TOTAL INTRAVENOUS ANAESTHESIA FOR PAEDIATRICS

A practical guidebook

1st Edition

College of Anaesthesiologists,
Academy of Medicine of Malaysia

Malaysian Society
of Anaesthesiologists

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Disclaimer: The contents of these guidelines are based on the consensus of the expert panel on the best practices as currently practiced by them, based on their knowledge of available scientific evidence and best clinical practice guidelines. Healthcare professionals are expected to exercise their clinical judgment when utilising the information within. The information is presented with the intention of guidance only and should not replace the responsibility of the user to make decisions appropriate to the circumstances of the individual patient and based on the correct and most current information of the drug(s) being considered. Doses should be titrated according to individual patient characteristics, anaesthetic needs and clinical effect.

This pocket reference serves as a resource for both first time users and experienced users of TIVA. It is mostly relevant for relatively healthy children (American Society of Anaesthesiology [ASA] physical status I or II), allowing for some degree of flexibility in different circumstances.

03 INTRODUCTION

Total intravenous anaesthesia (TIVA) is the technique of delivering and maintaining general anaesthesia using intravenous (IV) agents. Though inhalational anaesthesia is still widely used in children, the advent of newer drugs with favourable pharmacokinetic and pharmacodynamic properties have made TIVA a more popular choice in the past decade.[1,2] Inhalational anaesthesia comes with its own set of disadvantages such as irritability during induction and emergence, prolonged emergence, agitation, nausea and vomiting and environmental contamination. In TIVA the combined use of IV anaesthetic agents allow for reduced dosage resulting in reduced adverse effects and time to emergence.[2]

With the availability of short acting opioids and the understanding of the favourable pharmacokinetic and pharmacodynamic properties of propofol, TIVA has been gaining popularity among paediatric anaesthesiologists. Even though the volume of distribution and clearance of propofol are increased in children, the use of target-controlled infusions (TCI) of propofol and dosing requirements for paediatric patients are now being established. Propofol has an added benefit of having an antiemetic effect resulting in the reduction in post-operative nausea and vomiting. Remifentanil on the other hand has many properties of the “ideal IV anaesthetic” and unlike other opioids is independent of hepatic or renal clearance and therefore has a highly predictable termination of its effects regardless of dose and duration of infusion. This combination with their respective characteristics is an attractive one.[2]

03 INTRODUCTION

Some of the advantages of TIVA in children are very rapid inductions and achievement of equilibrium between plasma and effect site, improved quality of emergence from anaesthesia, smooth and peaceful recovery, no risk of environmental pollution, increased patient comfort, parental satisfaction in the post-operative period and can be administered in patients undergoing airway procedures. Furthermore, TIVA has been shown to reduce the incidence of one of the most common complications in paediatric anaesthesia which is laryngospasm in paediatric patients undergoing general anaesthesia. The disadvantages are pain experienced during propofol administration, the need of specialised perfusors, depth of anaesthesia monitoring and difficulty to estimate blood concentration of propofol in real time at the moment.[1]

TCI uses a simulated calculation programmed into perfusor using real-time pharmacokinetic models to deliver the bolus dose and infusion rates of anaesthetic agents to achieve user-defined target plasma or effect site concentration. These programs are incorporated in microprocessors within certain perfusors.[1] However, with majority of adult TCI models confining the age of use to patients above 16 years old and/or those above 30 kilogram (kg), there is limited availability of TCI systems for use in children. To date, there are only two TCI systems validated for use in children. These are the “Paedfusor” and the Kataria models, both for the use of TCI with propofol. “Paedfusor” has an age limit of above 1 year old and a minimum weight of 5 kg whereas the Kataria model limits the age to above 3 years and a minimum weight of 15 kg. Neither of these models allow for weight of over 61 kg in paediatric patients.

03 INTRODUCTION

As for opioids, we have yet to see pharmacokinetic models for TCI delivery in children. The Minto model for remifentanil accommodates for weights above 30 kg and height above 1.3 meters (m). Therefore, for children below these limits, mass rate infusion is employed. There are still considerable gaps in pharmacokinetic models for some drugs in ill children and for young children, infants and neonates. In view of this, caution is needed when these models are being used in this segment of patient population and the anaesthesiologist must still be knowledgable and experienced in titration of the IV agents to avoid awareness, pain and adverse effects.

