

# Total intravenous anaesthesia

Eoghan McGrenaghan  
Ming Wilson

## Abstract

Total intravenous anaesthesia (TIVA) is a technique to induce and maintain general anaesthesia exclusively with intravenous anaesthetic agents, thereby avoiding the use of inhalational agents. It is essential that all practicing anaesthetists are competent in the delivery of TIVA and able to perform it safely. TIVA is necessitated in a wide variety of clinical situations when the delivery of inhalational agents is absolutely or relatively contraindicated; for example, in patients with malignant hyperthermia or severe postoperative nausea and vomiting. In other situations, it may not be possible or practical to deliver inhalational anaesthesia such as during patient transfer or anaesthesia for airway surgery. This article describes the use of target controlled infusion models and principles, which enable anaesthetists to deliver TIVA safely. The Association of Anaesthetists of Great Britain and Ireland and the Society of Intravenous Anaesthesia have produced Guidelines for safe practice of TIVA in 2018.

**Keywords** Anaesthesia; intravenous; intravenous agents; target controlled infusions (TCI); total intravenous anaesthesia (TIVA)

**Royal College of Anaesthetists CPD Matrix:** 1A02; 1A03

It was documented in the fifth National Audit Project (NAP5) that total intravenous anaesthesia (TIVA) has been associated with accidental awareness in 28 cases, the majority of which were deemed to be preventable and due to poor understanding of the underlying pharmacokinetic principles. It concluded that all anaesthetists need to be skilled in the administration of TIVA and have a sound understanding of its principles to deliver it safely and it was felt that this is currently not the case.<sup>1</sup> A recent survey of anaesthetists working in the UK and Ireland found that the current training in TIVA was felt to be inadequate and at present many anaesthetists do not feel confident utilizing the technique.<sup>2</sup> Following the publication of NAP5 the Association of Anaesthetists of Great Britain and Ireland (AAGBI) and the Society of Intravenous Anaesthesia (SIVA) have produced Guidelines for safe practice of TIVA in 2018.<sup>3</sup>

## Background

The ideal anaesthetic agents for TIVA should have fast onset/offset times to enable prompt manipulation of depth of anaesthesia while also providing a quick patient wake up time.

**Eoghan McGrenaghan** MB BCh FRCA is a Specialist Anaesthesia Trainee at Salford Royal Hospital, Salford, UK. Conflicts of interests: none declared.

**Ming Wilson** MB ChB FRCA is a Consultant Anaesthetist at Salford Royal Hospital, Salford, UK. Conflicts of interests: none declared.

## Learning objectives

After reading this article, you should be able to:

- describe the indications for using TIVA
- discuss the advantages and disadvantages of TIVA
- set up a target controlled infusion to deliver induction and maintenance levels of intravenous anaesthesia

Propofol is the preferred intravenous anaesthetic agent due to its relatively rapid offset and clear-headed recovery. It is usually administered simultaneously with an opioid infusion most commonly remifentanyl due to its synergistic relationship with Propofol and its rapid onset and offset time. Its synergistic relationship with Propofol facilitates a decrease in the required Propofol target concentration to achieve appropriate levels of anaesthesia while minimizing haemodynamic instability. It also enables swift manipulation of effect site levels to ensure adequate levels of anaesthesia when the degree of surgical stimulus is increased suddenly.

## Indications for TIVA

Table 1 illustrates the various indications for TIVA.

