MALAYSIAN SOCIETY OF ANAESTHESIOLOGISTS

Year Book 2006/2007

Foreword

As a fellow of the Australian and New Zealand College of Anaesthetists, I receive the year book "Australasian Anaesthesia" from the College and I find this collection of lectures by fellows at local scientific meetings extremely useful. At a time when clinicians are expected to maintain professional competency, keeping abreast with current literature is one of many learning activities expected of us. For most practitioners, it is a demanding task to try to keep up with journal reading. A quick reference or a digest covering 'hot topics' or updates related to clinical practice is always much appreciated. It is with this in mind that the idea of introducing a similar year book was mooted.

In the past, regional scientific meetings organised by the MSA and 'evening talks' by industry sponsored foreign speakers provided most of our continuous professional development activities. However, with dwindling industry sponsorship and increasing expectation from our members, it becomes obvious that we must now aggressively pursue a CPD programme which is locally driven. The highly successful annual scientific meetings held in conjunction with the last two annual general meetings as well as the success of local intensive care conferences of the last four years have proved our ability to sustain a local CPDprogramme. This year book again proves our academic capability and reflects the MSA's commitment to promote continuous professional development.

In this year book, an update of thirteen clinical topics which have been peer reviewed is provided. It is my hope that members will find this book essential reading and beneficial to their daily practice.

This inaugural year book will not be possible without the hard work of its editors, Dr Rafidah Atan and Dr Nor'azim Yunos, to whom I am deeply indebted. They have shown their commitment and capability by successfully producing this book.

I am extremely grateful to my colleagues who have contributed to this publication. In spite of their busy clinical work, they have managed to write their chapters. It is a huge sacrifice spending hours researching and putting evidence together. The rest of us have benefited from their work. On behalf of the MSA, I express my profound gratitude and appreciation.

Ng Siew Hian

Preface

To be given the task to edit the first ever issue of the MSA Yearbook is truly a big honour. Such honour nevertheless carries with it the high expectation of all MSA members. It is therefore our sincere hope that this humble effort matches that expectation.

Our idea of the Yearbook is one that updates the reader on various aspects of anaesthesia and intensive care in a concise and 'easy' manner. This, however, by no means indicates a lesser quality. A special thank you goes to all authors and reviewers who have worked very hard, sacrificing their precious time in the process, in an attempt to produce a Yearbook that MSA members can be proud of. Similarly, our heartfelt gratitude goes to the 'silent contributors'; family members of those involved and their significant others.

We have made a conscious effort to involve as many members as possible either as main contributors, co-writers or peer reviewers, introducing some new talents in the process. We envisage the Yearbook to be a regular avenue for 'expert' authors to revisit the joy of writing scholarly articles and for 'novices' to discover their penchant for writing. We hope that subsequent editors will take on this idea as well.

Happy reading!

Rafidah binti Atan
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Acute Care

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INTRODUCTION

Acute care is the provision of appropriate care to a patient in life-threatening or impending life-threatening situation with the aim of preventing irreversible damage. To attain this goal, well trained care-providers in adequate numbers must be available, when necessary, to recognize, manage and reverse these situations.

Current surveys suggest that our health care services are inadequately equipped to cope with this need. Many doctors neither have the skills nor the knowledge necessary. Even in areas like intensive care where the provision of acute care is supposedly at its premium, care is often suboptimal out of hours.

SOURCE OF PROBLEMS AND INITIATIVES TO IMPROVE SITUATION

The importance of acute care has been unrecognized until recently and many medical schools have allowed thousands of doctors to be produced worldwide without adequate knowledge of handling the acutely ill. Many schools had hitherto assumed that if doctors are trained in the basics of medicine, they will instinctively be able to handle the acutely ill patient as well. They have failed to recognize that managing the acutely ill patient requires knowledge and skills that are unique to the discipline of acute care.

There are initiatives now in place especially in the United Kingdom, to catch up on these deficiencies in training, both in the undergraduate as well as postgraduate years. In the last few years, many medical schools have modified their curriculum to accommodate this need, and the United Kingdom Acute Care Initiative is one such move. The Royal College of Physicians in the United Kingdom has also produced working reports calling for acute care to be included in the specialty training curriculum at postgraduate level. This might require a review of the content of all postgraduate courses to accommodate dual training, emphasising not only general internal medicine but also acute care.

Recently, there is a parallel move worldwide to streamline health care systems to focus on acutely ill patients. The International Partnership on Acute Care Safety (IPACS), which is in turn endorsed by the WHO World Alliance for Patient Safety, has enlisted many health care bodies to look at improving systems in their respective countries to focus initially on acutely ill patients. IPACS hopes to ultimately benefit all patients using these systems improvement.

SCOPE OF SUBJECT

It is essential during the training of young doctors to emphasize on basic concepts in acute care. These include the importance of ensuring the integrity of all processes aiming for continued delivery of oxygen to all organs, chief of which are the brain and the heart. These processes involve ensuring airway patency for the passage of oxygen to the lungs, adequate breathing or ventilation to ensure that oxygen is continuously brought to the lungs at a rate commensurate with body requirements, and adequate circulation to ensure that the oxygen is subsequently delivered to the tissues by adequate flow of blood. Continuous oxygen delivery to all organs as a basis of life is poorly grasped by a significant number of health care providers. Most programs that teach care providers life-support fail to emphasize physiological aspects and trainees are left to rote-learn the program without understanding much of the process of oxygen delivery to the tissues to maintain life.

The knowledge base is extremely wide, so it appears rational to emphasize on certain principles of sustaining life.

A race against time

A lot has been said about the race against time for the acutely ill patient. For the trauma patient, the concept of the Golden Hour was first coined by Donald Trunkey. Subsequently the concept of the platinum ten minutes evolved – each an improvement in the previously accepted norm of trying to limit time to definitive care, in order to improve outcome. Impressive though these time frames may sound, minutes may be too long a delay in situations where cardiac output is absent, since it is enough for a mere 10 seconds of anoxia to the brain to produce loss of consciousness and four more minutes of uninterrupted anoxia to cause brain death.

Many studies have shown that in many acutely ill patients, premonitory signs and symptoms were missed by care providers, which if detected would have allowed more definitive management and prevented deterioration. Many modern hospitals currently have systems in place to rapidly alert relevant care providers, before deterioration of patients to the point of no return.

Airway, breathing and support of the circulation

Integrity or achieving integrity of the airway, breathing and circulation is essentially what acute care is all about. These three basic tenets of care will ensure adequate oxygen delivery to the tissues, necessary for the survival of the patient.

Recognizing an unstable patient

This is represented by a patient whose airway, breathing and circulation are not under good control either by the patient or his care-provider. An inadequate airway, a patient who is barely breathing and one whose blood flow to the tissues is suboptimal can deteriorate further and threaten the patient's survival. It is important to recognize these patients, the earlier the better, and to train all care-providers to be on the look out for them, and equip them with the necessary skills to minimize patient morbidity and mortality. If these three main causes of instability in an acutely ill patient are appropriately handled, further deterioration in most patients can be prevented. It is within the ability of all hospitals, in terms of personnel, equipment, drugs and other resources, to do this but in order to successfully manage life threatening situations with good outcomes, concerted effort on the part of administrators and medical staff will be required.

A threat to life as opposed to a threat to an organ

In acute care, a differentiation needs to be made between reversing circumstances, which are a threat to a patient's life, as opposed to those which are threatening an organ in the body. There is no doubt that both may be interlinked. A threat to important organs like the brain, the heart and the lungs may threaten life itself but threat to lesser organs like the eye may only mean loss of function to that particular organ. Under such circumstances, more priority must be given to managing that which threatens life first, before focusing on threats to an organ.

Damage control – do not save the limb and hazard the patient's life

In the current climate where the medical field has become super-specialized, there are fewer of us who look at the patient as a whole. We tend to focus on a disease condition or a problem in an organ or a problem in a limb, rather than getting the best outcome out of life threatening situations. Damage control is the theme which should be stressed in acute care. In an endeavour to salvage patients' limbs or other body parts, we may end up exposing patients to continued instability that can ultimately compromise the whole patient and result in a life threatening situation. Prolonged procedures on patients without due focus on optimal tissue oxygen delivery and survival can either cause an immediate life threat or cause subsequent damage. This occurs through the introduction of hypothermia, excessive blood loss and other physiological trespass from which patients may find difficulty in recovering.

The wider knowledge

Of course, besides the very basic tenets of the patent

airway, the process of breathing and ensuring flow to the tissues through an intact circulation, acute care providers need to know a myriad of other principles that can make a difference to outcome. This includes oxygen therapy, fluid and blood therapy, monitoring, eliciting signs of a rapidly deteriorating patient, keeping patients warm, effective communication to seek appropriate further support and even safe transport of acutely ill patients to other areas for more definitive care.

Parallel skills

Besides knowledge, there are skills that need to be learnt in parallel. These include airway control skills, skills to oxygenate and ventilate the patient with appropriate equipment, and maintenance of blood flow during cardiac arrest by way of closed cardiac massage. These skills are very basic and form part of basic life support skills. The ability to further enhance life-support management with appropriate drugs, defibrillation and other organ support form the basis of advanced life support. All these can be learnt separately as a module (eg module for airway management, oxygen therapy etc) and all care-providers can be tested for competency in each of the modules.

TEACHING OPPORTUNITIES

Acute care is needed by up to 16% of the patients admitted to the wards. Situations where teaching opportunities arise should not be difficult to come by. The recovery area in operating theatres is another fertile ground where teaching of acute care can be particularly rewarding. In these areas, there is a constant supply of patients whose airway, breathing and circulation may be compromised. The accident and emergency area is of course another ideal place for exposure of trainees to a variety of skills and processes in the management of acute care patients. Even the wards can be suitable if trainers take advantage of acute care situations, as and when they arise.

Teaching must be commensurate with the knowledge base of the trainee. As these life-sustaining processes are skills, teaching on the job involving small groups is the best means of achieving the goal. Obviously this is going to be labour intensive, as well as counting on the presence of enthusiastic trainees and trainers being at the correct place when a life threatening event occurs.

Simulation of the acute care situation allows programs to be arranged so that teaching and learning can occur at suitable times for both trainees and trainers. This, though realistic, may never approximate the real event but offers a good substitute. Here again, the throughput of the trainees may be limited because we have to understand that in skills learning, supervision of trainees is essential and thus, the numbers per supervisor have to be kept low for effective learning. Not all medical schools are equipped with this facility as they come with a fairly high price tag, both for purchase as well as maintenance.

THE TRAINEES

All care providers, whether in the capacity of a doctor, nurse or paramedic, should be equipped with the skill and know-how to do the job of sustaining life by ensuring oxygen is properly delivered to the tissues. Currently, medical students during their training are taught respiratory, cardiovascular and tissue physiology in great detail, but effort is often not made to correlate knowledge with principles involved in sustaining life in clinical practice. The skills involved are obviously harder to come by and unfortunately, physiological knowledge and clinical skills are often learnt separately, without attempts to integrate them, making it harder to understand and master the subject of acute care. As a result many young doctors graduate with few skills to provide acute care and learn by trial and error, over many years at the job, to acquire them. Most may not even bother, preferring to leave the job to others.

Post-graduate doctors are also a target group. It is only appropriate that whilst they may spend time acquiring skills and knowledge in a sub-discipline of medicine, they should also have the ability to save the lives of acutely ill patients. General practitioners are another set of care providers, identified for retraining of such knowledge and skills. We may have to change the mindset of all doctors not trained in acute care medicine to recognize the importance of acquiring such skills.

Nurses who form the bulk of care-providers in the ward should probably be the target of this initiative as well, as provision of acute care are fairly simple processes, requiring skills within the grasp of all care providers. As nurses outnumber doctors in all countries, this would be a good way of providing some temporary solution to the problem. They should also be provided with the basic knowledge to sustain life whilst awaiting further help.

THE TRAINERS

There are a limited numbers of doctors or specialists with the correct skills to teach acute care and they are already stretched with provision of care, much less to cope with training. The emergency room physician or acute care physician are rare breeds. The fully trained anaesthesiologists are physicians with much of the knowledge and skills required in acute care and they would be the most useful doctors in the medical speciality to fill the void. Most disciplines have a sub-field where management of the acutely ill patient is emphasized and these should be merged into one entity by all trainers under the umbrella of acute care.

Many colleges are recognizing the need as well as the lack of trainers for this new field. We are at an early stage of this recognition and are putting in much effort to address the problem, not only of training, but of provision as well. Currently in the United Kingdom, acute care medicine comes under the realm of the College of Physicians and has been set up as a sub-speciality of this college.

SUMMARY

Acute care is a new sub-discipline of medicine that is being recognized as being important in the provision of complete care to all patients. Many initiatives, both at the training as well as the provision level, are attempting to address the current shortfall in terms of human resources to cope with the acutely ill patient. When all systems are in place, the acutely ill patient will no longer become a formidable issue in the life of a doctor.

FURTHER READING

Practical Aspects of Acute Care. Drs. Chan Yoo Kuen & Ng Kwee Peng (eds) Publishers – University of Malaya Press, Kuala Lumpur 2005

Bion JF, Heffner JE Challenges in the care of the acutely ill. *Lancet* 2004; **363**: 970-977

Smith GB, Poplett N. Knowledge of aspects of acute care in trainee doctors. *Postgraduate Medical Journal* 2002; **78**:335-338

Perkins GD, Barret H, Bullock I, Gabbott DA, Nolan JP, et al. The Acute Care Undergraduate TEaching (ACUTE) Initiative: consensus development of core competencies in acute care for undergraduates in the United Kingdom. *Intensive Care Med* 2005;**31**(12): 1627-1633

Updates On Ambulatory Surgery

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Introduction

The first ether anesthetic was given for ambulatory surgery. James M. Venable had a small cystic tumor removed from the back of his neck by Dr Crawford W. Long on the evening of March 30, 1842.[1]

For the past 20 years day care surgery has undergone a rapid increase in volume. Currently an estimated 70% of surgical procedures in North America are completed in ambulatory settings. In Europe these figures vary widely but in England up to 65% of all surgical procedures are performed on a day case basis.[2]

The types of procedures which are considered suitable to be performed on outpatients vary considerably between different countries and even between different regions within a country.

Patients benefit from ambulatory surgery because it minimizes costs, decreases separation from home and family environments, reduces surgery waiting times, decreases likelihood of contracting hospital acquired infections, and appears to reduce postoperative complications.

Settings for outpatient surgery

The various designs of a prototypical ambulatory surgical unit include hospital integrated, hospital separated (but with access to a hospital), satellite ambulatory unit which operates under the same administration, totally independent free standing unit and office based unit. The majority of outpatient surgeries are still performed in hospital settings, either in integrated or separated units.

The decision as to where to perform the surgery depends upon the levels of ambulatory surgery. The levels of ambulatory surgery are classified as follows:

a) Minor ambulatory surgery (under local anesthesia)

b) Major ambulatory surgery (under G.A, central neural blockade with or without I.V. sedation)

c) In-patient ambulatory surgery

Screening of patients

At the present time, there are several commonly used approaches to screening patients for ambulatory surgery. These include the following:

1. Facility visit prior to the day of surgery
2. Office visit prior to the day of surgery
3. Telephone interviews/no visit
4. Review of health survey /no visit
5. Preoperative screening and visit on the morning of surgery
6. Computer – assisted information gathering

A visit by the anaesthetist on the day before surgery is desirable because it minimizes cancellation due to inadequate preoperative assessment and preparation, as well as reduces the patient's anxiety about anaesthesia and surgery. Unfortunately, this is not possible in many busy outpatient centres.

Selection of patient

This is the key to successful day care surgery, patients must be selected and prepared properly. Selection is

not simply a matter of choosing patients with conditions that may be treated on a day care basis, but also involves excluding patients who are unsuitable due to medical and social reasons. The complexity of surgery and the patient's medical condition must also be considered. Common exclusion criteria for patient selection are shown in Table 1.

Table 1: Exclusion criteria for outpatient surgery

1.	**Medical**
	a. Unfit ASA III & IV
	b. Obese: Body mass index >35
	c. Nature of pathology: large scrotal hernias, major intrathoracic, intrabdominal or intracranial surgery
	d. Procedures requiring more than one hour
	e. Surgery expected to have major fluid loss or blood loss
2.	**Patient**
	a. Concept of day care surgery unacceptable to the patient
	b. Psychologically unstable patient
	c. Patients who live far away from the hospital
	d. Infants < 3months of age and preterm babies
3.	**Social: No competent relatives or friends to**
	a. Accompany or drive patient home after the operation
	b. Attend to the patient at home for the next 24-48hours

Table 2: Controversial exclusion criteria

	Controversial exclusion criteria
	a. Extremes of age
	b. Morbid obesity
	c. COPD
	d. Fragile diabetes
	e. Patients prone to malignant hyperpyrexia
	f. Monoamine Oxidase Inhibitor use
	g. Acute substance abuse

The elderly and ASA physical status

Extremes of age are no longer a deterrent to outpatient surgery. A prospective trial involving a cohort of 15,172 patients undergoing ambulatory surgery found that age did not predict unanticipated admission.[3] Conversely, another cohort of 4,786 outpatients identified an association between age above 65 and an increased risk of intraoperative adverse events.[4] These events were mainly related to changes in haemodynamic variables and were found to increase in proportion with age.

A prospective study involving more than 13,000 patients by Natof at a freestanding ambulatory surgical centre demonstrated that ASA 3 patients in whom systemic diseases were well controlled preoperatively, were at no higher risk for postoperative complications than ASA 1 or 2 patients.[5] Chung et al. have recently published data examining predictors of adverse events in ambulatory surgery in the elderly as well as factors contributing to prolonged stay after ambulatory surgery in elderly patients.[6,7] These data demonstrated that outpatient surgery is safe in this patient population, with elderly patients sustaining more minor cardiovascular events than their counterparts and less, pain, drowsiness and postoperative nausea and vomiting.[6,7]

In summary, geriatric and higher-risk (physical status 3 and 4) patients may be considered for ambulatory surgery if their systemic diseases are well controlled and their medical conditions optimized before surgery.

The ex-premature infant

Premature infants less than 60 weeks postconceptual age should not be considered for ambulatory surgery. The risk of postoperative apnea has been evaluated in a number of retrospective and prospective studies. Cote' pooled individual patient data from 255 ex-premature infants in eight prospective studies[8] and calculated the probability of postoperative apnea occurring using a logistic regression model. Postoperative apnea occurred in approximately 25% of these patients. The incidence is inversely related to gestational age and post conceptual age (PCA), with an incidence of less than 5% when the PCA is over 60 weeks. A haematocrit level of less than 30% also correlated with the likelihood of apnea. A systematic review has demonstrated that caffeine reduces the rate of apnea[9] and some randomized control trials have demonstrated a reduced apnea rate with regional rather than general anesthesia.[10,11]

Cardiac disease

The patients with the greatest risk of complications from anaesthesia are those with cardiac disease, mainly uncontrolled hypertension, congestive cardiac failure (CHF) or angina. In a study of existing medical conditions as predictors of perioperative adverse events from ambulatory surgery, Chung et al found that patients with CHF had a 12% longer postoperative stay, which in some instances led to hospital admissions.[6] They also found a twofold increase in intraoperative cardiovascular events in patients with hypertension. However the study was of insufficient size to demonstrate an association between coronary artery disease (CAD) and intraoperative events.

The guidelines by the American Heart Association stratified risk according to the type of surgery, patient functional capacity and clinical predictors. Intermediate clinical predictors include mild ischaemic heart disease, prior myocardial infarction (over 1 month old), compensated heart failure, diabetes mellitus and renal insufficiency. These patients may undergo low-risk surgical procedures without further cardiac investigations.

Pulmonary disease

Chronic obstructive pulmonary disease (COPD), asthma and tobacco abuse often lead to pulmonary complications. Arozullah et al found that patients with COPD had twice the standard risk for pulmonary complications from ambulatory surgery as did patients without COPD.[12] In a recent prospective evaluation of preexisting medical conditions in ambulatory surgery, patients with asthma and smokers were identified as having an increased risk for postoperative respiratory events.[6] There was however no significant association between respiratory disease and length of stay in recovery after

ambulatory surgery.[7] This may be an indication that the events were relatively minor. Asymptomatic patients with asthma have very low complications, approaching that of non–asthmatic population.[13,14] However, those experiencing respiratory symptoms at the time of surgery faced a 50% incidence of postoperative respiratory complications compared with less than 2% of those without symptoms.

A cohort study of 489 patients evaluated the influence of smoking on the incidence of perioperative complications following ambulatory surgery.[14] Smokers experienced an increased risk of respiratory and wound complications. Patients who stopped smoking less than four weeks preoperatively suffered adverse events at a rate similar to current smokers. On the other hand, a randomized controlled trial of 120 patients undergoing joint arthroplasty demonstrated that smoking cessation six to eight weeks preoperatively yielded improvements in wound related complications.[15]

Morbid Obesity

The morbidly obese frequently have comorbidities, including CAD, CHF, hypertension, and obstructive sleep apnea. A health survey found that the prevalence of cardiovascular diseases was 37% in adults with a BMI of >30kg.m^{-2}, 21% in those with a BMI 25-30kg.m^{-2}, and only 10% in those with a BMI of < 25kg.m^{-2}.[16] Approximately 5% of morbidly obese patients have obstructive sleep apnea.[17] The study by Chung et al found a fourfold increase in adverse pulmonary events in morbidly obese patients compared with those of normal body weight. Although morbidly obese patients without systemic disease are acceptable candidates for ambulatory surgery, most centres prefer overnight hospitalization and postoperative observation for morbidly obese patients with pre-existing cardiac, pulmonary, hepatic or renal compromise or for patients with complex sleep apnea.

Diabetes Mellitus

IDDM is not considered a contraindication for ambulatory surgery. A study looking at preexisting medical conditions as predictors of adverse events in day case surgery did not find IDDM to be a significant predictor of intra- or postoperative events in ambulatory surgery.[18] Comorbid conditions including difficult airway, must be identified and managed appropriately. Recommendations to withdraw metformin >48hour preoperatively are not supported by evidence. Tighter control of perioperative blood glucose is encouraged.

Malignant Hyperthermia (MH)

MH is a rare condition and therefore has not been studied in large prospective trials. Knowledge of this condition and its management in the ambulatory setting is largely derived from case reports and retrospective reviews. Authorities support ambulatory surgery in MH patients as long as a minimum of four hours of temperature monitoring can be provided postoperatively. The Malignant Hyperthermia Association of the United States (MHAUS) advises that the MH patients may be discharged three to four hours following uneventful anesthetics.[19] The Malignant Hyperthermia Association of Canada (MHA Canada) recommends a four hour monitoring period.

Monoamine Oxidase Inhibitors

Monoamine oxidase inhibitors (MAOI) increase brain monoamine and cytoplasmic concentration of monoamine oxidase (MAO) substrates by inhibiting metabolism of cytoplasmic neurotransmitters.[20] Classic MAOI such as phenelzine and tranylcypromine, irreversibly inhibit MAO for two to three weeks until new enzyme is synthesized.[20] Moclobemide, a reversible inhibitor of MAO–A (RIMA) causes enzyme inhibition for less than 24hour. Selegiline, an anti-Parkinsonian agent, is a short acting, reversible MAO-B inhibitor at its usual dose. Serotonergic reactions to pethidine have been described for all MAOI, including moclobemide and selegiline. Pethidine blocks neuronal serotonin reuptake, resulting in serotonergic overactivity which manifests as agitation, hyper/hypotension, convulsions, hyperthermia, and coma.[21] Case reports of sporadic MAOI-related drug interactions led to many advisories to discontinue classic MAOI two to three weeks before surgery.[20,22,23] There is no

literature specifically concerning MAOI and ambulatory anesthesia. Although MAOI related drug interactions are possible and have been reported, patients continuing to take either classic or selective MAOI remain suitable candidates for ambulatory anesthesia if pethidine, cocaine and indirect acting catecholamines are avoided.[24]

Premedication

Ambulatory surgery is known to elicit anxiety. The use of premedication in outpatients has been a subject of considerable interest and debate. Inpatients usually receive premedication, but outpatients have not been given sedative premedication because of the mistaken belief that drugs could prolong recovery and delay discharge. Interestingly, most prospective studies have failed to demonstrate prolonged recovery times following premedication in outpatients. Shorter acting benzodiazepines can give reliable sedation, amnesia and anxiolysis without delaying recovery even after short procedures. A Cochrane Database Systematic Review concluded that there is no evidence of a difference in time to discharge from hospital in patients who received anxiolytic premedication.

Anaesthetic technique

The ideal anesthetic technique for ambulatory surgery should result in a rapid and smooth onset of action, intraoperative amnesia and analgesia, good surgical conditions and a short recovery period without side effects. Choice of anesthetic technique could either be general anesthesia, regional anesthesia, local anaesthesia or monitored anesthesia care. The choice of anesthetic technique can affect postoperative morbidity at home.[25]

General anesthesia

For many procedures, general anesthesia remains to be the most popular technique. The introduction of increasingly rapid and shorter acting volatile anesthetics (e.g. desflurane and sevoflurane), opioid analgesics (eg. remifentanil), and muscle relaxants has allowed practitioners to more consistently achieve a recovery profile that facilitates "fast tracking" following general anesthesia.[26,27] The use of electroencephalographic bispectral index monitoring can improve titration of maintenance anesthetic and thereby facilitate the early recovery process.[28,29] Intravenous (IV) agents are used for the induction of anesthesia in both adults and older children. Propofol is the IV induction agent of choice for outpatient anesthesia. It gives rapid emergence and very low incidence of postoperative side effects. Euphoria on emergence is often seen after propofol and postoperative nausea and vomiting (PONV) are rare, in particular when combined with the ultra short acting opioid remifentanil.[27,30] However, remifentanil has a limited role in ambulatory surgery because its advantages of rapid postoperative recovery and lack of residual respiratory depression are negated by the requirement for a longer acting opioid or alternative analgesic as soon as the infusion is stopped.[31] In spite of increasing interests in IV anesthetic techniques, inhaled anaesthetics remain to be the most popular agent for maintenance of general anesthesia. The newer halogenated ether compounds, sevoflurane and desflurane, have significantly lower blood:gas solubility characteristics, resulting in more rapid onset and recovery. In addition, these less-soluble volatile agents give more intraoperative hemodynamic stability because they are easily adjustable. Desflurane has rapidly gained popularity for maintenance of anesthesia during ambulatory surgery. It has the lowest blood:gas solubility of all volatile anaesthetics, and the most rapid awakening after ambulatory surgery. Sevoflurane has slightly faster awakening times and fewer postoperative side effects than isoflurane. Because it is non-irritating to the airway, sevoflurane can also be used for induction of anesthesia as an alternative to propofol in both adults and children. Maintenance with propofol infusion can improve the quality of recovery from general anaesthesia, but this does not result in earlier recovery or discharge when compared to both sevoflurane and desflurane. When these newer anaesthetic agents are combined with low dose remifentanil infusion, emergence from anesthesia is extremely rapid, facilitating the fast tracking process.[27]

Use of muscle relaxant in ambulatory surgery remains an open-ended problem. To date the ideal drug with rapid onset, minimal side effects and short duration of

action is not yet available. Suxamethonium still has a place for when muscle relaxation is needed only during intubation. Atracurium and rocuronium are non-depolarizing agents commonly used. Doses selected should seek the best compromise between ideal intubating conditions and duration of muscle relaxation required. Neuromuscular monitoring should be applied to minimize the risk of residual recurarization and reversal agents should be administered as needed.

Sugammadex may be the answer to the use of neuromuscular blocking agent for ambulatory surgery in the near future. It acts as a chelant by removing rocuronium from acetylcholine receptors, thus reversing neuromuscular blockade with no major adverse effects.

Although the facemask and oropharyngeal airways are often used for brief, superficial ambulatory procedure, tracheal intubation remains popular as it minimizes the risk of airway complications. However, the laryngeal mask airway (LMA) and the cuffed oropharyngeal airway (COPA) devices are now used where in the past either a face mask or tracheal tube would have been preferred.[32] These airway devices reduce requirement for anesthetic agents, cause less postoperative sore throat and less acute hemodynamic changes during induction and emergence, as well as allow avoidance of both muscle relaxants and reversal agents compared to the use of endotracheal tubes.

Regional anaesthesia

Regional anaesthesia, whether by epidural, spinal, peripheral nerve block or field block technique, offers a number of advantages to outpatients undergoing surgery. These techniques allow analgesia without sedation and provide prolonged postoperative analgesia. The decreased requirements for opioids reduces the incidence of PONV. Spinal anesthesia is the most common central neuraxial block in day surgery setting. It has distinct advantages over epidural anesthesia, with less time required to achieve an adequate block, lower incidence of incomplete sensory and motor block and pain during surgery.[33] A 17- nation European survey of 105 hospitals showed that almost 40% of all ambulatory surgery in the participating hospitals was performed under regional blocks. Spinal and epidural blocks were used in 20-30% of hospitals.

Lignocaine is most frequently used, though recent studies have shown that transient neurological symptoms (TNS) can occur in 16-40% of outpatients.[34,35,36] Alternative local anesthetic drugs such as bupivacaine in small doses (5-10mg) and ropivacaine are associated with very low incidence of TNS but are not always appropriate for day case surgery. Adjuvants such as fentanyl 10ug can improve the success rate of low dose hyperbaric bupivacaine (eg 5mg) spinal anaesthesia without prolonging discharge time.[37] A postoperative follow up did not show TNS in any of the 60 patients who received spinal mepivacaine as part of combined spinal-epidural (CSE) block for anterior cruciate ligament repair.[37]

A former barrier to outpatient spinal administration, namely post-dural puncture headache, has been largely eliminated with the introduction of conical–tipped needles that result in less dural trauma.[38] Although recovery after neuroaxial blockade is improved by decreasing the local anaesthetic dosage and adding a potent opioid analgesic (eg. fentanyl, sufentanil),[39] discharge times are still prolonged compared with general anesthesia or local anesthesia with sedation.[40,41] Increasingly, practitioners are turning to monitored anesthesia care (MAC) as an alternative to both general and regional anesthesia.[42]

The availability of improved sedation and analgesia techniques to complement local anaesthetic infiltration and peripheral nerve blocks has increased the popularity of performing surgery utilizing MAC.

Management of postoperative pain

Pain has been found to be a major factor complicating recovery and delaying discharge after ambulatory surgery.[46] A multimodal approach to providing postoperative analgesia is essential in the ambulatory setting.[42-45] The role of opioid in day case surgery is controversial because of their well known side effects, especially PONV. Although patients who receive opioids are more likely to experience PONV, average recovery times are not significantly prolonged by the

use of intraoperative opioid per se. Several studies have demonstrated early ambulation and discharge after fentanyl or alfentanil –based anaesthetic techniques.[47]

As a result of concerns regarding opioid–related side effects, there has been an increased interest in the use of potent non steroidal analgesics after ambulatory surgery, leading to an earlier discharge home. Other less expensive oral non-steroidal analgesics (e.g. ibuprofen, naproxen) may be acceptable alternatives to fentanyl and the parenteral non selective anti –inflammatory drugs if administered in a preemptive fashion.[48] Recently premedication with the COX-2 inhibitors has become more popular because they are devoid of potential adverse effects on platelet function.[50] Acetaminophen is a very cost effective alternative to the COX-2 inhibitors if it can be given in high enough doses prior to the end of surgery.[51,52] Pain should be controllable with oral analgesics before patients are discharged.

