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Total intravenous anaesthesia

By the perioperativeCPD team

Introduction

Total intravenous anaesthesia (TIVA) is a technique of general anaesthesia which uses a combination of agents given exclusively by the intravenous route without the use of inhalation agents. This module explains how TIVA/TCI works, the popular models used and how they affect different patient groups.

History

The history of intravenous (IV) drug administration starts in the 17th century when Christopher Wren injects opium into a dog using a goose quill. The next major advance didn't happen until the 1930's when hexobarbital and pentothal (sodium thiopental) were released. It was the introduction of first propofol (1986) and then the Diprufusor pump in the 1990's which enabled Target Controlled Infusions (TCI) to enter mainstream anaesthetics.

TIVA or TCI?

What is the difference between TIVA and TCI? In reality both terms are used interchangeably but there is a difference.

TIVA is Total Intravenous Anaesthetic, no volatile anaesthetic gases such as sevoflurane and desflurane. While it can be given using a TCI pump this is not necessary and it can be given through a simple mls/hour pump or even bolused by hand.

TCI or Target Controlled Infusion on the other hand, is giving an intravenous anaesthetic using a specialised microprocessor controlled syringe driver. With a TCI pump the anaesthetist enters the patient's details, selects the target concentration (plasma or effect-site) and the pump calculates the appropriate infusion rate.

Why use TIVA?

Intravenous (IV) anaesthesia whether TIVA or TCI has several advantages over inhalational anaesthetics:

- A faster/ cleaner recovery for short cases
- Less post-operative nausea and vomiting
- Less contamination from greenhouse gases than inhalational anaesthetics
- No risk of malignant hyperthermia

It also has disadvantages:

- Unidentified disconnection or extravasation (tissuing) of the propofol infusion can lead to awareness.
- Extra equipment, training and setup are needed.
- Recovery can be slow after very long operations.
- All concentrations whether it be plasma or effect site are estimates made by the pump programme, not the patients actual concentrations which cannot be measured clinically.

What drugs are used for TIVA?

Anaesthetic drugs with a fast onset/ fast recovery are best suited for TCI. The most common are propofol 1% and remifentanil, although alfentanil and sufentanil can also be used.
(Note: 2% propofol is sometimes used but all figures in this module relate to 1% propofol. Whichever strength is used it in your department, it should be the only one stocked to prevent errors.)

Why is a complex algorithm needed to run TCI?

When a drug is given intravenously it doesn't stay in the circulation for long. It is redistributed throughout the body to the tissues, muscles, organs, fat as well as being eliminated from the body by the kidneys, liver etc.

This explains why a bolus of propofol only has an effect for a few minutes as it is quickly redistributed though the whole body, not just to the brain where the site of action is. How long a drug is effective depends on its individual pharmacological characteristics and the physiology of the patient (see diagram 1).
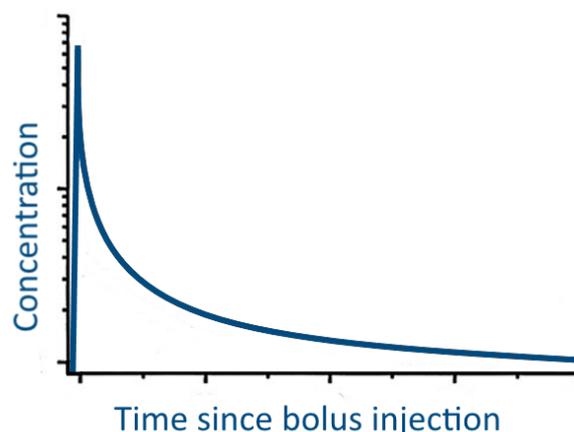

DIAGRAM 1: propofol concentration following a single bolus (indicative diagram not to scale)

What is the three compartment model?