## Pharmacokinetic principles

Effective TIVA relies on clinically adequate levels of Propofol and remifentanyl concentrations at the brain, the target effect site ( $C_{et}$ ) while maintaining an equilibrium with the levels in the plasma, the plasma effect site ( $C_{pt}$ ).<sup>4</sup>

Following the intravenous administration of a drug it is simultaneously subjected to distribution, metabolism and elimination resulting in exponential decline in three distinct phases. These complex processes can be described as a three-compartment model to allow the prediction of drug behaviour following its administration. These compartments are neither anatomical nor related to a corresponding organ but rather a theoretical construct.<sup>5</sup>

When an intravenous drug is administered it directly enters into the plasma which is the central compartment ( $V_1$ ) where it is then simultaneously redistributed to the other compartments while simultaneously undergoing elimination by metabolism and excretion. By knowing the rate at which the drug moves between these compartments and the theoretical volumes of these compartments, mathematical models can be used to predict the concentration of the drug in  $V_1$  after a specified dose is administered intravenously. In order to achieve this population studies have been performed to adjust for individual variables such as age, gender and weight allowing for predictive values by utilizing these mathematical models.

## Three compartment model

These compartments are described as a central compartment ( $V_1$ ) which represents plasma volume or initial volume of distribution and two other equilibrating compartments. Compartment 2 ( $V_2$ ) and compartment 3 ( $V_3$ ) are mathematical constructs

**Indications for TIVA**

Patient indications	Procedural/surgical indications	Other indications
Malignant hyperthermia	Airway surgery	Remote site anaesthesia where volatile agents may not be available
Severe PONV	Neurosurgery	Reduce atmospheric pollution
Neuromuscular disorders and intolerance of muscle relaxants	Surgery requiring neurophysiological monitoring	Day case surgery
	Patient transfer	

**Table 1**

to represent the speed at which the drug will redistribute to well-perfused ( $V_2$ ) and less well-perfused tissues ( $V_3$ ).  $V_2$  represents well-perfused tissue i.e. (muscle) and  $V_3$  represents poorly perfused tissue (i.e. fatty tissue) (Figure 1).<sup>5</sup>

Rate constants are used to describe the proportion of drug moving between the above compartments, for example  $K_{12}$  represents movement from  $V_1$  to  $V_2$  and  $K_{21}$  represents the movement of drug from  $V_2$  to  $V_1$ .  $K_{10}$  is a metabolic rate constant representing the proportion of drug being metabolized or eliminated in  $V_1$  at any given time.  $K_{e0}$  represents the proportion of drug diffusing from the central compartment to the effect site i.e. the brain.

**Steady-state and context sensitive half-time (CSHT)**

An initial fast bolus dose (600–1200 ml/hr) will result in a peak  $V_1$ , concentration which will rapidly decline due to redistribution and elimination. In order to maintain a constant concentration in  $V_1$  subsequent small doses will be continually required to

provide an acceptable level of concentration and therefore maintain an adequate level of anaesthesia. This will inevitably produce peaks and troughs potentially resulting in sub-therapeutic or toxic levels of the drug.

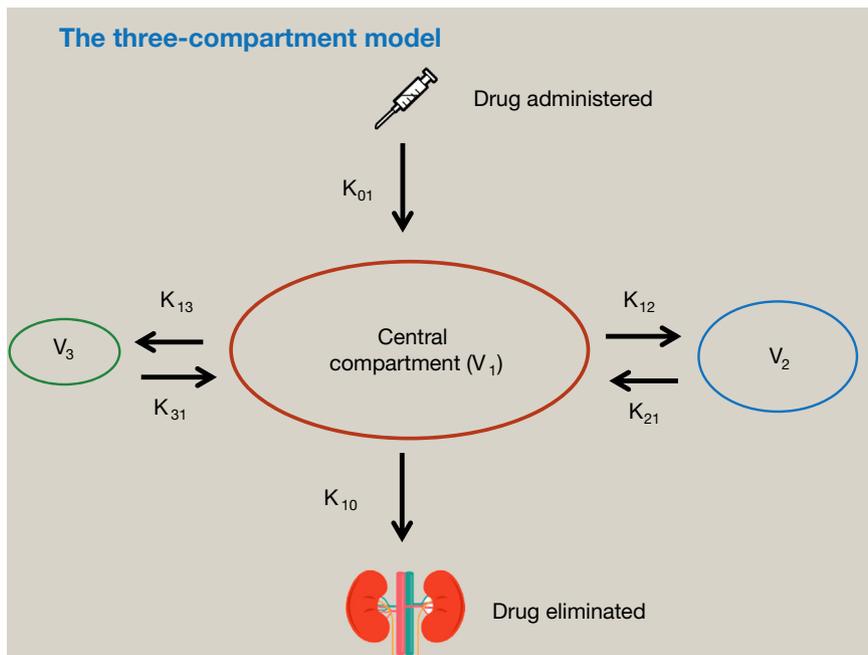
The delivery of a drug at a constant rate can produce a steady state within  $V_1$  but this may take a considerable period of time which may be impractical. For example, Propofol would require up to 24 hours before establishing a central steady state.<sup>5</sup> The CSHT of a drug increases as the duration of infusion increases until eventually reaching a plateau. This is because the peripheral compartment will not equilibrate with the central compartment following a brief infusion and the drug will be redistributed and eliminated. Following a prolonged infusion, a decline in the central compartment will be limited by the redistribution of the drug from the periphery.