Use of local anaesthetic techniques for intraoperative analgesia, as well as adjuncts to general (and spinal) anesthesia, can provide excellent analgesia during the early postoperative recovery and postdischarge periods.[53-55] Even simple wound infiltration and instillation techniques have been shown to improve postoperative analgesia following a variety of lower abdominal, peripheral extremity and even laparoscopic procedures. More recently, use of continuous local anesthetic delivery systems have been found to improve pain control after major ambulatory orthopaedic surgery by extending peripheral nerve blocks.[56-58] Patient-controlled local anesthetic delivery has also been described for improving pain relief after discharge home.[57]

Installation of 30 ml of bupivacaine 0.5% into the joint space reduces postoperative opiate requirements and permits earlier ambulation and discharge after arthroscopic surgery.[59] The addition of morphine (1-2mg), ketorolac (15-30mg), clonidine (0.1-0.2mg) and triamcinolone (10-20mg) to the intraarticular local anesthetic solution can further reduce pain after arthroscopic surgery.[59]

Postoperative nausea and vomiting

Despite pharmacological and technological advancements, nausea and vomiting still remain common problems for post surgical outpatients, seen in 20%-30% of patients after general anesthesia,[60] and reported by 35% of patients after discharge home.[61] Prophylactic measures are advised for the highly vulnerable patients – females, patients in the luteal and perimenstrual phases of the menstrual cycle, history of PONV, non smokers and those with motion sickness.[62] Droperidol, metoclopramide, and prochloperazine are effective against PONV in the ambulatory setting; however, their effectiveness is often negated by undesirable side effects such as extrapyramidal reactions, marked sedation and drowsiness. Anti-serotonin drugs (e.g. ondansetron, dolasetron), in contrast, provide effective PONV management without these undesirable side effects, and work by blocking central and peripheral receptors that modulate the vomiting reflex. Side effects, although infrequent, may include headache, dizziness, and transient elevation of liver enzymes.

Antiemetic prophylaxis with droperidol 0.625mg IV, droperidol 1.25mg IV, ondasetron 4mg IV or dolasetron 12.5mg is similarly efficacious in adults compared to metoclopramide 10mg IV.[63] Ondansetron, however, is more effective than droperidol in preventing vomiting in children.[63] While the timing of prophylactic ondansetron does not appear to affect the overall incidence of PONV, the need for rescue antiemetics to treat breakthrough PONV may be reduced when ondansetron is administered at the end of surgery.[64] In addition, dexamethasone prophylaxis (150ug/kg,up to 8 mg) appears to further decrease the risk of PONV, and provide an extended duration of action lasting up to 24-h postoperatively. Watcha has provided an algorithm ranging from routine multimodal antiemetic prophylaxis for the high risk patients to none for low risk patients (< 10% risk of PONV), and also identified risk factors.[70] Ultimately, a multimodal approach to antiemetic therapy, particularly in high risk patients, will provide the most effective outcome.[98,100] Recent studies have shown that alleviating dehydration with adequate

perioperative fluid therapy (20-mL/kg for 8-h NPO) will reduce the incidence of postoperative adverse outcomes, such as thirst, nausea and vomiting, in the outpatient.[72]

Conclusion

Ambulatory surgery has expanded rapidly in recent years. The number and complexities of surgery performed in the outpatient setting will no doubt continue to rise. Improvement of anaesthetic and surgical techniques, resulting in extremely good safety record, was a prerequisite for the radical increase in the number of surgical procedures performed in ambulatory surgical units. The correct evaluation of patients for ambulatory surgery is of critical importance. Careful patient selection can minimize adverse perioperative events and improve outcome measures.

The success of ambulatory surgery depends, to a large extent, on both effective control of postoperative pain and minimization of side effects such as sedation, nausea and vomiting.

References

1. Packard FR: History of medicine in the United States, New York, Paul B Hoeber, 1931.3
2. Jarrett PEM. Day care surgery. *Eur J Anaesthesiol* 2001;**18**:32-35.
3. Fortier J, Chung F, Su J. Unanticipated admission after ambulatory surgery-a prospective study. *Can J Anaesth*. 1998;**45**:612-9.
4. Chung F, Mezei G, Tong D: Adverse events in ambulatory surgery. A comparison between elderly and younger patient. *Can J Anaesth* 1999;**46**:309-21.
5. Natof HE: Preexisting medical problems. Ambulatory surgery. *IMJ 111 Med J* 1984; **166**:101-4
6. Chung F, Mezei G, Tong D. Preexisting medical condition as predictors of adverse events in day case surgery. *Br J Anaesth* 1999;**83**:262-70
7. Chung F, Mezei G: Factors contributing to a prolonged stay after ambulatory surgery. *Anesth Analg* 1999;**89**:1352-9
8. Cote CJ, Zaslavsky A, Downes JJ, et al. Postoperative apnea in former infants after inguinal herniorapphy. A combined analysis. *Anesthesiology* 1995;**82**:809-22.
9. Henderson –Smart DJ, Steer P. Prophylactic caffeine to prevent postoperative apnea following general anaesthesia in preterm infants .*Cochrane Database Syst Rev* 2002;**4**:CD000048.
10. Williams JM, Stoddart PA ,Williams SA, et al .Postoperative recovery after inguinal herniotomy in ex-premature infants :comparison between sevoflurane and spinal anesthesia. *Br J Anesth* 2001;**86**:366-371.
11. Somri M, Gaitini L, Vaida S, et al. Postoperative outcome in high risk infants undergoing herniorapphy; a comparison between spinal and general anesthesia. *Anesthesia* 1998;**53**:762-766.
12. Arozullah AM, Khuri SF, Henderson WG, Daley J;Participants in the National Veterens Affairs Surgical Quality Improvement Program. Development and validation of multifactorial risk index for predicting postoperative pneumonia after major non cardiac surgery. *Ann Intern Med* 2001;**135**:847-857.
13. Warner DO, Warner MA ,Barnes RD, et al. Perioperative respiratory complications in patients with Asthma. *Anesthesiology* 1996;**85**:460-7
14. Kumeta Y, Hattori A, Mimura M, Namiki A. A survey of perioperative bronchospasm in105 patients with reactive airway disease (Japanese). *Masui* 1995;**44**:396-401.
15. Moller AM, Villebro N, Pederson T, Tonnase H. Effects of preoperayive smoking intervention on postoperative complications; a randomized clinical trial .*Lancet* 2002;**359**:114-7.
16. Lean ME. Obesity and cardiovascular disease. The wasted years. *Br J Cardiology* 1999;**6**:269-73.
17. Young T, Palta M, Dempsey J,Skatrud J,Weber S, Badrr S. The occurrence of sleep disordered breathing among middle aged adults. *N Engl J Med* 1993;**328**:1230-5.
18. FriedmanZ,Wong DT, Chung F. What are the ambulatory surgical patient selection criteria in Canada? *Can J Anaesth* 2003;**50** (suppl) A16 Absract.

19. Malignant Hyperthermia Association of the United States. Medical FAQs.2003; URL;http//www.mhaus.org/index.cfm/fuseaction/Content.Display/PagePK/MedicalFAQs.cfm
20. Wells DG, Bjorksten AR. Monoamine oxidase inhibitors revisited. *Can J Anaesth* 1989;**36**:64-74.
21. Martyr JW, Orlikowski CE. Epidural anaesthesia, ephedrine and phenylephrine in a patient taking moclobemidew, a new monoamine oxidase inhibitors. *Anaesthesia* 1994;**49**:597-9.
22. Stack CG, RogersP, Linter SP, Monoamine oxidase inhibitors and anaesthesia. A review. *Br J Anaesth* 1988;**60**:222-7.
23. El Ganzouri AR, Ivankovich AD, Braverman B, Mc Carthy R. MAOI should they be discontinued preoperatively? *Anaesth Analg*.1985;**64**:592-6.
24. Gregory L, Bryson, Frances Chung Patient selection in Ambulatory Anaesthesia-An evidence based review Part 11
25. Kotiniemi LH, Ryhanen PT, Valanne J, Jokela R, Mustonen A, Poukkula E. Postoperative symptoms at home following day case surgery in children: a multicentre survey of 551 children. *Anaesthesia* 1998;**52**:563-9.
26. Song D, Joshi GP, White PF. Fast track eligibility after ambulatory anesthesia; a comparison of desflurane, sevoflurane and propofol. *Anaesth Analg* 1998;**86**:267-73.
27. Song D, White PF. Remifentanil as an adjuvant during desflurane anesthesia facilitates early recovery after ambulatory surgery. *J Clinical Anesth* 1999;**11**:364-7.
28. Song D, Joshi GP, White PF. Titration of volatile anaesthetic using bispectral index facilitates recovery after ambulatory anaesthesia. *Anesthesiology* 1997;**87**:842-4.
29. Gan TJ, Glass PS, Windsor A, et al. Bispectral index monitoring allows faster emergence and improved recovery from propofol , alfentanil, and nitrous oxide anesthesia :BIS utility study group. *Anesthesiology* 1997;**87**: 808-15.
30. Philip BK, Sanden PE, Chung F, et al. Remifentanil compared with alfentanil for ambulatory surgery using total intravenous anesthesia. *Anaesth Analg* 1997,**84**:515-20.
31. Van Vlymen JM, Fu W, White PF; Use of oropharyngeal airway as an alternative to the LMA with positive pressure ventilation. *Anesthesiology* 1999;**90**:1306-10.
32. Leach A. Old ideas ,new application *Br J Anaesth* 1998;**81**:113-14.
33. Rudkin GE. Local and regional anesthesia in the adult day surgery patient. Practical Anesthesia and Analgesia for Day Surgery Oxford: BIOS Scientific Publishers,1997;207-10.
34. Hampl KF, Heinzmann-Wiedener S,Luginbuehl. Transient neurologic symptoms after spinal anesthesia. *Anesthesiology* 1998;**88**:629-33.
35. Ligouri GA, Zayes VM, Chisolm MI. Transient neurologic symptoms after spinal anesthesia with mepivacaine and lidocaine. *Anesthesiology* 1999;**88**:619-23.
36. Pollock JE, Liu SS, Neel JM. Dilution of spinal lidocaine does not alter the incidence of TNS. *Anesthesiology* 1999;**90**:445-50.
37. Hodgson PS, Liu SS. Spinal anesthesia for day surgery. *Tech Reg Anesth.Pain Management* 2000;**4**:3-9.
38. Pawloski J, Sukhari R,Pappas et al. The anesthetic and recovery profile of two doses (60 and 80mg) of plain mepivacaine for ambulatory spinal anesthesia. *Anaesth Analg* 2000;**91**:580-4.
39. Vaghadia H, Mc LEOD DH, Mitchell GW et al. Small dose hypobaric lidocaine –fentanyl spinal for short duration outpatient laparoscopy. A.randomised comparison with a conventional dose hyperbaric lidocaine. *Anaesth Analg* 1997;**84**:59-64.
40. Song D, Greileich, Tongier K et al. Recovery profiles of outpatient undergoing unilateral inguinal herniorraphy. A comparison of the costs and recovery profiles of three anesthetic techniques. *Anaesth Analg* 1999;**88**:S30.
41. Li S, Coloma M, White PF, et al. A comparison of the costs and recovery profile of three anaesthetic techniques for ambulatory surgery. *Anesthesiology* . In press.
42. Sa' R ego MM, Watcha MF, White PF. The changing role of monitored anaesthesia care in the ambulatory setting. *Anaesth Analg* 1997;**85**:1020-36.
43. Kehlet H, Postoperative pain relief-What is the issue? [Editorial] *Br J Anaesth* 1994;**72**:387-40.
44. Erikson H, Tenhunen A, Kortilla K: Balanced analgesia improves recovery and outcome after outpatient tubal ligation. *Acta Anaesth Scand* 1996;**40**:151-5.
45. Michaloliakou C, Chung F, Sharma S. Preoperative multimodal analgesia facilitates recovery after ambulatory laparoscopic choleycstectomy. *Anaesth Analg* 1996;**82**:44-51.
46. Pavlin DJ, Chen C, Penaloza DA, et al. Pain as a factor complicating recovery and discharge after ambulatory surgery. *Anaesth Analg* 2002;**95**:627-34.

47. Zuurmond WWA, Van Leeuween L. Alfentanil vs isoflurane for outpatient arthroscopy. *Acta Anaesthesiol Scand* 1986;**30**:329-31.

48. White PF. The role of non opioid analgesic technique in the management of pain after ambulatory surgery. *Anaesth Analg* 2002;**94**:577-85.

49. Rosenblum M, Weller RS, Conrad PL, et al. Ibuprofen provides longer lasting analgesia than fentanyl after laparoscopic surgery. *Anaesth.Analg* 1991;**73**:255-9.

50. Raeder JC, Steine S, Vatsgar TT. Oral ibuprofen versus paracetamol plus codeine for analgesia after ambulatory surgery. *Anaesth Analg* 2001;**92**:1470-2.

51. Rusy LM, Houck CS, Sullivan LJ, et al. A double blind evaluation of ketorolac versus acetaminophen in paediatric tonsillectomy: analgesia and bleeding. *Anesth Analg* 1995;**80**:226-9.

52. Korpela R. Konvenoja P, Meretoja OA. Morphine sparing effect of acetaminophen in paediatric day care surgery. *Anesthesiology* 1999;**91**:442-7.

53. Tverskoy M, Cozacov C Ayache Met al. Postoperative pain after inguinal herniorapphy with different types of anaesthesia. *Anaesth Analg* 1990;**70**:29-35.

54. Harrison CA, Morris S, Harvey JS. Effect of Ilioinguinal and Iliohypogastric nerve block and wound infiltration with 0.5% bupivacaine on postoperative pain after hernia repair.*Br J Anaesth* 1994;**72**:691-3.

55. Ding Y, White PF. Post herniorraphy pain in outpatients after pre incision Ilioinguinal –hypogastric nerve block during monitored anesthesia care. *Can J Anaesth* 1995;**42**:12-5.

56. Grant SA, Nielsen KC, Greengrass RA, et al. Continuous peripheral nerve block for ambulatory surgery. *Reg Anesth Pain Med* 2001;**26**:209-14.

57. Illfeld BM, Morey TE, Wang RD, Enneking FK. Continuous popliteal sciatic nerve block for postoperative pain control at home. *Anesthesiology* 2002;**97**:959-65.

58. White PF, Issoui T, Skrivanek GD, et al .Use of a continuous popliteal sciatic nerve block for the management of pain after major paediatric surgery: does it improve quality of recovery? *Anesth Analg* 2003;**97**:1303-9.

59. Smith I, Shiverly RA, White PF. Effect of ketorolac and bupivacaine on recovery after outpatient arthroscopy. *Anesth Analg* 1992;**75**:208-12.

60. Watcha MF (2000) The cost effective management of postoperative nausea and vomiting. *Anesthesiology*;**92**:931-3.

61. Caroll NV, et al (1995) Postoperative nausea and vomiting after discharge from outpatient surgery centers. *Anesth Analg*;**80**:903-9.

62. Apfel CC, et al (1999) A simplified risk score for predicting postoperative nausea and vomiting: Conclusion from cross validations between two centers. *Anesthesiology*;**91**:693-700.

63. Hill RP,et al (2000) Cost effectiveness of prophylactic antiemetic therapy with ondasetron,droperidol or placebo. *Anesthesiology* **92**:958-67.

64. Frighetto L, et al, (1999) Cost effectiveness of prophylactic dolasetron, or droperidol vs. rescue therapy in the prevention of PONV in ambulatory gynaecologic surgery .*Can J Anaesth*;**46**:536-43.

65. Fortney JT, et al (1998) A comparison of the efficacy, safety and patient satisfaction of ondasetron versus droperidol as antiemetic for elective outpatient surgical procedures. *Anesth Analg*;**86**:731-8.

66. Domino KB, et al. (1999) Comparative efficacy and safety of ondasetron, droperidol and metaclopramide for preventing nausea and vomiting: a meta analysis. *Anesth Analg*;88:1370-9.

67. Sun R et al (1997). The effect of timing ondasetron administration in outpatients undergoing otolaryngologic surgery. *Anesth Analg*;84: 331-6.

68. Henzi I et al (2000) Dexamethasone for the prevention of postoperative nausea and vomiting : a quantitative systemic review. *Anesth Analg*;**90**(1):186-94.

69. Scuderi PE, et al (1999) Antiemetic prophylaxis does not improve outcomes after outpatient surgery when compared to symptomatic treatment .*Anesthesiology*;**90**:360-71.

70. Watcha MF, White PF (1999) Postoperative nausea and vomiting: Prophylaxis vs. treatment. *Anesth Analg*;**89**:1337-9.

71. Tramer MR, et al (1997) A quantitative systemic review of ondasetron in the treatment of established postoperative nausea and vomiting. *BMJ*;**314**:1088-92

72. Yogendran S et al (1995) A prospective randomized double –blinded study of the effect of intravenous fluid therapy on adverse outcomes on outpatient surgery. *Anesth Analg*;**80**:682-6.

Field Anaesthesia: A Report of Mercy Malaysia's Mission 1 to Kashmir following the 2005 South Asia Earthquake

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On October 8, 2005 at approximately 8.50 a.m., a massive earthquake with a magnitude of 7.6 on the Richter scale struck south Asia, involving three nations – Pakistan, India and Afghanistan, killing 73,000 people and completely destroying homes, schools, hospitals and businesses. The epicenter was located right in the middle of the disputed mountainous regions along the Pakistani-Indian border. Faced with the Himalayan terrain and the coming harsh winter, this natural disaster was set to become one of the worst humanitarian crises that the region had ever faced in centuries.

Malaysian Medical Relief Society (MERCY Malaysia) deployed its first mission to Pakistan within 48 hours of the incident. It consisted of an orthopaedic surgeon, an anaesthetist, a physician, a nurse, two logisticians and a non-medical team leader. MERCY Malaysia Mission One was part of a multi-organizational Malaysian Team assembled by the Malaysian Prime Minister. Other organizations involved included the Special Malaysian Disaster Relief and Rescue Team (SMART), Malaysian Red Crescent Society (MRCS) volunteers, as well as doctors and medical assistants from the Emergency Department, Hospital Kuala Lumpur.

We first arrived in Islamabad on October 11 after a grueling 13-hour flight on board the Royal Malaysian Air Force (RMAF) C-130 Hercules. After liaising with Pakistani and United Nations (UN) officials, Muzafarrabad was chosen as our destination. Located some 20 to 30km from the epicenter, it is the capital of the State of Azad Kashmir, the Pakistani-controlled part of the former princely state of Kashmir. Following the earthquake, the disputing parties in the area declared a cease-fire to allow swift delivery of humanitarian aid. We departed by bus from Islamabad on October 12 and due to hazardous landslides, were forced to stop overnight in a hill station called Murree, therefore arriving in Muzafarrabad only a day later.

In Muzaffarabad, we witnessed the devastation caused by the earthquake (figure 1). Only then did we realize the gravity of the disaster. We were informed by UN officials that all search and rescue (S&R) operations had been called off, as it was already into Day 6 after the initial disaster. For our SMART team, it was a case of 'not too little, but too late'.

A field had been converted into a large helipad with numerous helicopters from the UN, Pakistani and foreign military, transporting medical and humanitarian aid together with casualties from affected areas unaccessible by road. Patients were laid on a 'triage' area near the helipad. The local field hospital located next to the helipad, run by the

Figure 1: Muzaffarabad: Survivors covering their faces from the stench of decomposing bodies underneath the rubble

Pakistani military was overwhelmed. Other non-governmental organizations (NGOs) e.g Medicins Sans Frontieres (MSF) transferred some of these patients to their own field hospitals which were set up elsewhere.

We made ourselves useful by treating patients at the 'triage' area whilst waiting for definitive management. A large number of patients had sustained spinal cord injury secondary to vertebral fractures caused by falling debris of ceilings and as a result, had distended bladders. Others had dirty open wounds with limb fractures splinted by hastily made cardboard splints. Treatment for these patients included bladder cathetherisation, simple surgical debridement, toilet and suturing, analgesia and changing of splints.

On October 16, the Malaysian Team was selected to go on a medical relief and evacuation mission. A Luftwaffe (German Air Force) Sikorsky CH-53 helicopter transported us to a remote village inaccessible by road. Within just 4 hours, the team had treated a total of 60 patients. Approximately 25 of these patients were treated for minor surgery such as debridement, toilet and suturing; done mainly under procedural sedation. More definitive treatment such as limb amputations and skin grafts were required for 10 patients and we therefore evacuated them.

On October 17, MERCY Mission 1 parted company with the rest of the Malaysian team, as we felt our services were very much needed elsewhere. Up to this point MERCY Mission 2 had been busy providing surgical services in a field hospital set up by Pakistani Islamic Medical Association (PIMA) in the neighboring city of Bagh. Our journey from Muzaffarabad to Bagh took the whole day, travelling through treacherous mountain roads littered with debris and rubble. The earthquake had marred the breathtaking views of majestic mountain ranges, beautiful conifer forests and idyllic picturesque villages.

Bagh literally means garden in Farsi, but it was certainly no garden when we arrived. It was heavily damaged with 60% of its buildings collapsed. There was no water and only intermittent electricity. Moving masses of people, with belongings, lingered about looking for safe shelters. The district hospital was non-functional.

Mercy Malaysia and our local partner operated a total of 5 tents. We had a field operation theatre (OT), a clinic, a rudimentary pharmacy, a ward tent crammed with 20 patients and a small tent containing a basic sterilization area. Unlucky patients overflowed outside, sleeping in the open air.

The OT that was set up in a tent is shown in Figure 2. There were two operating tables but only one Boyle anaesthesia machine equipped with halothane vaporizer and very limited oxygen supply. Pulse oximetry powered by battery was the only monitoring device available. Over the next 2 days, we treated approximately 35 patients. The majority of cases were fractures (both open and closed) and infected wounds.

Mercy Mission 1 and Mission 2 finally left for Islamabad after two weeks, on October 19. Subsequent missions, up to Mercy Mission 27, continued our effort. We had a two day break before returning to Kuala Lumpur on October 21.

Technique of Anaesthesia and Perioperative Care

Although we arrived in Bagh approximately 10 days after the initial earthquake, throngs of patients were still coming in. Those with major trauma would have probably succumbed to injuries in the initial few days. Some patients had to travel long distances, some

patients, considering the extent of their wounds. Their injuries were the result of trauma from collapsed buildings, as most were not built to withstand earthquakes. Cases of infected wounds involving the limbs, scalp and perineum required repeated debridements (figure 3). Some gangrenous and severely crushed injuries ended up with amputations. A few cases of open fractures required external fixators. Numerous closed fractures required traction or closed manipulation and reduction(CMR) followed by full length casting . Open reduction and internal fixation were not practiced as OT sterility was questionable.

Figure 2: Field OT in Bagh.

Each morning during the ward rounds, an OT list was prepared, although this subsequently had continuous additions of fresh arrivals. We were fortunate to work with volunteers of Al-Khidmat Foundation who functioned not only as our nurses and attendants, who prepared and carried patients, but also as our interpreters. Preoperative anaesthetic assessment was limited, and if there was any, usually involved a quick examination in the OT. No patient was turned away for 'further optimization'. Consideration had to be given to the long distance traveled by patients, limited ward space, increasing number of patients turning up and limited medical resources. Our aim was to treat each patient as quickly as possible and allow home rehabilitation. We were lucky to have radiographs available. The field hospital had been set up next to a small private hospital equipped with basic X-ray facility, which was subsequently abandoned for fear of aftershocks. This did not seem to deter the brave radiographers from providing the much needed investigations.

Blood investigations were unfortunately unavailable. Fasting time was not an issue, as most patients had not had a decent meal for the past few days. Despite that, we were very likely to have anaesthetized a number of unfasted patients as well.

Although we had a Boyle anaesthetic machine at our disposal, general anaesthesia with Halothane was scarcely used due to the very limited availability of oxygen, volatile anaesthetic and power supply. During our short stint in Bagh, Mission 1 used Halothane anaesthesia for only one case, which was a small toddler with scalp abscess in whom there was difficulty establishing intravenous (i.v.) access.

Our technique of choice for most cases, was spontaneous ventilation under iv ketamine anaesthesia for both induction and maintenance. A typical induction dose/regime would be iv midazolam 3 to 5 mg followed by iv ketamine 1 to 1.5 mg/kg. In paediatric patients, ketamine would be the sole iv anaesthetic used. We did not supplement anaesthesia with iv atropine, as excessive salivation was very rarely a problem. Surgical anaesthesia was achieved within 30 seconds. Patients then breathed spontaneously on room air. Maintenance was with intermittent boluses of iv ketamine, usually one quarter to half the induction dose every 5 to 10 minutes, administered when patients have increased vocalization or purposeful movements in response to surgical stimuli. Duration of all operations were less than an hour.

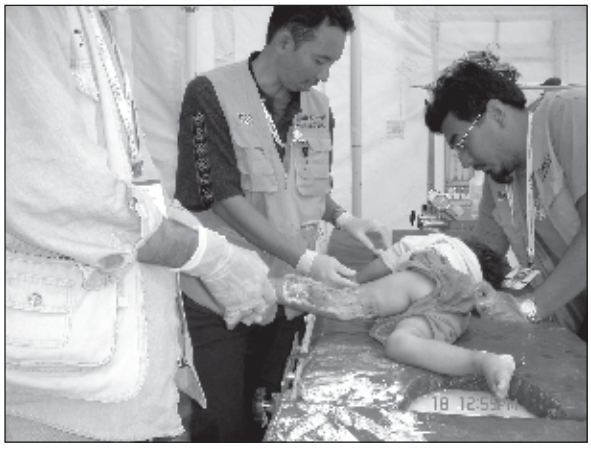

Figure 3: A child undergoing Ketamine anaesthesia for surgical debridement.

Patients tend to maintain their airway very well under ketamine anaesthesia. Some required some degree of chin-lift, but none needed oral airway or intubation. There were no cases of aspiration. Ketamine and its efficacy and safety in field and military anaesthesia has been well documented by Australian civilian and military surgical teams serving in disaster- stricken areas of Papua New Guinea, Dili and Banda Aceh.[1,2,3]

Pulse oximetry was only used during the one case of Halothane general anaesthesia, because of limited battery reserve. As there was no other form of monitoring, we had to resort to intermittent manual monitoring in the form of palpating the carotid pulse for pulse rate and volume, and feeling for breath during chin-lift maneuvers for airway patency and determination of breath rate.

Intraoperatively, crystalloids in the form of normal saline 0.9% or Hartmann's solution were infused routinely.

Although equipment and local anaesthetic (LA) for spinal anaesthesia were available, it was not performed, as we felt it to be too time consuming and uneconomical considering the amount of time available and the number of patients. However, we did perform wrist and femoral blocks. One wrist block was initially performed under ketamine anaesthesia. Once the effects of ketamine wore off, the block was then used for intraoperative anaesthesia. We found that this technique avoided delays whilst waiting for the regional block to set in. Femoral block using perivascular technique was also used for intra and postoperative analgesia.

All patients with infected wounds were given i.v. antibiotics and tetanus prophylaxis. As the pharmacy was well stocked with locally produced cephalosporins, broad spectrum cephalosporins such as cefuroxime or ceftriaxone were given.

Following the surgical procedure, patients were then sent to the ward immediately for recovery. In the case of the child who received Halothane anaesthesia, he was monitored in OT until he showed signs of waking up. There was neither space nor staff to run a recovery area.

Postoperative requirements of opiates were minimal. Undoubtedly, oligoanalgesia was rampant, although none of the patients complained of pain.

Discussion

Based on our limited experience and other well published experiences of Australian surgical teams, ketamine appears to be the anaesthetic agent of choice for disaster situations.[1, 2, 3] Its positive points include airway preservation,[5,6] stimulation of the cardiovascular system,[6] minimal need for complex equipment e.g. Boyle anaesthetic machine or oxygen supply,[4] minimal need for recovery ward[5] and reduced need for administration by trained anaesthetists.[5,10] The unpleasant psychogenic side-effects were not seen in our patients even for those undergoing repeated procedures. Pleasant dreams have instead been described in patients from the Banda Aceh experience.[1]

Ketamine appears ideal for superficial and deep surgery e.g. wound debridement.[1,3] but is not the anaesthetic of choice for surgery involving body cavities i.e. intraabdominal operations and burr-hole procedures in the Papua New Guinea experience.[3] It is safe and effective for children undergoing painful or disturbing procedures. For this group of patients, the i.m. route is a valid alternative to the i.v. route. The optimal i.m. dose of ketamine for procedural sedation in children was determined to be 4 to 5 mg/kg.[12] There is, however, yet to be a prospective randomised control study to validate this premise.

The safety and efficacy of regional techniques in field anaesthesia was demonstrated by the Regional Anaesthesia Section at Walter Reed Army Medical Center during a deployment in Burkina Faso.[7] In their series, 110 out of 118 surgical procedures were conducted under regional anaesthesia. The commonest technique was central neural blockade. Other techniques used were LA infiltration, thoracic paravetebral block, brachial plexus blocks, lumbar and sacral plexus blocks. The authors emphasized on the importance of intensive regional anaesthesia training to ensure the success of regional blocks in austere environments. Continuous lumbar plexus and sciatic nerve blocks for anaesthesia and analgesia have been successfully used in an American soldier

during the 2nd invasion of Iraq (the authors used the name 'Operation Iraqi Freedom').[8]

The use of volatile agents is still applicable in field anaesthesia, albeit only in body-cavity surgeries. We were fortunate to have a Boyle anaesthetic machine on loan by a private hospital. In reality, however, it is a logistical nightmare to transport the machine to a distant place. Other more portable and versatile options have been described in the literature. The ULCO Portable Field Anaesthesia Machine which weighs only 32 kg when fully loaded,[9] was used by the Australian Defence Force (ADF).[3] It can be used in both drawover and plenum modes.[9] The Triservice Apparatus (TSA) which is essentially two Oxford Miniature Vaporisers (OMV) connected in series[13] can only function as a drawover device but is favoured by the British military.[10] Drawover systems require much less oxygen when compared to plenum systems. Another example of a drawover system is Ohmeda Universal PAC drawover apparatus,[14] which has also been used in combinations with other anaesthetic circuits in the field.

Total intravenous anaesthesia using target-controlled infusion of Propofol has also been used by the ADF in Dili.[11]

Oxygen supply is a precious commodity in disaster areas. Oxygen concentrators, producing 3-4 L/min of 90 – 95% oxygen were used by the ADF successfully.[12]

Monitoring of patients in the field should ideally include all minimum monitoring standards i.e electrocardiogram, pulse oxymetry, non-invasive blood pressure and capnometer. New portable devices that are available commercially include finger pulse oxymeter, portable gas analyzer, hand-held capnometer and compact combined pulse oxymeter/capnometer robust enough for different environments.[12]

Patients at risk for aspiration undergoing volatile anaesthesia should undergo rapid sequence intubation with cricoid pressure to minimize the risk of aspiration. The Laryngeal Mask Airway (LMA) was extensively used in wound debridement procedures under general anaesthesia by the ADF in Papua New Guinea.[2]

Conclusions

Volunteerism is clearly not for everyone. Unfavorable living conditions, appalling toilets, psychological trauma, concern for personal safety and unfamiliar food affected everyone in our team, one way or the other. Courage, compassion, humility, hardiness and flexibility are among the traits that volunteers should have. Different people volunteer for different reasons but most enjoy the experience and keep on volunteering.

MERCY Malaysia has always been dependent on local partners in delivering emergency medical help to disaster areas. The experience gained from this South Asia earthquake medical relief work has exposed its volunteers to field surgery and anaesthesia. During the writing of this article, MERCY Malaysia is setting up an Emergency Response Unit (ERU) capable of being an independent surgical and medical unit.

The provision of field anaesthesia presents unique challenges not often seen in hospital-based practice. Poorly prepared patients may require life-saving surgeries under austere conditions. From our limited experience after the South Asia earthquake, we've found that most surgery conducted under these conditions was superficial in nature. Intravenous ketamine was the anaesthetic agent of choice in most instances.

