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### Paediatric total intravenous anaesthesia

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#### **Key points**

- Paediatric total i.v. anaesthesia (TIVA) can facilitate surgery, reduce airway responsiveness, and minimize complications such as postoperative nausea and vomiting and emergence agitation.
- Bolus doses of propofol are largely determined by the volume of distribution, while required infusion rates are predominantly determined by the clearance.
- Manual infusions remain an important option in clinical practice due to variability within and between target-controlled infusion models.
- Adjuvant agents, such as remifentanil and dexmedetomidine, play an important role in minimizing propofol requirements.
- Avoidance of neuromuscular block, and the adjuvant use of processed EEG, is recommended to aid titration and lower the potential risk of awareness.

Total i.v. anaesthesia (TIVA) has been used in adult practice since 1982 with target-controlled infusion (TCI) regimes available since 1989. Conversely, the use of TIVA in paediatric practice is far less routine with a survey finding only 10% of paediatric anaesthetists using it weekly or more. It has previously been the subject of a special edition of the journal *Pediatric Anaesthesia* and the use for paediatric anaesthesia care is an increasing component at

international meetings: educational sessions at the European Society for Paediatric Anaesthesia (2013), ASA (2014), and the Society for Intravenous Anaesthesia meeting in November 2015.

Despite a number of obstacles (including interindividual pharmacokinetic and pharmacodynamic variability and safety concerns regarding propofol infusion syndrome—PrIS), there are notable benefits to TIVA and particular areas where it is indicated for anaesthetic or surgical reasons, where it may surpass volatile anaesthesia.<sup>3</sup> It is a mandatory technique when inhalation agents are contraindicated.

#### **Indications (see Table 1)**

#### Advantages and disadvantages

For physiological and clinical<sup>3</sup> reasons (Table 2), TIVA has increasingly established a significant role in surgery in or around the airway (e.g. ENT) by obtunding airway reflexes (Table 2). The changes in airway reactivity facilitate extubation and result in a minimal incidence of laryngospasm and stridor after extubation. It is readily titratable, so that spontaneous ventilation (SV) may be maintained.<sup>4</sup> It does not rely on the airway for delivery or on airway and pulmonary dynamics for anaesthetic maintenance. Therefore, there is no risk of ambient pollution and exposure of surgical and operating theatre staff to volatile anaesthetics when the airway is shared. TIVA has been seen to be beneficial in those with preoperative respiratory symptoms by reducing the frequency of complications.<sup>5</sup>

Emergence delirium (or agitation) (ED/EA) is common, especially subsequent to sevoflurane anaesthesia, and may

precipitate maladaptive behaviour, memory impairment, and problems with subsequent anaesthetic experiences in paediatric practice. Propofol use, at induction and as maintenance of anaesthesia, has been seen to reduce the risk of ED in comparison with sevoflurane.<sup>6</sup>

Prevention of postoperative nausea and vomiting (PONV) with propofol improves patient experience and may avoid associated complications such as dehydration, electrolyte abnormalities, and delayed discharge. The incidence of PONV in children over 3 yr is double that of adults. Propofol reduces early PONV with number needed to treat quoted as 5.53 in adult practice and is therefore felt likely to benefit children over 3 yr old.<sup>7</sup>

With the current concern surrounding the effects of anaesthesia on the developing brain, propofol may exert some neuroprotective effects; animal studies have shown reduced 'hypoxia-mediated increases in lactate dehydrogenase' and increased neurogenesis. The reduced incidence of emergence delirium has been hypothesized to be a result of this neuroprotective effect. This is thought not to be true for the neonatal brain as propofol does cause apoptosis similarly to isoflurane and ketamine in this population in animal studies. §