Most anaesthetic drugs conform closely to the three compartment pharmacological model which describes how drugs are distributed and eliminated from the body after an IV injection.
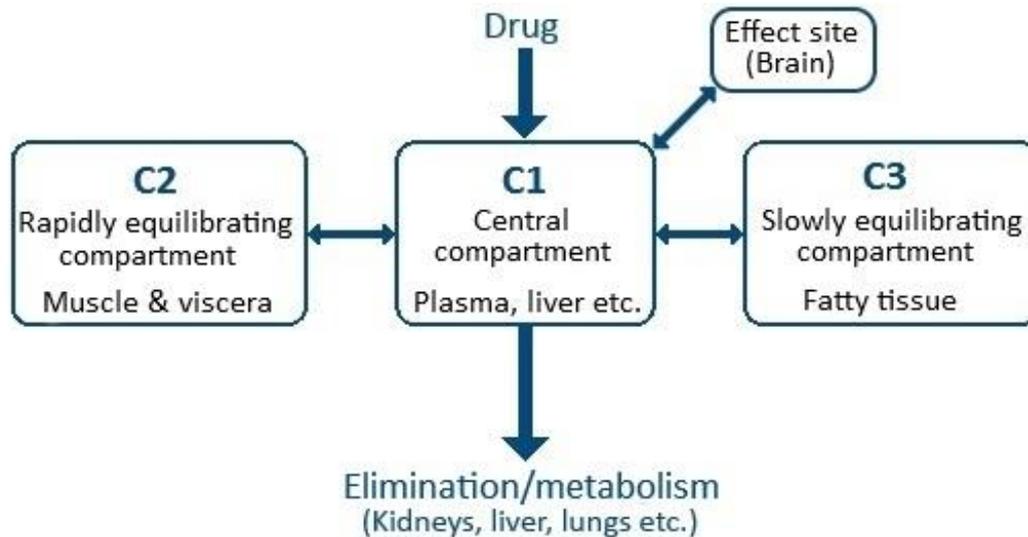

DIAGRAM 2: the three compartment model

The drug (i.e. propofol) is initially injected/infused into the central compartment which consists primarily of plasma. Then some of it is distributed to the two other compartments (C2 & C3) as well as the brain which is considered a separate compartment in this model.
(These compartments are only theoretical and do not represent actual body compartments.)

- C1 is the central blood compartment where drug distribution is virtually instantaneous.
- C2 consists of highly perfused tissue such as muscles. Drugs move in and out of them relatively fast.
- C3 contains less well perfused tissue such as fat; as a result movement of drug into and out of this compartment is slower.
- The Effect site for propofol is the brain.

Drugs are removed by the body only from the central compartment (C1) by being eliminated or metabolised.

Once an infusion is stopped, drugs will move back out of C2 and C3 back into C1 as the levels in the central compartment drop.

How does a TCI pump calculate the infusion rate?

Using the patient's details (height, weight etc.) the desired concentration is set by the anaesthetist and the pump calculates and combines 3 separate infusions using the B.E.T model (see below). The infusion rate is adjusted every 10 seconds.

Bolus- An initial bolus to fill the central compartment (plasma) as soon as possible.

Elimination- This is a constant rate infusion to replace the drug lost through elimination from the central compartment.

Transfer- This infusion compensates for the loss through distribution to the peripheral compartments (C2 & C3). It reduces over time as the levels equilibrate between the compartments.

When is the patient asleep?

The normal induction concentration using TIVA is between 4-6 µg/ml although this, like all anaesthetic drugs depends on the patient's age health and other drugs administered (esp. opioids). There is no one concentration that is appropriate for all patients and titration to individual patient response and surgical stimulus is recommended.

The starting concentration may need to be as high as 8µg/ml in a young, fit, anxious male and considerably lower in older, frail or unwell patients. In this latter group it is better to start low i.e. 1-2µg/ml and slowly increase the rate.

Experienced operators often note at which effect-site concentration the patient loses response to noxious stimulus (jaw thrust) and use this to tailor TIVA levels to the individual patient.

During maintenance of anaesthesia a target concentration of 3.0-6.0 µg/ml is suggested. This can be dropped to 2.5-4.0 µg/ml when opioids are used because there is a synergistic effect when propofol and opioids are given together and this allows for a reduction in the dose of propofol of up to 50%.

Where remifentanil is administered with the propofol, target remifentanil concentrations of 2-6 ng/ml are commonly used. With concentrations greater than 1.5 ng/ml the patients may need assisted ventilation.

Note: Propfol concentrations are micrograms/millilitre (µg/ml) where remifentanil concentrations are nanograms/ millilitre (ng/ml)

Circumstance	Suggested concentration (micrograms/ml)	Notes
Induction	4-6	
Slow induction (i.e. elderly)	1-3	
Maintenance	3-6	
Maintenance with opioids	2.5-4	
Concentration on waking	1-2	Warning: This is extremely variable
Remifentanil concentration when used with propofol	2-6 ng/ml	Nanograms/millilitre

TABLE 1: Suggested effect site concentrations

What is the difference between plasma concentration and effect site concentration?

