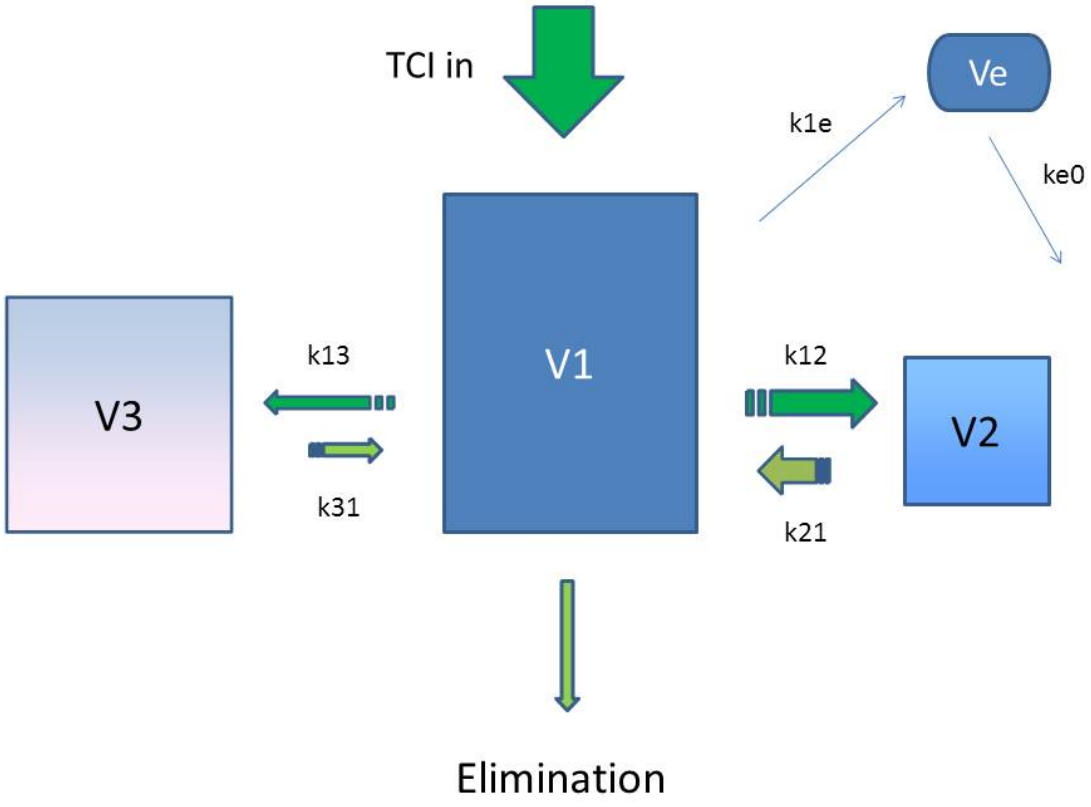
The very basics of Total Intravenous Anaesthesia (TIVA)

As the name implies, this technique of general anaesthesia avoids any use of volatile agents or nitrous oxide and induces and maintains balanced general anaesthesia with the use of intravenous drugs only. The anaesthetic machine delivers simply oxygen enriched air to the patient via a standard ventilator and houses the regular options of patient monitoring modules.

Clearly the delivery of such anaesthesia is simplified by using syringe pumps rather than free hand incremental blousing, but this freehand technique of an analgesic and hypnotic given intravenously is often used for very short surgical procedures eg endoscopy or reduction of limb fractures and such.

What are the assumptions made when giving a TIVA anaesthetic? Well, it helps to have the following pictorial representation in your mind…

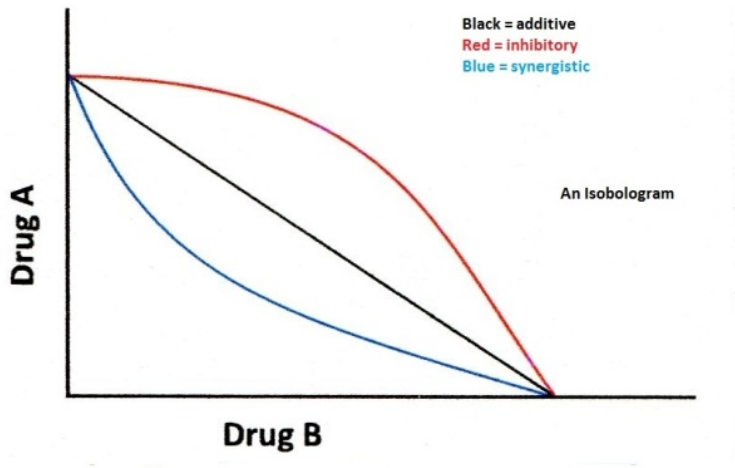


… no its not as complicated as it may look at first.