**The effect site**

The effect site is the location where a drug has its intended effect and in the case of anaesthetic agents this will be the brain rather than the plasma. By including this in the three-compartment model a pharmacokinetic-pharmacodynamic model is created. By specifying a rate constant for movement of a drug into and out of a compartment ( $k_{e0}$ ) it is possible to predict the expected time for a clinical effect to be achieved. The theoretical volume of this compartment is negligible, meaning that it does not have any impact on the behaviour of the pharmacokinetic model.<sup>5</sup>

**TIVA via manual regimes**

Manual infusion regimes are now rarely used as they have been found to be laborious and prone to error. However, as their design provides useful insight into the requirements of a variable rate infusion to maintain a constant central compartment



**Figure 1**

concentration we will discuss it for completeness. The bolus, elimination transfer (BET) scheme dictates the three components of TIVA.

### Bolus (B)

An initial bolus dose is delivered to fill  $V_1$  and provide rapid induction of anaesthesia. If a Propofol bolus was not delivered it would take a constant Propofol infusion at 10 mg/kg/hr 45–90 minutes to achieve clinically useful plasma levels in an 85 kg adult male.<sup>4</sup>

### Elimination (E)

To maintain a constant  $V_1$  concentration a final constant infusion rate must match elimination of the drug when redistribution is complete, and the drug has equilibrated between the peripheral and central compartments.

### Transfer (T)

An interim infusion rate is required to maintain the  $V_1$  concentration by matching the rate of transfer of the drug from central to the peripheral compartments. Manual regimes risk excessive doses for some patients and inadequate doses in others. The pharmacokinetic and pharmacodynamics variability between patients dictate the clinical effect of the drug and a more accurate technique is required to reliably deliver appropriate concentration in response to varying degrees of surgical stimulation.

### Target-controlled infusions (TCIs)

TIVA can be delivered by several methods (intermittent bolus, fixed rate infusion, infusion based on a manual algorithm, TCI and a mixture of these). By encompassing several techniques which may not produce an equivalent efficacy or safety profile it is not possible at present to recommend a standard technique. There are ongoing debates as to whether TIVA is associated with a higher incidence of awareness when compared to intravenous induction and volatile maintenance.

The amount of Propofol in the blood and brain required to ensure an appropriate level of anaesthesia is dependent on a multitude of factors and varies between individual patients, making it impossible to predict what is required in advance. The variation is commonly witnessed in older patients requiring a lower Propofol concentration than younger patients. The Propofol plasma concentration routinely required for maintenance of anaesthesia will usually be between 1.5 and 6.0 µg/ml.<sup>6</sup>

In order to ensure that an adequate depth of anaesthesia is achieved by TIVA, a dedicated pharmacokinetic pump should be used. These pumps utilize complex algorithms which calculate the distribution of agents between compartments and allow for rapid adjustments of targets to achieve the desired clinical effect. The first commercially available TCI system was the 'Diprifusor' in 1998 for the induction and maintenance of anaesthesia in adults. The use of TCI pumps to deliver TIVA is now commonly used for anaesthesia in the operating theatre.

