Total intravenous anaesthesia in children: a practical guide

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Abstract

Total intravenous anaesthesia (TIVA) is increasingly used for maintenance of anaesthesia in both adults and children. This article will discuss topics relevant to administration of TIVA in children – the potential benefits of TIVA, challenges and some clinical examples of its use.

Keywords Children; intravenous; pharmacology; propofol; remifentanil; TIVA

Royal College of Anaesthetists CPD Matrix: 1A02, 2D02, 2D06

Learning objectives

After reading this article, you should be able to:

- describe the pharmacology of total intravenous anaesthesia (TIVA)
- discuss the benefits of TIVA in children
- recognize the limitations of TIVA

What is TIVA?

Total intravenous anaesthesia (TIVA) is the use of intravenous agents for induction and maintenance of anaesthesia. The most frequently used agent is propofol (2,6-di-isopropylphenol). Other agents used for TIVA include ketamine, midazolam, dexmedetomidine and opioids. In recent years, most TIVA systems use propofol with or without adjuvants.

Pharmacology of propofol

Propofol is a highly lipophilic hypnotic agent formulated in a lipid emulsion and is an excellent hypnotic. Propofol has minimal or no analgesic properties, so any TIVA technique involving propofol requires a clear analgesic management plan, be that intravenous or regional anaesthesia. Intravenous analgesia is often given in the form of opioids or α_2 agonists, however many other agents have also been used. This article will principally focus on the use of propofol alongside remifentanil.

Propofol follows a three-compartment model (Figure 1), in which anaesthesia is achieved by an initial bolus of 3–5 mg/kg. This quickly crosses the blood–brain barrier to lead to the hypnotic effect in the central nervous system (the effect site). Modern infusion pumps can deliver these bolus infusions with rates of up to 1200 ml/hour.[1]

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Maintenance of anaesthesia is by continuous infusion at a lower rate. The rate of infusion depends on the rate of transfer between the various theoretical compartments of the body. These compartments consist of organs with similar blood flow or lipid solubility. After the initial bolus, propofol is distributed to the central compartment [C1], a very well-perfused compartment including the liver and the brain. There is then redistribution to organs with good perfusion [C2], with further redistribution to the poorly perfused adipose tissue [C3] with its large volume.[2]

The relatively quick emergence from a bolus of propofol occurs because of this redistribution into the other compartments, rather than elimination. Redistribution will be higher in healthy children than adults due to their high cardiac index. To prevent emergence, the propofol in the central compartment has to be replaced.

Elimination (clearance) is only from the central compartment and occurs after propofol is metabolized by the liver, mainly by conjugation, with renal excretion of the conjugates. Because clearance is only from the central compartment, propofol does accumulate, especially in the poorly perfused adipose tissue. After a long infusion, even after stopping propofol, propofol will make its way along a concentration gradient (now reversed) from the adipose tissue back into the well-perfused tissues and continue to contribute to hypnotic effect on the brain. This increases time to wake-up after a long infusion. Propofol has a context-sensitive half-time of 20 minutes after an infusion of 4 hours or up to 45 minutes after 12 hours of an infusion.[1]

Remifentanil is a short-acting synthetic opioid working on μ-receptors. It is highly lipid soluble and undergoes rapid blood–brain equilibration. It has an ester linkage that undergoes rapid hydrolysis by non-specific tissue and plasma esterases. This means it is does not accumulate and its context-sensitive half-time (the time for plasma concentration to fall by 50% after stopping a steady state infusion) remains fairly constant even after prolonged infusions. It is metabolized to remifentanil acid that has virtually no clinical effect. This quick offset means it is not be suitable for postoperative analgesia. The use of opioids such as remifentanil allows anaesthesia with lower concentrations of propofol.

Target-controlled infusions (TCI)

Pharmacokinetic models: TCI pumps are programmed with pharmacokinetic parameters for compartment models (e.g. a two-compartment model might contain clearance, intercompartment clearance, central and peripheral volumes). These programmes determine infusion rates to maintain a certain plasma concentration (Cp) or effect site concentration (Ce) in the CNS. Original TCI models were designed using pharmacological data derived from tests in healthy adults. Adult data are not suitable for children due to the increased volume of distribution and higher clearance values in children. There are now data available