It shows a central compartment into which the drugs are administered (V1), then there are 2 peripheral compartments – V2 vessel rich (eg muscle) and a second bigger one – V3 vessel poor (eg fat). Clearly, as it is blood that delivers the drug, V2 will fill at a faster rate (more blood vessels) than V3. Note the small volume Ve which represents the effect site of the

drug action. The drugs are trying to reach here but as their delivery follows simple rules of concentration gradients, all areas that the blood delivers the drug too are also in competition to reach equilibrium with the central compartment. This represents a 3 compartment (pharmacokinetic) model and is how we explain the decline in measured blood concentrations following an intravenous bolus of drugs used in anaesthesia. At steady state, the drug concentration in the central compartment will equal the concentration in the 2 peripheral compartments and also the effect site. However, there are "unbalancing factors" working constantly against this equilibration or steady state and those are the processes of metabolism and elimination. Hence, when steady state is reached and in order to maintain this steady state, the drugs still have to be delivered into the central compartment at a rate that equals the metabolism and excretion of each individual drug (elimination). As each drug is unique, and will be metabolised and excreted in different percentages and at different rates (ie they have different pharmacokinetic profiles), the subsequent delivery of each drug will be at a different rate. So the first very obvious observation is that it is nonsensical to mix 2 drugs, with two different pharmacokinetic profiles, in one syringe! Yes, people can by experimentation get a mixture that "works" (keeps a patient asleep) but by definition, it will not be by an optimal concentration of each drug in the body and so recovery will be sub-optimal due to relative overdosage of one drug and / or underdosage of the other.

Syringe pumps have been programmed especially to deliver TIVA by a process of allowing you to choose a steady state concentration of the drugs you choose to use (usually Propofol and Remifentanil) and this technique is called Target Controlled Infusions (TCI). Being aware of the synergistic effect of opioids and hypnotics (Propofol / Remifentanil just as Sevoflurane / Fentanyl) allows us to choose a target level on the pumps to deliver the correct amount of each drug to equilibrate with the effect site as per the pharmacokinetic profile for each drug which will determine how quickly or slowly it will as an individual drug, enter V2, V3 and Ve. Knowing the level to choose is where the art of anaesthesia comes in, just as you know what to set a vaporiser at depending on the agent within it. The isobolgram below defines the 3 possible drug interactions



It is true that we can measure the end tidal volatile agent concentration (a figure and NOT a definitive indicator of a correct level for an individual patient) and that currently we cannot do this routinely for IV drugs (although of course there is the capability of measuring Et Propofol now), but you must remember that the accuracy of such Et volatile measurement can show 25% inaccuracy in patients; everyone knows that EtCO2 is NOT equal to PaCO2.