To date there is a lack of guidelines for the administration of TIVA in paediatrics. This has prompted the writing committee to spearhead the first edition of a practical guidebook to assist those involved in paediatric anaesthesiology, particularly for those interested in TIVA for paediatric patients. The content and recommendations in this guidebook is based on the writing committee's knowledge, experience and available scientific evidence on this subject.

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USES & BENEFITS OF TOTAL INTRAVENOUS ANAESTHESIA IN PAEDIATRICS

TIVA can be used in virtually any type of case unless contraindicated.

Appropriate uses of TIVA

1.	Neurosurgical procedures
2.	Surgical procedures requiring neurophysiological monitoring, such as spine surgery
3.	Cardiac catheterisation
4.	Ambulatory surgery
5.	Malignant hyperthermia susceptible patients
6.	Patients at risk of post-operative nausea and vomiting
7.	Airway surgery (e.g. bronchoscopy or laser surgery)
8.	Lobectomy via thoracotomy/pneumonectomy/video-assisted thoracoscopic surgery
9.	Procedural sedation and monitored anaesthesia care

04

USES & BENEFITS OF TOTAL INTRAVENOUS ANAESTHESIA IN PAEDIATRICS

Relative contraindications of TIVA

1. Neonates
2. Mitochondrial disease
3. Medium chain acyl-CoA dehydrogenase deficiency (MCADD)

Benefits of using TIVA

1. Can be employed in remote areas
2. Less airway complications – particularly laryngospasm, hence can be extubated any time with spontaneous breathing
3. Less nausea and vomiting
4. Improved quality of recovery
5. Less emergence delirium/agitation
6. Reliable delivery of anaesthesia when airway/ventilation is difficult
7. Decrease operation theatre (OT) pollution

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PRINCIPLES OF TOTAL INTRAVENOUS ANAESTHESIA

1. **Ensure adequate hypnosis.**
   a. Application of pharmacokinetic and pharmacodynamic knowledge will ensure correct dosage that leads to smooth anaesthesia and quick recovery.
   b. Depth of anaesthesia monitoring (e.g. Bispectral index [BIS]) helps to ensure adequate hypnosis without over depressing the cardiovascular system; however, it is not essential for all patients.

2. **Ensure adequate analgesia/suppression of reflex.**
   a. Titrate remifentanil infusion to intensity of surgical stimulus.
   b. Higher doses of remifentanil can prevent movement. This cannot be achieved with the longer acting opioids such as morphine and fentanyl, without delayed recovery.
   c. Ensure adequate post-operative analgesia as remifentanil has short duration of action. Administer morphine or any other appropriate analgesic at least 45 minutes before end of surgery. For surgical procedures pre-emptive multimodal analgesia is required before remifentanil infusion has been switched off.

3. **Ensure haemodynamic stability.**
   a. Haemodynamic instability may occur despite adequate hypnosis and analgesia.
   b. Consider hypotensive agents if blood pressure (BP) is persistently elevated.
   c. Consider fluids, vasoactive agents or inotropic agents if BP is persistently low.
   d. Consider atropine if bradycardia develops.

05 PRINCIPLES OF TOTAL INTRAVENOUS ANAESTHESIA

4. **Ensure muscle relaxation.**
   a. Propofol has weaker muscle relaxant properties than inhalation agents. Thus, more frequent doses of neuromuscular blockers may be required when using propofol for maintenance of anaesthesia without remifentanil.

06
GENERAL CONSIDERATIONS

1. **Ensure that the necessary information is available for calculation of the infusion rate.**
   This includes weight, age, height and gender.

2. **Select the appropriate pharmacokinetic model.**
   Avoid modifying adult models and only use paediatric models to avoid under dosing especially in children who are less than 30 kg. For children above 61 kg use the Marsh adult model.