Table 1 Indications for use or consideration of TIVA in paediatric cases

Patient	Malignant hyperthermia history, susceptibility, or risk Muscular dystrophy, core myopathy, or neuromuscular disease		
	Previous history of PONV or motion sickness		
	Risk or previous history of emergence delirium		
	History of acute or chronic reactive airways		
	Fear of facemask		
	Minimization of allergy risk		
Surgical	Airway surgery or shared airway procedures		
	Requirement for evoked potential monitoring,		
	e.g. scoliosis surgery		
	Neurosurgical procedures		
	Middle ear surgery		
	Procedures with high PONV risk, e.g. strabismus, T&A		
Procedural	Remote site anaesthesia, e.g. MRI		
	Muscle biopsy for neuromuscular diagnosis		

The disadvantages of TIVA in children include practical issues such as pain on injection and others seen in Table 2. If i.v. access, without undue distress, is not possible in the awake child, then a TIVA infusion may still be used for maintenance of anaesthesia subsequent to an inhalational induction once the cannula is placed. Methods of preventing the pain of injection include co-administered lidocaine (0.2–0.5 mg kg $^{-1}$ , common practice), pre-treatment with other agents such as opioids (e.g. 0.5  $\mu g \ kg^{-1}$  remifentanil),  $^9$  use of a larger vein, lower initial infusion rates, or alternative propofol formulations with altered lipid content (the addition of lidocaine nullifies the differences between formulations).  $^7$ 

Overall cost-effectiveness is difficult to assess with drug costs, disposables, equipment, and patient outcomes all requiring consideration. Propofol and remifentanil have decreased in cost since their introduction and usage is inversely proportional to weight; becoming cheaper in comparison with sevoflurane or desflurane anaesthesia as weight decreases<sup>3</sup> (cost for 60 min: sevoflurane \$54.75, TIVA 10 kg patient \$2.95, TIVA 20 kg patient \$5.91—unpublished hospital data).

There are concerns about awareness when TIVA is used in children, although one study has shown the risk to be lower with TIVA compared with inhalation anaesthesia in paediatric practice.<sup>3</sup> In the recent Fifth National Audit Project, the incidence was higher with TIVA (compared with volatile anaesthesia) in adults, but there was only one paediatric vignette, in a 15 yr old, associated with TCI propofol and neuromuscular block. The risk may be reduced by avoiding neuromuscular block and by using processed EEG (pEEG) monitoring in patients over 2 yr of age or dependent on the monitor available (monitors are not well validated in children and are not valid in infants less than age 2 yr). Caution should be exercised in the light of the recent publication regarding pEEG in awake patients.<sup>10</sup>

Pharmacokinetic and pharmacodynamic variability between paediatric patients, <sup>11, 12</sup> the effect of maturation on propofol metabolism in early life and specific issues in the critically ill, limits use; the extremely variable pharmacokinetics of propofol in neonates and the non-linear changes in both volume of distribution and clearance indicate that it should be used with extreme caution in neonates and ex-premature infants and in the critically ill with organ dysfunction. Caution is also required where vasodilatation would be hazardous, such as in the shocked child or those with certain types of congenital heart disease.

Table 2 Advantages and disadvantages of TIVA in paediatrics<sup>3</sup>

	Advantages		Disadvantages
Clinical	Reduced airway reactivity, laryngospasm and bronchospasm	Clinical	Risk of bacterial contamination
	Improved ciliary function		Pain on injection
	Bronchodilation and preserved hypoxic pulmonary vasoconstriction		Risk of associated metabolic phenomena; PrIS, lactic/metabolic acidosis
	Reduced emergence delirium	Practical	Need for i.v. access and infusion pump(s)
	Reduced PONV		Potential for disconnection, risk of awareness
	Use in neuromuscular disease, core myopathies		Lack of EEG monitoring availability or reliable depth of anaesthesia monitor
Practical	No interference with evoked potential monitoring		No practical, cost-effective point-of-care propofol measurement systems
	Titratable, ease of delivery via pump		•
	Maintenance of SV for remote site anaesthesia	Other	Caution in prolonged procedures or obese patients due to long context-sensitive half-life of propofol
Other	No vapour atmospheric pollution		Environmental effect of plastic waste and waste propofol
	Associated with overall reduced costs		Disposables may be costly

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