### Key components

- User interface.
- Microprocessors with pharmacokinetic software.
- Infusion pump which delivers up to 1200 ml/hour.
- Visual and audible safety systems.

TCI pumps display the brain or target effect site ( $C_{et}$ ), and the plasma effect site ( $C_{pt}$ ). A typical system calculates the bolus dose and speed of subsequent infusion required to maintain the target plasma drug concentration ( $C_{pt}$ ). Calculations are repeated every 10 seconds and the infusion rate is continued until the  $C_{pt}$  is achieved. The diffusion of the drug from plasma to the brain occurs exponentially initially until equilibrium is achieved 4–5 half times. If  $C_{pt}$  is increased a bolus is delivered to  $V_1$  and the infusion rate increases to match the additional transfer and elimination at the higher concentration. When  $C_{pt}$  is decreased, the infusion stops until the plasma concentration declines to the new target and is restarted at a lower rate, diffusion of the drug from the brain occurs with the same half-time.

### Pharmacokinetic models

Different pharmacokinetic models have been incorporated into the pumps and there is debate about which models most closely represent the match between calculated and actual Propofol concentrations. However, currently there is no evidence supporting one over another and all have proved reliable in clinical practice. All models have similar limitations in terms of accuracy and stability of plasma and effect site concentrations due to inherent assumption made when predicting target site levels and inter-individual variability.<sup>7</sup> Close clinical monitoring of the patient remains an important part of the anaesthetist's role. Table 2 illustrates the main differences between the Marsh and Schnider Models.

The Marsh model assumes that  $V_1$  is directly proportional to weight only, therefore ignoring age. The age is entered but not used directly in the calculation. However, the pump will not function if an age less than 16 years is entered. The Marsh model utilizes total body weight.<sup>5</sup>

The Schnider model is incorporated into the newer-generation TCI pumps. It is a three-compartment Propofol model where age and height are entered into the system. As it takes age into account it is considered more appropriate in the elderly population allowing for reduced clearance. The Schnider model adjusts some of the pharmacokinetic parameters for age but this does not necessarily prevent haemodynamic instability. A gender-specific lean body mass is calculated and used to adjust the elimination

### Differences between the Marsh and Schnider models

	Marsh model	Schnider model
Central compartment ( $V_1$ )	In 70 kg person - larger $V_1$ (15.9 L)	In a 70 kg person — smaller $V_1$ (4.27 L)
Onset of clinical effects on induction of anaesthesia	Slower	Faster
Initial bolus dose (mg)	Larger	Smaller
Time to deliver dose (seconds)	Longer	Shorter
Time to reach target concentration (minutes)	Longer	Shorter

Table 2

rate constant  $K_{10}$ . Due to the small fixed volume of  $V_1$  in the Schnider model it is recommended to use effect-site targeting to ensure an adequate initial bolus.<sup>4</sup>

The major difference between the Marsh and Schnider model is the volume of  $V_1$ . The central compartment in Schnider is fixed in the sense that it is the same for each patient at 4.27 L in a 70 kg person which is smaller than that used in Marsh (15.9 L), therefore varying the estimated concentration following a bolus. This results in almost a fourfold difference in the peak plasma concentration when a bolus is administered. When using Marsh in the less robust patient it is advised to start at a low  $C_{pt}$  and gradually increase until the desired clinical effect is achieved.<sup>4</sup>

### Remifentanyl

Opioids are a key component of a balanced TIVA technique as they enable the response to noxious stimuli to be controlled. Due to its negligible CSHT, Remifentanyl is an ideal co-agent to be administered with Propofol. It has a synergistic interaction with Propofol and rapid elimination. This enables a decreased Propofol concentration intraoperatively and the rapid offset of remifentanyl avoids respiratory depression postoperatively. However, it is important to note that remifentanyl will not provide postoperative analgesia.