TCI pumps use either of two methods to calculate the concentration of drug in the body.

Plasma concentration models where the pump calculates and maintains an estimated concentration of drug in the plasma (C1).

However IV anaesthetics work on the central nervous system, specifically the brain (the effect site) and it takes time for the drug concentration in the brain to equilibrate with that in the plasma, especially when using propofol which moves slowly between compartments.

Effect site models give a larger initial bolus than the plasma concentration models. This higher initial bolus ensures the effect site (brain) levels of the drug rise faster, giving a quicker induction.

Note: All the TCI calculations and concentrations are estimates as there is no way in clinical practice to measure the actual plasma or brain (effect site) concentrations in any given patient.

What are the propofol TCI models for adults?

There are two main models for TCI, Marsh (plasma concentration) and Schnider (effect site).

The Marsh (plasma concentration) model is the most popular. It is a fairly simple model which uses a patient's body weight to calculate the infusion rate and adjusts the infusion rate every 10 seconds.
Although an age is entered it is only used to ensure the patient is over 16, otherwise the pump does not operate.
It gives a smaller induction dose then the Schnider but a larger volume overall throughout the case. This smaller induction dose leads to a lag in induction time.
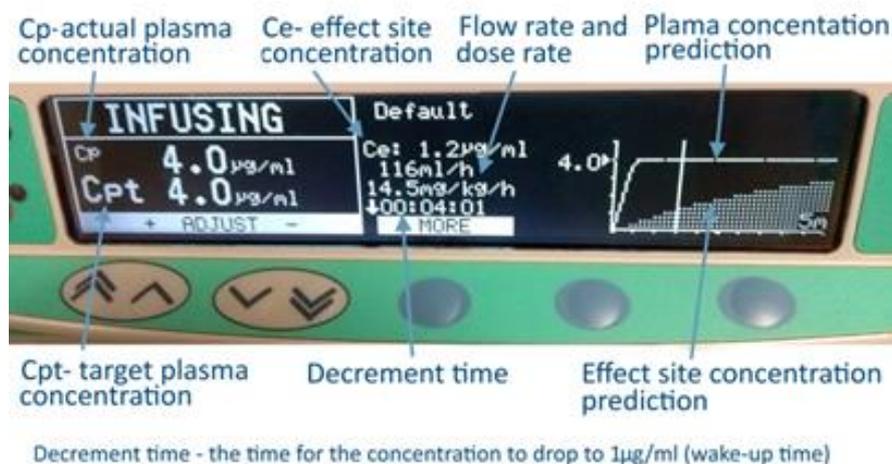

Decrement time - the time for the concentration to drop to 1μg/ml (wake-up time)

Diagram 3: Marsh model (plasma concentration Alaris PK pump

The Schnider (effect site) model is newer and it uses patient weight, height, age and sex to calculate a lean body mass and bases its infusion rate on these parameters.
It gives a larger bolus rate initially (overshoot) and then less propofol during the case. The overshoot leads to a faster induction.

Although other modes are available within these models they are for experienced, expert users only.

Which is the best mode for the elderly?

Like many areas of anaesthesia there is debate over which model is best for elderly or frail patients, although neither is wholly accurate.

Although age is entered for the Marsh (Plasma site) model it is not used in the calculations. A 70kg 98yr old will receive the same infusion rate as an 18 yr old of the same weight which is not clinically correct.

Many consider the Schnider (effect site) model better. While it gives a larger induction bolus it gives a lower total volume throughout the case which may be beneficial to frail patients.

Whichever mode is selected a lower target concentration should be used initially (1-2 μg/ml) with incremental increases every few minutes or as the haemodynamic factors allow.

Are there different models for paediatrics?

The use of TCI in children is a specialised area of practice.

There are two models specific for paediatric, the Paedfusor and the Kataria models, both which are for ages up to 16 years old and 61kg weight. If the patient is above either of these parameters the adults models may be used.

If propofol infusions are used for extended periods (i.e. more than 24hrs) in children there is a very small risk of propofol infusion syndrome which can lead to cardiac failure, rhabdomyolysis, metabolic acidosis, and kidney failure, and it can be fatal.