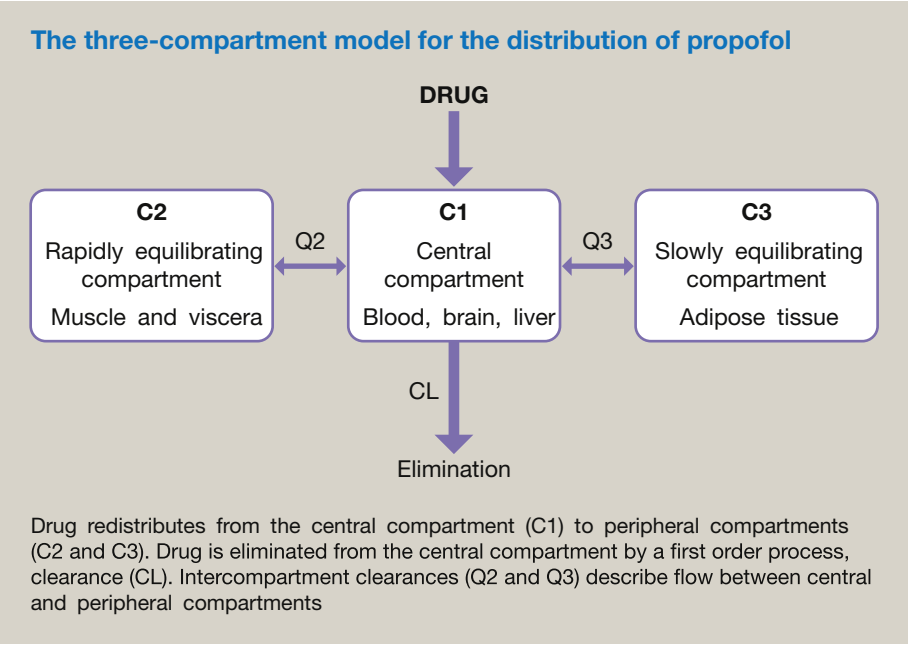

Figure 1

from healthy children over the age of 1 year; these data have been incorporated into many available paediatric pumps. Children tend to require higher initial boluses and maintenance infusion rates due to having higher volumes of distribution, cardiac outputs and clearance rates. There are still limited data in the neonatal and infant populations, where pharmacokinetics have been shown to be variable and unpredictable partly due to the immature hepatic enzyme system.[2]

Infusion regimens have been described that allowed anaesthesia and suitable operating conditions with simple manual pumps. Making adjustments to increase depth of anaesthesia requires further boluses plus an increase in infusion rates. The introduction of TCI pumps has simplified this process. TCI pumps require patient demographics (age, weight) and then use modelling based on pharmacokinetic data to predict dose. Given the widespread availability of these pumps, we recommend their use where possible.

The most widely used paediatric pharmacokinetic parameter sets ('models') used in TCI pumps are the Kataria and Paedfusor models, although many others have been described. The Kataria model has a lower limit of 3 years or 15 kg, whilst the Paedfusor has limits of 1 year or 5 kg. They have both been widely used and seem to perform well, although the Paedfusor model has had the more extensive investigation. They may overestimate initial boluses so care should be taken especially in patients who are potentially haemodynamically unstable. Unlike most adult TCI models, these have no effect site prediction (Ce), so plasma concentration will not reflect the concentration in the brain until equilibration has occurred. This is particularly relevant after a bolus, where it may take up to 5 minutes for the Ce to be equivalent to the Cp. Therefore care should be taken to confirm loss of consciousness prior to insertion of an airway device or administration of neuromuscular blockade at the start of anaesthesia.

One challenge facing the anaesthetist is the increasing incidence of obesity in children. The dose for obese children does not increase in a linear fashion with weight. This is because there is not a linear correlation between clearance and the volume of the central, well-perfused compartment and body weight. It has been suggested that ideal body weight should be used for induction doses and then an allometric scaling factor of 0.75 on total body weight be used to calculate maintenance infusion.[3] However, the use of two weights is not practical for a TCI pump. A rule of thumb is to calculate the ideal body weight and add 20% — this additional weight aliquot takes into account the increased muscle mass that is present in obese patients.

There are TCI models for remifentanil but these have been derived from a very limited populations. The rapid equilibration means that a steady state is achieved very quickly so a selected rate can be used — a microgram per kilogram body weight per minute rate (μg/kg/minute) is commonly used. A rate of 0.1 μg/kg/minute will provide reasonable intraoperative analgesia while rates can be increased up to 0.5 μg/kg/minute for very stimulating procedures.

Between-individual PK variability means that patients will still require different drug concentrations. TCI modelling does not make adjustments for covariates such as anxiety, concurrent opioid use or co-morbidity that may increase or decrease requirements. Closed loop systems that adjust infusions in response to changes in clinical measurements, using processed electroencephalography monitors or auditory evoked potentials, are in development and may further aid safe administration of TIVA. They are unlikely to be predictive so would still need external, medical input; these are not yet available in clinical practice.

Other drugs

There are a variety of intravenous agents that can induce anaesthesia or can be given alongside propofol. Fentanyl and alfentanil both can be given intermittently or as infusions. Unlike remifentanil, they accumulate and cause increased recovery time after prolonged infusion.