References

1. Paix BR, Capps R, Neumeister G, Semples. Anaesthesia in a Disaster Zone: A Report on the Experience of an Australian Medical Team in Banda Aceh Following the 'Boxing Day Tsunami". *Anaesth Intensive Care* 2005;**33**:629-634
2. Taylor RP, Emonson DI, Schlimmer JE. Operation Shaddock—the Australian Defence Force response to the tsunami disaster in Papua New Guinea. *Med J Aust* 1998;**169**:606-609
3. Bradley JP, Lee D. Asia Pacific Forum: Anaesthesia in the United Nations Military Hospital, Dili, East Timor. *Anaesth Intesive Care* 2001;**29**: 527-529
4. Dobson MB. Anaesthesia for difficult locations-developing countries and military conflicts. In: Prys-Roberts C, Brown Burnell R Jr, eds International Practice of Anaesthesia Vol 2 pp1- 10
5. King M. Primary Anaesthesia. Oxford University Press, 1990; pp60.
6. Morgan GE, Mikhail MS. (eds) Nonvolatile Anaesthetic Agents. In:Clinical Anesthesiology. Appleton and Lange, 1999, pp141
7. Buckenmaier CC, Lee EH, Shields CH, Sampson, Chiles JH. Regional Anaesthesia in Austere Environments. *Reg Anesth Pain Med* 2003:**28**, 321-327
8. Buckenmaier CC,.McKnight GM, Winkley JV, Bleckner, Shannon C, Klein MK, Lyons RC, Chiles JH. Continous Peripheral Nerve Block for Battlefield Anaesthesia and Evacuation. *Reg Anaest Pain Med* 2005;**30**: 202-205
9. Perndt HKS. The ULCO Anaesthesia Suitcase. *Anaest Intensive Care* 2002;**30**: 800-803
10. Mellor AJ. Anaesthesia in Austere Environtments. *J R Army Med Corps* 2005;**5**: 272-276
11. Harding JN, Wilson M.Use of Target-Controlled Infusion of Propofol for Military Field Anaesthesia. *ADF Health* 2003;**4**:23-26.
12. Tang KC, Chiu JW, Low E. Airway and Ventilatory Equipment in Field Anaesthesia: What's New? *Military Med* 2004;**169**:342-349
13. Green SM et al. What is the optimal dose of intramuscular ketamine for pediatric sedation? *Acad Emerg Med* 1999;**6**:21-26
14. Houghton IT. The Triservice anaesthetic apparatus. *Anaesthesia* 1981; **36**:1094-108
15. Lunn DV. The Ohmeda Universal PAC drawover apparatus. A Technical and clinical evaluation. *Anaesthesia* 1995;**50**(10): 870-874

Prevention and Management of Hypotension during Regional Anaesthesia for Caesarean Section

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Introduction

Audit studies on anaesthesia-related maternal mortality worldwide have repeatedly emphasised that the risk of mortality is higher with general anaesthesia (GA) compared to regional anaesthesia (RA).[1,2] As such, it is strongly recommended that caesarean section (CS) should be performed under regional anaesthesia unless specifically contraindicated. Regional anaesthetic techniques for CS include single-shot spinal, combined spinal-epidural (CSE) and epidural anaesthesia.

Single-shot spinal anaesthesia is often the RA technique of choice because of its rapid, reliable and profound sensory and motor blockade. However, maternal hypotension is the most frequent complication of this technique; the incidence of spinal-induced hypotension is reported to be in the range of 40-85%.[3] Hypotension often results in unpleasant maternal symptoms such as nausea, vomiting and light-headedness. There is a distinct association of intraoperative nausea and vomiting with maternal hypotension, and strict control of blood pressure can dramatically reduce emetic symptoms.[4] When hypotension is severe and sustained (systolic BP < 80 mmHg greater than 4 min duration), uteroplacental perfusion may be jeopardized resulting in fetal acidosis and neonatal depression. Several strategies are currently used to prevent or minimize hypotension but there is no established ideal technique.

In a meta-analysis by Reynolds,[5] it was noted that there was a significant reduction in neonatal umbilical cord blood pH following CS under spinal anaesthesia than either epidural or general anaesthesia. This could be secondary to hypotension associated with spinal anaesthesia, or a side-effect of ephedrine used in its treatment or prevention. They also noted that routine co-administration of phenylephrine with ephedrine is associated with higher umbilical arterial and venous pHs, and with less fetal acidosis, than when ephedrine is used alone. However, the authors concluded that the differences observed, though significant, were not large; and that in many instances the advantages of spinal anaesthesia outweighed the concerns regarding funic pH and base deficit.

Haemodynamic consequences of spinal anaesthesia are manifold. Sympathetic blockade induces reductions in systemic vascular resistance (SVR), venous return, stroke volume, cardiac output and blood pressure.[6] Regional perfusion is altered by shunting of blood into the mesenteric bed, which may result in decreased uteroplacental blood flow. When the block extends above T4, the cardiac sympathetic nerves are affected, resulting in hypotension and bradycardia.

Prevention of Spinal-induced Hypotension

Suggested prophylactic measures against spinal-induced hypotension include recognition and modification of factors affecting outcome of spinal anaesthesia, measures to increase central blood volume (positioning, leg compression, fluid preload), and the use of vasopressors, either singly or in combination. However, as stated in a recently published Cochrane Collaboration Systematic Review, no intervention reliably prevents hypotension during spinal anaesthesia for caesarean section.[7] Furthermore, prophylactic management has been associated with side-effects – large volumes of intravenous fluids increase the risk of iatrogenic pulmonary oedema in high risk pregnant patients, prophylactic vasopressors can cause hypertension and prophylactic ephedrine has been associated with fetal acidosis.[8]

a) Factors Affecting Outcome of Spinal Anaesthesia

Many different factors may influence the outcome of spinal anaesthesia in terms of sensorimotor blockade and haemodynamic consequences. Factors such as the amount of local anaesthetic injected, baricity and temperature of the local anaesthetic solution,[9-12] positioning of the patient during [13-14] and after [15-17] spinal injection, and the speed of injection,[18-19] are expected to be of importance in the development of hypotension following spinal blockade.

In an in vitro study on a spinal canal model, Lui concluded that baricity was an important determinant of local anaesthetic distribution in the subarachnoid space.[11] Hallworth investigated the effect of posture and baricity on the spread of intrathecal bupivacaine for elective CS and found that hypotension incidence and ephedrine use increased with decreasing baricity, with the hypobaric sitting position having the most frequent incidence of hypotension (76%) as well as cervical blocks (24%).[12]

Inglis compared the right lateral with the sitting position during induction of spinal anaesthesia, and found that the incidence of hypotension was higher in the lateral group.[13] The Oxford position (full lateral with shoulder elevation), first described by Carrie,[20] was shown to be associated with a slower onset of the spinal block, more stable blood pressure, less ephedrine use, a more predictable final block height and later requirement for postoperative analgesia compared to the sitting position.[21]

The speed of intrathecal injection may be important, as it was noted that slow injection (2 ml/min) significantly reduced incidence (68% versus 92% control) and severity of hypotension.[19] However, in a much earlier study, Bucx did not find clinically relevant influence on the maximum level of sensory blockade when 0.5% bupivacaine at room temperature was injected with a ten-fold difference in speed.[18] The incidence of hypotension was not investigated in Bucx's study.

The addition of various doses of different intrathecal opioids may allow reduction in the local anaesthetic dose, with an equivalent success rate and less severe side-effects such as hypotension, nausea and vomiting, and prolonged motor blockade.[22] Ben-David reported that bupivacaine 5 mg with fentanyl 25 µg provided adequate surgical anaesthesia with less hypotension, vasopressor requirements, and nausea than bupivacaine 10 mg.[23]

In terms of central neuraxial block technique, Goy reported that subarachnoid block induced by CSE produced greater sensorimotor anaesthesia and prolonged recovery compared with single shot spinal technique, with a greater incidence of hypotension and vasopressor use despite using identical doses and baricity of local anaesthetic.[24] The low dose sequential CSE technique, with a small intrathecal dose topped up via the epidural route if required, is another method to reduce the likelihood of hypotension. This technique has been successfully utilized in the anaesthetic management of patients with significant cardiac disease for CS.[25]

b) Central blood volume expansion

Methods used to for central blood volume expansion include patient positioning, leg compression, and intravenous fluid administration.

i) ***Positioning***

One should be meticulous in making sure that left uterine displacement is properly instituted in order to avoid aortocaval compression. This entails some degree of left pelvic tilt, in the form of 15° left lateral tilt as advocated by Crawford,[26] or the supine wedged position (wedge placed under the right hip), or maintenance of full lateral position until the moment of skin preparation. Rees studied the effects of positioning following initiation of spinal anaesthesia for CS, and recommended the use of the lateral position rather than tilt for elective cases because aortic compression was more pronounced in the tilt position.[15] However, block onset was found to be quicker when the patient was turned directly to the tilt position and hence would be advantageous in urgent Caesarean delivery.[16] In another study using CSE for CS, Mendonca found that early

hypotension was less frequent and was easier to treat when the patients were placed in the full left lateral position compared with the tilted supine position.[17]

It must be noted that the supine tilted position may be less than Crawford's recommendation of 15°, due to unreliable estimation of the degree of tilt.[27] This is an important finding as lesser degrees of tilt are associated with residual inferior vena cava compression, and it could make anaesthetists discount inadequate tilt as a cause of hypotension or collapse in a pregnant woman. Indeed Crawford's recommendation might seem rather empirical, as aortocaval compression has even been demonstrated with up to 34° of lateral tilt.[28]

ii) ***Leg compression***

Leg compression is a mechanical means of central blood volume expansion. Various methods have been described, such as leg wrapping with Esmarch bandage, anti-thromboembolic stockings, inflatable boots or splints, and leg elevation while tilting the OT table head down. Rout regarded the use of leg compression immediately post-spinal as a simple means of reducing the accompanying hypotension and advocated its wider usage.[29] In a systematic review on the effects of an increase of central blood volume before spinal anaesthesia for CS, Morgan noted that leg wrapping and anti-thromboembolic stockings decreased the incidence of hypotension compared with leg elevation or control.[30]

iii) ***Intravenous fluids***

The use of intravenous fluid as volume preload prior to subarachnoid block is an established part of anaesthetic practice. Intravenous fluid preloading is thought to minimize severity of hypotension and reduce vasopressor requirements by expanding the central blood volume. In addition, it may result in reduction of red blood cell loss by haemodilution. However, there are wide variations in the type, amount, speed, and timing of intravenous fluid administration. Routine fluid preload consists of 15-20 ml/kg Ringer's lactate over 20 min before the subarachnoid block. In a survey of practice among the anaesthetists in the UK, the fluid chosen by 83.3% of the preloaders was Hartmann's solution and the usual volume was 1000 ml.[31] However, the incidence of hypotension remains disappointingly at 40% even with fluids.[30]

The use of colloids has also been advocated, ranging from a combination of 6% hetastarch & Ringer's lactate, 10% hydroxyethyl starch, and gelatin solution. Problems associated with colloid solutions, namely cost, risks of fluid overload, anaphylactoid reactions and coagulopathy should be taken into consideration. In the same systematic review, Morgan found that crystalloid preload was inconsistent in preventing hypotension, whereas colloid appeared to be effective in all but one study.[30]

The timing of fluid administration has also been investigated, and rapid crystalloid loading appears more effective when delayed until intrathecal injection and then very quickly infused – a "coload" rather than preload. Dyer found that requirement for vasopressor therapy was reduced in the coload group, and may be advantageous in terms of managing maternal blood pressure prior to delivery.[32] It certainly seems more logical to give a fluid load during the onset of vasodilation rather than before.

c) **Vasopressor Prophylaxis**

There is a confusing array of choices and preferences for vasopressors, such as the use of ephedrine versus α-adrenergic agonists, single versus combination therapy, and prophylactic versus therapeutic use. Similarly, the route of administration (intramuscular, intravenous bolus or intravenous infusion) and the dose (bolus doses or infusion) are many and varied. In the UK survey conducted in 1999, ephedrine was the sole vasopressor used by 95.2% of the respondents.[31] This is likely to change with the increasing popularity and widespread use of α-adrenergic agonists, phenylephrine in particular.

Ayorinde evaluated pre-emptive intramuscular

phenylephrine and ephedrine for reduction of spinal anaesthesia-induced hypotension during CS.[33] He found that pre-emptive IM phenylephrine 4 mg and ephedrine 45 mg reduced the severity of hypotension and the total dose of rescue IV ephedrine used. However, the use of intramuscular injection for rescue therapy is becoming less popular in view of its unpredictable systemic absorption and peak effect, and the possibility of rebound hypertension.

Prophylactic administration of vasopressors has been recommended as a proactive rather than reactive step, as placental hypoperfusion may occur before maternal hypotension is manifest. Vasopressor prophylaxis aims to reduce the incidence and severity of hypotension, as well as the total dose of rescue vasopressor therapy. However, it may result in problems of its own, such as over-treatment with reactive hypertension, tachyphylaxis to ephedrine, and maternal bradycardia associated with phenylephrine. In addition, the vast majority of patients who develop hypotension respond to therapy with bolus doses of vasopressor. The safety and efficacy of vasopressor prophylaxis should be established before it could be embarked upon as a standard practice.

Choice of Vasopressors

Historically, ephedrine has been regarded as the vasopressor of choice in obstetric anaesthesia. Ralston[34] showed that, in gravid ewes, ephedrine was more effective for increasing arterial BP with better preservation of uteroplacental blood flow compared with other vasopressors. In contrast, α-adrenergic agonists increased uterine vascular resistance and thus reduced uteroplacental blood flow – reduction by 45% in metaraminol and 62% in methoxamine. This finding was reiterated by McGrath, who experimented on ewes receiving ritodrine infusion and found that ephedrine increased uterine blood flow while phenylephrine increased uterine vascular resistance.[35] However, it is doubtful whether such experiments conducted on sheep could be extrapolated to humans because of species difference. In addition, the sheep were not under regional anaesthesia and were not placed in supine position with left lateral tilt (as in Caesarean delivery). Furthermore, the test drug was administered to increase BP by 50% instead of being used as treatment for hypotension.

Interest in phenylephrine in obstetric anaesthesia was rekindled by Ramanathan, who compared ephedrine with phenylephrine during epidural anaesthesia for CS.[36] He concluded that bolus doses of phenylephrine 100 μg provided an adequate perfusion pressure with similar maternal and fetal outcomes to ephedrine group, and that an α-agent such as phenylephrine did not cause fetal acidosis when used for treating maternal hypotension. Following this, there was an increasing use of α-agonists and other vasopressors such as phenylephrine, methoxamine, metaraminol, adrenaline, dopamine, paredrine, mephentermine, vasopressin and angiotensin II.

In the 1990s, the status of ephedrine as the vasopressor of choice in obstetric anaesthesia has been increasingly questioned. Being a combined α- and β-adrenergic receptor agonist, ephedrine has less effect on SVR and venous capacitance vessels compared to a pure α-agonist, and the cardiovascular system remains vasodilated and relatively under-filled. Blood pressure is maintained by β-mediated increases in myocardial contractility, heart rate and cardiac output to offset decreases in SVR, hence the development of unwanted maternal tachycardia as a side-effect of ephedrine administration.[3] It is also difficult to titrate, has a relatively slow onset and long duration of action, and may demonstrate tachyphylaxis during which large doses are frequently required. The incidence of nausea and vomiting is significantly higher than phenylephrine despite similar BP control.[4] Ephedrine also readily crosses the placenta and may increase fetal metabolic rate secondary to ß-adrenergic stimulation; it may even result in fetal acidosis from direct fetal effects.[8]

In contrast, phenylephrine, being a pure α-agonist, increases preload by vasoconstriction. It demonstrates a selective vasoconstrictive effect on mesenteric bed than on uteroplacental vasculature and may in fact improve uteroplacental perfusion and fetal acid-base status.[3] Reflex bradycardia occurs

in up to 20% of patients receiving phenylephrine. It is aggravated by sympathetic denervation in high block but is often well-tolerated, transient, and responsive to treatment with atropine or glycopyrrolate.

Lee *et al* [37] performed a systematic review of randomized controlled trials on ephedrine versus phenylephrine for the management of hypotension during spinal anaesthesia for CS. They found no difference in efficacy of management (prevention and treatment) of maternal hypotension in both groups. Phenylephrine was associated with a higher incidence of maternal bradycardia and higher umbilical arterial pH values. However, there were no differences in the incidence of true fetal acidosis (umbilical arterial pH < 7.2) or Apgar score of < 7 at 1 and 5 min. They found no support for the traditional idea of ephedrine as the vasopressor of choice for the management of maternal hypotension, thus its routine use could not be recommended.

The use of prophylactic ephedrine for the prevention of hypotension during spinal anesthesia for elective CS was also reviewed by Lee *et al*.[8] They found that the efficacy of ephedrine for preventing hypotension was small. The use of larger doses of ephedrine (>14 mg) did not eliminate hypotension but caused reactive hypertension and a minor decrease in umbilical arterial pH. As in the previous systematic review, they concluded that prophylactic IV ephedrine could not be recommended.

In the literature, various regimes of vasopressor prophylaxis and rescue therapy have been studied and advocated. Examples include prophylactic phenylephrine infusion 100 µg/min and rescue IV ephedrine bolus or phenylephrine infusion; and prophylactic infusion of 2 mg/min ephedrine with 10 µg/min phenylephrine and rescue ephedrine bolus of 6 mg.

In a study on phenylephrine prophylaxis, Ngan Kee[38] compared the use of phenylephrine infusion at 100 µg/min for 3 min immediately after intrathecal injection, then at 100 µg/min when systolic BP was less than baseline. This was, compared to controls of IV bolus 100 µg when SBP was less than 80% baseline. He found that phenylephrine prophylaxis resulted in significantly lower incidence (23% versus 88%) and magnitude of hypotension, higher total phenylephrine dose and similar fetal outcome in terms of umbilical cord blood gases and Apgar scores.

In another study by the same author [39] to compare phenylephrine infusion regimens for maintaining maternal blood pressure during spinal anaesthesia for CS; phenylephrine infusion of 100 µg/min was administered for 2 min immediately after intrathecal injection, then at 100 µg/min to maintain systolic BP at either 100%, 90% or 80% of baseline. It was found that titration of phenylephrine to maintain SBP at 100% of baseline achieved the best outcome with the lowest episodes of hypotension, the lowest incidence of nausea and vomiting, and the highest umbilical artery pH.

Word of Caution

It has been demonstrated that extrapolation of results from animal studies to humans can be fraught with uncertainties, due to species differences in α- and ß-adrenergic receptor, and differences in vascular responses to vasopressors.

In addition, many of these randomized controlled trials are conducted on healthy non-labouring parturients with term, low risk fetuses for elective CS. Question marks must be raised when dealing with less than healthy mothers, labouring mothers, fetuses at risk (intrauterine growth retardation, preterm, fetal distress) and CS done under emergency situations. Erkinaro demonstrated that in a chronic sheep model of increased placental vascular resistance, phenylephrine impaired uterine and placental haemodynamics and increased fetal lactate concentrations.[40] Datta compared healthy with diabetic parturients and showed that while healthy mothers had a slight decrease in umbilical arterial pH following transient hypotension under spinal anaesthesia, diabetic mothers had clinically significant reductions in umbilical arterial pH following similar degrees of hypotension.[41]

Summary

There is a lack of efficacy of individual modalities in preventing spinal anaesthesia-induced hypotension, and a single perfect antidote for prevention and treatment of maternal hypotension may never be found. A multimodal approach, including fluid preloading and prophylactic vasopressor use, may represent the optimal approach. The position of ephedrine as the vasopressor of choice in obstetric anaesthesia has been challenged, and the use of pure α-agonist such as phenylephrine may be more advantageous. As long as hypotension is transient, the choice of vasopressor should depend on the clinical situation, considering not only the blood pressure but the heart rate as well.[42] As Riley suggested in an editorial, "Spinal anaesthesia for Caesarean delivery: keep the pressure up and don't spare the vasoconstrictors".[43]

References

1. Why mothers die. Report on confidential enquiries into maternal deaths in the United Kingdom 2000-2002. London; 2004.
2. Hawkins JL, Koonin LM, Palmer SK, Gibbs CP. Anesthesia-related deaths during obstetric delivery in the United States, 1979-1990. *Anesthesiology* 1997;**86**:277.
3. McKinlay J, Lyons G. Obstetric neuraxial anaesthesia: which pressor agents should we be using? *Int J Obstet Anesth* 2002;**11**;117-21.
4. Balki M, Carvalho JCA. Intraoperative nausea and vomiting during cesarean section under regional anesthesia. *Int J Obstet Anesth* 2005;**14**:230-41.
5. Reynolds F, Seed PT. Anaesthesia for caesarean section and neonatal acid-base status: a meta-analysis. *Anaesthesia* 2005;**60**:636-53.
6. Mark JB, Steele SM. Cardiovascular effects of spinal anesthesia. *Intern Anesth Clin* 1989;**27**:31-9.
7. Emmett RS, Cyna AM, Andrew M, Simmons SW. Techniques for preventing hypotension during spinal anaesthesia for caesarean section. *Cochrane Pregnancy and Childbirth Group Cochrane Database of Syst Rev* 2006;**3**.
8. Lee A, Ngan Kee WD, Gin T. Prophylactic ephedrine prevents hypotension during spinal anesthesia for Cesarean delivery but does not improve neonatal outcome. *Can J Anesth* 2002;**49**:588-99.
9. Heller AR, Zimmermann K, Seele K, Rossel T, Koch T, Litz RJ. Modifying the baricity of local anesthetics for spinal anesthesia by temperature adjustment – model calculations. *Anesthesiology* 2006;**105**:346-53.
10. Horlocker TT, Wedel DJ. Density, specific gravity, and baricity of spinal anesthetic solutions at body temperature. *Aneth Analg* 1993;**76**:1015-8.
11. Lui ACP, Munhall RJ, Winnie AP, Selander D. Baricity and the distribution of lidocaine in a spinal canal model. *Can J Anaesth* 1991;**38**:522-6.
12. Hallworth SP, Fernando R, Columb MO, Stocks GM. The effect of posture and baricity on the spread of intrathecal bupivacaine for elective cesarean delivery. *Anesth Analg* 2005;**100**:1159-65.
13. Inglis A. Daniel M. McGrady E. Maternal position during induction of spinal anaesthesia for caesarean section. A comparison of right lateral and sitting positions. *Anaesthesia* 1995;**50**:363-5.
14. Russell IF. Effect of posture during the induction of subarachnoid analgesia for caesarean section. Right v. left lateral. *Br J Anaesth* 1987;**59**:342-6.
15. Rees SGO, Thurlow JA, Gardner IC, Scrutton MJL, Kinsella SM. Maternal cardiovascular consequences of positioning after spinal anaesthesia for Caesarean section: left 15o table tilt vs. left lateral. *Anaesthesia* 2002;**57**:15-20.
16. Hartley H, Seed PT, Ashworth H, Kubli M, O'Sullivan G, Reynolds F. Effect of lateral versus supine wedged position on development of spinal blockade and hypotension. *Int J Obstet Anaesth* 2001;**10**:182-8.
17. Mendonca C, Griffiths J, Ateleanu B, Collis RE. Hypotension following combined spinal-epidural anaesthesia for Caesarean section. Left lateral position vs. tilted supine position. *Anaesthesia* 2003;**58**:428-31.
18. Bucx MJ, Kroon JW, Stienstra R. Effect of speed of injection on the maximal sensory level for spinal anesthesia using plain bupivacaine 0.5% at room temperature. *Reg Anesth* 1993;**18**:326-7.
19. Simon L, Boulay G, Ziane AF, et al. Effect of injection rate on hypotension associated with spinal anesthesia for cesarean section. *Int J Obstet Anesth* 2000;**9**:10-4.

20. Carrie LES. Spinal and/or epidural blockade for Caesarean section. In: Reynolds F, ed. Epidural and Spinal Blockade in Obstetrics. London: Bailliere Tindall, 1990; 139-50.
21. Stoneham MD, Eldridge J, Popat M, Russell R. Oxford positioning technique improves haemodynamic stability and predictability of block height of spinal anaesthesia for elective caesarean section. *Int J Obstet Anaesth* 1999;**8**:242-8.
22. Dyer RA, Joubert IA. Low-dose spinal anaesthesia for Caesarean section. *Curr Opin Anaesthesiol* 2004;**17**:301-8.
23. Ben-David B, Miller G, Gavriel R, Gurevitch A. low-dose bupivacaine-fentanyl spinal anesthesia for cesarean delivery. *Reg Anesth Pain Med* 2000;**25**:235-9.
24. Goy RWL, Sia ATH. Sensorimotor anesthesia and hypotension after subarachnoid block: combined spinal-epidural versus single-shot spinal technique. *Anesth Analg* 2004;**98**:491-6.
25. Hamlyn EL, Douglass CA, Plaat F, Crowhurst JA, Stocks GM. Low-dose sequential combined spinal-epidural: an anaesthetic technique for caesarean section in patients with significant cardiac disease. *Int J Obstet Anesth* 2005;**14**:355-61.
26. Crawford JS. Principles and practice of obstetric anaesthesia. 5th Ed. Oxford: Blackwell Scientific, 1984: 286-7.
27. Jones SJ, Kinsella SM, Donald FA. Comparison of measured and estimated angles of table tilt at Caesarean section. *Br J Anaesth* 2003;**90**:86-7.
28. Kinsella SM, Whitwam JG, Spencer JAD. Aortic compression by the uterus: identification with the Finapress digital arterial pressure instrument. *Br J Obstet Gynaecol* 1990;**97**:700-5.
29. Rout CC, Rocke DA, Gouws E. Leg elevation and wrapping in the prevention of hypotension following spinal anaesthesia for elective caesarean section. *Anaesthesia* 1993;**48**:304-8.
30. Morgan PJ, Halpern SH, Tarshis J. The effects of an increase of central blood volume before spinal anesthesia for cesarean delivery: a qualitative systematic review. *Anesth Analg* 2001;**92**:997-1005.
31. Burns SM, Cowan CM, Wilkes RG. Prevention and management of hypotension during spinal anaesthesia for elective Caesarean section: a survey of practice. *Anaesthesia* 2001;**56**:794-8.
32. Dyer RA, Farina Z, Joubert IA, et al. Crystalloid preload versus rapid crystalloid administration after induction of spinal anaesthesia (coload) for elective caesarean section. *Anaesth Intens Care* 2004;**32**:351-7.
33. Ayorinde BT, Buczkowski P, Brown J, et al. Evaluation of pre-emptive intramuscular phenylephrine and ephedrine for reduction of spinal anaesthesia-induced hypotension during Caesarean section. *Br J Anaesth* 2001;**86**:372-6.
34. Ralston DH, Shnider SM, DeLorimier AA. Effects of equipotent ephedrine, metaraminol, mephentermine, and methoxamine on uterine blood flow in the pregnant ewe. *Anesthesiology* 1974;**40**:354–70.
35. McGrath JM, Chestnut DH, Vincent RD, et al. Ephedrine remains the vasopressor of choice for treatment of hypotension during ritodrine infusion and epidural anesthesia. *Anesthesiology* 1994;**80**:1073-81.
36. Ramanathan S, Grant GJ. Vasopressor therapy for hypotension due to epidural anesthesia for caesarean section. *Acta Anaesthesiol Scand* 1988;**32**:559-65.
37. Lee A, Ngan Kee WD, Gin T. A quantitative, systematic review of randomized controlled trials of ephedrine versus phenylephrine for the management of hypotension during spinal anesthesia for cesarean delivery. *Anesth Analg* 2002;**94**:920-6.
38. Ngan Kee WD, Khaw KS, Ng FF. Lee BB. Prophylactic phenylephrine infusion for preventing hypotension during spinal anesthesia for cesarean delivery. *Anesth Analg* 2004; **98**:815-21.
39. Ngan Kee WD, Khaw KS, Ng FF. Comparison of phenylephrine infusion regimens for maintaining maternal blood pressure during spinal anaesthesia for Caesarean section. *Br J Anaesth* 2004;**92**:469-74.
40. Erkinaro T, Kavasmaa T, Pakkila M, Acharya G, Makikallio K, Alahuhta S, Rasanen J. Ephedrine and phenylephrine for the treatment of maternal hypotension in a chronic sheep model of increased placental vascular resistance. *Br J Anaesth* 2006;**96**:231-7.
41. Datta S, Brown WU Jr. Acid-base status in diabetic mothers and their infants following general or spinal anesthesia for cesarean section. *Anesthesiology* 1977;**47**:272-6.
42. Vallejo MC, Ramanathan S. Should -agonists be used as first line management of spinal hypotension? (Editorial) *Int J Obstet Anaesth* 2003;**12**:243-5.
43. Riley ET. Spinal anaesthesia for Caesarean delivery: keep the pressure up and don't spare the vasoconstrictors. (Editorial) *Br J Anaesth* 2004;**92**:459-61.

Use of Medical Simulation in the Practice of Anaesthesia

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Introduction

Medical simulation is an exercise designed to mimic a real life situation in which the learner is given an opportunity to reason through a clinical problem and make diagnostic and treatment decisions in real time without fear of patient compromise. It also refers to the artificial representation of a complex real-world process with sufficient fidelity to achieve a particular objective, either for the purposes of training or performance testing.

Simulator refers to a computerized mannikin with a realistic cardiopulmonary system that interfaces with standard equipment (monitors, intubation supplies, etc.). High fidelity physiology and pharmacology programs control the mannikin and mimic human responses. It even has a "voice" to provide realistic patient encounters.

The introduction of high fidelity simulation and its associated training program into the medical training has made an impact on safety aspects of patient health care, especially in anaesthesiology.[1]

History

While simulation has been practiced from the early times (as in the rehearsal of animal hunting activities or preparing for warfare), the needs of World War II greatly accelerated simulation technology for use of in flight training.

The first recorded use of a medical simulator is that of a mannikin created in the 17th Century by a Dr Gregoire of Paris (Buck, 1991). He used a pelvis with skin stretched across it to simulate an abdomen, and with the help of a dead fetus explained assisted and complicated deliveries to midwives.

In spite of this early start, medical simulators did not really gain widespread use in the following centuries, principally for reasons of cost, reluctance to adopt new teaching methods, and scepticism that what was learned from a simulator could be transferred to actual practice.

All of these reasons are still relevant today, however the combination of improved technology and increasing pressures on educators have promoted simulation as one option to address the problems associated with traditional clinical skills teaching. With the availability of inexpensive computer technology in recent years, simulation technology has blossomed again. This is especially in the field of medicine, where applications range from scientific modeling to clinical performance appraisal in the setting of crisis management.

In the last 10 years, simulation using high-fidelity patient simulators for the purpose pf training health-care professionals has grown and expanded rapidly. There are now approximately 200 simulation training centres operating internationally. Malaysia currently has two such centres and one of them is the University Malaya Simulation Centre that was opened in 2001. Located in the Faculty of Medicine, it is supported by a government grant and provides multidisciplinary training for doctors and nurses at both undergraduate and postgraduate levels.

Type of simulators

Computer-based simulators used in medical education fall into four general categories:

(1) Screen-based text simulators,

(2) Screen-based graphical simulators,

(3) Mannikin-based simulators,

(4) Virtual reality trainers.

The Virtual Anesthesiology Training Simulation System from CAE/Eagle/MedSim (the name reflects a series of corporate sales and takeovers) is a modern anesthesiology simulator conceived for a number of training applications, such as to train anesthesiology residents, for practice with new technology or instruments, for rehearsing anesthetic emergencies, and possibly for future testing, certification, or recertification of anesthesiologists. It is also of potential use outside the operating room, in situations like Critical Care Training and Emergency Room Training.