The Minto model is popular as it is applicable to a wide range of patient characteristics. Age is used for calculation of its pharmacokinetic parameters but as in the Schnider model, its adjustment does not alter pharmacodynamics response. A sex specific lean body mass is calculated and used to adjust the patient's parameters.

### Practical aspects

Multiple approaches can be utilized for the simultaneous induction of Propofol and remifentanyl TCI. If the targeted effect site is chosen in both then they can be commenced together. However, there is an increased risk of apnoea if remifentanyl is started prior to propofol or if plasma target is selected in both. If effect site Propofol and plasma remifentanyl are selected, the synergistic effect will be lost as Propofol will achieve target concentration much more rapidly, increasing the risk of haemodynamic instability.<sup>5</sup>

Due to the synergy between remifentanyl and Propofol the ability to choose high remifentanyl/low Propofol effect site concentration, or the converse, is enabled. This allows for a quicker wake up for the patient if utilizing a high remifentanyl combination; however, it increases the risk of apnoea and bradycardia.<sup>5</sup>

If the pump battery fails intraoperatively when not connected to the main power supply most pumps will not recall the programme, or the amount of drug previously delivered. The three options are to switch to a volatile-based technique, restart the pump in a manual mode or restart the pump in TCI mode. All of these options risk haemodynamic instability.<sup>5</sup>

Termination of infusions can be performed simultaneously at the end of the operation or the remifentanyl can be continued at a lower dose, e.g. 1–2 ng/ml to facilitate a smoother wake up and avoid coughing.<sup>7</sup>

Delivery of longer-acting opioids should be administered 40 minutes prior to wake up to avoid increased postoperative pain

when the remifentanyl infusion is terminated as no postoperative analgesia will be provided once the infusion is terminated and there is a risk of acute opioid tolerance.<sup>7</sup>

### Typical target concentrations in routine practice

If a rapid onset of anaesthesia is required, an initial  $C_{pt}$  (Marsh) or  $C_{et}$  (Schnider) Propofol concentration 4–6 µg/ml will be appropriate in healthy young or middle-aged patients. Maintenance of 3–6 µg/ml/min without opioids and 2.5–4.0 µg/ml/min with opioids are typical. If the patient is very anxious or robust this may be higher, alternatively if they are elderly, frail or critically ill it will be lower.

In elderly frail patients an alternative technique of starting a slower induction at an initial Propofol concentration of 1 µg/ml with gradual 0.5–1.0 µg/ml increases until there is loss of consciousness. This will help avoid hypotension on induction while allowing the anaesthetist to assess the target concentration required to prevent a response to noxious stimulus. The clinical calibration of the individual patient's response to Propofol should routinely take place at induction with the documentation of the  $C_{et}$  when the patient experiences loss of response to speech, and loss of movement in response to a noxious stimulus e.g. firm pressure on the angle of the mandible.

The latter concentration can be used to guide the approximate concentration likely to be required during the maintenance of anaesthesia.<sup>3</sup> Patients with a Propofol concentration greater than 1.5 µg/ml are unlikely to spontaneously ventilate and will require ventilation.

### Special considerations

#### TIVA in paediatrics

TIVA in paediatrics is a lot less routine than adults but has many specific advantages to paediatric anaesthesia. These include decreased emergence delirium, reduced airway reactivity and less postoperative nausea and vomiting. However, the pharmacokinetic and pharmacodynamics variability, the effect of propofol metabolism in early life, specific issues in the critically ill and the non-linear changes in volume of distribution and clearance mean TIVA should be used with extreme caution in the neonatal and ex-premature infants.<sup>8</sup>