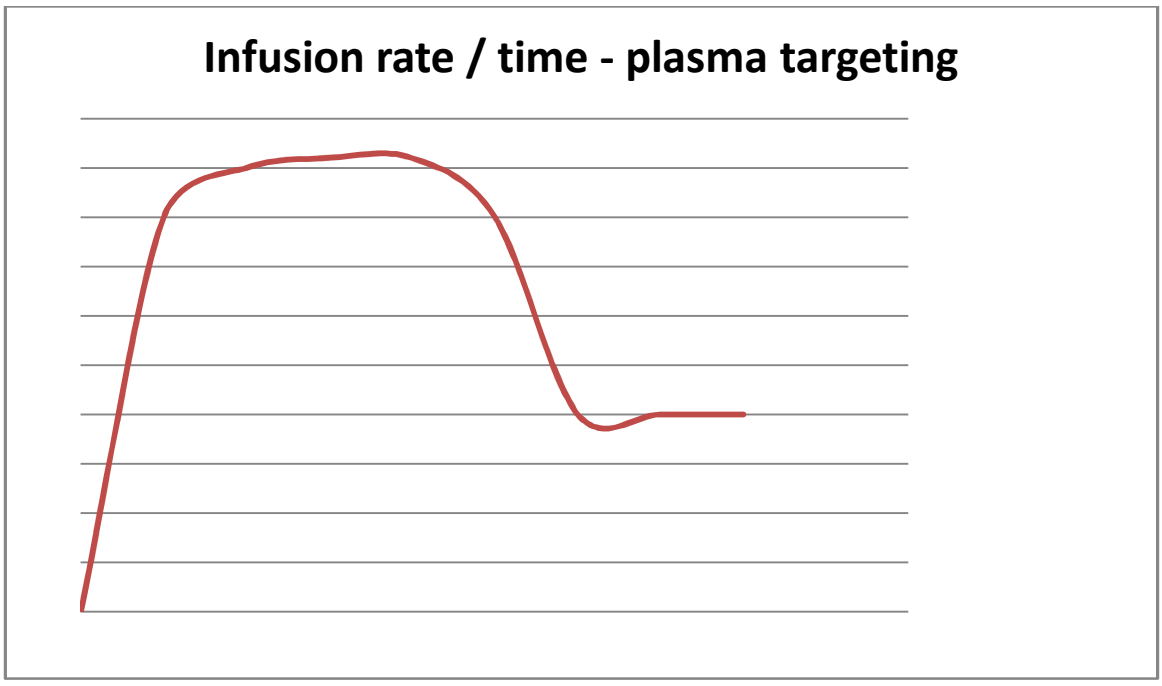
So how are the infusion rates for IV drugs calculated? Put simply, studies of declining arterial and venous blood levels following an IV bolus have been measured, alongside BIS monitoring, and the time to peak effect noted (ie the time lag between administration of the drug bolus and the lowest BIS number recorded). Together and with the addition of other factors (patient demographics) accurate (usable) formulae have been derived to define the pharmacokinetics (how the drug behaves in the body or how the body treats the drug) of each drug. It is sufficient to say for the purpose of this document that these formulae have been tried and tested and work!

We have to tell the syringe pumps a few things about the drug – what drug, what concentration; about the syringe – what make and size as different 50 ml syringes have different bores and hence the volume swept to deliver a set dose will vary; the sex of the patient, the age of the patient, the height of the patient and the weight of the patient. All of the 4 patient based demographics are what we take into account anyway, when we stand poised with a 20ml syringe full of 1% Propofol, though I would respectfully suggest that the pumps actually take a little more consideration than us as individual Anaesthetists when induction commences!