This high level Human Patient Simulator (HPS) consists of a lifelike patient mannikin; which breathes spontaneously, has palpable pulses, heart and lung sounds and responds appropriately to stimuli such as electrical current from a neuromuscular blockade monitor. It can also present a wide range of responses such as arm motion, eyelid open/closure, pupil dilatation/contraction, and tongue and airway swelling. The mannikin can be intubated and connected to life-support systems, such a mechanical ventilators or intravenous cardiac inotrope infusion pumps.[2] A hybrid (mechanical and mathematical) lung model allows the patient mannikin to consume oxygen and produce carbon dioxide. The HPS is able to recognise and respond to a wide variety of pharmacological agents and physiology events. The simulator can be programmed to present a variety of medical problems (e.g. mitral and aortic stenosis, intracranial hypertension) and altered physiologic states including cardio respiratory events such as haemorrhage, anaphylaxis, pneumothorax, and aspiration; and metabolic events, as well as a difficult airway and equipment malfunction. Almost any specialty can be accommodated, including pediatrics and obstetrics.

Figure 1

High Fidelity Simulator : SAM of UM

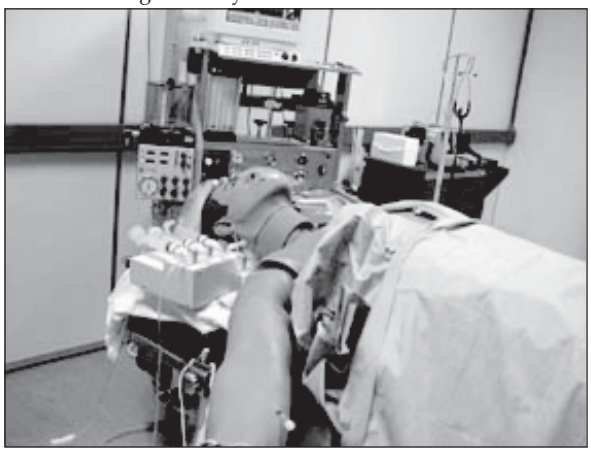
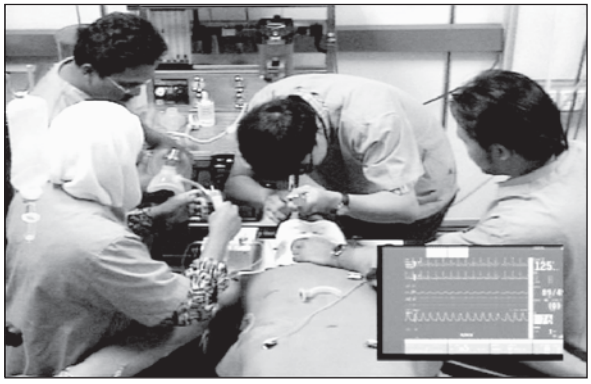


Figure 2

Teaching Crisis Management in Trauma Patient



Uses of medical simulation

In recent decades, the simulation technology has been leading the change in new teaching techniques. This change is evident in anaesthesia education, where there is a shift from structure-based curriculum to competence-based curriculum. In the latter, accomplishments of preset competencies determine the learning process. Medical simulation – with its improved computer-based programs, increasingly sophisticated task trainers and simulator facilitators – allows for new teaching methods that fulfill this shift in education approach.

In anaesthesia, the major purpose of simulators is to rehearse the management of both frequently

occurring and rare events during anaesthesia. The principal objective of simulators is to provide the highest transfer of skills from the training device to the operation systems.

There are five essential elements of medical simulation training which include curriculum, training tools, performance evaluation, data collection, and debriefing. Since the introduction of the first fully interactive patient simulator in the 1960s, the health care industry has rapidly embraced the use of medical simulators as a component of medical training. Today, there are more than 40 virtual reality, graphical, mannikin-based and screen-based simulators available for initial and ongoing training of health care professionals.

How Can Simulation Improve Patient Safety?

Simulation offers methodical training, performance assessment and refinement in practice; which may indirectly improve patient safety. It acts as a platform for the change in learning culture and improvement in quality and risk management activities.

The following areas below underpin the contribution of simulation towards improvement in patient safety in anaesthesia.

1. Education

- Introduction to anaesthesia for medical students
- Introduction to anaesthesia for medical officers

2. Training

- Specific professional group - Training curriculum focuses on skills & behaviours required for tasks on the job
- Advanced airway management skills
- Anesthesia Crisis Resource Management (ACRM)

3. Research

- A wide variety of research on human performance in health care requires simulation
- "Educational research" & performance assessment
- Clinical techniques (e.g. pediatric sedation)
- Human machine interaction
- Decision making

4. Risk Management

- Appropriate simulation training may reduce:
  - The frequency of adverse clinical events
  - The impact of clinical events that do occur
  - The likelihood of litigation after an event
  - A jury's perception that the institution did not take patient safety seriously

5. Performance Assessment

Simulation is a key research tool in human performance because it provides:

- Reproducibility
- Controllability
- Criticality

all in a confidential environment with no risk to patients

While application of simulation in the areas of education, training and research has been well established, more needs to be done for risk management and performance assessment.[2]

Why has simulation become more popular as a teaching and assessment tool?

In the past, health care professionals learnt on the job, which some still believe is the best way to gain experience. However, there are a number of barriers to this type of traditional clinical teaching. These include:

a) Humanitarian issues – practicing on patients is not ethical. We have moved into an age of where learning on patients is no longer acceptable if there is an alternative.

b) There has been a decrease in the number of inpatients, in part due to an increasing number of day case patients and also the fact that chronic conditions are being cared for in the community. This has led to a decrease in exposure and access of the trainees to ward patients.

c) The training time for postgraduate medical education has decreased and will continue to decrease further. With the implementation of new

training schemes, experience cannot be built upon over time as before.

d) Some situations are so rare that to gain experience would take many lifetimes.

e) Legal/litigation issues. The possibility of educational establishments being sued by patients and ex-students for not teaching and assessing clinical skills as laid down by the regulatory bodies could arise.

f) Record keeping, reproducibility, assessment and validity are issues all brought to the forefront with clinical governance and revalidation. Simulation is seen as away of addressing some of these issues.

g) Students learn more effectively in a non-threatening environment.

h) There is increasing emphasis on multidisciplinary learning, and clinical skills teaching is an ideal forum for this.

Is patient simulator ready for competence testing?

Despite increasing use and popularity of simulation in medical education, most professional societies, medical associations, and licensing boards are opposed to its use as a primary component of the certification process. This hesitancy is partly because it has been difficult to tie simulator outcomes to real-life procedural outcomes. In short, there is a paucity of data to support the validity, reliability, and reproducibility of simulator training or its translation into clinical practice.

How successful is the implementation of simulator training in Malaysia?

The progression of simulator training program is still slow in Malaysia, due to the lack of financial and human resources, time, and validation of education or evaluation model. Currently, the high fidelity human patient simulators in Malaysia are used to run programs such as advanced airway management, advanced trauma care and anaesthetic crisis resource management (ACRM). We conducted an evaluation of simulation-based activities in University Malaya Medical Centre and the results were very positive; majority of the participants regarded the tool as realistic and helped them to improve their skills in anaesthesia with further training.[3]

What is in the future?

The high cost of purchase and maintenance of the full-scale (FS) simulators compared to the less-expensive training methods has created controversy within the anaesthesia profession, with cost-effectiveness being the main concern. At some simulation centres, simulator training is compulsory for anaesthesia trainees. In Denmark, all trainees are expected to undergo a 3-day national compulsory course in clinical decision making at the Simulation Centre in Herlev.[4,5] However, there is limited evidence that people actually perform better and learn faster or of change in patient outcome as a result of patient simulation training. Weller et al [6] showed that in a survey study of anaesthetists who had attended a simulation-based course in anaesthesia crisis management in the preceding year, the respondents highly valued the course and perceived a change in their practice as a result of the training. The Simulation Centre in Bristol, England is now conducting a study to examine whether simulation training used in crisis management courses for neonatal emergencies is more effective than standard training in reducing perinatal mortality.

In short, the future of simulation in anaesthesia will be influenced by its cost-effectiveness and the validation of its effect on actual patient outcome. Nevertheless, to quote Dr Gaba:

" No industry in which human lives depend on the skilled performance of responsible operators has waited for unequivocal proof of the benefits of simulation before embracing it… Neither should anesthesiology."

Gaba DM. Anesthesiology 76:491-494, 1992

Reference

1. Gaba DM. Applications of Simulation in Anesthesiology.
2. Doyle D.J. Simulation in Medical Education: Focus on Anesthesiology.. Available from: URL: http://www.med-ed-online.org
3. Ringsted C, Østergaard D, Scherpbier A: Embracing the new paradigm of assessment in residency training: An assessment programme for first-year residency training in anaesthesiology. *Med Teach* 2003; **25**: 54–62
4. Østergaard, Doris MD. National Medical Simulation training program in Denmark. *Crit Care Med* 2004;**32**(2): S58-S60
5. Wang CY, Ng KP, Mohd Isa M, Mah Y, Ong G, Kaur R. Human Patient Simulator: The Malaysian Experience. *13th World Congress of Anaesthesiologists 2004;* abstract S027.
6. Weller J, Wilson L, Robinson B. Survey of change in practice following simulation-based training in crisis management. *Anaesthesia* 2003;**58**(5): 471-473.

Propofol Infusion Syndrome

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Propofol infusion syndrome

Propofol infusion syndrome (PRIS) is a constellation of signs originally described in children but has since been shown to occur in adults as well. First seen in critically ill paediatric patients sedated with propofol, it has since been described in adult neurosurgical intensive care units as well as in anaesthesia. Up till 2006, 24 paediatric and 14 adult cases have been reported.[1]

In view that propofol is immensely popular and is beginning to be used by non-anaesthesiologists, this review article aims to describe the syndrome, explain its suggested pathophysiology and possible treatment.

PRIS and the paediatric patient

In 1990, the death of a two-year-old child with croup was reported in Denmark. The child was sedated in the intensive care unit with propofol averaging 10mg/kg/hr over 4 days. The patient developed hepatomegaly, heart failure and hypotension. Unfortunately, as it was reported in an obscure paper,[2] the mortality was not given much attention. It is now recognized that this may have been the first mortality reported due to PRIS.

It was not until two years later that mortality linked to the use of propofol was reported in English. Parke et al[3] reported five cases of mortality in children ranging from age of 4 weeks to 6 years who were diagnosed with croup or bronchiolitis. These young patients had received propofol infusions at 7 – 10 mg/kg/hr for between 66 to 115 hours. The features were similar among the children – lipemia, hepatomegaly, metabolic acidosis followed by bradyarrhythmia and progressive cardiac failure.

This report prompted the manufacturer to warn physicians, that propofol at the time, was not licensed for use in the paediatric population.[4,5] Confusion reigned however, as the United States Food and Drug Administration (US FDA) found no direct link to paediatric deaths and instead urged the manufacturer to "pursue pediatric indication".[6]

Sporadic cases continued to be reported in the literature. In 1998, Bray[7] reported a series of 18 critically ill paediatric patients who died after developing similar features of bradycardia, asystole, metabolic acidosis, lipemia, hepatomegaly and rhabdomyolysis. This was followed by a warning from the US FDA itself which halted a randomized controlled trial (RCT) which showed that paediatric patients given propofol sedation had higher death rates (9.5%) compared to those who received other agents (3.8%). Unfortunately the RCT was terminated and its results were not published. The Canadian health authorities also issued a warning that propofol was contraindicated in the paediatric age group.

Despite these warnings, many disputed the existence of PRIS.[8,9] Despite the lack of large scale RCTs evaluating the safety of the drug for procedural sedation or for the induction and maintenance of general anaesthesia,[10] propofol has been used in large paediatric centers with no apparent untoward incidents.[11] The United Kingdom Committee on Safety of Medicines currently states that propofol is contraindicated for sedation of children aged 16 and below.[12]

PRIS in adults

The first recorded case of mortality in adults associated with PRIS was reported in 2000.[13] The patient was an 18-year-old man involved in a motor vehicle accident. He sustained head and chest trauma, multiple fractures, facial burns, multiple lacerations and abrasions. He was sedated with propofol during transport to hospital as well as in the emergency department. Post operatively he was transferred to the ICU and continued to receive propofol as an infusion. On day 3, his creatine kinase (CK) level was elevated. Although he did not have compartment syndrome, the

raised CK was attributed to extensive soft tissue injuries and fractures. He was treated with diuretics and alkalinisation of urine.

On day 5, he developed atrial fibrillation with rapid ventricular response. His electrocardiogram (ECG) showed intraventricular conduction block, a new left axis deviation and possible anterolateral infarction. This changed to left bundle branch block over 4 hours.

He developed progressive metabolic acidosis with hyperkalaemia and rising methaemoglobinaemia (13%). Global hypokinesia was demonstrated on echocardiogram. He developed bradycardia and hypotension unresponsive to atropine, epinephrine and fluids. He subsequently went into pulseless electrical activity and asystole.

Haemoglobin electrophoresis showed normal level of methaemoglobinaemia. The pseudomethaemoglobinaemia arose due to a lab error in spectrophotometry due to high turbidity from a hyperlipidaemic blood sample. The patient had received a total dose of 530 mg/kg of propofol for 39 hours and 700 mg/kg for 59 hours.

In 2001, Cremer et al[14] reported the first series of adult deaths. Five patients with head injuries inexplicably had fatal cardiac arrests in a neurosurgical intensive care unit after introduction of 2% propofol for sedation. This prompted a retrospective analysis of head-injured patients aged 16 to 55 years admitted to the unit from 1996 to 1999 who were mechanically ventilated for more than 48 hours. This unit practiced a head injury protocol where patients had intracranial pressure (ICP) monitoring, were moderately hyperventilated based on jugular-venous oximetry and received propofol sedation. Larger doses of propofol were used to reduce cerebral metabolic requirements of oxygen ($CMRO_2$) and ICP.

Of the 67 cases analysed, 7 possible cases of PRIS were identified. These patients had increasing need for inotropic and vasopressor support 24-48 hours after propofol was started. They received higher mean doses of propofol compared to other cases, and all had received more than 5mg/kg/hr of propofol for more than 58 hours.

Based on their findings, Cremer et al calculated that the crude odds ratio for occurrence of PRIS was 1.93 (95% CI 1.12-3.32) per unit (mg/kg/hr) increase in mean propofol use. PRIS did not occur in patients who received less than 5 mg/kg/hr. The incidence was 17% in those who received between 5 to 6 mg/kg/hr and rose to 31% in those receiving more than 6mg/kg/hr of propofol.

PRIS has been reported to occur when propofol was used in large doses for even short periods of time for anaesthesia as well.[15,16]

Pathophysiology of PRIS

The pathophysiology of PRIS is unclear, although it is likely to be multifactorial. A number of priming factors such as central nervous system activation in the critically ill patient have been identified which puts the patient at risk of PRIS. High dose propofol along with supportive therapy such as catecholamines and corticosteroids act as triggering factors.[17]

In animal models, propofol has been shown to uncouple oxidative phosphorylation and energy production in the mitochondria, hence impairing oxygen utilization and inhibiting electron flow along the electron transport chain.[18,19] It antagonizes β-adrenoceptors and calcium channel proteins causing diminished cardiac contractility.[20,21]

In humans, muscle cytochrome oxidase deficiency was demonstrated in one child who developed PRIS after propofol sedation,[22] while the muscle biopsy of another child showed decreased complex IV activity and low cytochrome oxidase ratio[24]. These are suggestive of mitochondrial respiratory chain enzyme deficiency.

In critically ill patients, catecholamine-mediated lipolysis of adipose tissues produces free fatty acids (FFA) which form the most important substrates for production of energy. FFA undergo β-oxidation in the mitochondria, a process which generates electrons which are then transferred to the respiratory chain.

Wolf et al[24] found evidence of impaired fatty acid oxidation in a 2-year-old boy who had clinical features of PRIS. The boy had raised plasma concentration of

malonyl carnitine and C5-acylcarnitine which subsequently normalized following recovery. These findings suggest that there were altered long-chain FFA entry into the mitochondria caused by inhibition of carnitine palmitoyl transferase I and uncoupling of β-oxidation with the respiratory chain at complex II. This results in failure of long-chain FFA entering the mitochondria, while medium- and short-chain FFA which freely cross the mitochondrial membranes could not be utilized. This leads to an imbalance of energy production and demand. An accumulation of unutilized FFA also results, which have pro-arrhythmogenic properties.[25]

Low carbohydrate supply is a risk factor for PRIS. The body reverts to lipolysis to meet energy demands, leading to further accumulation of FFA. Children are at a higher risk due to low glycogen storage.[26] Wolf et al[27] reported the case of an 11-year-old child, who received propofol for more than 5 days for treatment of epilepsy, developing high C4-acylcarnitine levels associated with low carbohydrate intake. Fat overload may also be a contributory factor. A 10-year-old boy developed PRIS after receiving a ketogenic diet, which contains 90% energy in the form of long-chain triglycerides, for control of refractory epilepsy.[28]

An interesting relationship has been shown between high catecholamine levels and propofol pharmacokinetics in an animal study.[29] As catecholamines increase cardiac output, mean propofol arterial concentration was linearly reduced, causing a reversal of anaesthesia. This was attributed to increased first-pass dilution and clearance of propofol resulting from increased cardiac output. Propofol antagonism of β-adrenoceptors[20] may also contribute. Catecholamine surges in acute neurological dysfunction is well recognized and may cause increasing doses of propofol usage to ensure adequate sedation. This negative inotropic effects of propofol in turn drives increased usage of catecholamines to maintain cardiac output, resulting in a positive feedback mechanism and progressive myocardial depression.

Possible treatments

The early cases of PRIS carried high mortality. With increasing awareness, several possible treatments have been suggested.

The first recorded survival was reported in 1992.[30] The patient was a 20-month-old child who developed asystolic cardiac arrest after receiving propofol 5 – 10 mg/kg/hr for 56 hours. The patient was successfully resuscitated and underwent venovenous haemofiltration. Extracorporeal membrane oxygenation (ECMO) was successfully used to treat a 13-year-old male with PRIS.[31]

It has been suggested that stopping the propofol infusion, institution of supportive measures and dialysis are the cornerstone of management. Weaning patients off catecholamine support and early nutrition to prevent breakdown of fats may be useful, as evidenced by Corbett et al's[32] success in the managing a head-injured patient with PRIS. This patient had the propofol infusion ceased, was weaned off his catecholamine support and started on appropriate tube feeding. His renal function which was initially impaired, improved after cessation of propofol. He received metoprolol and captopril for treatment of moderate to severe global left ventricular dysfunction (ejection fraction 25 – 30%) and moderate right ventricular dysfunction. The patient was subsequently discharged home.

Despite progress being made, prevention is always better than cure. It would be prudent to keep propofol infusions at less than 5 mg/kg/hr for less than 48 hours. If higher doses are required, or sedation is needed for longer periods of time, one should consider the use of other sedative agents.

Conclusions

Propofol infusion syndrome is a rare occurrence which carries a high mortality rate. More cases may be seen in the future as the popularity of propofol as a sedative and anaesthetic agent for short procedures increases. A heightened awareness of PRIS and its presentation, such as unexplained metabolic acidosis and myocardial depression may uncover more cases, contribute to earlier cessation of the drug and an improved outcome. The pathophysiology of PRIS has not been fully elucidated but the effects of propofol on free fatty acid metabolism and mitochondrial respiratory chain and its relationship with catecholamines contribute to the occurrence of this syndrome. Treatment of this syndrome is by stopping the infusion and providing supportive therapy.

References

1. Fudickar A, Bein B, Tonner PH. Propofol infusion syndrome in anaesthesia and intensive care medicine. *Curr Opin Anaesthesiol* 2006; **19**: 404-10.
2. Notits fra Bivirkningsnaevnet. Propofol (Diprivan) bivirkninger. Ugeskr Laeger 1990; **152**: 1176.
3. Parke TJ, Stevens JF, Rice AS, Greenaway CL, Bray RJ, Smith PJ et al. Metabolic acidosis and fatal myocardial failure after propofol infusion in children: five case reports. *BMJ* 1992; **305**: 613-6.
4. Edwards KG. 'Diprivan' ICU sedation in children: unlicensed use. Serious adverse events including fatalities. Letter to doctors. Macclesfield, UK: ICI Pharmaceuticals 1992 April 29.
5. Edwards KG, Arnold BDC. Propofol infusion in children [Letter]. *BMJ* 1992; **305**: 952.
6. FDA's Anesthetic and Life Support Drugs Advisory Committee. ICI's Diprivan (propofol) anesthetic has no direct link to pediatric deaths in ICUs, FDA advisory committee finds; FDA asks ICI to pursue pediatric indication. FDC Reports 1992; 54:14.
7. Bray RJ. Propofol infusion syndrome in children. *Paediatr Anaesth* 1998; **8**: 491-9.
8. Reed MD, Blumer JL. Propofol bashing: The time to stop is now! *Crit Care Med* 1996; **24**: 175-6.
9. Susla GM. Propofol toxicity in critically ill pediatric patients: show us the proof. *Crit Care Med* 1998; **26**: 1959-60.
10. Hatch DJ. Propofol infusion syndrome in children. *Lancet* 1999; **353**: 1117-8.
11. Crawford MW, Dodgson BG, Holthy HHK, Roy WL. Propofol syndrome in children. *CMAJ* 2003; **168**(6): 669.
12. Committee on Safety of Medicines, Medicines Control Agency. Propofol (Diprivan) infusion: sedation in children aged 16 or younger contraindicted. Current problems in Pharmacovigilance 2001; 27: 10.
13. Perrier ND, Baerga-Varela Y, Murray MJ. Death related to propofol use in an adult patient. *Crit Care Med* 2000; **28**(8): 3071-4.
14. Cremer OL, Moons KGM, Bouman EAC, Kruijswijk JE, de Smet AMGA, Kalkman CJ. Long-term propofol infusion and cardiac failure in adult head-injured patients. *Lancet* 2001; **357**: 117-8.
15. Burrow BK, Johnson ME, Packer DL. Metabolic acidosis associated with propofol in the absence of other causative factors. *Anesthesiology* 2004 Jul; **101**(1); 239-43.
16. Liolios A, Guerit JM, Scholtes JL, Raftopoulos C, Hantson P. Propofol infusion syndrome associated with short-term large-dose infusion during surgical anesthesia in an adult. *Anesth Analg* 2005; **100**: 1804-6.
17. Vasile B, Rasulo F, Candiani A, Latronico N. The pathophysiology of propofol infusion syndrome: a simple name for a complex syndrome. *Intensive Care Med* 2003; **29**: 1417-25.
18. Branca D, Roberti MS, Lorenzin P, Vincenti E, Scutari G. Influence of the anaesthetic 2,6 diisoprophylphenol on the oxidative phosphorylation of isolated rat liver mitochondria. *Biochem Pharmacol* 1991; **42**: 87-90.
19. Schenkman KA, Yan S. Propofol impairment of mitochondrial respiration in isolated perfused guinea pig hearts determined by reflectance spectroscopy. *Crit Care Med* 2000; **28**: 172-7.
20. Zhou W, Fontenot HJ, Wang SN, Kennedy RH. Propofol induced alterations in myocardial beta-adrenoceptor binding and responsiveness. *Anesth Analg* 1999; **89**: 604-8.
21. Zhou W, Fontenot HJ, Liu S, Kennedy RH. Modulation of cardiac calcium channels by propofol. *Anesthesiology* 1997; **86**: 670-5.
22. Cray SH, Robinson BH, Cox PN. Lactic acidemia and bradyarrhythmia in a child sedated with propofol. *Crit Care Med* 1998; 2089-92.
23. Mehta N, DeMunter C, Habibi P, Nadel S, Britto J. Short-term propofol infusions in children. *Lancet* 1999; **354**: 866-7.
24. Wolf A, Weir P, Segar P, Stone J, Shield J. Impaired fatty acid oxidation in propofol infusion syndrome. *Lancet* 2001; **357**: 606-7.
25. Jouven X, Charles MA, Desnos M, Ducimetiere P. Circulating nonesterified fatty acid level as a predictive risk factor for sudden death in the population. *Circulation* 2001; **104**: 756-61.
26. Short TG, Young Y. Toxicity of intravenous anaesthetics. *Best Pract Res Clin Anaesthesiol* 2003; **17**: 77-89
27. Wolf AR, Potter F. Propofol infusion in children: when does an anaesthetic tool become an intensive care liability? *Paediatr Anaesth* 2004; **14**: 435-8.

28. Baumeister FA, Oberhoffer R, Liebhaber GM. Fatal propofol infusion syndrome in association with ketogenic diet. *Neuropaediatrics* 2004; **35**: 250-2.

29. Myburgh JA, Upton RN, Grant C, Martinez A. Epinephrine, norepinephrine and dopamine infusions decrease propofol concentrations during continuous propofol infusion in an ovine model. *Intensive Care Med* 2001; **27**: 276-82.

30. Barclay K, Williams AJ, Major E. Propofol infusion in children (Letter). *BMJ* 1992; **305**: 953.

31. Culp KE, Augoustides JG, Ochroch AE, Milas BL. Clinical management of cardiogenic shock associated with prolonged propofol infusion. *Anesth Analg* 2004; **99**: 221-6.

32. Corbett SM, Moore J, Rebuck JA, Rogers FB, Greene CM. Survival of propofol infusion syndrome in a head-injured patient. *Crit Care Med* 2006; **34**(9): 2479-83.

Central Venous Oxygen Saturation: How To Use It

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The aim of cardiovascular monitoring is to recognise impending tissue hypoxia. Early recognition and treatment of tissue hypoxia is important in the management of the critically ill. If untreated, global tissue hypoxia leads to anaerobic metabolism, lactate production and oxygen debt. The magnitude and duration of oxygen debt have been implicated in the development of multi-system organ failure and increased mortality. Unfortunately, the routine continuous monitoring of the systemic blood pressure, heart rate and central venous pressure is unable to provide information about the imbalances between whole body oxygen supply and demand in these patients.

Measurement of mixed venous oxygen saturation (SvO_2) from the pulmonary artery has been advocated as an indirect indicator of the adequacy of tissue oxygenation. To enable measurement of this parameter, pulmonary artery catheterisation is necessary. Due to its inherent risks and lack of convincing data of its usefulness, pulmonary artery catheterisation is not routinely carried out as part of the cardiovascular monitoring in the critically ill patient.

Central venous catheterisation, an easier and safer procedure, is frequently performed in the critically ill patient. It is mainly used to monitor central venous pressure and administer vasoactive drugs. In the late 1960s, Goldman studied the measurement of central venous oxygen saturation ($ScvO_2$) in patients with myocardial infarction while Scheinman investigated if the $ScvO_2$ reflects changes in SvO_2. Whether $ScvO_2$ exactly mirrors SvO_2, especially in the critically ill patients, has always been a question. Rivers, in a prospective randomised trial, demonstrated that there was improved survival outcome with early intervention directed by $ScvO_2$ in patients with severe sepsis and septic shock.[1] Since then, there has been a resurgence in interest in the measurement of $ScvO_2$ in critically ill patients.

Physiology of mixed venous oxygen saturation (SvO_2)

Calculation of O_2 consumption *(VO_2)* according to the Fick principle is given as the product of cardiac output *(CO)* and arteriovenous O_2 content difference *(a-v[O_2])*.

$$VO2 = CO \times a\text{-}v[O_2]$$

a-v[O_2] is the difference between arterial O_2 content and venous O_2 content *($CaO2 - CvO_2$)*

Therefore $$VO_2 = CO \times (CaO_2 - CvO_2)$$

Rearranging the formula for O_2 consumption

$$CvO_2 = CaO_2 - \frac{VO_2}{CO}$$

O_2 content ($[O_2]$) is the sum of oxygen bound to haemoglobin [product of haemoglobin concentration (Hb) and O_2 saturation (SO_2)] and physically dissolved oxygen [PO_2].

$$[O_2] = [Hb \times 1.36 \times SO_2] + \{[PO_2 \times 0.003]\}$$ — negligible

Substituting O_2 content in the formula for O2 consumption

$$CvO_2 = CaO_2 - \frac{VO_2}{CO}$$

$$Hb \times 1.36 \times SvO_2 = Hb \times 1.36 \times SaO_2 - \frac{VO_2}{CO}$$

$$SvO_2 \approx SaO_2 - \frac{VO_2}{CO}$$

SvO_2 indicates the balance between oxygen supply and demand. SvO_2 can be decreased when O_2 supply does not increase proportionately to an increased O_2 demand. Thus fever, pain or stress may decrease SvO2 when the increase in whole-body O_2 demand is not matched by an appropriate increase in O_2 delivery.

Limits of mixed venous oxygen saturation (SvO_2)[2]

SvO_2 level	Consequences
$SvO_2 > 75\%$	Normal extraction O_2 supply > O_2 demand
$75\% > SvO_2 > 50\%$	Compensatory extraction Increasing O_2 demand or decreasing O_2 supply
$50\% > SvO_2 > 30\%$	Exhaustion of extraction Beginning of lactic acidosis O_2 supply < O_2 demand
$30\% > SvO_2 > 25\%$	Severe lactic acidosis
$SvO_2 < 25\%$	Cellular death

SvO_2 can also decrease due to a lower arterial O_2 content or cardiac output, or both. Conditions causing this drop in O_2 delivery include anaemia, hypoxia, hypovolemia or heart failure.

Can $ScvO_2$ function as a surrogate for SvO_2?

In healthy humans, the oxygen saturation in the inferior vena cava is higher than in the superior vena cava as the lower body extracts less O_2 than the upper body. The reason is many of the vascular circuits that drain into the inferior vena cava use blood flow for non-oxidative phosphorylation needs (e.g. renal and hepatic blood flow).

Measurement of $ScvO_2$ in the superior vena cava reflects the degree of O_2 extraction from the brain and the upper part of the body. Since the pulmonary artery contains a mixture of blood from both the superior as well as the inferior vena cava, SvO_2 in the pulmonary artery is greater than $ScvO_2$ in the superior vena cava. In non-shock states, a good correlation between $ScvO_2$ and SvO_2 has been shown, with $ScvO_2$ being less than SvO_2 by about 2 - 3%. If the tip of the central venous catheter is located inside the right atrium, there is mixing of blood from the inferior vena cava and measurement of $ScvO_2$ may be higher than if the tip is located in the superior vena cava.

The difference between $ScvO_2$ and SvO_2 is not constant and may be affected by changes in the regional blood flow and oxygen supply to demand ratio. In shock states, there is a consistent reversal of the relation between $ScvO_2$ and SvO_2 where superior vena cava $ScvO_2$ is always greater than SvO_2 with the difference ranging from 5-18%. Redistribution of blood flow away from the splanchnic, renal, and mesenteric bed toward the cerebral and coronary circulation, including more desaturated blood (< 30%) from the coronary sinus, contributes to this observation. Thus, $ScvO_2$ consistently overestimates the true SvO_2 under shock conditions and the changes of these two parameters occur mostly in a parallel manner.

Measurements of $ScvO_2$ and SvO_2 are not equivalent i.e. the absolute values differ. It had been shown in animal studies that SvO_2 and $ScvO_2$ closely paralleled each other in various pathologic states. However, studies in humans had shown conflicting results.[3, 4, 5]

$ScvO_2$ monitoring: continuous vs. intermittent

Central venous O_2 saturation can be measured either intermittently using central venous blood gas analysis or continuously using fibreoptic oximetry catheters. It is vital to measure central venous oxyhaemoglobin saturation using oximetry if intermittent blood gas analysis is used. $ScvO_2$ computed from partial pressure oxygen (PvO_2) will not be accurate. The PvO_2 range is within the steep section of the oxyhaemoglobin dissociation curve where a small change in PvO_2 will cause a significant change in $ScvO_2$.