Table 1. Pharmacokinetic model selection for total intravenous anaesthesia using target controlled infusions

Drug	Target	Pharmacokinetic model
Propofol	Plasma concentration	Kataria : > 15 kg (3 - 16 years); Max: 61 kg Paedfusor: > 5 kg (1 -16 years); Max: 61 kg
Remifentanil	Plasma/ effect-site concentration	Minto model: > 30 kg MASS rate infusion: < 30 kg

3. **Start TCI at a high concentration and titrate downwards.**

4. **Depth of anaesthesia monitoring such as BIS, Entropy and auditory evoked potential (AEP) can be used to help titrate the depth of anaesthesia but not mandatory for all patients particularly in those under 1 year of age.**

06
GENERAL CONSIDERATIONS

5. **Drug dosage should always be adjusted according to the response of the patient.**

6. **For surgical procedures pre-emptive multimodal analgesia is required before remifentanil infusion has been switched off.**

7. **Consider minimising dose of propofol in all paediatric patients using a combination of opioids and local anaesthetic (LA) blocks.**

8. **For obese children use the total body weight (TBW) to calculate the dose needed for infusion. Start with a lower target concentration and consider depth of anaesthesia monitoring.**

9. **A fully functional anaesthetic machine together with inhalation anaesthetic agents, vaporisers and gas monitors are essential.**

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EQUIPMENT REQUIREMENTS: GENERAL PRINCIPLES

1. A checklist minimises errors during TIVA pre-anaesthetic setup (see Appendix 1).
2. Conduct an apparatus check before administration of anaesthesia. Ensure that the batteries of the pumps are charged.
3. Backup equipment is useful, but not mandatory.
4. Ensure the occlusion alarm has been set.
5. Select a syringe of an equivalent volume from the pump library.
6. Use non-return/one-way valves on any intravenous line.
7. If a one-way valve is not available, use a dedicated intravenous cannula appropriate for the patient's age.
8. Due to the risk of disconnection, it is advisable to use Luer Lock systems.
9. Clearly label intravenous connectors and valves.
10. Minimise dead space.

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EQUIPMENT REQUIREMENTS: GENERAL PRINCIPLES

11. Avoid non-invasive blood pressure (NIBP) monitoring on the same arm as the intravenous infusion.
12. It is advisable to choose a large peripheral vein.
13. Sites of intravenous infusions should be visible and intermittently monitored for dislodgement or extravasation, wherever possible.
14. Check for leakage at all points intermittently.
15. Check for kinks in the infusion tubing intermittently.
16. Remove air bubbles from syringe.
17. Do not run vasoactive drugs and TCI through the same intravenous line.
18. Avoid high concentrations of drugs running at low speeds.

08 INDUCTION OF ANAESTHESIA

Table 2. Dosage schemes for induction of total intravenous anaesthesia

Drug	Target controlled infusion	MASS rate infusion	Comments
Propofol	TCI 5-6 µg/ml till LOC.	Not recommended.	Administer at "Flash" rate.
Remifentanil *For patients > 30 kg use the Minto model TCI.*	Spontaneous breathing: 1-2 ng/ml[§].	A bolus of 0.2-0.3 µg/kg. Then infusion at 0.1 - 0.2 µg/kg/min.	Administered over 60 seconds.
	Intubated patients: 4-5 ng/ml.	A bolus dose of 0.5 - 1.0 µg/kg. Then a mass rate infusion of 0.3-0.5 µg/kg /min.	

In addition to the above, induction via volatile agents can be done. If gas induction is done, consider starting propofol at 4 µg/ml.

LOC – Loss of consciousness

[§] Bradycardia with or without hypotension seen when targeting the effect-site may be greater than when targeting the plasma concentration.

09 MAINTENANCE OF ANAESTHESIA

Table 3. Dosage schemes for maintenance of total intravenous anaesthesia

Drug	Target controlled infusion	MASS rate infusion
Propofol	Range: 2.5-4.0 µg/ml* - Try to minimise target concentration of propofol. -Titrate according to patient response or depth of anaesthesia monitoring.	Not recommended.
Remifentanil¶ *For patients > 30 kg use the Minto model TCI.*	Spontaneous breathing: 1-2 ng/ml.	0.05 - 0.2 µg/kg/min.
	Intubated patients: 3-8 ng/ml†.	0.2-1.0 µg/kg/min.