Compartment volumes in children are about twice the size of that of adults when compared to their respective body weight. This results in children being delivered a larger initial bolus dose and infusion rate relative to body weights. This difference normalizes at the age of 16 years. There is also a greater rate of clearance, peaking at 1 year of age resulting in a higher maintenance rate. Prolonged infusion will also accumulate peripherally to a greater extent when compared to adults producing a slower patient wake up post termination of infusion. For average length procedures up to 50% more propofol will be used in paediatric models when compared to an adult utilizing the Marsh model.<sup>3</sup>

The 2018 guidelines for the safe practice of TIVA have commented that using TIVA in paediatrics requires specific training to allow for the pharmacokinetic and pharmacodynamics variation as well as practical differences across the various age ranges. Processed EEG (pEEG) feedback may be particularly useful for

titration of anaesthesia.<sup>3</sup> The two most widely used and validated paediatric TCI programmes used in practice are Kataria and Paedfusor models.

The Kataria model is suitable for children between the ages of 3–16 years with a weight range between 15 and 61 kg in comparison to the Paedfusor, which is a variant of the Marsh model that is appropriate in children aged between 1 and 16 years who weigh between 5 and 61 kg. Paedfusor features non-linear scaling of  $V_1$  volume above the age of 12 years.<sup>8</sup> Teenage children who weigh more than 61 kg can be managed using the Marsh adult model.<sup>3</sup>

Pain is a common issue on induction of TIVA in paediatrics and can be very distressing. This can be diminished by prior administration of intravenous lidocaine, opioids or nitrous oxide.<sup>8</sup>

Simultaneous delivery of remifentanyl TCI can be administered to children over the age of 12 and weighing more than 30 kg using the Minto model, but under this age and weight it is necessary to use a manual infusion e.g. 0.25–0.5  $\mu\text{g}/\text{kg}/\text{min}$  as a TCI model is not yet available<sup>2</sup>

Propofol infusion syndrome is a very rare, but potentially fatal condition which has been associated with Propofol infusions in the paediatric population. It results from interference with mitochondrial energy production resulting in rhabdomyolysis, acidemia and multi-organ failure. The risk factors for this are prolonged Propofol infusions, high delivery rates at 6 ml/kg/hr, critical illness, low sugar intake and co-administration of catecholamines and steroids.<sup>2</sup> It is rarer still in the context of TIVA for surgery.

### TIVA in critical care

Fixed rate propofol infusion are commonly used for sedation on intensive care units but if procedures are required to be performed or muscle relaxants are to be administered then care must be taken to avoid awareness. Due to organ dysfunction in the critically ill patient the pharmacokinetics of TIVA will be altered, decreasing the accuracy of the TCI model to predict plasma Propofol concentrations increasing the risk of haemodynamic instability. The guidelines for the safe practice of TIVA recommend titration to clinical effect and the utilization of processed EEG monitoring in these circumstances.<sup>3</sup>

### TIVA and obesity

When using TIVA in obese patients there is a lack of evidence with regards to if it is better to use total body weight or adjusted body weight. The Marsh and Schnider models may be inaccurate in the obese patient. Marsh TCI pumps will only allow a maximum of 150 kg and Schnider will only accept variables resulting in a BMI of less than 35  $\text{kg}/\text{m}^2$  for females and 42  $\text{kg}/\text{m}^2$  in males. The Society for Obesity and Bariatric Anaesthesia (SOBA) has published guidelines on using TIVA in obese patients. The current advice is to be cautious, titrate to clinical effect and continually clinically assess whilst utilizing processed EEG to avoid awareness or haemodynamic instability.<sup>3</sup>

### TIVA and accidental awareness

When contrasting the safety profile of TIVA with an inhaled anaesthetic the ability to monitor end tidal anaesthetic gas

concentration continuously is a major factor. Monitoring the end tidal anaesthetic gas concentration provides an ability to quickly recognize inadequate anaesthesia. However, with TIVA the potential for an interruption via disconnection of the infusion tubing or cannula creates a potential for it to go unrecognized and may result in the patient experiencing unintended awareness.<sup>1</sup>

