Total intravenous anaesthesia

Advances in pharmacokinetic understanding have popularised the safe and effective use of total intravenous anaesthesia delivered by continuous infusion. This article explores why the practical and outcome benefits have made total intravenous anaesthesia an increasingly accepted alternative to use of inhalational agents.

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Introduction

Advances in pharmacokinetic understanding have popularised the safe and effective use of total intravenous anaesthesia delivered by continuous infusion. Administration of inhalational agents remains the most common method of maintaining general anaesthesia, but this article explores the practical and outcome benefits that have made total intravenous anaesthesia an increasingly accepted alternative.

Target controlled infusions

While monitoring the end-tidal concentration of volatile agents is standard practice, there are currently no methods of monitoring plasma drug concentrations in real time. Total intravenous anaesthesia therefore relies on target controlled infusions to ensure adequate and stable drug concentrations at the site of effect.

Target controlled infusion pumps allow the clinician to enter the desired drug concentration to be achieved in the plasma or brain for various intravenous agents. Infusion rates are calculated based on patient variables such as age, sex, height and weight, and infusions are administered and titrated in an automated fashion. Most target controlled infusion systems use a three-compartment pharmacokinetic model, which commonly requires a starting bolus to 'fill' the initial volume of distribution (plasma compartment), followed by a decelerating infusion to compensate for drug elimination and diffusion to two other quickly- and slowly-equilibrating compartments (Nimmo et al, 2019).

Why use total intravenous anaesthesia?

Total intravenous anaesthesia has many, well-evidenced benefits over inhalational anaesthesia. A reduction in postoperative nausea and vomiting is the most notable benefit of propofol-based total intravenous anaesthesia (Johnson, 2017). A meta-analysis including 20 991 patients demonstrated a 39% reduction in relative risk of postoperative nausea and vomiting using total intravenous anaesthesia compared with inhalational anaesthetics (Irwin et al, 2020). A short-acting opioid like remifentanil is commonly administered alongside an anaesthetic agent such as propofol to provide analgesia and dramatically reduce the requirements for anaesthetic agents. The risk of postoperative nausea and vomiting is minimised in practice, but not completely reduced, as a result of the increased risk of using an opioid in conjunction with propofol, as opposed to propofol alone (Johnson, 2017).

Positive modulation of $GABA_A$ (gamma-aminobutyric acid) plays a key role in the anaesthetic effect of propofol. In-vitro studies show that propofol acts upon other receptors concomitantly, including inhibiting the phosphorylation of a subunit of the NMDA (N-methyl-d-aspartate) receptor, to mediate pain signalling. Furthermore, propofol's anti-inflammatory and antioxidant properties significantly impact on the analgesic effect of total intravenous anaesthesia (Irwin et al, 2020). Propofol-based total intravenous anaesthesia achieves a statistically significant reduction in acute pain intensity 24 hours postoperatively. Incidence of chronic pain syndromes is also reduced, compared to that seen if sevoflurane is used (Irwin et al, 2020).

Total intravenous anaesthesia is increasingly used in cancer surgery. An estimated 60% of cancer patients undergo removal surgery (Yap et al, 2019). Major surgery invariably

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entails physiological stress, which in turn alters local and cellular immunity, thought to drive cancer recurrence and metastasis. A meta-analysis of 21 000 patients concluded that using total intravenous anaesthesia for numerous types of cancer surgery is associated with an increase in recurrence-free and overall survival (Yap et al, 2019). In addition, there is strong preclinical evidence that volatile anaesthesia may potentiate the spread of cancer via several mechanisms, for example by reducing the activity of cytotoxic natural killer cells (Yap et al, 2019).

Performing total intravenous anaesthesia also confers practical benefits. The rapid onset and offset characteristics of a propofol and remifentanil combination reduces emergence delirium phenomena, when compared with sevoflurane (Irwin et al, 2020). This makes total intravenous anaesthesia ideal for short surgical cases and to facilitate endoscopy or imaging, without the need for a vaporiser.

Awareness

Accidental awareness is routinely cited as a major disadvantage to total intravenous anaesthesia. A nearly two-fold increased risk has been reported with total intravenous anaesthesia based on case reports and audit, although a large majority of cases are deemed preventable, being linked to poor application of understanding or technical errors (Johnson, 2017). Nevertheless, using processed electroencephalograms is highly recommended for cases requiring neuromuscular blockade (Nimmo et al, 2019).

Conclusions

All anaesthetists should be competent to safely administer total intravenous anaesthesia. Although there is concern about accidental awareness, the risk of this can be mitigated through the use of increasingly sophisticated target controlled infusion systems. Total intravenous anaesthesia effectively reduces postoperative nausea and vomiting and may improve postoperative chronic pain and cancer recurrence. While inhalational anaesthesia has a long and colourful history, total intravenous anaesthesia remains in its relative infancy, although given its promising potential it is likely to play an established role in the future of everyday anaesthetic practice.

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