* The lower limit of the target concentration is 2 µg/ml when depth of anaesthesia monitoring is used.
† For more stimulated cases go to higher concentration.
¶ A lower dose of remifentanil can be used with a LA block.

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ALGORITHM FOR THE PRACTICAL MANAGEMENT OF TOTAL INTRAVENOUS ANAESTHESIA: SPONTANEOUS BREATHING

Suggested total intravenous anaesthesia regimen

1. Start remifentanil infusion (Refer to Table 2).
2. After the target concentration of remifentanil has been reached, start propofol TCI at a target concentration of 5 µg/ml.
   a. If loss of consciousness (LOC) is not achieved within 1 minute, step up the target concentration by 0.5 µg/ml every 30 seconds (sec) until LOC is achieved.
3. Insert laryngeal mask airway (LMA) when patient is relaxed.
4. Perform LA block if necessary.
5. During surgery, adjust target concentrations of propofol TCI within a range of 2.5-4.0 µg/ml and remifentanil infusion, according to the clinical responses of the patient and the co-administration of other agents.
   Note: If depth of anaesthesia monitoring is not used, the propofol target concentration should be gradually decreased to and then maintained at 3 µg/ml. It may be necessary to assist ventilation if respiratory rate (RR) drops to < 10/min.
6. Increase remifentanil infusion when surgical stimulation is expected.

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ALGORITHM FOR THE PRACTICAL MANAGEMENT OF TOTAL INTRAVENOUS ANAESTHESIA: SPONTANEOUS BREATHING

7. Administer morphine or any other appropriate analgesic at least 45 minutes before end of surgery. For surgical procedures pre-emptive multimodal analgesia is required before remifentanil infusion has been switched off.

8. Stop propofol during skin closure.

9. Stop the remifentanil infusion during dressing.

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ALGORITHM FOR THE PRACTICAL MANAGEMENT OF TOTAL INTRAVENOUS ANAESTHESIA: VENTILATED

Suggested total intravenous anaesthesia regimen

1. Start remifentanil infusion (Refer to Table 2).
2. After the target concentration of remifentanil has been reached, start propofol TCI at a target concentration of 5 µg/ml.
   a. If LOC is not achieved within 1 minute step up the target concentration by 0.5 µg/ml every 30 sec until LOC is achieved.
3. Administer muscle relaxant to facilitate endotracheal tube (ETT) placement.
4. If intubation is planned, titrate remifentanil infusion upwards (Refer to Table 2).
5. Manage hypotension with intravenous fluids.
6. Insert ETT/LMA when patient's supraglottic airway is relaxed.
7. Perform LA block if necessary.

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ALGORITHM FOR THE PRACTICAL MANAGEMENT OF TOTAL INTRAVENOUS ANAESTHESIA: VENTILATED

8. During surgery, adjust target concentrations of propofol TCI within a range of 2.5-4.0 µg/ml and remifentanil infusion, according to the clinical responses of the patient and the co-administration of other agents.
Note: If depth of anaesthesia monitoring is not used, the propofol target concentration should be gradually decreased to and then maintained at 3 µg/ml.

9. Increase remifentanil infusion when surgical stimulation is expected.

10. Administer morphine or any other appropriate analgesic at least 45 minutes before end of surgery. For surgical procedures pre-emptive multimodal analgesia is required before remifentanil infusion has been switched off.

11. Stop propofol during skin closure.

12. Reverse paralysis upon return of muscle power.

13. Stop remifentanil infusion after reversal of neuromuscular blockers.

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PREVENTING POST-OPERATIVE PAIN AFTER REMIFENTANIL

1. Consider regional anaesthetic techniques/local infiltration whenever possible.
2. Administer IV morphine 0.1-0.2 mg/kg at least 45 minutes before end of operation.
3. Consider IV paracetamol 30 minutes before end of surgery, unless contraindicated.
4. If the patient reports severe pain in the recovery room, consider a bolus of IV fentanyl 0.5 - 1 µg/kg or/and IV morphine 0.05 mg/kg boluses. Repeat morphine boluses as required.
5. Consider anti-emetics when opioids are used.