Is TIVA accurate for obese patients?

As with the elderly, neither the Marsh or the Schnider models are accurate when used on with obese patients. The maximum body weight accepted by Marsh model is 150 kg and it bases infusion rates on actual body weight. This may result in a relative overdose to obese patients.

The Schnider model only accepts a BMI <35 kg m^{-2} for females or <42 kg m^{-2} for males and calculates a lean body mass which it uses for its calculations.

When using TIVA in obese patients, titration to clinical effect and EEG monitoring is recommended.

Why are the models so inaccurate?

Both the Marsh and Schnider models where developed and tested using only a very small number of subjects (18 for Marsh and 24 for Schnider) who were all young, fit, healthy and ASA 1. New TCI models have been developed that are expected to be more accurate for all patient groups including up to 250kg They are currently undergoing extensive trials and hopefully will be available soon.

What model is used for remifentanil?

Remifentanil uses the Minto model which calculates a sex-specific lean body mass for anyone over 12yrs age. It can be used in either plasma or effect site concentrations, although the difference in modes is minimal.

Where remifentanil is administered with propofol, target remifentanil concentrations of 2-6 ng/ml are commonly used.

Minimising the risk of awareness

Rates of awareness are higher with TIVA than when using volatile anaesthetics. Proper equipment and precautions can prevent the majority of these.

The syringes and infusion set through which TIVA is delivered must have luer-lock connectors to reduce the risk of accidental disconnection and an anti-syphon valve on the drug delivery line(s) to prevent uncontrolled infusion from a damaged syringe.

Where more than one infusion is given through a single i.v. cannula (or central venous catheter lumen) an anti-reflux valve should be present to prevent backward flow of drug up the infusion tubing. It is particularly important that this is present on the IV fluid administration line.

IV access should be visible, well secured and checked regularly. If either the patient in paralysed, or the cannula is not visible, then EEG monitoring/BIS is recommended.
Finally, if using 2 or more syringes, the pumps should not be programmed until the syringes are loaded to prevent errors.
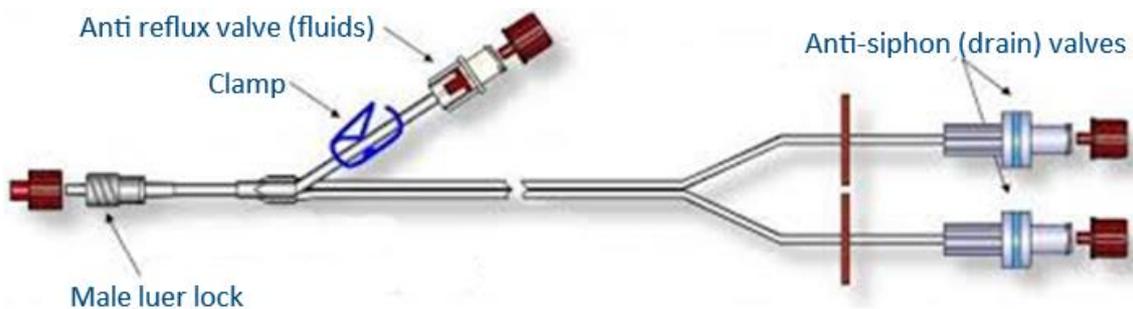

Diagram 4: TIVA infusion set

Ending a TIVA case

Towards the end of the case as the surgical stimulus is reduced the target concentration can be gradually reduced, although the effect site concentration should not be dropped below 2.0 µg/ml.
If remifentanil is used a longer acting opioid such as morphine or oxycodone ought be given 15-20 minutes before the end of the case to prevent any gap in analgesia.

The countdown timer (Decrement time) on Alaris pumps will give an estimated time for the concentration to drop to 1.0 µg/ml as a rough indication of a wakeup time but this depends on the amount of analgesia given and the length of the case.
Experienced operators often note at which effect-site concentration the patient loses response to noxious stimulus (jaw thrust) and use this as an indication to the level they may wake up at. Beware this is a guide only and very variable.

All infusion lines should be flushed prior to handover in PACU, especially the remifentanil line to prevent inadvertent boluses post-operatively.

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The Society for Intravenous Anaesthesia (https;//siva.ac.uk)