The Safe Anaesthesia Liaison Group<sup>9</sup> (SALG) produced recommendations in 2009 to minimize the risk of complications with TIVA. These included the use of non-return valves on intravenous infusion lines, clear labelling of connectors and valves, cannula site visible at all times and that all relevant clinical staff are competent in the use and aware of the limitations of the equipment.<sup>4</sup>

However, regardless of these guidelines the fifth National Audit Project (NAP5) found that of the 28 cases reviewed, 21 involved TIVA being utilized for the induction and maintenance of anaesthesia in a theatre setting with 7 cases being reported when anaesthesia was being initiated or continued outside of the operating theatre. The most common cause of unintended awareness was a result of a paralysed patient being administered an inappropriately low dose fixed rate propofol infusion. More than three-quarters of these cases were considered to be preventable.<sup>1</sup>

### TIVA outside of theatre

The NAP5 report also highlighted the time delay when converting from inhalational anaesthesia to TIVA when transferring patients to critical care and the failure of administering a bolus dose of propofol to ensure adequate effect site concentration.<sup>1</sup> Conversely however, TIVA minimized risk of unintended awareness when transferring the patient from the anaesthetic room to the operating theatre as there was no need to disconnect from the breathing circuit and interrupt inhaled anaesthetic delivery. There were relatively few reports of unintended awareness with TCI in contrast with non-TCI infusions, indicating the issue does not lie with the pharmacokinetic models delivered by these pumps.<sup>1</sup>

Out of theatre use of TIVA was identified as a higher risk setting for unintended awareness. Most notable low dose fixed rate infusions without a prior bolus dose of Propofol and an absence of pEEG monitoring. In these settings when inhaled anaesthesia is not available it is crucial for all anaesthetists to be competent in the delivery of TIVA. The Guidelines for the safe practice of TIVA recommend the use of TCI and pEEG monitoring when delivering a TIVA outside of theatre.<sup>3</sup>

It is crucial to ensure that the brain concentration of the Propofol is adequate before the volatile anaesthetic agent falls particularly when administering a neuromuscular blocking drug prior to transfer as reported in NAP5<sup>1</sup>.

### Monitoring the patient during TIVA

This inherent risk of accidental awareness under general anaesthesia (AAGA) when delivering TIVA has resulted in the National Institute of Health and Care Excellence (NICE, 2012) recommending the use of depth of anaesthesia monitoring; especially when neuromuscular blocking agents are used. The interpretation of pEEG does have pitfalls that anaesthetists need to

appreciate as they can result in error of analysis. These can result from artefacts, poorly placed electrodes and electrical interference it is therefore very important anaesthetists receive appropriate training in interpreting pEEG to ensure TIVA is performed safely.<sup>10</sup> Processed EEG monitors do not just provide a derived index value to the anaesthetist but a variety of information to assess for example the EEG waveform, signal quality, EMG activity and degree of burst suppression which should all be interpreted by the anaesthetist in combination with other patient monitoring and clinical experience.<sup>3</sup>