When using $ScvO_2$ to make clinical decisions, it should not be based on a single measurement, but rather on trends of $ScvO_2$ to detect an imbalance between oxygen delivery and consumption. Continuous monitoring of $ScvO_2$ and SvO_2 in the framework of haemodynamic

goals and treatment algorithms has resulted in improved patient outcome. However, it is unclear if intermittent measurements of $ScvO_2$ can substitute continuous monitoring of $ScvO_2$ in these algorithms.

Clinical uses of $ScvO_2$ monitoring

Septic shock

Although the blood flow to the splanchnic region is increased in septic shock, the lower ratio of O_2 supply to demand in the this region results in greater O_2 desaturation from venous blood that drains into the hepatic vein and inferior vena cava, respectively. On the other hand, cerebral blood flow is maintained causing the measurement of $ScvO_2$ to be higher than SvO_2. On average $ScvO_2$ exceeds SvO_2 by 8% in patients with septic shock.[3]

Rivers et al. demonstrated that using $ScvO_2$ as a resuscitation end-point in addition to mean arterial pressure and central venous pressure provides significant outcome benefit for patients with severe sepsis and septic shock over standard therapy.[1] Those in the early goal-directed therapy group were resuscitated to $ScvO_2$ greater than 70% using continuous $ScvO_2$ monitoring.

While $ScvO_2$ is an excellent tool in the early resuscitation period of shock, there is still controversy as to whether it is a suitable parameter for follow-up therapy in the intensive care unit. Varpula et al. found that the difference between these two oxygen saturation parameters varies highly in the intensive care unit treatment period and concluded that SvO_2 is not to be estimated on the basis of $ScvO_2$.[5]

Heart failure and cardiogenic shock

Heart failure is characterised by a limited cardiac output. To meet the needs during an increase in O_2 demand, the O_2 extraction in tissue is increased as these patients are unable to sufficiently increase their cardiac output. Therefore, in these patients, SvO_2 is tightly correlated with cardiac output and a drop in SvO_2 is a good and early marker of cardiac deterioration, most commonly seen in acute heart failure in acute myocardial infarction. Goldman et al. found that $ScvO_2$ less than 60% showed evidence of heart failure, shock or both.

However patients with chronic heart failure may live with SvO_2 in the low range of 30 - 40% without apparent tissue hypoxia, presumably because they have adapted to higher O_2 extraction. These patients can increase their O_2 consumption to a limited degree because O_2 extraction is close to its limits as is cardiac output. Anders examined the use of lactic acid levels and $ScvO_2$ to stratify and treat patients with acutely decompensated end-stage congestive heart failure who presented to the emergency department.[6] $ScvO_2$ was significantly lower in the high lactic-acid group than in the normal lactic-acid group. There was a significant prevalence of undetected cardiogenic shock with $ScvO_2$ ranging from 26.4 to 36.8% in the presence of normal vital signs.

Cardiac arrest

Patients with cardiac arrest routinely have $ScvO_2$ values of 5-20% during cardiopulmonary resuscitation. Those with return of spontaneous circulation had a higher initial mean and maximal $ScvO_2$ than did those without.[7] No patient attained return of spontaneous circulation without reaching a $ScvO_2$ of at least 30%. A $ScvO_2$ of greater than 72% was 100% predictive of return of spontaneous circulation. However, a very high $ScvO_2$ (>80%) in the presence of a very low O_2 delivery after successful CPR is also an unfavorable predictor of outcome as it is indicates impairment of tissue O_2 utilisation probably due to a prolonged cardiac arrest. Continuous $ScvO_2$ monitoring can provide an objective measure to confirm the adequacy or inadequacy of cardiopulmonary resuscitation in providing O_2 delivery but its practicality is doubtful.

Trauma and haemorrhage

Scalea et al. had shown that patients presenting with trauma and hemorrhage required additional resuscitation or surgical procedures when $ScvO_2$ remained less than 65% despite stable systemic blood pressure, heart rate and central venous pressure.[8] These patients had more serious injuries and significantly larger estimated blood losses and required more transfusions than those patients with $ScvO_2$ saturation > 65%. They also demonstrated prolonged cardiac dysfunctions and elevated lactate levels.

Major surgery

Pearse et al. measured $ScvO_2$ besides cardiac index and O_2 delivery index in patients after major general surgery and found that a $ScvO_2$ cut-off value of 64.4%

(sensitivity 67%, specificity 56%) could be used to discriminate patients with a complicated or uncomplicated post-operative course.[9] The lowest $ScvO_2$ was independently associated with post-operative complications. In the first hour after surgery, significant reductions in $ScvO_2$ were observed but there were no significant changes in cardiac index or oxygen delivery index during the same period. Reduction in $ScvO_2$ is due to increased post-operative oxygen consumption from various factors e.g. pain, emergence from anaesthesia and shivering.

Limitations of mixed and central venous oxygen saturation for the assessment of tissue oxygenation

Inadequate tissue oxygenation may exist despite normal central and mixed venous oxygen saturations. Normal or high $ScvO_2$ and SvO_2 do not rule out tissue hypoxia in the organ or at regional level. Venous oximetry can reflect the adequacy of tissue oxygenation only if the tissue is still capable of extracting O_2.

Venous oximetry should not be used alone in the assessment of the cardiovascular system but in combination with other haemodynamic parameters and indicators of organ perfusion such as serum lactate concentration and urine output.

Conclusion

Low values of SvO_2 or $ScvO_2$ indicate a mismatch between O_2 delivery and tissue O_2 demand. $ScvO_2$ values differ from SvO_2 values and this difference varies with cardiac output and regional O_2 consumption. Much remains unknown about $ScvO_2$. Further work is needed to understand changes of $ScvO_2$ over time in assessing treatment and in different types of patients.

References

1. Rivers E, Nguyen B, Havstad S, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med* 2001;345(19): 1368-77
2. Marx G, Reinhart K. Venous oximetry. *Curr Opin Crit Care* 2006;1 2:263–268.
3. Reinhart K, Kuhn HJ, Hartog C, Bredle DL. Continuous central venous and pulmonary artery oxygen saturation monitoring in the critically ill. *Intensive Care Med* 2004;**30**(8): 1572-8
4. Chawla LS, Zia H, Gutierrez G. Lack of equivalence between central and mixed venous oxygen saturation. *Chest* 2004;**126**:1891-96
5. Varpula M, Karlsson S, Ruokonen E. Mixed venous oxygen saturation cannot be estimated by central venous oxygen saturation in septic shock. *Intensive Care Med* 2006 (electronic reference http://dx.doi.org/10.1007 /s00134-006-0270-y)
6. Ander DS, Jaggi M, Rivers E, et al. Undetected cardiogenic shock in patients with congestive heart failure presenting to the emergency department. *Am J Cardiol* 1998;**82**(7): 888-91.
7. Rivers EP, Martin GB, Smithline H, et al.. The clinical implications of continuous central venous oxygen saturation during human CPR. *Ann Emerg Med* 1992; **21**; 1094-1101
8. Scalea TM, Hartnett RW, Duncan AO, et al. Central venous oxygen saturation: a useful clinical tool in trauma patients. *J Trauma* 1990; **30**:1539-43
9. Pearse R, Dawson D, Fawcett J, Rhodes A, Grounds RM, Bennett ED. Changes in central venous saturation after major surgery, and association with outcome. *Crit Care* 2005;**9**(6):R694-9.
10. Bloos F, Reinhart K. Venous oximetry. *Intensive Care Med* 2005;**31**(7):911-13.
11. Rivers E, Ander DS, Powell D. Central venous oxygen saturation monitoring in the critically ill patient. *Curr Opin Crit Care* 2001;**7**;204-211

Invasive Haemodynamic Monitoring

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Introduction

Invasive haemodynamic monitoring has revolutionised critical care practice. Assessment and interventions for critically ill patients have been transformed by the appropriate acquisition of haemodynamic data, the appropriate interpretation of the data obtained, and the subsequent decision making that alters therapeutic interventions. Invasive haemodynamic monitoring provides a tool to monitor cardiovascular physiology, to titrate interventions and to evaluate the response to the therapies instituted. For the results of haemodynamic monitoring to be utilized effectively, the bedside clinician must have a solid foundation in understanding the technical and physiologic implications that can impact the values obtained.

I will address the issues of invasive haemodynamic monitoring under the following headings.

Measuring Cardiac Output
Measuring Oxygen Utilisation
Continuous Monitoring
Less Invasive Monitoring
Functional Haemodynamic Monitoring

1) Measuring Cardiac Output

In the early 1970's when Drs Swan and Ganz brought this valuable tool, Pulmonary Artery Catheter (PAC), to assess intracardiac pressures, patients had to be transported to the cardiac catheter lab to obtain these measurements. Once the PAC becomes readily available these parameters could be obtained at the bedside and without the need for fluoroscopy. Early in the clinical use of PAC the pressures and cardiac determinations were the primary parameters obtained. Yet despite it being available the concept still required more than two decades to gain acceptability in the routine practice of most clinicians.

Changes in haemodynamic monitoring over the past 10 years have followed two paths. First, there has been a progressive decrease in invasive monitoring, most notably a reduction in the use of the pulmonary artery catheter because of a presumed lack of efficacy in its use in the management of critically ill patients, with an increased use of less monitoring requiring only central venous and arterial catheterization to derive the same data. Second, numerous clinical trials have documented improved outcome and decreased costs when early goal-directed protocolised therapies are used in appropriate patient populations.

The problem facing the clinicians when trying to evaluate the effectiveness of the PAC is an important one that goes beyond PAC use. Unlike the introduction of new medications, technologies are not required to demonstrate an impact on patient outcome prior to approval for use. Virtually none of the current technologies, ranging from noninvasive blood pressure monitoring to echocardiography, have been well studied for their impact on patient outcome. Monitoring and diagnostic technologies, of which the PAC is a member, do not directly impact patient outcomes. The outcome of the patient is based on the clinician's interpretation of the information provided by the technology.

For PAC utilization to accurately measure cardiac output (CO) using thermodilution technique there are some specific assumptions that must be taken into consideration.

- The bolus must be injected within 4 seconds;
- The amount of the solution must be accurate;
- The temperature of the injectate must be precisely measured;
- The catheter must be properly placed within the heart and pulmonary artery;
- The computer must have the appropriate computation constant

Another factor that can result in non-reproducible values is the timing of the injectate to the respiratory cycle. CO can differ from inspiration to expiration.

Determinations that are not within a 5% to 10% range are frequently deleted from the series. Averaging strategies can produce varied CO values. For reproducibility rather than accuracy, potential physiologic events are often deleted. Apart from the inherent variables cited above, the PAC is not without its detractors. In general there is a reduction in PAC utilization over the past 10 years. The decisions usually quoted for using less of invasive haemodynamic monitoring by the PAC are

1) increased risk to the patient with PAC insertion and placement
2) the ability to measure similar variables via other less invasive techniques e.g. CVP, echocardiography (TEE or TTE),
3) increased cost
4) inaccurate measurement and misuse of PAC derived variables
5) incorrect interpretation and application
6) lack of proven benefit of PAC in the overall patient management.

However if we look at each of the reasons cited, we see that they can be countered.

1) The risks of PAC insertion is not much different from that of a CVP catheter insertion (hemorrhage, pneumothorax, large vessel damage, arrhythmias) – the only specific PAC complication is pulmonary artery rupture
2) Although CVP catheters can also give central venous saturation as a surrogate (as mixed venous saturation in PAC) and cardiac output (via other means e.g. PiCCO derived), it does not give pulmonary circulation data
3) In Malaysia cost consideration is indeed a factor to decide, but the cost of a PAC has come down in recent times
4) Inaccuracies of PAC measurement usually are seen during measurements of PCWP and PAOP rather than mixed venous saturation
5) Inaccuracies of interpretation and application can be reduced with better education and familiarization – it is more of user fault than equipment fault
6) Most of the studies that examine PAC derived data and patient outcome do not examine them with a defined treatment plan. Hence lack of proof of benefit does not equate to proof of lack of benefit.

One must also realize that there is no such thing as a normal cardiac output, and accurate measures of cardiac output are less important than measures of cardiac output changes in response to treatment and time. Thus if one wants to accurately define adequacy of cardiac output then we must also measure whether the oxygen delivery is adequate to match the oxygen demand. Hence measures of mixed venous oxygen are essential - whether one uses the PAC to obtain mixed venous saturation or one uses the CVP to obtain central venous oxygen as a surrogate of mixed venous saturation.

2) Measuring Oxygen Utilisation

The primary clinical application of mixed venous oxygen (SvO_2) monitoring is the assessment of tissue oxygenation. Tissue oxygenation is the key parameter that is affected by changes in cardiac output and blood pressure. Since SvO_2 reflects the balance between oxygen delivery and oxygen consumption, SvO_2 values are often tied to assessments of the adequacy of haemodynamic values. Questions such as 'What blood pressure or cardiac output is acceptable for a given patient?" can be better evaluated through the use of SvO_2.

The benefit of the SvO_2 value is that it is a reflection of the overall balance of oxygen delivery and consumption. A normal SvO_2 value-about .60 to .75-indicates that the balance between oxygen delivery and consumption is adequate. If the SvO_2 drops below .60, then either oxygen delivery is inadequate (as in low cardiac output states like congestive heart failure) or oxygen consumption is too high (as in respiratory failure). The lower the SvO_2 value, the more likely a problem exists in terms of tissue oxygenation. SvO_2 values in the .30 to .49 region have been associated with disruptions in the ability to produce adenosine triphosphate (ATP).

Elevated SvO_2 values also are potentially dangerous, indicating an obstruction or maldistribution of blood flow to tissues in which cells are unable to use oxygen. In the case of either obstruction or maldistribution, an SvO_2 value over .75 is an indicator of a threat to tissue oxygenation in that tissues are either not using or not receiving oxygen. Most of the hemoglobin (SvO_2) is being returned to the lungs without having oxygen removed.

If blood pressure (BP) is considered low (e.g. 80/50 mm Hg) but the SvO_2 is normal, then the blood pressure is not likely to be harming tissue oxygenation. If the BP is low and the SvO_2 is low, then treatment of the blood pressure is more important.

Central venous saturation (CeVOX) as a surrogate of mixed venous saturation is becoming more utilized especially when PAC utilization is not an option (e.g. pediatrics, or unstable patients).

Using pulse oximetry (SpO_2) and SvO_2 is termed "dual oximetry". Oxygen extraction can be obtained by simply subtracting SvO_2 from SpO_2. Certain monitors either provide a pulse oximeter to obtain SpO_2 or have the capability to have the value slaved in. Once both SpO_2 and SvO_2 are available, dual oximetry parameters can be obtained and displayed.

3) Continuous Monitoring

Continuous Cardiac Output (CCO)

There are two clinically acceptable methods available to measure CO: bolus thermodilution (BTD-CO) and continuous cardiac output (CCO). The bolus method only allows intermittent measurement of cardiac output and introduces the potential for user variability. With the intermittent method, an injectate temperature cooler than blood temperature is used for the input signal.

The introduction of continuous cardiac output measurement allows for near real-time measurement of blood flow and stroke volume. Since the process is automated, it also reduces user variability. A modified pulmonary artery catheter with a 10cm thermal filament is used. The thermal filament is maintained in the right ventricle and continuously transfers heat directly into the blood according to a random pattern. A temperature change (less than 0.04ºC) is detected downstream on a thermistor at the distal tip of the pulmonary artery catheter. A computer calculates CO via a thermodilution washout curve. A digital CO is displayed continuously on the CCO monitor and is updated every 30 seconds to provide an average flow over the previous 3 – 5 minutes. CCO requires no user calibration procedures.

Advantages of CCO include the ability to continuously measure blood flow (i.e. cardiac output) and detect changes in cardiac output and stroke volume early and eliminate clinician error due to improper injectate solution, volume, and/or temperature. Fewer erroneous data are obtained due to dysrhythmias or respiration variation. Limitations of CCO include time delays in the response of the CCO catheter, need for an invasive catheter, and increased cost of the catheter.

CCO values are influenced by the same assumptions as intermittent thermodilution determinations – there must be forward flow; a steady baseline PA temperature; adequate mixing of the blood and input signal; and proper catheter placement. Many of the technique- related potentials for error are eliminated, such as amount of fluid injected, timing of the injectate, proper injectate sensing, and computation constant.

Continuous Venous Saturation (Mixed and Central)

The technology for continuous SvO_2 monitoring has been in place for over 20 years. Refinements in the optical processing of reflected light has minimized problems of accuracy. However, manufacturers still recommend an in vivo calibration on a daily basis to confirm accuracy of the device.

The continuous SvO_2 monitoring pulmonary artery catheter functions by using light-emitting diodes that send light (specifically along the light spectrums of red and infrared light) into the blood. This allows the detection of oxygen-carrying hemoglobin (oxyhemoglobin) and non-oxygen carrying hemoglobin (deoxyhemoglobin) by comparing the amount of red and infrared light that is reflected. Light bounces off hemoglobin (among other things), and the reflected light is analyzed by an optical module. The ratio of red to infrared light that is reflected is a function of how much oxyhemoglobin and deoxyhemoglobin is present. Changes in hemoglobin should be monitored. Continuous monitoring of patient variables has provided the clinician with the ability to observe adverse events in a more timely fashion. Physiologic changes can be acted upon in amore timely manner than with intermittent assessment

In its ultimate form it continuously measures temperature, heart rate, mixed venous O_2 saturation (SvO_2), cardiac output, right ventricular ejection fraction and end diastolic volume, central venous pressure and pulmonary arterial pressure. When

coupled with non-invasive pulse oximetry, it can also give total oxygen delivery (DO_2) and consumption (VO_2). These measures will be made more effective if coupled with parallel measurements of tissue wellness with other techniques.

Continuous CeVOX is also available in the market now e.g. PreSep catheter by Edwards.

4) Less Invasive Haemodynamic Monitoring
Pulse Contour Analysis

The possibility of determining the CO using the arterial pulse wave has intrigued both scientists and clinicians for decades. Preliminary successes have been achieved using techniques involving determination of the area under the arterial pressure curve, as well as other methods involving analyses of various subtleties of the wave. The issue has been quantifying the relationship between the amount of blood flow and the pressure wave associated with it. This relationship can vary widely from one individual as clinical conditions change. Knowing this relationship for an individual patient and circumstance allows for the calculation of a constant (K), which can be used for subsequent CO assessments. Techniques using the arterial wave have thus previously required initial calibration with another method of CO assessment.

There are four devices that track stroke volume (SV) by analysis of the arterial pressure waveform

- 1) the PiCCO monitor (Pulsion, Munich, Germany)
- 2) the LiDCO plus System (LiDCO, Cambridge, UK)
- 3) the PRAM system (FIAB SpA, Florence, Italy)
- 4) the Vigileo system and Flo Trac System (Edwards Lifesciences, USA)

PiCCO

The clinical validation studies for pulse contour were done with the arterial catheter in the femoral position. The accuracy of pulse contour seems to lessen when the arterial waveform analysis is obtained from a peripheral location. The PiCCO system may only be used with a cannula placed in the femoral or axillary artery. Kinking of the cannula may necessitate recalibration or even replacement of the arterial cannula followed by recalibration. As circulatory compliance changes in response to primary physiological changes or vasoactive drugs, the morphology of the arterial waveform alters. This is not problematic unless the pulse rate is particularly irregular.

The PiCCO continuous cardiac output shows good agreement with intermittent thermodilution of PAC, requiring recalibration only during major changes in systemic vascular resistance e.g. after phenylephrine infusion. This system also gives additional values over and above the conventional data obtained from the PAC catheter. Global end diastolic volume (GEDV) approximates intrathoracic blood volume (ITBV) and extravascular lung water (EVLW) as a surrogate for cardiac preload. ITBV and EVLW have traditionally been measured by the double indicator technique (thermodilution and indocyanine green) via a pulmonary artery catheter. Using EVLW to guide fluid management in medical intensive care patients has been suggested to reduce the duration of mechanical ventilation and length of stay in the ICU. The ITBV has been suggested to be a better indicator of cardiac preload than pulmonary artery occlusion pressure (PAOP) and central venous pressure.

Lithium Dilution Cardiac Output (LiDCO)

A small dose of lithium chloride is injected via a central or peripheral venous line; the resulting arterial lithium concentration-time curve is recorded by withdrawing blood past a lithium sensor attached to the patient's existing arterial line. In terms of accuracy, clinical studies have demonstrated that the LiDCO method is at least as accurate as thermodilution over a wide range of cardiac outputs. It is more reliable than conventional thermodilution cardiac output measurement. The dose of lithium needed (0.15 – 0.3 mmol for an average adult) is very small and has no known pharmacological effect. Recalibration is unnecessary for at least 8 hours. This approach differs slightly from that of the PiCCO™ system; LiDCO analyses the arterial waveform throughout the cardiac cycle whereas PiCCO™ utilizes only the area under the systolic portion of the curve.

Only three studies in humans have been published in peer-reviewed journals, two in cardiac surgical patients and one in critically ill paediatric patients.

Pressure Recording Analytical Method (PRAM) System

The PRAM system is based on the physics of perturbations. It analyses all of the arterial wave using a collecting signal of 100Hz. The most important points on the waveform are the diastolic pressure, the systolic pressure and the point of closure of the aortic valve. The SV is calculated from the area under the curve in the interval between the diastolic part of the curve and the dicrotic notch. In this way the system is analysed individually and does not require calibration to correct for compliance. PRAM has already been validated in cardiac surgery against the PAC.

Edwards Vigileo and Flo Trac System

The Edwards Vigileo system, using the FloTrac sensor attached to arterial pressure tubing, needs no such calibration and provides continuous CO measurements from the arterial pressure wave.

The system consists of a sensor (FloTrac, Edwards LLC) and a processing/display unit (Vigileo, Edwards LLC). The processing unit applies a proprietary algorithm to the digitized wave, and reports CO, cardiac index, stroke volume , stroke volume index and stroke volume variation (SVV). The system calculates the arterial pressure using arterial pulsatility (standard deviation of the pressure wave over a 20-s interval), resistance and compliance, according to the following general equation:

Stroke volume = K x Pulsatility

where K is a constant quantifying arterial compliance and vascular resistance, and pulsatility is proportional to the standard deviation of the arterial pressure wave over a 20-s interval. K is derived from patient characteristics (gender, age, height and weight) as well as waveform characteristics (e.g., skewness and kurtosis of individual waves). This calibration constant is recalculated every 10 min. There was close correlation between the algorithm and continuous thermodilution CO.

This technology represents a highly innovative and potentially significant advance in haemodynamic assessment. The lack of necessity for calibration with a more invasive method of CO assessment provides for easy and expeditious use in a myriad of clinical venues, including the emergency room, cardiac care unit, operating room, trauma bay, medical/surgical intensive care units and intermediate care units.

This represents an advantage over the PiCCO system, which requires a centrally placed arterial catheter (femoral, axillary or long radial). To obtain information about systemic vascular resistance, a central venous catheter can be transduced and interfaced with the Vigileo. This allows the clinician to provide optimal fluid, vasodilator and inotropic therapy without the need for pulmonary artery catheterization.

The FloTrac Vigileo system also reports SVV. This is the change in SV in one respiratory cycle. Patients suffering hypovolemia exhibit an exaggerated SVV. A large SVV (>10%) thus indicates that the patient is likely to respond favorably to fluid administration.

If a central venous pressure catheter has been placed, its signal can be interfaced with the Vigileo, allowing for the calculation of systemic vascular resistance (SVR) and SVR index (SVRI). When use with a central venous oximetry catheter, the Vigileo also provides continuous central venous oxygen saturation ($ScvO_2$). The Vigileo reports haemodynamic parameters at 20-s intervals, performing its calculations on the most recent 20s of data.

Potential weaknesses of the system include possible inaccuracy in the presence of arterial wave artifact, compromise of the arterial catheter, aortic regurgitation, intense peripheral vasoconstriction and irregular pulse.

Functional Haemodynamic Monitoring

Specific haemodynamic variables are commonly measured and displayed at the bedside, and their values are often used in clinical decision making. However the utility of each variable as a single absolute value is questionable. This gives rise to the concept of functional haemodynamic monitoring. It can either be viewed as a solitary value and interpreted according to its value and patternwhich

may be called static functional monitoring. It can also be viewed to evaluate the effect of treatment looking at trends of change, hence implying its therapeutic application which can be looked as a dynamic functional haemodynamic monitoring. Although trends in specific variables over time are useful in defining haemodynamic stability, their rapid change in response to application of a therapy has greater clinical utility. For example, an elevated CVP implies right ventricle pressure overload, it provides no information on the precise etiology. Assessing preload adequacy is more definitive in managing a patient with elevated CVP – e.g. volume challenge with fluids or passive leg raising (similar to a slight Trendelenberg position). Recent monitoring devices have incorporated this as part of their system e.g. SVV value in PiCCO and Flo Trac system.

One must not only look at the effect of respiration or ventilation on the CVP but one must also give close attention to CVP waveform interpretation. Examples are given.

Conclusion

The effectiveness of haemodynamic monitoring depends both on available technology and on our ability to diagnose and effectively treat the disease processes for which it is used. Within this context haemodynamic monitoring represents a functional tool that may be used to derive estimates of performance that may in turn direct treatment. It must be stressed that no monitoring device, no matter how accurate or complete, could be expected to improve patient outcome, unless coupled to a treatment that itself improves outcome.

Further reading

1. M Singer, E D Bennett. Invasive Haemodynamic Monitoring in the United Kingdom. *Chest* 1989; **95** : 623 – 626.
2. M Singer. Cardiac Output 1998 (Review). *Heart* 1998; **79**: 425 – 428.
3. M Pinsky. Haemodynamic Monitoring Over the Past 10 Years. *Critical Care* 2006; **10**: 117.
4. D Prentice, T Aherns. Controversies in the Use of the Pulmonary Artery Catheter (Haemodynamic Monitoring). *J of Cardiovasc Nursing* 2001; **15**(2):1-5.
5. S Tibby, I A Murdoch. Monitoring Cardiac Function in the Intensive Care (Review). *Arch Dis in Childhood* 2003; **88**(1):46 – 52.
6. J M Headley. Invasive Haemodynamic Monitoring: Applying Advanced Technologies. *Crit Care Nurs Quart* 1998; **21**(3): 73 – 84.
7. M Pinsky, J L Vincent. Let Us Use the Pulmonary Artery Catheter Correctly and Only When We Need It. *Crit Care Med* 2005; **33**(5): 1119 – 1122.
8. R L Reed. Mixed Venous Saturation as a "stand-alone" Indicator of the Oxygen Extraction Ratio. *Int Care* 2004; **11**(3): 103 – 108.
9. J D Edwards, R Mayall. Importance of the Sampling Site of Mixed Venous Oxygen Saturation in Shock. *Crit Care Med* 1998; **26**(8): 1356 – 1360.
10. K Reinhart, H J Kuhn, D L Bredle. Continuous Central Venous and Pilmonary Oxygen Saturation Monitoring in the Critically Ill. *Int Care Med* 2004; **30**: 1572 – 1578.
11. J C Cheney, S Derdak. Minimally Invasive Haemodynamic Monitoring for the Intensivist: Current and Emerging Technology (Review). *Crit Care Med* 2002; **30**(10); 2338 – 2345.
12. 12)C Zollner, M Haller, M Weis, K Morstedt, P Lamm, E Kliger, A E Goetz. Beat to Beat Measurement of Cardiac Output by Intravascular Pulse Contour Analysis: a Prospective criterion Standard Study in patients After Cardiac Surgery. *J Cardiothoracic Vasc Anesth* 200; **14**(2): 125 – 129.
13. G R Manecke. Edwards FloTrac Sensor and Vigileo Monitor. *Expert Rev Med Devices* 2005; **2**(5): 523 – 527.
14. R M Pearse, K Ikram, J Barry. Equipment Review: An Appraisal of the LiDCOplus Method of Measuring Cardiac Output. *Crit Care* 2004; **8**(3):190 – 195.
15. S Romano, M Pistolesi. Assessment of Cardiac Output from Systemic Arterial Pressure in Humans. *Crit Care Med* 2002; 30(8): 1834 – 1841.

16. S Scolletta, S M Romano, B Biagioli, G Capannini, P Giomarelli. Pressure Recording Analytical Method (PRAM) for Measurement of Cardiac Output During VariousHaemodynamic States. *Br J Anaes* 2005; **95**(2): 159 – 165.

17. M Pinsky, D Payen. Functional Haemodynamic Monitoring. *Crit Care* 2005; **9**(6): 566 – 572.

18. 18)G Marx, T Cope, L McCrossan, S Swaraj, C Cowan, S M Mostafa, R Wenstone, M Leuwer. Assessing Fluid Responsiveness by Stroke Volume Variation in Mechanically Ventilated Patients with Severe Sepsis. *Euro J Anaes* 2004; **21**: 132 – 138.

Triage In The Intensive Care Unit

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The demand for beds in the intensive care unit in both general hospitals and teaching hospitals in Malaysia usually far exceeds their availability. A national survey carried out from May to July 2005 on intensive care beds in all hospitals in Malaysia,[1] showed that the number of ICU beds made up only 1.5% of the total hospital beds i.e. 2.4 ICU beds per 100,000 population. This figure is rather dismal when compared to developed countries (United Kingdom 8.5, Germany 28.5, France 38.4, United States 30.5). A 3 year audit on adult intensive care units[2] further revealed that as much as 56% of patients referred were denied admission due to the non-availability of beds, resulting in patients being mechanically ventilated in the general wards and an increased in mortality (51.8%) of those denied admission. The situation is expected to worsen as our population expands and ages. In addition, advances in medicine have led to more complicated procedures and treatments, resulting in patients needing admission to ICU for monitoring purposes.

The reasons for this shortfall in ICU beds in Malaysia are unknown as no local studies have looked into this shortage. We may speculate that the main reasons for Malaysia are likely to be financial and manpower shortage. It is impossible for a developing country like Malaysia to match the United States where ICU expenditure accounts for up to 13.3% of total hospital costs, 4.2% of national expenditure and 0.56% of their Gross Domestic Product. However, many other factors may also play a role. Lack of pooling of resources within and between hospitals, persistent admission of patients with no hope of survival and delays in discharging patients that no longer require intensive care may all be contributory.[3]

As the demand for intensive care services outstrips the availability, prioritizing patients who will benefit most from intensive care has been at the forefront of intensive care practice in recent years. 'Triage' as it is known, is derived from the French word 'trier' which means to put aside and was first practiced by the French military in the 19th century. For triage to take place, the patient has to be identified first (pre ICU triage). Various medical factors like age, severity of illness, diagnosis, quality of life and advance directives have been used in the triage decision. However, non medical factors like the availability of beds, type of referral (patient, chart or telephone review), time of triage, seniority of the ICU physician, interpersonal relationships and financial gain can also affect the triage decision.[4] For pre ICU triage to be effective, it is impossible to ignore the fact that ICU beds can be blocked by patients who no longer require intensive care (post ICU triage). This has led to the development of intermediate or 'step down' units to cater for this group of patients.