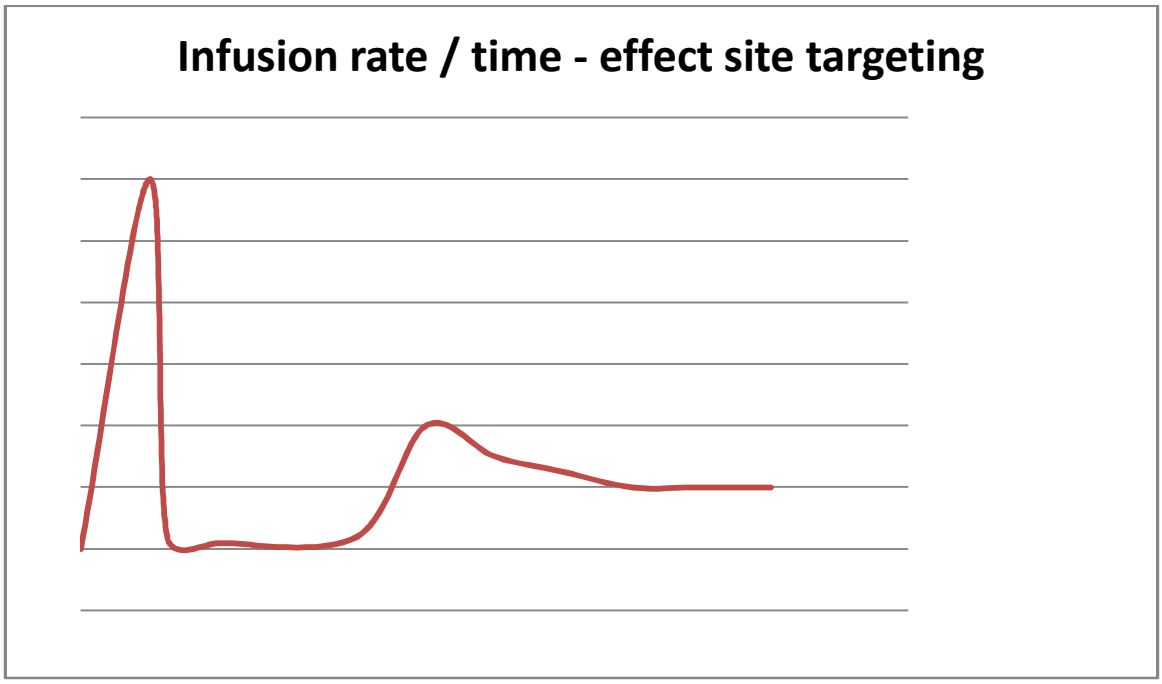
At this point, just one other option needs to be explained. The pumps can be set to target to “plasma level” or to “effect site”. This is very straightforward and where we bring in the other term of pharmacodynamics (or what the drug does to the body). The effects are seen as hypotension, bradycardia, maybe bronchospasm etc. In other words the side effects of ANY drug which we USUALLY define as undesirable effects. Such effects will be proportional to the peak plasma level of the drug which in turn will depend on the total dose administered as a bolus and the rate of administration of the drug. This is the case whether it is a hand that has pushed the plunger on a syringe or a syringe pump. So you will correctly observe that these undesirable effects are less likely to occur if the plasma level of a drug is controlled by defining a maximum level that it can reach; this is only controllable by a mathematically programmed syringe pump and simply CANNOT be calculated by hand delivery. Hence, we may choose to set the pump to “plasma” targeting for ASA 3, 4 or 5 patients so that they don’t suffer the hypotensive hit of a high peak plasma level. Clearly induction will be “gentle” and slower as the plasma level is controlled at what we want the eventual steady state to be and equilibration between the compartments is slower due to the reduced concentration gradients that drive the equilibration….just as if we were inducing such a patient “freehand” ie we would in this circumstance NOT simply rapidly inject 15 mls of 1% Propofol IV into such a patient. We try to replicate what our programmed pump will do in this circumstance. The pumps will deliver by a controlled

infusion to reach the plasma level chosen, rather than giving a bolus resulting in a high overshoot. A freehand induction whether with an IV agent followed by a volatile agent or with a manual TIVA regimen simply cannot be achieved. TCI pumps are essential.

The graph shows the pump giving a moderately fast infusion rate initially to achieve the chosen plasma level, followed by a slower and slowing infusion rate as steady state is reached between all the compartments and the infusion rate eventually settles to match the metabolism and elimination rate.



What about ASA 1 and 2 patients who might be able to cope with a pharmacodynamic "hit"? Well we can target these patients to "effect site". Here, the pumps will deliver a bolus, resulting in a high peak plasma level and hence the measurable pharmacodynamic effect. However, as a high peak plasma level is obtained, the relative concentration gradients are larger, equilibration will occur more rapidly and hence induction will be quicker. This mimics a traditional IV freehand induction and choosing a high initial volatile agent level to get a "wash in" effect to rapidly establish a steady state at the effect site, before reducing the level to that of satisfactory maintenance. The two techniques are working identically. However, do remember that the Et volatile agent measurement is simply that and says nothing about the effect site concentration. It tells you the MAV value you are delivering, but NOT the effect site concentration. It is measuring, if you like, the lung concentration…but like Propofol and Remifentanil, volatile agents work on receptors in the brain and not the lung!



So this is a very basic summary of what TIVA is, how we understand its workings and how it is delivered. It is deliberately fundamental at this stage, but we shall move on to discuss the essential safety aspects of delivering TIVA by TCI and then a final section will look more closely at the pharmacokinetic algorithms available in the TCI pumps and consider extremes of patient demographics which is as relevant to volatile agent anaesthesia as it is to TIVA.

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