### Recommendations from the guidelines for the safe practice of TIVA 2018<sup>1</sup>

1. All anaesthetists should be trained and competent in the delivery of TIVA. Schools of Anaesthesia and training bodies should provide teaching, training and practical experience of TIVA to all anaesthetic and intensive care medicine trainees. Consultant and staff grade, associate specialist and specialty doctor (SAS) anaesthetists have a responsibility to ensure that they have the knowledge and skills required to deliver TIVA competently and safely.
2. When general anaesthesia is to be maintained by Propofol infusion, use of a target-controlled infusion (TCI) is recommended.
3. Starting target concentrations should be chosen depending on the characteristics of the patient, co-administered drugs and clinical situation. Older, frail or unwell patients may benefit from setting a low initial target Propofol concentration, and making repeated small incremental increases.
4. Within an anaesthetic department, it is preferable to stock only one concentration of Propofol and to dilute remifentanyl to a single, standard concentration.
5. The infusion set through which TIVA is delivered should have a Luer-lock connector at each end, an antisiphon valve on the drug delivery line(s) and an anti-reflux valve on any fluid administration line. Drug and fluid lines should join as close to the patient as possible to minimize dead space. The use of administration sets specifically designed for TIVA is recommended.
6. Infusion pumps should be programmed only after the syringe containing the drug to be infused has been placed in the pump.
7. The intravenous cannula or central venous catheter through which the infusion is being delivered should, whenever practical, be visible throughout anaesthesia.
8. Anaesthetists should be familiar with the principles, interpretation and limitations of processed electroencephalogram (EEG) monitoring. Observation of the EEG trace and electromyography activity is likely to improve the clinical utility of the monitoring.
9. Use of a processed EEG (pEEG) monitor is recommended when a neuromuscular blocking drug is used with TIVA.
10. When TIVA is administered outside the operating room, the same standards of practice and monitoring should apply as for anaesthesia in the operating room.

### Conclusion

TIVA is an essential technique that all practicing anaesthetists are required to perform confidently and competently for a variety of clinical situations. Following the publication of NAP5 it is clear that a lack of training and education in the use of TIVA can result in unintended awareness. It is therefore crucial that all anaesthetists using this technique are familiar with the indications, limitations and have an understanding of the underlying pharmacokinetic principles to ensure safe delivery in the appropriate clinical settings. ◆

### REFERENCES

1. Nimmo AF, Cook TM. 5th national Audit Project (NAP5). Accidental Awareness during general Anaesthesia in the United Kingdom and Ireland Report and findings—chapter 18. Total intravenous anaesthesia. The Royal College of Anaesthetists and the Association of Anaesthetists of Great Britain and Ireland, September 2014.
2. Madhivathanan P, Kasivisvanathan R, Cohen A. Training in total intravenous anaesthesia: a regional survey. *Anaesthesia* 2010; **65**: 540–2.
3. Nimmo AF, Absalom AR, Bagshaw O, et al. Guidelines for the safe practice of total intravenous anaesthesia, Association of anaesthetists of Great Britain and Ireland (AAGBI) and the society for intravenous anaesthesia (SIVA). 2018, <https://doi.org/10.1111/anae.14428>. [Accessed November 2018].
4. Al-Rifai Z, Mulvey D. Principles of total intravenous anaesthesia: basic pharmacokinetics and model descriptions. *Cont Educ Anaesth Crit Care Pain* 16: 92–97.
5. Hawthorne C, Sutcliffe N. Total intravenous anaesthesia. *Anaesth Intensive Care Med* 17: 166–168.
6. Reves JG, Glass PSA, Lubarsky DA, McEvoy MD, Martinez-Ruiz R. Intravenous anesthetics. In: Miller RD, ed. *Miller's anaesthesia*. Philadelphia: Churchill Livingstone, 2007; 719–768.
7. Al-Rifai Z, Mulvey D. Principles of total intravenous anaesthesia: practical aspects of using total intravenous anaesthesia. *Cont Educ Anaesth Crit Care Pain* 2016; **16**: 276–80.
8. Gaynor J, Ansermino JM. Paediatric total intravenous anaesthesia. *Cont Educ Anaesth Crit Care Pain* 2016; **16**: 369–73.
9. Safe Anaesthesia Liaison Group. Guaranteeing drug delivery in TIVA. 2009, [http://www.aagbi.org/sites/default/files/tiva\\_info.pdf](http://www.aagbi.org/sites/default/files/tiva_info.pdf). [Accessed 21 June 2018].
10. Goddard N, Smith D. Unintended awareness and monitoring of depth of anaesthesia. *Cont Educ Anaesth Crit Care Pain* 2013; **13**: 213–7.