Age has been used to triage ICU patients, as it is a simple and objective measure of life expectancy. The average life expectancy has increased substantially worldwide and by the year 2020, the male life expectancy in Malaysia is predicted to rise to 75 years while for females it is 78 years. It would be difficult to set an arbitrary cut off point and ethically questionable to exclude older patients on the basis of age alone. In a survey of 600 ICU clinicians, only 12% stated that age should limit ICU admission; most indicated that quality of life, probability of survival, reversibility of acute illness and co-morbidities were more important considerations when triaging.[5] In the Support Prognostic Model, which was done to understand prognosis and preference for outcomes and risks of treatments, age was found to be only a minor contributor towards predicting 180 day survival compared to acute physiological changes and Glasgow Coma Scale.[6] In another study by Nicholas F on influence of patient's age on survival,[7] although mortality was found to be higher in the older age group, this is because of a greater severity of illness in the elderly, with age being only a minor component contributing to excess mortality. A similar study looking into the outcome of intensive care in the elderly,[8] showed that the number of organ system failures was associated with increased ICU and 1 year mortality while age was not.. Age was also found to

have little impact on 1-year survival in over 65 years of age whereas severity of illness, length of stay, prior ICU admission and respiratory failure were much better predictors.[9] Similarly in the Malaysian population, a 2 year review of ICU survivors and non-survivors in the year 2003-2004,[10] also revealed that age was not found to be an independent risk factor for death. However, Joynt studied 236 ICU refusals and showed that patients above the age of 65 years were more likely to be refused admission (OR 2.58 [1.69 – 3.94]).[11] A similar study by Sprung showed that the 92 ICU refusals were older (OR 1.02 p 0.04).[12] A study carried out in Israel on survival in critically ill patients hospitalized in and out of intensive care units under paucity of intensive care beds showed that the ICU population had a significantly much younger age group compared to the other departments. [13] This is in contradiction to single and multi centre studies carried out in France by Garrouste-Orgeas that showed that age was not a factor in ICU refusal.[14] It would appear that the importance of age as a triage tool is not uniform and can vary depending on the centre. From these studies, it would seem that the withdrawal of therapy and triage decisions should not be solely or primarily based on age alone.

In 1988, a consensus panel in the United Kingdom stated that the 'Selection for intensive care should be based on broad concepts of prognosis derived from statistical analysis of comparable cohorts of patients backed up by sound clinical trials'. Twenty years later, we all know that the applicable instruments are hardly available. All the current severity of illness scoring systems suffer from very low sensitivity (APACHE II 51%, MPM 11.7%, SAPS II 21.2%) although specificity is better (APACHE II 85.4%, MPM 84.5%, SAPS II 96.8%)[15,16] This means that a proportion of those who are not expected to survive in fact survive, making these scoring systems useless for predicting individual patients' outcomes. Furthermore only MPM_0 has been validated for immediate assessment and can be applied at the time of ICU admission. All the other scoring systems include variables of physiological abnormality after a specified time in the ICU. In comparison, it has been shown that physicians could better discriminate survivors from non-survivors as measured by area under the receiver operating characteristic curve (0.89 for physicians vs. 0.83 for APACHE II, $p < 0.001$).[17] Although medical intensive care personnel were fairly accurate discriminators, there was a tendency to underestimate survival that was affected by the level of training and forecasting accuracy.[18] Albeit an improvement in sensitivity, physicians' estimates still had a poor sensitivity of 24% (compared to the sensitivity of MPM_0 2%). If survival was combined with poor functional outcome as an end point, there was an improvement in sensitivity to 35%. The benefits of combining an objective prognostic measure with a physicians estimate can be seen in the SUPPORT trial[6] in which a model was developed for predicting 180-day survival. In this study, the discriminatory ability of the model was increased from 0.79 to 0.82 when the physician's estimates were included. It would appear that scoring systems used in conjunction with the clinical judgment of the physician represent the best tools we have at the moment.

Severity of illness has been used to identify those patients who will benefit most from ICU care by refusing care to those who are 'too well' and those who are 'too sick' to benefit from intensive care. In practice, it is difficult to identify these 2 groups of patients. There is a tendency for ICUs to refuse admission with increasing severity of illness as shown by Joynt and Sprung using MPM (OR 1.0[0-0.33], 1.49[0.34-0.66], 2.4[0.66-1.0]) and APACHE II (OR 1.0[1-10], 3.3[11-20], 27.5[21+]) scoring respectively.[11,12] Both studies also showed excess in mortality most marked in those patients in the middle range of severity of illness refused intensive care. When appropriately referred patients for intensive care were refused admission to the ICU, there was a relative risk of death of 1.6 compared with a group of appropriately admitted cases with medium APACHE II scores (11-20). This would suggest that if these patients were admitted, lives would be saved. However, it is this middle territory of disease severity where there is a lack of discriminatory tools available to identify those who might benefit from ICU.

The diagnosis can also have an influence on the triaging decision. Diagnosis affecting the cardio-respiratory system (OR refusal 0.53), sepsis (OR 0.46) and chronic renal disease (OR 0.45) were associated with admission in 2 studies.[11, 4] However, this in contrast to the study by Sprung which showed that refusal was associated with the cardio respiratory system (OR 1.7), sepsis (OR 2.4) and neurological system (OR 1.4).[12] Not surprisingly, the highest refusal rates were associated with metastatic cancer (OR 5.82),

chronic respiratory diseases[19] and diseases that are expected to cause death in <1 year (OR 2.67).[14] There also appears to be a bias against medical patients whereby surgical and postoperative patients were more likely to be granted admission.[11,12,14] One can only speculate that surgical patients may derive greater benefit from ICU as shown by a higher mortality among medical patients compared to surgical patients.[12] Another point to note is that all these studies were performed by anaesthetists who have a closer working relationship to their surgical counterparts.

Quality of life measure as a triaging tool appears attractive as it provides information on the previous functional status of the patient and what can be achieved with further intervention. Quality of life measures like the Nottingham Health Profile and Katz's Activities of Daily Living require cooperative and conscious patients which may not be applicable to the critically sick. Refusals for ICU admission have been associated with quality of life factors like 'needing help at home' (p 0.02), resident in a long term care facility (p 0.002) and dependency (p 0.002).[4]. This was similar to the large multi centre French study that found higher refusal rates in dependent and institutionalised patients.[14] A lower hospital mortality was found in patients who were able to live at home without any help (Hazard Ratio 0.440 0.28-.68)[4] and had no chronic health problems.[13] Although functional status is used as an indicator of quality of life, Wilson and Cleary found that despite poor function in activities of daily living,[25] patients may actually perceive good health status and overall happiness. When examining quality of life 1 year after ICU admission, Konopad[26] found that even though patients had lower levels of activity, these patients perceived better overall health status. Furthermore, functional status can change as 30% of patients with marked limitations of function at admission demonstrated improvement after 2 months. Most physicians agree that the family should play an active role in decision making but patients' and families' opinions were more often obtained by ICU physicians when the patients were physically capable of expressing their wishes. This may mean that triaging physicians who deemed ICU admission inadvisable may have been reluctant to ask the families involved for their opinion.One study in France[24] even showed that only 79% of patients would designate their spouse as their surrogate decision maker. The question of the patient surrogate may be very different in Malaysia given the role of the extended family which can involve more than one individual. On the issue of advanced directives, one Scandinavian study showed that only 1% of ICU patients[27] had advance directives. This figure is probably much lower in Malaysia.

It is interesting to note that the way and to whom a referral is made can also affect the triage decision. Phone triage and patients with unknown cardio respiratory function have been significantly associated with admission compared to patient review by the triaging physician.[4,14] Furthermore, there is evidence to show that senior ICU triaging physicians are more likely to refuse ICU admission compared to their junior counterparts.[4,14] This could imply that experience is vital in the triaging process whereby more senior staff with prior experience is possibly better at identifying situations where ICU admission is not necessary. It is also comforting to note that physicians are reluctant to deny ICU admission in the face of limited information.[4,14]

One of the most common problems faced by the ICU triaging physician is deciding who should go to ICU when there is a lack or no beds in the ICU. Evidence shows that there is a tendency to refuse admission (OR 3.2 p 0.02) when the unit is full.[4,12,14] However, triaging decisions during these times were not significantly associated with an increased mortality with other factors like APACHE II, medical status and diagnosis positively correlating to mortality.[12,20] There was also a tendency for refusing patients who were referred out of hours whilst patients referred in the day were more likely to be admitted (OR refusal 0.52).[14] These findings are not surprising but the higher rate of refusals in the night may indicate that a shortage of staff during those periods may have an effect on the triaging decision.

The increasing need to improve triaging decisions led to the development of the Medical Emergency Teams (MET) in Australia and Critical Care Outreach Teams (CCOT) in the United Kingdom in the 90's. The primary objective of these teams were to identify critically ill patients earlier, avert ICU admission through early and appropriate management, improving outcome and to educate ward staff on managing critically ill patients. Earlier studies were promising with Schein showing a 50% reduction in cardiac arrest after the introduction of the MET.[28] A

prospective controlled trial of the effect of the MET on postoperative patients showed that there was a significant relative risk reduction of 36% for postoperative death, 44.4% for emergency ICU admissions and reduction in duration of hospital stay from 23.8 days to 19.8 days.[21] In contrast, a recent study on 20,000 patients in Australia did not show any benefit of the MET on reducing the incidence of cardiac arrest or death.[29] A study carried out at the University of Malaya showed that critically ill medical inpatients at risk of death could be identified by the Modified Early Warning Score. This may mean that the MET may still have a role in triaging by allowing critically ill patients to be highlighted earlier. This allows the ICU physicians to make better assessments of their patient in terms of patient preferences, pre hospital quality of life and reversibility of their current condition. This information may not have otherwise been possible in an acutely sick and deteriorating patient.

In order to standardize the process of triaging to fulfil the 4 principles of medical ethics (beneficence, non malificience, autonomy and distributive justice), guidelines on triaging have been issued by the Society of Critical Medicine in 1999.[22] The guidelines put forward several principles:

1) Admission criteria should only select those who are likely to benefit from ICU care.
2) To use tools for assessing severity of illness and prognosis of critically ill patients combined with clinical judgment.
3) Admission to be based on several models utilizing prioritisation, diagnosis and objective parameter models.
4) ICU director should have authority and responsibility to admit or discharge patients when the ICU is full.
5) Triage policies should be written in advance.
6) Triage decisions should be made explicitly and without bias (ethnic, social status, sexual preference and financial status are not to be considered)
7) Triage decision may be made without patient or surrogate consent.
8) Religious or moral convictions may be the basis for providing treatment provided the costs are not borne by society and the provision does not foreclose treatment to other patients.
9) Policies should be reviewed annually by a multi professional team.

However, the society clearly states that these are only guidelines and individual institutions need to create their own criteria to meet their specific requirements. A recent Scandinavian survey showed that only 8% of intensivists were aware of published guidelines on triaging.[23] In order to show compliance with triaging guidelines, a French study on 26 ICUs showed that on average only 4 (range 0-8) out of 20 recommendations were observed when patients were refused ICU admission. The situation was even worse when there was a full unit or if triaging was done over the phone.[19] Therefore it appears that guidelines are difficult to put into practice in real life.

In Malaysia where there is a shortage of beds, improving the efficiency of the ICU has become of paramount importance. This can be achieved by pooling of resources like having a central or regional bed manager to identify available ICU beds in the region. An early warning system should also be put into place in the general wards to identify patients who are at risk of deterioration. Physicians in the ward need to issue and record "do not resuscitate" (DNR) orders in the notes of terminally ill patients. Withdrawal and withholding therapy should be practiced. A set of local guidelines also needs to be developed to meet the multi cultural and religious needs of the Malaysian society.

For the foreseeable future, triage to ICU will continue to be dealt with on an individual basis. None of the current triaging tools in use have been shown to be perfect and we are left with a combination of these tools which are only useful for research and audit purposes. Furthermore as more treatment options become available, the triaging process may need to be constantly re-evaluated. The wide variation among individual physicians, which may compromise the principle of distributive justice, needs to be addressed and mutual principles need to be adopted. Hence, subjective patient assessments with ethical guidance will remain as the main determinant of ICU triage.

References

1. Tai LL, Ng SH. A National Survey of Intensive Care Resources in Malaysia. Nov 2005.
2. Tong MG,Tan CC. National Audit on Adult ICUs. 2005 Report.
3. Levin PD, Sprung CL. The Process of Intensive Care Triage. *Intensive Care Med* 2001; **27**: 1441-1445.
4. Garrouste-Orgeas M, Montuclard L, Timsit JF, Misset B, Christias M, Carlet J. Triaging patients to the ICU: a pilot study of factors influencing admission decisions and patient outcomes. *Intensive Care Med* 2003; **29**: 774-781.
5. Society of Critical Care Medicine: Attitudes of critical care medicine professionals concerning distribution of intensive care resources. *Crit Care Med* 1994; **22**: 358-362.
6. Knaus WA, Harrell FE, Lynn J. The Support Prognostic Model: Objective Estimates of Survival for Seriously Ill Hospitalized Adults. *Ann Intern Med* 1995; **122**(3): 191-203.
7. Nicolas F, Le Gall JR, Alperovitch A. Influence of patients' age on survival, level of therapy and length of stay in intensive care units. *Intensive Care Med* 1987; **13**(1): 9-13.
8. Kass JE, Castriotta RJ, Malakoff F. Intensive care unit outcome in the very elderly. *Crit Care Med* 1992; **20**(12): 1666-71.
9. Rockwood K, Noseworthy TW, Gibney RT. One-year outcome of elderly and young patients admitted to intensive care units. *Crit Care Med* 1993; **21**(5): 687-91.
10. SH Ng, LL Tai, CC Tan, MG Tong. National Audit on Adult ICUs. 2004 Report
11. Joynt GM, Gomersall CD, Tan P. Prospective evaluation of patients refused admission to an intensive care unit: triage, futility and outcome. *Intensive Care Med* 2001; **27**: 1459-1465.
12. Sprung CL, Geber D, Eidelman LA. Evaluation of triage decisions for intensive care admission. *Crit Care Med* 1999; **27**(6): 1073-1079.
13. Simchen E, Sprung CL, Galai N. *Crit Care Med* 2004; **32**(8):1654-1661.
14. Garrouste-Orgeas M, Montuclard L, Timsit JF. Predictors of intensive care unit refusal in French intensive care units: A multiple centre study. *Crit Care Med* 2005; **33**(4): 750-755.
15. Schafer JH, Maurer A, Jochimsen F. Outcome prediction models on admission in a medical intensive care unit: do they predict individual outcome. *Crit Care Med* 1990; **18**(10): 1111-8.
16. Wong DT, Crofts SL, Gomez M. Evaluation of predictive ability of APACHE II system and hospital outcome in Canadian intensive care unit patients. *Crit Care Med* 1995; **23**(7): 1177-83.
17. McClish DK, Powell SH. How well can physicians estimate mortality in a medical intensive care unit. *Medical Decision Making*. 1989; **9**(2): 125-32.
18. Christensen C, Cottrell JJ, Murakami J. Forecasting survival in the medical intensive care unit: a comparison of clinical prognoses with formal estimates.*Methods of Information in Med* 1993; **32**(4): 302-8.
19. Azoulay E, Pochard F, Chevret S. Compliance with triage to intensive care recommendations. *Crit Care Med* 2001; **29**(11): 2132-2136.
20. Metcalfe MA, Sloggett A, McPherson K. Mortality among appropriately referred patients refused admission to intensive care units. *Lancet* 1997; **350**: 7-12.
21. Bellomo R, Goldsmith D, Uchino S. Prospective controlled trial of effect of medical emergency team on postoperative morbidity and mortality rates. *Crit Care Med* 2004; **32**(4): 916-921.
22. Society of Critical Care Medicine. Guidelines for ICU Admission, Discharge and Triage. *Crit Care Med* 1999; **27**(3): 633-638.
23. Taligren M, Klepstad P, Petersson J. Ethical issues in intensive care-a survey among Scandinavian intensivists. *Acta Anaesthesiol Scand* 2005; **49**(8);1092-1100.
24. Azoulay E, Pochard F, Chevret S. Opinions about surrogate decision designation: a population survey in France. *Crit Care Med* 2003; **31**: 1711-4
25. Wilson I, Cleary P. Linking clinical variables with health-related quality of life: A conceptual model of patient outcomes. *JAMA* 1995; **273**: 59-65
26. Konopad E, Noseworthy TW, Johnston R: Quality of life measures before and one year after admission to an intensive care unit. *Crit Care Med* 1995; **23**:1653-1659
27. Goodman MD, Tarnoff M, Slotman G. Effect of advance directives on the management of elderly critically ill patients. *Crit Care Med* 1998; **26**: 701-4

28. Schein R, Hazday N, Pena M, Ruben B, Sprung C. Clinical antecedents to inhospital cardiopulmonary arrest. *Chest* 1990; **6**:1338-92

29. MERIT study investigators. Introduction of the Medical Emergency Team (MET) System: A cluster-randomised controlled trial. *Lancet* 2005; **365**: 2091-97

30. Toh KW, Tan PSK, Ong GSY, Kow SP. A Prospective Study of Intervention by the Critical Care Outreach Team on Outcome in Malaysian Medical In-Patients. 2nd National Conference on Intensive Care Sep 2004; Free Paper

VAP: Everything You Want to Know

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Ventilator-associated pneumonia or VAP is one of the most dreaded yet common nosocomial infections occurring in the critically ill.

VAP is defined as pneumonia occurring in patients more than 48 hours after endotracheal intubation and mechanical ventilation. It is commonly classified as early onset if it develops during the first 4 days of ventilation and late-onset if it develops at day 5 or more of ventilation. Early-onset VAP is usually associated with antibiotic-sensitive organisms and a better outcome compared to late-onset VAP which is associated with antibiotic-resistant organisms and a higher mortality.

Epidemiology

The incidence of VAP in the majority of reports varies between 8 and 28% and this is probably due to the different diagnostic criteria defining VAP. The oft-quoted overall prevalence of nosocomial pneumonia by the European Prevalence of Infection in Intensive Care or the EPIC study is 10%. Cook et al in their prospective cohort study showed that although the cumulative risk of VAP increased over time, the daily hazard rate decreased after day 5 ie 3.3% at day 5, 2.3% at day 10 and 1.3% at day 15

The development of VAP leads to increased duration of mechanical ventilation and this results in prolonged ICU and hospital stay. A study by Heyland showed that patients with VAP stayed an average of 4.3 days longer in the ICU compared to patients without VAP. This increase in the duration of ICU as well as hospital stay would invariably lead to rising health care costs.

The mortality attributable to VAP is difficult to quantify, as there are many compounding factors affecting the mortality of critically ill patients. Reported crude mortality rates of VAP vary between 24 to 50% and can reach up to 76% in specific settings or when lung infection is caused by high risk pathogens.

Risk factors

Multiple risk factors have been identified in the development of VAP. Intubation is perhaps the most significant risk factor and has shown to increase the risk of nosocomial pneumonia by 6- to 21-fold. Other risk factors include reintubation and unplanned extubation, severity of illness on admission (APACHE II score > 16), acute and chronic lung disease, excessive sedation, patients admitted with trauma or burns, witnessed arrest and aspiration and the use of paralytic agents.

Pathogenesis

The pathogenesis of VAP involves bacterial colonization of the aerodigestive tract. Subsequent aspiration of these contaminated secretions into the lower airways is the main route by which the bacteria invade the lower airways and cause VAP

Although less common, inhalation of pathogens from contaminated aerosols and direct inoculation of contaminated condensates from ventilator tubings could also result in VAP

Some investigators have postulated that the endotracheal tube of ventilated patients could become colonized with the bacteria which is encased in a biofilm. Subsequently embolization of these bacteria into the alveoli during suctioning or bronchoscopy may result in VAP.

Prevention

Prevention is the cornerstone to decreasing the incidence of VAP. General as well as specific infection control measures should be put in place at all times in the intensive care unit.

Perhaps the most important and effective general infection control measure taken to prevent all nosocomial infections is hand washing. Adequate hand washing facilities and alcohol hand rubs help decrease cross contamination of multidrug resistant organisms between patients. Constant and continuous education of health care workers on the epidemiology and prevention of VAP is advocated. Zack et al have showed that a formal education program on risk factors on the development of VAP and correct practices on the prevention of VAP directed at intensive care nurses can decrease the incidence of VAP.

Specific preventive strategies are targeted at preventing aspiration. Barring no contraindications, intubated patients should be nursed in the semi recumbent position. This is defined as elevation of the head of the bed between 30 – 45 degrees. Endotracheal cuff pressure should be monitored regularly ensuring cuff pressure is kept between 25 – 30mmHg. Preventing unplanned extubation as well as reintubation are other important measures in preventing aspiration.

Use of special endotracheal tubes which allow continuous aspiration of subglottic secretions has been shown to decrease early onset pneumonia and is recommended if available in patients who are going to be ventilated for more than 4 days

Enteral feeding may similarly increase the risk of aspiration. It is however preferred over parental nutrition as it prevents intestinal villous atrophy and may attenuate bacterial translocation. Caveats when patients are enterally fed: prevent gastric over distension, monitor and treat large gastric volumes and lastly ensure patients are in the semi recumbent position.

Intubation per se has been shown to increase the incidence of VAP by manifold. Thus early liberation from ventilation is warranted. Daily sedation vacation and weaning protocols can decrease time spent on the ventilator and hence decrease the incidence of VAP. Similarly, non invasive ventilation should be used whenever possible in selected patients with respiratory failure.

Stress ulcer prophylaxis with H_2 antagonist such as ranitidine is advocated in the prevention. Despite sucralfate showing a trend towards reduced VAP, its use when compared to H_2 antagonist has been shown to have a slightly higher rate of clinically significant gastric bleeding.

Routine change of ventilator circuits is not advocated as the tubings become colonized as soon as they are changed. What is more important is to prevent the condensates that accumulate within the circuit tubings from entering the endotracheal tube. Scheduled drainage of these condensates is thus necessary to prevent this.

Diagnosis

Diagnosing VAP accurately and early is neither easy nor straightforward. It is however crucial as early and appropriate antibiotics have been shown to decrease morbidity and mortality.

The latest American Thoracic Society guidelines in diagnosing VAP divide diagnostic strategy into a clinical and bacteriological one, incorporating both features in the final recommendation.

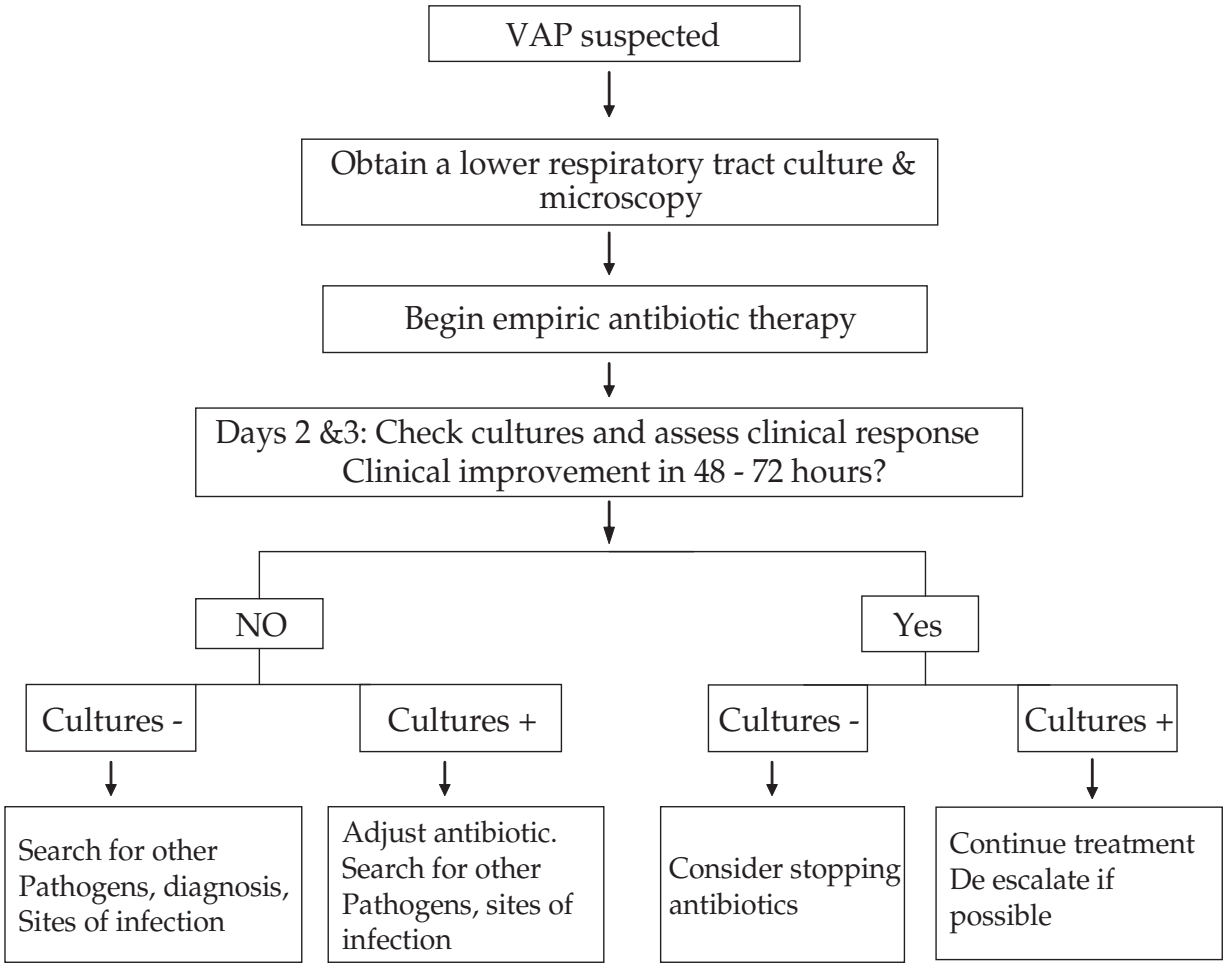
When the clinical approach is used, VAP may be suspected if there is a new or progressive infiltrate on the chest X-Ray with two of three clinical signs of infection (fever, leucocytosis or leucopenia, purulent secretions). Empiric antibiotic may be started based on the above. The initial empiric antibiotic should be based on the risk factors for specific pathogens as well local patterns of antibiotic resistance and organism prevalence. Sampling of the lower respiratory tract secretions for culture and blood culture is recommended prior to starting antibiotics.

To improve specificity in the clinical diagnosis of VAP, the Clinical Pulmonary Infection Score or CPIS was introduced by Pugin et al. This score had some limitations as it included microbiological cultures to diagnose VAP. Singh et al modified the CPIS using only physiological and radiological parameters.

A score of more than 6 was required to diagnose VAP. Using the modified CPIS, patients with a low clinical suspicion of VAP can be have their antibiotics safely discontinued after 3 days.

The bacteriological approach to diagnose VAP uses quantitative cultures of the lower respiratory tract secretions ie endotracheal aspirates, bronchoalveolar lavage (BAL) or protected specimen brush (PSB) specimens. Growth above specific threshold is required to diagnose and determine the causative microorganism. Quantitative cultures are useful to diagnose VAP in patients with low or equivocal clinical suspicion of infection. However false negative cultures is a possibility in patients who have recently been started on antibiotics, especially in the preceding 24 hours

Below is a summary of the management strategies for patients with suspected VAP



Treatment

Appropriate antibiotic selection with adequate dosing ensures a favorable outcome in patients with VAP. Some patients are at high risk of developing VAP with multidrug-resistant organisms. Risk factors to the development of multidrug-resistant pathogens include antimicrobial therapy in the preceding 90 days, current hospitalization of 5 days or more and the presence of immunosuppressive disease or therapy. Identifying these groups of patients is important to ensure that the initial antibiotics target these organisms.

Reducing the duration of treatment in patients with VAP has led to good outcomes with more antibiotic free days and less super infection. A large multi-center trial showed that there was no difference in terms of mortality, relapse or length of ICU stay in patients treated with 8 or 15 days of antibiotics. In another study, Singh and co-workers used the modified CPIS to guide them on the duration of antibiotics with low risk patients (CPIS 6 or less) having only 3 days of antibiotics compared to the conventional 10 -14 days. These patients had a better outcome when compared to the conventional group.

Shortening the course of treatment to VAP appears to limit cost and the potential for resistance while preserving a clinically acceptable response. Another aspect when treating VAP is de-escalation of antibiotics. This practice is currently recommended to ensure the culprit pathogen is treated yet at the same time prevent superinfections and the emergence of resistance strains

Conclusion

Preventing, diagnosing and treating VAP continues to be a challenge to the intensivist. Great efforts should be made to decrease the incidence of VAP as it represents a major health care burden, increasing morbidity and mortality of critically ill patients. Preventing VAP should be made an important focus for quality improvement and infection control in the ICU

Further Reading

1. American Thoracic Society. Guidelines for the management of adults with with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. *Am J. Resp Crit Care Med* 2005;**171**: 388 – 416
2. Cook DJ, Walter SD, Cook RJ, Griffith LE et al. Incidence and risk factors for Ventilator-associated pneumonia in critically ill patients. *Ann Intern Med* 1998; **129**:440
3. Chastre J, Fagon JY. Ventilated – associated pneumonia. *Am J Resp Crit Care Med* 2002;**165**:867-903
4. Singh N, Rogers P et al. Short course empiric antibiotic therapy for patients with pulmonary infiltrates in the intensive care unit: prospective evaluation of the CPIS score as an early predictor of outcome. *Am J Resp Crit Care Med* 2000;**162**:505 -511

Volatile Anaesthetics and Cardioprotection

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There is evidence indicating that volatile anesthetics protect the myocardium against reversible and irreversible ischemic injury. Volatile agents reduce arterial and coronary perfusion pressure, cause dose-related depression of myocardial contractility, produce coronary vasodilatation, affect electrophysiologic function, and modify autonomic nervous system activity to varying degrees. The anti-ischemic effects of volatile anesthetics may therefore be mediated, at least in part, by favorable alterations in myocardial oxygen supply-demand relations, preservation of energy-dependent cellular functions, and increased coronary blood flow. It seems unlikely however that changes in myocardial metabolism and coronary perfusion caused by volatile anesthetics are solely responsible for protection against ischemic damage. Inhalational anaesthetics given before ischaemia, in fact trigger an endogenous cardioprotective mechanism known as preconditioning. Even when administered after ischaemia, volatile anaesthetics continue to provide specific protection against reperfusion injury – including after cardioplegic arrest.

Ischaemic Preconditioning

Ischaemic preconditioning (IPC) is a phenomenon in which a short period of ischaemia protects against a subsequent and more prolonged episode of ischaemia.

During myocardial ischaemia, cardiac myocytes demonstrate reduced contractility within a few seconds and stop contracting within the first few minutes. This 15-minute period of ischaemia, however, induces numerous changes in the non-contracting myocytes, including a marked decrease in high-energy phosphates and the adenine nucleotide pool, depletion of glycogen, accumulation of lactate and H^+ and mild intracellular edema observed on ultrastructure. Once blood flow is re-established, the myocytes eventually recover. However if ischaemia continues for longer than 15 minutes, cellular necrosis will begin followed by the process of apoptosis, which will occur even after reperfusion if ischaemia is severe. In contrast, short periods of transient myocardial ischaemia appear to protect the heart from extensive damage during subsequent longer periods of ischaemia. This phenomenon was first described by Murry et al.[1] Importantly, if the time between preconditioning and prolonged ischaemia was longer than 2 hours, the effect of preconditioning decreased.[2] However, if this period between the preconditioning ischaemia and prolonged coronary artery occlusion was extended to 24 h, the IPC phenomenon was restored, indicating the existence of an additional delayed preconditioning effect, called the "second window" of preconditioning.[3]

Anaesthetic Preconditioning

The administration of some anesthetics produces a preconditioning-like effect, protecting the myocardium from the effects of myocardial infarction and myocardial dysfunction.