13 BIBLIOGRAPHY

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APPENDIX 1: TIVA CHECKLIST

PLEASE ENSURE THAT THIS CHECKLIST HAS BEEN COMPLETED BEFORE STARTING TIVA FOR YOUR PATIENTS

1. TCI pumps with power cables. ☐
2. Drug filled syringes with perfusor tubings. ☐
3. Dedicated IV line or non-return valves with 2 three way taps connected to patient's IV cannula. Ensure secured tightly. ☐
4. Propofol 1% (10 mg/ml) & remifentanil (Minto model: 50 µg/ml or MASS rate infusion: 20 µg/ml). ☐
5. TCI programme for **propofol**
   - Kataria or Paedfusor Model (Details for Age, Weight, Height and Sex must be entered). ☐
   - Choose plasma concentration. ☐
   - Set target concentration (i.e. 5–6 µg/ml for Target Concentration) (ensure correct units). ☐
   - Connect to 3 way connector attached to patient's IV cannula. ☐
6. TCI Programme for **remifentanil**
   - Ensure correct dilution for remifentanil. ☐
   - Minto or MASS rate infusion model, plasma or effect-site concentration. ☐
   - If effect-site concentration, aim for 1-2 ng/ml for spontaneous breathing or 4-5 ng/ml for intubated patients (ensure correct units). ☐
   - Adjust according to surgical stimulus. ☐
   - Connect to 3 way connector attached to patient's IV cannula. ☐

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APPENDIX 1: TIVA CHECKLIST

PLEASE ENSURE THAT THIS CHECKLIST HAS BEEN COMPLETED BEFORE STARTING TIVA FOR YOUR PATIENTS

7. Ensure no leakages and that patient's IV cannula is always visible during the surgery (if possible). ☐

8. No other drugs should be administered via the TCI infusion line (unless absolutely necessary e.g. during induction). A separate IV line should be used for infusion of IV fluids. ☐

9. Infusion lines should be checked every 15 minutes during surgery, if possible (akin to checking for disconnection of the breathing circuit). ☐

10. If BIS is used, check placement before and after surgical draping. Be careful of surgical antiseptic solution getting between the skin and the BIS electrode. ☐

At conclusion of case, ensure all tubings/IV cannulae which had propofol and remifentanil are flushed to prevent inadvertent boluses in the ward.

15 APPENDIX 2: REMIFENTANIL

Remifentanil is an opioid agonist with rapid onset and an ultra-short duration of action. It rapidly equilibrates with the brain and has a constant context-sensitive half time of 3 to 6 minutes. The time taken to reach a steady-state concentration is 5–10 minutes.

However, severe adverse events may occur if remifentanil is used incorrectly.

1. Haemodynamic effects
   (a) Dose-dependent hypotension and bradycardia.
   (b) Bradycardia can be reversed with glycopyrrolate, atropine or ephedrine.
   (c) Hypotension - reduce rate of infusion or administer fluids.

2. Respiratory effects
   (a) Depression of respiration in a dose-related fashion.
   (b) Spontaneous respiration occurs at 4 to 5 ng/ml.

3. Muscle rigidity
   (a) Related to the dose and speed of administration.
   (b) Occurs when > 1 µg/kg is administered in less than 60 seconds.
   (c) Decreased by decreasing infusion or administering a neuromuscular blocker.

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APPENDIX 2: REMIFENTANIL

4. In view of the above an IV bolus should only be given
   (a) To intubated patients during the maintenance of general anaesthesia.
   (b) For induction of anaesthesia in non-intubated patients.
   (c) Up to < 1 µg/kg over 60 seconds.

5. Stopping remifentanil
   (a) There is rapid dissipation of respiratory depressant effect.
   (b) Analgesic effects fade off very fast after terminating an infusion - need to ensure rescue analgesics are given before or soon after end of surgery.

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APPENDIX 3: PREVENTING PAIN DURING INDUCTION OF PROPOFOL TCI

1.	Use a fast running IV line.
2.	Initiation of remifentanil infusion before propofol.
3.	Lower the TCI of propofol, or step up slowly to achieve the target.
4.	IV Lignocaine 0.5 - 1.0 mg/kg prior to propofol induction.

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