One has to distinguish between triggers, i.e. mechanisms at the beginning of the signal transduction cascade, and mediators, which finally mediate cardioprotection during the long infarct-inducing (index) ischaemia. It is hypothesized

that volatile anesthetics stimulate a trigger that initiates a cascade of events leading to activation of an end-effector that is responsible for resistance to injury. To date, adenosine type 1 (A_1) receptors, protein kinase C (PKC), inhibitory guanine nucleotide binding (G_i) proteins, reactive oxygen species, and mitochondrial and sarcolemmal K_{ATP} (mito K_{ATP} and sarc K_{ATP}, respectively) channels have been shown to mediate anaesthetic preconditioning (APC).[4]

K_{ATP} Channels

Mitochondrial adenosine triphosphate-sensitive potassium (K_{ATP}) channels have been implicated as the end-effector in this protective scheme, but sarcolemmal K_{ATP} channels may also play a role. K_{ATP} channels are heteromultimeric complexes containing an inward-rectifying potassium (K_{ir}) channel and a sulfonylurea receptor (SUR). Opening of K_{ATP} channels is an important step in the signal transduction cascade of anaesthetic-induced preconditioning. The administration of a non-specific K_{ATP} channel-blocker, glibenclamide, prior to the administration of the volatile anaesthetics completely abolishes cardioprotection.

In vitro experiments suggest that volatile anesthetics are capable of modifying K_{ATP} channel activity. Isoflurane stimulates outward K^+ current through sarc K_{ATP} channels in isolated ventricular myocytes during patch clamping. Volatile anesthetics also reduced sarc K_{ATP} channel sensitivity to inhibition by ATP, thereby increasing open state probability.[5]

G Protein–coupled Receptors

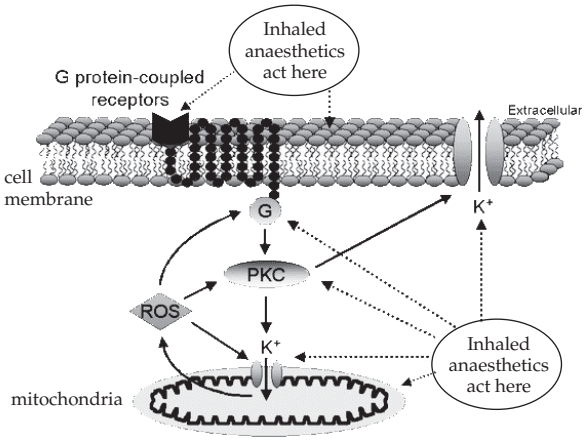
Volatile anesthetics modulate K_{ATP} channel activity through second messenger signaling. Overall, APC seems to be associated with the activation of separate receptor-mediated pathways that are mostly linked to inhibitory G-protein (G_i), namely adenosine (A_1, A_3), purinoceptors (P_{2Y}), endothelin (ET_1), acetylcholine (M_2), α1- and β-adrenergic, angiotensin II (AT_1), bradykinin (B_2) and opioid (δ_1, κ) receptors, which couple to a highly complex network of kinases.[4]

Protein Kinase C

Protein Kinase C (PKC) is an essential component of the signaling pathways associated with preserving cellular viability. The diverse PKC isoform family is a large group of serine/threonine protein kinases that are distinguished by variable regulatory domains and cofactors and also display diverse tissue and species distributions. Activation of G protein-coupled receptors (e.g., A_1, bradykinin, δ_1 opioid) stimulate PKC during IPC. Volatile anesthetics have also been shown to stimulate PKC translocation and activity, possibly by interacting with the regulatory domain of the enzyme. Recent findings strongly suggest that volatile anesthetic-induced PKC activation is required to open K_{ATP} channels and produce myocardial protection.[4]

Reactive Oxygen Species

Large quantities of reactive oxygen species (ROS) are released during reperfusion of ischemic myocardium that damage proteins responsible for intracellular homeostasis, depress contractile function, and produce membrane damage. Halothane, isoflurane, and enflurane have been shown to attenuate the toxic effects of ROS on left ventricular pressure development in isolated hearts. The protective effects of sevoflurane were associated with reduced dityrosine formation, an indirect marker of ROS and reactive nitrogen species. These results support the hypothesis that volatile anesthetics reduce the release of deleterious quantities of ROS associated with coronary artery occlusion and reperfusion. Other findings strongly suggest that a variety of preconditioning stimuli; direct mito K_{ATP} channel openers, opioids, and volatile anesthetics, stimulate a small burst of ROS that initiate downstream signaling events and produce protection from subsequent ischemic injury. For example, pretreatment with low concentrations of ROS have been shown to mimic the beneficial actions of IPC. Free radical scavengers administered before or during brief ischaemia markedly attenuated the protective effect of the preconditioning stimulus on infarct size. Alternatively, different ROS may exert opposing actions on mito K_{ATP} channel activity.



Mitochondrial adenosine triphosphate–sensitive potassium (K_{ATP}) channels have been implicated as the end-effector in this protective scheme, but sarcolemmal K_{ATP} channels may also play a role. Volatile anesthetics signal through adenosine and opioid receptors, modulate G proteins, stimulate protein kinase C (PKC) and other intracellular kinases, or have direct effects on mitochondria to generate reactive oxygen species (ROS) that ultimately enhance K_{ATP} channel activity. Volatile anesthetics may also directly facilitate K_{ATP} channel opening.[4]

Mechanism of Cardioprotection

The protective effect of anaesthetic preconditioning is mediated by opening mito K_{ATP} channel,[6] which also mediates the protective effect of ischaemic preconditioning. Alteration of the mitochondrial oxidation–reduction balance by mito KATP channel opening may also act to promote cellular protection.

A similar cardioprotective effect was confirmed for enflurane, isoflurane, sevoflurane and desflurane and the noble gas xenon under a variety of experimental conditions in vitro and in vivo; cardioprotection against reperfusion damage was also maintained when the heart was already protected against ischaemic damage by cardioplegic solutions (see review by Preckel[7]). The amount of cardioprotection in all these studies was substantial, leading to an infarct size reduction of about 50%. In addition, several specific mechanisms could be identified: a direct action at the myocardial cell against immediate damage by an interaction with the ryanodine receptor of the sarcoplasmic reticulum and an action against the neutrophil mediated secondary damage.[8] Han and co-workers not only demonstrated that isoflurane reduces the inhibitory effect of ATP on K_{ATP} channel opening[9] but also that the isoflurane metabolite trifluoroacetic acid directly activates K_{ATP} channels. In contrast, a study by Zaugg and co-workers found that the administration of isoflurane or sevoflurane in isolated rat cardiomyocytes did not increase the open-state probability of mitochondrial K_{ATP} channels directly, but that this effect depended on activation of PKC.[10] In one study, it was shown that the cardioprotection induced by both volatile anaesthetics did not depend on opening of sarc K_{ATP} channels.

In early preconditioning, the in vivo experiments confirmed the results of previous in vitro studies that opening of mitochondrial and/or sarcolemmal K_{ATP} channels is a key mechanism of the signal transduction cascade of pharmacologically induced preconditioning by volatile anaesthetics. Activation of adenosine receptors and inhibitory G-proteins trigger the cardioprotection conferred by isoflurane-induced preconditioning. Opening of stretch-activated channels is also involved; administration of gadolinium (a blocker of these channels) prior to isoflurane administration also blocked the preconditioning effect. Only two studies have investigated whether isoflurane-induced early preconditioning is dose-related. The data collected provided evidence that the threshold for induction of preconditioning by a 30-minutes period of isoflurane inhalation is 0.25 MAC in dogs. Protection was only dose-dependent in the presence of a low coronary collateral blood flow. In contrast, in a recent study by our laboratory we could in fact show that lower doses of isoflurane increase PKC-ε activation and decreased infarct size to a greater extent than higher doses.

Isoflurane administration before myocardial ischaemia also reduces contractile dysfunction ('stunning'): pharmacologically induced preconditioning against stunning involves activation of adenosine-A_1 receptors, PKC and K_{ATP} channels. In all of these studies, K_{ATP} channel blockers were administered before the preconditioning stimulus and not during the index ischaemia. Therefore, these results suggest that opening of K_{ATP} channels is not an end-effector (mediator) of pharmacologically induced preconditioning as previously thought,[11] but rather acts as a trigger, i.e. an early part of the signal transduction pathway.

Xenon administered for 3 to 5 minutes before ischaemia reperfusion in an in vivo rat model significantly reduced the infarct size, and that this cardioprotection was in fact mediated via an increased phosphorylation and translocation of PKC-ε.

Roscoe and co-workers showed in isolated isolated human atrial tissue that adenosine A_1 receptor activation and K_{ATP} channel opening is essential for pharmacologically induced preconditioning by isoflurane.[12] In contrast, no protective effect was found for halothane. In the same study, patch clamp measurements did not demonstrate a direct effect for either volatile anaesthetic on K_{ATP} channel-opening probabilities. Desflurane preconditions human atrial myocardium by activation of adenosine A_1 receptors, α- and β-adrenoceptors and mito K_{ATP} channels.[13] Zaugg and co-workers demonstrated that preconditioning induced by 10 minutes administration of 2 MAC sevoflurane preserves myocardial and renal function in patients undergoing coronary artery bypass graft surgery under cardioplegic arrest and that PKC-δ and -ε are activated and translocated in response to sevoflurane in the human myocardium.[14]

In contrast to early preconditioning, the phenomenon of late preconditioning, though less pronounced, protection occurs 12±24 h after the initial preconditioning stimulus and lasts for up to 72 h (second window of protection or late/delayed preconditioning). It was long thought not to be mediated by volatile anaesthetics. Consistent with this delayed type of protection, late preconditioning is dependent on de novo synthesis of cardioprotective proteins. In contrast to most classic or early preconditioning models, late preconditioning consistently protects against stunning.[15] Opioids can also stimulate late preconditioning in vivo.[8]

Intravenous anaesthetics have shown little evidence of cardioprotection during ischaemia reperfusion situations. Propofol, for example, is known as an oxygen free radical scavenger and inhibits calcium influx across plasma membranes, but does not improve post-ischaemic myocardial function.[16] Ketamine can block this channel and prevent the cardioprotective effect of ischaemic preconditioning at clinically relevant concentrations. The effect is stereospecific for the R(-)-isomer and does not occur with S(+)-ketamine. Cardioprotection by late preconditioning is also blocked by a single bolus dose of racemic ketamine, but not by S(+) ketamine.[17] Barbiturates may also block the ATP regulated potassium channels, a blocking effect on preconditioning may only occur at supratherapeutical doses.[18]

Potential harmful mechanisms

Opening of the (mitochondrial) K_{ATP} channel is a central mechanism in the signal transduction of preconditioning. Both barbiturates and ketamine can block K_{ATP} channels in isolated cells. While thiopental appeared to be safe and did not block experimental preconditioning at clinical doses,[18] several studies found that ketamine completely blocked the cardioprotection of ischaemic preconditioning both in vitro and in vivo; the effect was stereospecific for the R(-)-isomer. A recent study from our laboratory showed that lidocaine blocks ischaemic preconditioning only when used at supratherapeutic concentrations.[19]

While the clinical importance of these findings is still unknown, it is probably safer to avoid racemic ketamine in clinical settings where ischaemia reperfusion is likely to occur. Sulphonylurea oral anti-diabetics such as gliblenclamide can block the K_{ATP} channel and prevent cardioprotection by preconditioning. Recent evidence suggests that a patient with type II diabetes and coronary artery disease may profit from changing the treatment to insulin (by having less ischaemia-induced myocardial dysfunction).[20]

Clinical trials to prove clinical relevance

Evidence is now needed from clinical trials involving actual patients with coronary artery disease undergoing surgery to confirm that exposure to volatile anaesthetics does offer cardioprotection. Although animal studies have mostly succeeded in demonstrating cardioprotection with volatile anaesthetics, the same cannot be assumed to occur in humans. In fact, two previous trials conducted in coronary surgery, each involving more than 1000 patients had found no difference in terms of outcome, including the incidence of myocardial ischaemia, between intravenous and volatile anaesthetic

regimens.[21,22] In view of recent interests in the cardioprotective effects of volatile anaesthetics, some trials are revisiting the topic.[23]

A review of the clinical studies conducted to date reveal that these studies on anaesthetic preconditioning are aimed at either of the following:

i) Finding evidence that the administration of volatile anaesthetics result in preconditioning. This is achieved by demonstrating an increase in the level of markers of preconditioning.

ii) Demonstrating cardioprotective effects when volatiles are included in the anaesthetic regimen as indicated by:

- Improved ventricular function e.g. maintained haemodynamic variables, reduced inotropic requirements and normal measures of contractility
- Reduced incidence of dysrhythmias on reperfusion
- Reduced period of myocardial stunning and earlier functional recovery
- Reduction in infarct size or prevention of infarct
- Reduced length of hospital or intensive care unit stay

Ischaemic preconditioning and clinical relevance

There is plenty of evidence suggesting the benefits of ischaemic preconditioning, which is the counterpart of anaesthetic preconditioning. Preinfarction angina, for example is found to reduce the size of hypokinetic segments on echocardiography and peak CKMB levels.[24] In a review of ischaemic preconditioning written in 2006,[25] Kloner summarised the following findings regarding manifestations of preconditioning in the human heart; 'that repeat angioplasty balloon inflations result in less chest pain, ST segment elevation, and lactate production than upon an initial inflation; that a second episode of ischemia induced by exercise or pacing is associated with less chest pain, ST segment change, and lactate production than a first episode; that pre-infarct angina reduces infarct size and is associated with better clinical outcome; that intermittent aortic cross clamping preserves myocardial ATP during coronary artery bypass surgery; that certain preconditioning mimetic agents can reduce ischemia during balloon inflation or exercise testing in both an early preconditioning and delayed fashion'. The preconditioning mimetic agents referred to in this review include adenosine, adenosine agonists, K_{ATP} channel/opener and nitrate-like agent nicorandil, delta opioids, volatile anaesthetics and nitroglycerin. This review also outlined various factors that may result in attenuation or abolishment of ischaemic preconditioning namely diabetes mellitus, hyperglycaemia, certain oral hypoglycaemic agents like glibenclamide (sulphonylureas), hypercholesterolaemia and high cholesterol diet. For the last factor, pravastatin apparently restores ischaemic preconditioning even at a dose that did not normalize serum cholesterol levels.

Anaesthetic preconditioning and clinical relevance

It is rather disappointing that clinical studies on anaesthetic preconditioning, on the other hand, fail to mimic the almost unequivocal benefit seen in animal studies or the convincing evidence from studies on ischaemic preconditioning. There may be many reasons for this failure. Complex considerations need to be undertaken in reproducing the findings from animal studies in that of real patients with coronary artery disease undergoing surgery. Various designs were devised to meet the obvious difficulties faced in conducting such trials. The ischaemia must be induced in a predictable, standardized and reproducible manner. Exposures to volatile anaesthetics at a standardized time, either pre-ischaemia, post-ischaemia or throughout the anaesthetic period are then studied to determine whether the exposure will in fact prevent adverse outcomes. All this must be done while also randomizing the subjects to different interventions. These issues pose serious practical as well as ethical problems and some would consider the conduct of these studies as going against many things accepted as good clinical practice. The interpretation of the results must then take into account the fact that factors such as surgical expertise, anaesthetic expertise, haemodynamic strategies, to name a few, may also interfere with outcome measurements.

As a result of the above difficulties, most clinical trials on anaesthetic preconditioning were conducted in patients undergoing cardiac surgery. In this setup, the occurrence of ischaemia can be predicted and

subsequent reperfusion is a routine part of the procedure. Furthermore, compared to non-cardiac surgery, complications can be more expediently dealt with; elegant techniques of measurement of variables such as contractility are possible and intensive monitoring after surgery as well as measurements of cardiac enzymes in the post operative period is routinely done.

Although cardiac surgery provides the most ethical, predictable and safe scenario for the conduct of such studies, the actual relevance of the findings remain questionable, as these are not the only group of patients at risk where the occurrence of perioperative ischaemia is concerned. It is reported that perioperative ischaemia occurs in 18 to 74% of patients with coronary artery disease undergoing non cardiac surgery[26]. Most of these clinical trials also involve the institution of cardiopulmonary bypass (CPB), which in itself induces preconditioning.[29] Any proof of preconditioning or its beneficial effects must ideally differentiate between that which is due to the anaesthetic agent and preconditioning induced by the institution of CPB. Furthermore, in cardiac surgery, definitive treatment for the ischaemia is achieved at the end of the surgery, which can certainly improve patient outcome. This does not occur in patients with ischaemic heart disease undergoing non cardiac surgery, and the findings of studies in cardiac surgery may not be suitably translated to them. From the above discussion, it is evident that this latter group is more likely to benefit, if anaesthetic preconditioning is shown to improve outcome of perioperative ischaemia.

Apart from the issue of differences in the target group concerned, other issues like the timing and dosing of such exposure need to be resolved if the information is to be used in clinical practice. Review of the current literature reveals that these clinical studies use rather diversely different protocols, measure quite different endpoints and produce different conclusions, leaving readers wondering about the application of anaesthetic preconditioning as well as the adequacy of evidence to promote such management.

It is evident from animal and human studies that study protocols mainly target three timings of exposure to volatile anaesthetics:

1. Preconditioning protocols where the volatile exposure occurs exclusively during the preischaemic phase. Often this involves a washout period prior to the ischaemic insult, so that the volatile anaesthetic is exclusively present only during the preconditioning phase. A large proportion of earlier clinical studies were studying this form of exposure.
2. Reperfusion protocols where volatile anaesthetics are introduced only after the ischaemic insult has occurred and during the reperfusion period. So far these have been mainly conducted in animal studies.
3. Protocols where exposure to volatile agents occur throughout the anaesthetic, including both the preischaemia and reperfusion period. These trials involving patients are published as studies which compare outcome between total intravenous anaesthetic regimens and volatile incorporated regimens. It indirectly challenges the long held belief that the anaesthetic regimen has no bearing on patient outcome.

With regard to outcome measures, some trials involving patients were only aimed at determining if a preconditioning phenomenon had in fact occurred on exposure to volatile anaesthetics. These trials studied levels of various markers of preconditioning such as protein kinase C and tyrosine kinase. Some other trials sought to compare differences in the extent of ischaemic damage following ischaemia for which levels of markers such as troponin T, troponin I, creatine kinase-MB levels and degree of ST segment changes were compared. Other outcomes of interests that have been looked into include measurement of myocardial function such as echocardiographic measurements of contractility, intraventricular pressure measurements, inotropic support requirements, cardiac index measurements and rates of complications such as arrhythmia. Recent clinical trials on anaesthetic preconditioning have taken all this a step further by looking at more definitive measures of patient outcome such as hospital and intensive care unit (ICU) length of stay and other measures of morbidity.

Preconditioning studies

In clinical trials involving preconditioning protocols during coronary surgery, the index ischaemia is taken

to occur during aortic cross-clamping. Volatile anaesthetics, in most instances, were introduced upon commencement of CPB, just prior to aortic cross clamping. This is usually followed by a period where washout of the volatile is allowed to occur. The volatile anaesthetic is therefore present only in the preischaemia period.

A fair number of these studies report equivocal findings between the experimental and the control group. This may be contributed by another common feature shared between many of these clinical studies utilising preconditioning protocols; small sample size. Most studies involve only around 20 subjects, although some included more, up to 50 to 72 subjects. It is therefore unclear if this lack of power contributes to the lack of positive findings. Furthermore, even with positive findings, there is an issue raised as to whether the institution of CPB induces ischaemic preconditioning in itself and this needs to be differentiated from benefits due to anaesthetic preconditioning conferred by the volatile agents.

The first of these preconditioning studies were conducted by Belhomme et al in 1999 involving 20 patients.[27] In this protocol, the treatment group was exposed to isoflurane at 2.5 MAC for 5 minutes upon institution of the CBP. A 10 minute washout period then followed prior to aortic cross-clamping. The findings of this study showed that although the treatment group had an increase a marker of protein kinase C activation (taken to indicate the occurrence of preconditioning), there was no difference in postoperative release of creatinine kinase MB and troponin I compared to the control group.

In another study of 20 patients, an effort was made by Pouzet et al to differentiate between preconditioning conferred by the volatile anaesthetic and preconditioning conferred by the institution of CPB alone.[28] In the treatment group, sevoflurane was administered at 2.5 MAC during the first 10 minutes of CPB whilst the control group received no exposure to sevoflurane. The findings showed that two markers of preconditioning studied were significantly increased and occurred to a similar extent in both groups and the authors concluded that there was no evidence to indicate that exposure to volatiles resulted in greater preconditioning. Furthermore, there was again no difference in the level of Troponin I in both groups. The sevoflurane group however, also showed an increase in levels of a third marker, tyrosine kinase. Although the authors did not make any implications of the last finding, De Hert, in a narrative review took this be indicative of greater preconditioning in the sevoflurane group.[29]

Subsequent studies attempted to determine if anaesthetic preconditioning resulted in improved ventricular function. A study on 22 patients conducted by Penta de Peppo et al[30] found that enflurane administered at 1.3% for 5 minutes immediately before CPB enhanced left ventricular function as indicated by measures of contractility derived via echocardiography. There was again no difference from the control group in terms of extent of ischaemic damage as indicated by creatine kinase-MB and troponin I levels.

Tomai et al studied 40 patients,[31] the treatment group of which received isoflurane at 1.5% for 15 minutes, followed by a washout period of 10 minutes before the start of CPB. The study found no difference between the two groups with regard to postoperative cardiac function and peak troponin I values except in a subgroup of patients with ejection fraction less than 50%, where the release of troponin I levels 24 H postoperatively were slightly lower in the treatment group.

Administration of isoflurane 0.5-2.0% until start of CPB resulted in better postoperative cardiac index and a lesser degree of ST segment changes compared to the control group in a study of 49 patients by Haroun- Bizri.[32] The incidence of reperfusion arrhythmias were however similar in both groups.

And the largest of these preconditioning studies were conducted by Julier et al, involving 72 patients, which found that administration of sevoflurane 4% for the first 10 minutes of CPB before aortic cross-clamping resulted in a lower release of a biochemical marker for myocardial contractile dysfunction (brain natriuretic peptide) although again no differences could be found in the occurrence of arrhythmias, creatine kinase MB and cardiac troponin T release.[33] Contrary to the findings of Haroun Bizri et al, this study found no difference in perioperative ST segment changes compared to the control group.

From the analysis of these studies involving preconditioning protocols, questions arise if the variable findings occurred as a result of differences in the type, concentrations and timing of administration of the volatile agents used. It appears that consistency is achieved in demonstrating that the phenomenon of preconditioning also occurs in humans with exposure to volatiles. However, there is lack of evidence to indicate that when volatiles are administered exclusively in the preischaemic period to humans, reduced ischaemic damage and better myocardial function results.

Volatile incorporated versus total intravenous anaesthesia

Other clinical trials then attempted to compare anaesthetic regimens incorporating volatile agents with anaesthetic regimens which only involved intravenous agents. In the treatment group of these studies, exposure to volatile agents occur throughout the anaesthetic, as opposed to the preconditioning protocols discussed earlier where volatile exposure only occur during the preischaemic period. In contrast to preconditioning studies, these studies tend to report, rather consistently, positive results supportive of volatile incorporated anaesthetic regimens. Indirectly, this approach also questions the previously held belief that the choice of anaesthetic regimen has no bearing on patient outcome.[21,22]

De Hert et al studied 20 patients comparing myocardial function during and after coronary surgery between two anaesthetic regimens, using sevoflurane and propofol respectively.[34] Better preserved cardiac performance was observed in the sevoflurane group as demonstrated by a pressure catheter placed in both the left ventricle and the left atrium which measured both contraction and relaxation response to increased cardiac load. There was also less need for inotropic support (dobutamine) during weaning from CPB for the sevoflurane group. The plasma concentrations of cardiac troponin I were also lower in this treatment group.

The same group of researchers subsequently repeated the study in a group of high risk patients (n=45), as defined by elderly patients with three vessel disease and ejection fraction of less than 50%, using desflurane, sevoflurane and propofol respectively and found similar protective effects, namely better preserved cardiac function, less need for haemodynamic support post CPB and less myocardial damage with both volatile groups.[35]

In a correspondence published in 2003 in Anaesthesiology, Van der Linden and a group of researchers which also included De Hert, reported a before and after analysis of the routine use of volatile anaesthetics during anaesthesia for cardiac surgery.[36] In this observational analysis, 107 patients underwent coronary surgery in the 'before' period during which the anaesthetic only involved usage of midazolam and high dose sufentanil. This centre for coronary surgery was then rebuilt, equipping the anaesthetic machine and the CPB circuits with vaporizers and end tidal anaesthetic concentration monitoring. A total of 91 patients subsequently underwent coronary surgery in the 'after' period, when the anaesthetic technique was modified to using a lower dose of midazolam and sufentanil but routinely including sevoflurane at 0.5 to 2.0%. During both time periods, the same surgical and anaesthetic team performed all the procedures and patient characteristics, medication, intraoperative data and haemodynamic strategies were the same. The findings of this observational analysis reported consistently lower Troponin T levels, lower need for inotropic support during weaning from CPB and lower incidence of low cardiac index (as defined by the need for inotropic support for cardiac index lower than 2.0 1 • min^{-1} • m^2) for patients anaesthetized in the 'after' period with sevoflurane routinely included in the anaesthetic regimen.

El Azab et al in a small trial of 20 patients comparing sevoflurane with midazolam-sufentanil anaesthesia found that sevoflurane anaesthesia resulted in decreased levels of plasma tumor necrosis factor (TNF), an ischaemia-reperfusion injury marker.[37] Less patients in the sevoflurane group needed inotropic support to maintain haemodynamic stability and the length of stay in the intensive care unit was significantly lower in the sevoflurane group.

There is hitherto only one study which looked at the cardioprotective effects of volatile agents in off pump coronary surgery. Conzen et al demonstrated in a study of 20 patients that sevoflurane anaesthesia resulted in better cardiac function and reduced serum troponin I

levels although no significant effect on creatine kinase-MB could be found.[38] It was suggested that this off-pump study, with the elimination of preconditioning by CPB, can be better translated to patients undergoing non cardiac surgery.

As was outlined in this section earlier, these studies where exposure to volatile anaesthetics occur throughout the pre and post-ischaemia period, showed consistently positive findings in favour of a volatile-incorporated anaesthetic.

Implications on outcome of patients

The final question of interest after demonstrating the occurrence of anaesthetic preconditioning and studying its effects on cardioprotection, is whether the outcome of patients with coronary artery disease is significantly improved if volatile anaesthetic regimens are used during surgery.

De Hert again published another clinical trial, this time including a larger sample of 320 patients.[39] Four fast-track anaesthetic protocols were compared, two based on total intravenous regimen using propofol and midazolam respectively and two based on volatile anaesthetics namely sevoflurane and desflurane respectively. The study found that both volatile anaesthetic groups had shorter ICU and hospital length of stay, less incidence of patients requiring ICU admission for > 48 hours, lower levels of troponin I, lower incidence of raised levels of troponin I > 4 ng/mL, lower need for inotropic support and less incidence of prolonged need for inotropic support. The four groups were similar in terms of duration of postoperative ventilation, incidence of post operative atrial arrhythmia, reintubation and pulmonary oedema.

Conclusion

The findings of clinical trials in the latter period, where volatile anaesthetics are used throughout the surgery certainly seem encouraging and more supportive of the cardioprotective effects of volatile agents. There is a need to take a closer look at these findings especially in the light of earlier studies which have found no added benefit of using volatile anaesthetic regimens in patients undergoing cardiac surgery.

Why is there a difference? Other questions one might ask include: do different agents have differing effects on preconditioning? Are some agents better than others? Some trials have already looked into these and there is suggestion that not all volatiles are created equal.[40] Clinical trials then need to look at patients with coronary disease who undergo non-cardiac surgery, while overcoming the greater challenges posed considering all the factors that are against the conduct of such studies. It would be, however, a worthwhile effort as the anaesthetic specialty ultimately needs to decide how this information can be utilized, especially in patients undergoing non cardiac surgery. We also need to look at what factors abolish these effects and therefore to be avoided in patients with coronary disease who come under our care. These factors have been impressively studied by our cardiology colleagues and may also apply to anaesthetic preconditioning. For example, many of the trials on anaesthetic preconditioning had excluded patients under glibenclamide and theophylline, as these agents are shown to abolish ischaemic preconditioning.

The medical fraternity as a whole is studying other preconditioning mimetics, apart from volatiles, and these agents may also be utilized by anaesthetists. The effects of preconditioning on other tissues are also being studied and there is possibility for us to tap into these when considering protection of other organs such as the kidney, brain and liver. In fact, anaesthetic preconditioning affecting endothelial cells has been shown to occur and may play a role in protection against ischaemia-reperfusion injury in humans.[41] Although the possibilities are indefinite, the prospects of these are certainly exciting and we hope that this quest to find better techniques that improve the outcome of our patients will bear fruit in the near future.

References

1. Murry CE, Jennings RB, Reimer KA. Preconditioning with ischemia: a delay of lethal cell injury in ischemic myocardium. *Circulation* 1986;**74**:1124-36.
2. Murry CE, Richard VJ, Jennings RB, Reimer KA. Myocardial protection is lost before contractile function recovers from ischemic preconditioning. *Am J Physiol* 1991;**260**:H796-804.
3. Kuzuya T, Hoshida S, Yamashita N, et al. Delayed effects of sublethal ischemia on the acquisition of tolerance to ischemia. *Circ Res* 1993;**72**:1293-9.
4. Tanaka K, Ludwig LM, Kersten JR, Pagel PS, Warltier DC. Mechanisms of Cardioprotection by Volatile Anesthetics. *Anesthesiology* 2004;**100**:707-21
5. Han J, Kim E, Ho WK, Earm YE: Effects of volatile anesthetic isoflurane on ATP-sensitive K+ channels in rabbit ventricular myocytes. *Biochem Biophys Res Commun* 1996;**229**:852–6
6. Kersten JR, Schmeling TJ, Pagel PS, Gross GJ, Warltier DC: Isoflurane Mimics Ischemic Preconditioning via Activation of K sub ATP Channels: Reduction of Myocardial Infarct Size with An Acute Memory Phase. *Anesthesiology* 1997;**87**:361-370,
7. Preckel B & Schlack W. In Vincent J Le (ed.) Effect of Anesthetics on Ischemia-Reperfusion Injury of the Heart. Berlin:Springer;2002:165-176.
8. Weber NC, Schlack W. The concept of anaesthetic-induced cardioprotection: mechanisms of action. *Best Practice & Research Clinical Anaesthesiology* 2005;**19**(3):429–443,
9. Han J, Kim E, Ho WK & Earm YE. Effects of volatile anesthetic isoflurane on ATP-sensitive K+ Channels in rabbit ventricular myocytes. *Biochem. Biophys. Res. Commun* 1996;**229**:852–856.
10. Zaugg M, Lucchinetti E, Spahn DR et al. Volatile anesthetics mimic cardiac preconditioning by priming the activation of mitochondrial KATP channels via multiple signaling pathways. *Anesthesiology* 2002;**97**:4–14
11. Kersten JR, Gross GJ, Pagel PS &Warltier DC. Activation of adenosine triphosphate-regulated potassium channels: mediation of cellular and organ protection. *Anesthesiology* 1998;**88**:495–513.
12. Roscoe AK, Christensen JD, Lynch C 3rd. Isoflurane, but not halothane, induces protection of human myocardium via adenosine A1 receptors and adenosine triphosphate-sensitive potassium channels. *Anesthesiology* 2000;**92**:1692–1701.
13. Hanouz JL, Yvon A, Massetti M et al. Mechanisms of desflurane-induced preconditioning in isolated human right atria in vitro. *Anesthesiology* 2002;**97**:33–41.
14. Julier K, Da Silva R, Garcia C et al. Preconditioning by sevoflurane decreases biochemical markers for myocardial and renal dysfunction in coronary artery bypass graft surgery: a double-blinded, placebo controlled, multicenter study. *Anesthesiology* 2003;**98**:1315–1327.
15. Zaugg M, Lucchinetti E, Uecker M, et al. Anaesthetics and cardiac preconditioning. Part I. Signalling and cytoprotective mechanisms. *Br J Anaesth* 2003;91:551– 65.
16. Ross S, Munoz H, Piriou Vet al. A comparison of the effects of fentanyl and propofol on left ventricular contractility during myocardial stunning. *Acta Anaesthesiol. Scand.* 1998;**42**:23–31.
17. Mullenheim J, Frassdorf J, Preckel B, Thamer V, Schlack W. Ketamine, but not S(+)-ketamine, blocks ischemic preconditioning in rabbit hearts in vivo. *Anesthesiology.* 2001; **94**(4): 630-6.
18. Mullenheim J, Molojavyi A, Preckel B, Thamer V, Schlack W. Thiopentone does not block ischemic preconditioning in the isolated rat heart. *Can J Anaesth*. 2001; **48**(8): 784-9.
19. Barthel H, Ebel D, Mullenheim J et al. Effect of lidocaine on ischaemic preconditioning in isolated rat heart. *Br. J. Anaesth*. 2004; **93**: 698–704.
20. Scognamiglio R, Avogaro A, Vigili de KS et al. Effects of treatment with sulfonylurea drugs or insulin on ischemia-induced myocardial dysfunction in type 2 diabetes. *Diabetes* 2002; **51**: 808–812.
21. Slogoff S, Keats AS. Randomized trial of primary anesthetic agents on outcome of coronary artery bypass operations. *Anesthesiology* 989; **70**:179–88
22. Tuman KJ, McCarthy RJ, Spiess BD, et al. Does choice of anesthetic agent significantly affect outcome after coronary artery surgery? *Anesthesiology* 1989; **70**:189 –98
23. De Hert SG, Van der Linden PJ, Cromheecke S, et al. Choice of primary anesthetic regimen can influence intensive care unit length of stay after coronary surgery with cardiopulmonarybypass. *Anesthesiology* 2004; **101**: 9 –20.
24. Ottani F, Galvani M, Ferrini D, et al. Prodromal angina limits infarct size: a role for ischemic preconditioning. *Circulation* 1995;**91**:291–7.

25. Kloner RA, Rezkalla SH. Preconditioning, postconditioning and their application to clinical cardiology. *Cardiovasc Res.* 2006;**70**(2):297-307.
26. Mangano DT. Perioperative cardiac morbidity. *Anesthesiology* 1990;**72**:153– 84.
27. Belhomme D, Peynet J, Louzy M, et al. Evidence of preconditioning by isoflurane in coronary artery bypass graft surgery. *Circulation* 1999;**100**(suppl II):II-340-II4.
28. Pouzet B, Lecharny JB, Dehoux M, et al. Is there a place for preconditioning during cardiac operations in humans? *AnnThorac Surg* 2002;**73**:843– 8.
29. De Hert SG, Turani F, Mathur S, Stowe DF. Cardioprotection with volatile anesthetics: mechanisms and clinical implications. *Anesth Analg.* 2005;**100**(6):1584-93
30. Penta de Peppo A, Polisca P, Tomai F, et al. Recovery of LVcontractility in man is enhanced by preischemic administration of enflurane. *Ann Thorac Surg* 1999;**68**:112– 8.
31. Tomai F, De Paulis R, Penta de Peppo A, et al. Beneficial impact of isoflurane during coronary bypass surgery on troponin I release. *G Ital Cardiol* 1999;**29**:1007–14.
32. Haroun-Bizri S, Khoury SS, Chehab IR, et al. Does isoflurane optimize myocardial protection during cardiopulmonary bypass? *J Cardiothorac Vasc Anesth* 2001;**15**:418 –21.
33. Julier K, da Silva R, Varcia C, et al. Preconditioning by sevoflurane decreases biochemical markers for myocardial and renal dysfunction in coronary artery bypass graft surgery: a doubleblinded placebo-controlled, multicenter study. *Anesthesiology* 2003;**98**:1315–27.
34. De Hert S, ten Broecke P, Mertens E, et al. Sevoflurane but not propofol preserves myocardial function in coronary surgery patients. *Anesthesiology* 2002;**97**:42–9.
35. De Hert S, Cromheecke S, ten Broecke P, et al. Effects of propofol, desflurane, and sevoflurane on recovery of myocardial function after coronary surgery in elderly high-risk patients. *Anesthesiology* 2003;**99**:314 –23.
36. Van der Linden P, Daper A, Trenchant A, De Hert S. Cardioprotective effects of volatile anaesthetics in cardiac surgery. *Anesthesiology* 2003;**99**:516 –7.
37. El Azab SR, Rosseel PM, De Lange JJ, et al. Effect of sevoflurane on the ex vivo secretion of TNF-alpha during and after coronary artery bypass surgery. *Eur J Anaesthesiol* 2003;**20**:380–4.
38. Conzen PF, Fischer S, Detter C, Peter K. Sevoflurane provides greater protection of the myocardium than propofol in patients undergoing off-pump coronary artery bypass surgery. *Anesthesiology* 2003;**99**:826 –33.
39. De Hert SG, Van der Linden PJ, Cromheecke S, et al. Choice of primary anesthetic regimen can influence intensive care unit length of stay after coronary surgery with cardiopulmonary bypass. *Anesthesiology* 2004;**101**:9 –20.
40. Roscoe A, Christensen J, Lynch C III. Isoflurane, but not halothane, induces protection of human myocardium via adenosine A1 receptors and adenosine triphosphate-sensitive potassium channels. *Anesthesiology* 2000;92:1692–701.
41. Lucchinetti E, Ambrosio S, Aguirre J, et al. Sevoflurane inhalation at sedative concentrations provides endothelial protection against ischemia-reperfusion injury in humans. *Anesthesiology* 2007;**106**(2):262-8.

Anaesthesia for Pituitary Tumor Surgery

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Introduction

Pituitary tumors can be generally divided into two groups: functioning pituitary tumors and non-functioning pituitary tumors. They account for 10-15% of all intracranial neoplasms, with the majority of pituitary tumours being non-functional macroadenomas.[1] Functioning pituitary adenomas often present with symptoms of hormonal hypersecretion, and although medical therapy is available for most of these hyperfunctioning states, it is not curative. As a result, transsphenoidal pituitary surgery has become a commonly performed neurosurgical procedure, posing unique challenges to the anesthesiologist, due to distinct medical co-morbidities associated with the various adenomas.[2]

Clinical Presentation

This can be attributed to both pressure effects on local structures adjacent to the pituitary gland as well as hormonal effects to distant organs. Most patients present with symptoms and signs of visual field defects, headaches, hormone hypersecretion and hypopituitarism either alone or in combination. A functioning pituitary tumor may present with Cushing's syndrome (adenocorticotropin), acromegaly (growth hormone,GH) and hyperprolactinemia (prolactin).

Non-functioning pituitary tumors which include chromophobe adenoma, craniopharyngioma, meningioma, aneurysm and rarely metastatic or granulomatous lesions, are usually larger than functioning ones because of delay in presentation. Increased intracranial pressure and panhypopituitarism are therefore common presenting symptoms.[3]

Pituitary tumors can also be part of multiple endocrine neoplasia type I which is a syndrome of GH-producing, prolactin-producing or chromophobe adenomas of the pituitary; primary hyperparathyroidism and insulin-producing or gastrin-producing tumors of the pancreas.[4]

Classification of pituitary tumor

Pituitary tumours may be classified according to the size and extend of sellar involvement. The Hardy Classification of pituitary tumor is as follows:[5],

- Grade I: Normal size sella, mild thinning of the floor, less than 10mm in diameter, microadenoma
- Grade II: Sella enlarged but intact, no extrasellar extension
- Grade III: Localized erosion of sellar floor, extension into sphenoid sinus or suprasellar space.
- Grade IV: Diffuse erosion of the sellar floor. "Phantom" sella, extension into sphenoid sinus or suprasellar space.

Surgical treatment[2]

Except for prolactinomas, the first line treatment for pituitary adenomas that hypersecrete or cause mass effects is usually transsphenoidal surgery. This should always be preceded by measurement of prolactin and thyroxine levels and the patient should be covered with

either hydrocortisone or dexamethasone. The use of endoscopic instruments and intraoperative fluoroscopy are standard equipments for transplenoidal surgery but with the introduction of computerized real time, three dimensional image processing, the efficacy of surgery is further enhanced. This is particularly when local landmarks have been lost or disturbed by previous explorations.

Transsphenoidal microsurgical excision is considered the therapy of choice for all pituitary tumors without marked extrasellar extension. Mortality associated with this procedure is less than 1% and morbidity such as carotid artery injury, visual loss, ophthalmoplegia is rare. Other advantages include preservation of normal pituitary function, lower incidence of permanent diabetes insipidus, less blood loss and no external scarring.[6]

The transfrontal approach is reserved for tumor of uncertain diagnosis and those that extend into the anterior and middle fossae. Morbidity and mortality is higher compared to the previous technique.[7]

Treatment of craniopharyngiomas in young children is controversial and range from attempts at total excision to conservative surgery (cyst aspiration, ventricular shunting) plus radiation.[8]

For micro-prolactinomas, long term treatment with bromocriptine or an alternative dopamine agonist is the most common treatment of choice. Surgery is rarely curative for macroadenomas and often results in hypopituitarism. Dopamine agonists are the treatment of choice as serum prolactin return to normal in over 75% of patients and result in long term shrinkage of most tumors.[9]

Pre-operative Evaluation and Anaesthetic Concerns[3]

In preoperative assessment of patients presenting for pituitary surgery, a detailed pulmonary and airway assessment must be taken into account. Features of acromegaly or cushingoid features suggest a potential difficult airway due to large tongue in the former and relative short neck with buffalo hump in the latter. Thickening of the laryngeal and pharyngeal soft tissues leading to a reduction in the size of the glottic opening, hypertrophy of the periepiglottic folds and macroglossia can all contribute to airway obstruction. Fiberoptic intubation may be necessary, but may prove difficult in these patients because of distorted anatomy and resistance to advancement of the endotracheal tube. An obstructive respiratory syndrome is observed in 25% of female and 70% of male patients. Obstructive sleep apnea (OSA) secondary to upper airway obstruction can affect up to 70% of acromegalic patients.[10,11]

Cardiac disease is a major cause of morbidity and mortality in acromegalic patients. Electrocardiography changes such as ST segment depression, T-wave abnormalities, and conduction defects are common while hypertension occurs in approximately 40% of acromegalic patients. Left ventricular hypertrophy can occur in the presence of systemic hypertension, but also occurs in at least 50% of normotensive acromegalic patients. Echocardiography reveals an increase in left ventricular mass, stroke volume, cardiac output, and isovolumic relaxation time. A poorly compliant left ventricle and its accompanying need for high filling pressures may be considered the hallmark of acromegalic cardiomyopathy.

Visual field defect is due to direct pressure of the tumour on the anterior chiasm leading to the classic symptoms of bitemporal hemianopia.

In Cushing's disease, the hypersecretion of adrenocorticotropic hormone (corticotropin) stimulates the adrenal gland to produce cortisol, androgens, and to a lesser extent mineralocorticoids. The patients may also be hypertensive, and have hirsutism, thin skin with purple striae, easy bruising, acne, proximal muscle weakness, osteoporosis, emotional lability, psychosis, hypokalemic metabolic alkalosis, hyperpigmentation, glucose intolerance, increased susceptibility to infection and impaired wound healing. Evaluation of cardiovascular function, electrolytes and plasma glucose are required. Cortisol release will be increased during surgical stimulation. Skeletal muscle weakness may affect the responses to muscle relaxants. Stress-dose steroids will be required intraoperatively.

Diabetes mellitus can be seen in one third of patients with Cushing's disease and need to be controlled prior to surgery.

Premedication is rarely indicated in patients for pituitary surgery unless the patient is anxious or hypertensive. Patients with sleep apnea are usually not premedicated so as to avoid further airway compromise.

Endocrinologic consideration[12]

Before pituitary surgery, all patients with pituitary disease should be subjected to a diagnostic test of Hypothalamic-Pituitary Axis function. Hormonal assay to be done include serum cortisol, serum GH level, serum prolactin and serum thyroid stimulating hormone, TSH. The decision regarding the perioperative use of glucocorticoid cover depends on the result of the preoperative screening test. There are various intraoperative glucocorticoids replacement regimes recommended for the perioperative period in the presence of actual or potential anterior pituitary insufficiency.

If the ACTH 1-24 (Synacthen) test is abnormal, then the patient should be commenced on standard maintenance doses of glucocorticoid (15-30 mg hydrocortisone daily, depending on factors such as age, sex, and body habitus) in the lead-up to surgery. These patients should be treated perioperatively with 48 hours of supra-physiological glucocorticoid therapy, with rapid dose reduction. A suggested dose regimen, using hydrocortisone, is:

i) 50 mg every 8 h on day of surgery,

ii) 25 mg every 8 h on day one post-operatively, and

iii) 25 mg at 0800 h on day two post-operatively

Oral thyroid replacement is indicated in patients with pan-hypopopituitarism.

Diabetes insipidus rarely occurs intra-operatively but is not uncommon post-operatively. Therefore monitoring urine volume, specific gravity and serum electrolytes is necessary during intra-operative and post-operative periods. Treatment should be considered if there is a significant discrepancy in fluid intake and output, an increasing serum sodium (above 145 mmol l^{-1}), and when excessive urine output significantly interferes with sleep. Desmopressin (DDAVP) works quickly and effectively without undesirable increases in arterial blood pressure. An initial dose of 0.1 mg of DDAVP can be administered orally or alternatively, if the patient is unable to take oral medications, 1 µg of DDAVP can be administered subcutaneously.

Conduct of Anaesthesia

These are usually elective procedures but occasionally urgent transsphenoidal or transcranial surgery is indicated to decompress the optic nerves and chiasm as in the case of a haemorrhagic infraction of pituitary tumor which may produce the signs and symptoms of subarachnoid hemorrhage, sudden loss of consciouness, meningeal symptoms, blindness, ophthalmoplegia and panhypopituitarism.

Intraoperative anaesthetic technique[13]

The goals of anaesthesia are smooth induction, airway control with endotracheal intubation and adequate depth of anaesthesia to obtund sympathetic reflexes. Anaesthetic techniques that can be used in the majority of patients include the use of narcotics, inhalation or total intravenous anaesthesia with muscle relaxants. It is important that patients do not cough after reversal as this may lead to CSF rhinorrhoea.

Intravenous induction is commonly used unless difficult airway is suspected especially in acromegalic patients. Total intravenous anaesthesia using propofol has the advantages of providing anaesthesia with lower blood pressure and better recovery profile; otherwise general anaesthesia using inhalational agent, air and oxygen is other alternative. Either a RAE tube or armored tube can be used to secure the airway.

Standard intra-operative monitoring includes standard ECG monitoring, pulse oximetry, $ETCO_2$, NIBP, urine output and core temperature. Invasive arterial pressure monitoring is considered essential as we may need to treat sudden surges in intraoperative blood pressure as well as to manage troublesome intraoperative bleeding. Central venous pressure monitoring will facilitate the fluid replacement therapy in patients as some may develop diabetes insipidus post-operatively. Unless faced with technical problems, invasive monitoring such as CVP and arterial pressure monitoring is used routinely for our patients undergoing pituitary surgery. Radial artery cannulation is to be avoided in acromegalic patients who show signs of carpel tunnel syndrome.

Intermittent doses of muscle relaxant technique are usually adequate and should be titrated to a TOF count of 0-1. For transsphenoidal approach technique, short acting opiates such as fentanyl is usually adequate for the pain relief in the majority of patients.

Patient Positioning and surgery

For transsplenoidal surgery, the patient is placed in a semi-recumbent, reclining, or lawn-chair position, with the operative site above the level of the heart to allow for free drainage of blood from the region of the sella and the sphenoid sinus. The patient is positioned in the head-up position either rested on the horseshoe ring or fixed by 3 pins.

The operative table will need to be positioned so that the room can accommodate the fluoroscopic or image guidance systems which will be used intraoperatively to confirm the position and trajectory of the transsphenoidal speculum.

Air embolism is rare if the gradient between the head and operative field is 15 degrees or less. Excessive bleeding from cavernous sinus may occur and may need temporary or permanent packing of the sinus. Postoperative ophthalmoplegia, facial anesthesia and contralateral hemiparesis or hemiplegia my result from direct pressure or vasospasm.

For removal of the lateral portions of tumors, particularly those with suprasellar extension, the surgeon may request for a valsalva maneuver to cause the remaining tumor to prolapse into view. Alternatively, the injection of 10 ml of air or saline via a lumbar catheter often will deliver the remaining suprasellar portion of the tumour into the sella.[14]

Bothersome bleeding during intrasellar exploration can be effectively controlled with adequate local anesthetic nitration of the nasal passages combined with appropriate anaesthetic depth and in some instances hypotension anaesthesia.

There is an incidence between 1 and 4% of CSF leak when surgeons use the trans-splenoidal approach and this may require a repair in a later stage. For treatment of postoperative rhinorrhea, the placement of a continuous closed system or intermittent CSF drainage via a lumbar subarachnoid catheter may be considered to allow the leak to seal. The lumbar catheter can either be inserted as a prophylactic procedure prior to the operation in the awake patient or postoperatively if CSF leak is encountered intraoperatively.[14]

Post-operative Care

Patients should be instructed that mouth breathing will be required in the postoperative period because of bilateral nasal packs.

The incidence of PONV after transsphenoidal procedures seems to be less frequent than that reported for supra and infratentorial craniotomy.[15] Nevertheless it is important that any PONV need to be treated aggressively as it may dislodge the fat graft placed within the sella and sphenoid sinus.

Patients are usually extubated immediately after the surgery and admitted to a high dependency unit for post-operative care. Immediately post-anaesthetic concerns include compromised airways (due to bilateral nasal packing) or bleeding into airway. Diabetes insipidus can set in quite early if not during the surgery. Monitoring for visual field defects is necessary as any worsening of visual field may indicate compression to the chiasma due to bleeding or direct surgical damage.

Follow up

Provided there are no postoperative complications, glucocorticoid supplementation should be withdrawn after 48 hours, and measurement of morning plasma cortisol levels performed daily between day 3 and 5 postoperatively. Daily clinical assessment of the patient, together with these cortisol results, will determine the subsequent use of glucocorticoid replacement therapy.

Frequency of follow up depends on the size of the residual tumor, the presence or absence of residual visual field defects, and the possibility of further endocrine loss following radiotherapy.

References

1. Levy A, Lightman SL. The pathogenesis of pituitary adenomas. *Clin Endocrinol* 1993;**38**:559-70
2. Fortnightly Review: Diagnosis and management of pituitary tumors. A Levy, S L Lightman. *BMJ* 1994;**308**:1087-91
3. Cortell JE, Smith DS, editors. Anaesthesia and Neurosurgery 4th ed. Mosby; 2001:591-609.
4. O' Brien T, O'Riordan DS, Gharib H, et al: Results of treatment of pituitary disease in multiple endocrine neoplasia, type I. *Neurosurgery* 1996;**39**:273-279
5. Hardy J.The transsphenoidal surgical approach to the pituitary. *Hospital Practice* 1979;**7**:81-89
6. Ciric I, Ragin A, Baumgartner C, et al. Complications of transsphenoidal surgery: results of a national survey, review of the literature, and personal experience. *Neurosurgery* 1997; **40**:225-237
7. Hoffman LD, DeSilva M, Humprey RP, et al: Aggressive surgical management of craniopharyngiomas in children. *J Neurosurg* 1992;**76**:47-52
8. Carazzuti V, Fischer EG, Welch K, et al. Neurologic and psychophysiological sequelae following different treatments of craniopharyngioma in children. *J Neurosurg* 1983;**59**:409 – 417
9. Molitch ME: Medical treatment of prolactinomas. *Endocrinol Metab Clin North Am* 1999;**28**:143–169
10. Piper JG, Dirks BA, Traynelis VC, VanGilder JC. Perioperative Management and Surgical Outcome of the Acromegalic Patient with Sleep Apnea. *Neurosurgery* 1995;**36**(1):70–75
11. Breivik H. Perianaesthetic management of patients with endocrine disease *Acta Anaesthesiologica Scandinavica* 1996;**40**(2):1004-1015
12. Inder WJ, Hunt PJ. Glucocorticoid Replacement in Pituitary Surgery: Guidelines for Perioperative Assessment and Management. *Journal of clinical endocrinology and metabolism*. 2002;**87**(6):2745-2750
13. Nemergut EC, Dumont AS, Barry UT, Laws ER. Perioperative Management of Patients Undergoing Transsphenoidal Pituitary Surgery. *Anesth Analg* 2005;**101**:1170 –81
14. Jane et al. Pituitary Surgery: Transsphenoidal Approach. *Neurosurgery* 2002;**51**:435-444
15. Flynn BC, Nemergut EC. Postoperative Nausea and Vomiting and Pain After Transsphenoidal Surgery: A Review of 877 Patients *Anesth Analg* 2006;**103**:162–7

Contemporary Issues in Effective Paediatric Pain Management

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Pain is defined as unpleasant sensory, emotional and/or motor perception resultant from actual or potential tissue damage. It is considered as "the fifth vital sign" by the new *Joint Commission on Accreditation of Healthcare Organization* (JCAHO), which requires healthcare professionals to address, assess and to treat regularly in order to alleviate unnecessary suffering to the patients of all age groups.[1] However, pain remains one of the most misunderstood, underdiagnosed and hence undertreated complex clinical symptom especially among the paediatric age groups. That the experiencing of pain is basically subjective makes its objective measurement extremely difficult.

Traditionally, healthcare professionals tend to believe that young infants or neonates do not feel much pain. This is attributed to a misconception that in this group of patients, their nervous system is relatively immature and therefore unable to perceive much nociception. These myths have been proven to be inaccurate as researchers have shown that the foetal central nervous system is relatively well-developed in as early as the 26th week of gestation, with neurochemical and anatomical capabilities of experiencing nociception. In this respect, suboptimal pain treatment rendered to premature babies and neonates may have implications that extend beyond infancy, including hypersensitivity to noxious stimuli in the later life.[2]

Paediatric patients are unique when it comes to pain management. On one hand, they are exceptionally sensitive to opioids owing to the fact that their central nervous system, hepatic and renal functions are relatively immature. On the other hand, their total requirement of opioids may be higher than the adults (in terms of per body weight requirement), which can be attributed to their higher degree of extra-cellular fluid compartment as well as volume of distribution. Besides, it is also important to note that patients presenting for repeated procedures may actually require more analgesia for the same degree of painful stimulus and this should be taken into consideration in the planning of their pain management.

As paediatric patients traverse over various developmental stages, it is important to take into account their respective physiological, psychological and emotional responses to pain perception while formulating their pain management plan. Identification of the presence and severity of pain in these patients is a challenging endeavour and requires experience as well as patience on the part of the clinician. When dealing with pre-verbal age groups in particular, their inability to convey the pain perception often leaves interpretation of the level of pain perplexing. A relatively inexperienced healthcare provider or parent may sometimes mistake the uncommon presentations of pain to non-noxious manifestations such as hunger, wetting or fear of unfamiliar surroundings, subsequently leading to delayed or inadequate pain treatment. Hence, pain assessment of paediatric patients should be undertaken with techniques which are appropriate to their developmental level. Members of the pain team need to go down to the child's level in order to gain an insight into the child's condition. For children who are unable to communicate or are at age less than 3 years, they should be assessed using the *FLACC scale* (appendix 1). In contrast, the FACES pain rating scale as advocated by Baker & Wong,1987 should be used for those aged 3 and above (appendix 2).

As for children who are able to use descriptory words and understand well the concepts of rank and order, methods of pain assessment such as the numerical scale, colour scale or word scale can be utilized instead.[3] Whenever possible, all manners of description of pain such as the location, duration, character and intensity should be explored among the older age groups as they often provide valuable information that contributes to successful pain management.

The common pitfalls of paediatric pain management include under dosing on the clinician's part for fear of adverse complications such as respiratory depression and cardiovascular compromise, especially in non-intubated children. The misconceived parental worry of addiction and subsequent physical dependence as well as the possible undesirable long term effects of analgesics to their children do not help either. All these often lead to a less aggressive approach with subsequent administration of subtherapeutic doses to the patients especially among the pre-verbal age groups and neonates.[4] Such undertreatment can be circumvented by formulation of a comprehensive pain management plan encompassing careful incremental titration of analgesics and proper monitoring of the patients. The development of institutional protocol and guidelines will help to "safe-guard" the process of pain management. In addition, healthcare professionals should engage in continuous medical education and alleviation of unfounded parental fears. Nevertheless, the role of family members in the pain management of patients should not be underestimated, for they can assume active and important roles such as early detection of untoward incidents or help in the administration of analgesics in suitable conditions (e.g. parent-controlled analgesia or parent monitored analgesia).

In recent years, the multi-modal approach utilizing a combination of techniques and/or medications has gained popularity and been proven to achieve greater success in pain management of paediatric patients. This approach effectively modulates pain perception at multiple levels. In addition, its advantage of avoiding excessive dosage of any single analgesic is often extolled.

It is imperative that the attending anaesthesiologist formulate a suitable anaesthetic and pain management plan in accordance to the patient's needs as well as the nature of the surgery. This would entail a comprehensive pre-operative assessment and preparation. Apart from conducting a thorough history and physical examination, these preoperative visits by the anaesthesiologist are helpful in establishing a rapport with the patient and the parents as well as alleviating their anxiety. Issues which may influence the pain management plan such as co-morbid diseases, surgical site, postoperative disposition and family consent for pain management techniques should be addressed and agreed upon during this preoperative session. In view of the fact that children abhor needles and its associated pain, inhalational induction should be considered before embarking on obtaining intravenous access. Alternatively, EMLA cream (Eutatic Mixture of Local Anaesthetic) should be applied to prospective venupuncture sites at least one hour before-hand prior to sending to the operating theatre. Besides sedative pre-medication, pre-emptive analgesia such as oral paracetamol or NSAIDs (Non-Steroidal Anti-Inflammatory Drugs) may be prescribed as it would minimize subsequent postoperative analgesic consumption as well as improve time to first rescue analgesia post-operatively.

The presence of the parents or guardians in the operating theatre on the day of surgery will help to avoid unwarranted agitation of the patient prior to induction of anaesthesia. This practice should be encouraged in all cases, if possible. A balanced anaesthesia approach which utilizes opioids, in conjunction with inhalational agent administration (with muscle relaxant as well in certain cases) remains the much favoured technique. Other agents which aid intra-operative analgesia such as ketamine, tramadol, codeine and clonidine may be considered in selective cases. However, some of these agents are not available in our local setting.

By and large, young children who undergo day care operations usually experience minor or manageable post-operative pain. They can be treated with simple paracetamol, regional, peripheral nerve blockade and/or simple local infiltration. Conversely, for those who are admitted electively and subjected to more complex procedures, opioids should be administrated judiciously and titrated to the needs of the patient especially if nursed in a non-high dependency setting post-operatively. In critically ill patients who remain intubated post-operatively, opioid infusion provides effective pain relief as well as decrease in sedation needs in the ICU setting. In the normal ward setting, patient-controlled analgesia with morphine (or sometimes, parent or nurse-controlled analgesia) may be considered for suitable patients if they can understand and obey instructions well.[5,6]

In certain cases, intraoperative surgical pain can be alleviated with central neuraxial blocks/analgesia techniques such as epidural (either caudal, lumbar or

thoracic depending on the desired level of analgesia), subarachnoid or plexus blockade. These techniques are highly effective, coupled with relatively low complication rates in experienced hands and are widely practiced nowadays. The benefits of the epidural analgesia may also be extended to the post-operative period.

Apart from these factors, good surgical skills with minimal tissues handling or damage and strict perioperative infection control are pivotal, considering the fact that uncomplicated wound healing is usually associated with lesser pain perception.

The therapeutic effects of the non-pharmacological methods are essential and should not be underestimated. Active participation and support from ward nurses, physiotherapists, play therapists and child psychologist are important as well in ensuring effective pain alleviation.[7] Maintenance of good communication among members of a cohesive team will eventually contribute to the improvement and success of the overall pain management.

Quality assurance measures include proper database and record-keeping, which should be handled by dedicated staff. These audits are important in streamlining pain management protocol and guidelines for the benefit of the patients. The audits will also ensure consistency in practices and avoidance of unnecessary errors. Efforts should be made to provide for sufficient funds for the purpose of promoting continuous education as well as equipment upgrading and purchases. All the members of the pain management team should meet on a regular basis to facilitate the smooth running of team, tackle on-going problems, and provide consultations and discussions on implementation of new guidelines or protocols.

The advancement and refinement of paediatric anaesthesia over the years has seen the effectiveness of various pharmacological and non-pharmacological methods of analgesia established from research in paediatric patients rather than mere extrapolation from studies on adult patients. As the understanding of paediatric pain improves, pain management has become an indispensable and integral part of paediatric anaesthesia. As such, continuous educational programmes should be made freely available to inculcate all healthcare professionals with a better understanding of effective paediatric pain management.

In summary, effective paediatric pain management is an intergration of good understanding of paediatric pain issues, quality assurance and continuous education.

Reference

1) Ellis J, O' Connor BV, Cappelli M, Goodman JT, Blouin R, Reid CW. Pain in hsopitalized pediatric patients: How are we doing? *Clinical Journal of Pain*. 2002; **18**:262-269.

2) Anand KJ, Brown MJ, Causon RC. Can the human neonate mount an endocrine and metabolic response to surgery? *J Pediatr Surg*. 1985;**20**(1):41-48.

3) Amy LD, David CB, Marc HG. Pain assessment for pediatric patients in the Emergency Department. *Pediatrics*. 2006; **117**(5):1511-1518.

4) Jan PH, Huda Huijer AS, Marcel A, Ruud JG. Are children given insufficient pain-relieving medication postoperatively? *J of Advanced Nursing*. 1998; **27**(1):37.

5) Monitto CL, Greenberg RS, Kost-Byerly S, Wetzel R, Billett C, Lebet RM, Yaster M. The safety and efficacy of parent-/nurse-controlled analgesia in patients less than six years of age. *Anesth Analg*. 2000; **91**(3):573-579.

6) Tarja P, Katri VJ, Anna-Maija P. Parents' roles in using non-pharmacological methods in their child's postoperative pain alleviation. *J of clinical nursing*. 2002; **11**(4):526.

Appendix 1:

The FLACC is a behaviour pain assessment scale © University of Michigan Health System

- this is a behaviour scale that has been tested with children age 3 months to 7 years.
- each of the five categories (Faces, Legs, Activity, Cry, Consolability) is scored from 0-2 and the scores are added to get a psychological status, anxiety and other environment factors.

FACE	**(0)** no particular expression or smile	**(1)** occasional grimace or frown withdrawn disinterested	**(2)** frequent to constant frown, clenched jaw, quivering chin
LEGS	**(0)** normal position or relaxed	**(1)** uneasy, restless, tense	**(2)** kicking, or legs drawn up
ACTIVITY	**(0)** lying quietly, normal position, moves easily	**(1)** squirming, shifting back and forth, tense	**(2)** arched, rigid or jerking
CRY	**(0)** no cry (awake or asleep)	**(1)** moans or whimpers, occasionally complaint	**(2)** crying steadily, screams or sobs, frequent complaints
CONSOLABILITY	**(0)** content, relaxed	**(1)** reassured by occasional touching, hugging or "talking" to, distractible	**(2)** difficult to console or comfort

Appendix 2:

- The Faces Pain Score, by Baker & Wong (1987).
- The pain team should be informed as soon as the score is ≥ 6 while in the ward.