NEW TOYS OR NEW TOOLS? TOWARDS TRUE TARGET CONTROLLED ANAESTHESIA

Dr Ross Kennedy

Christchurch Hospital
Christchurch

Most anaesthetists understand the term target controlled anaesthesia but the standard usage is usually applied in a very limited way. In this presentation I will suggest that most of what we do is target controlled. Titration to effect underpins they way in which we control many aspects of anaesthesia and is a form of target control. However improvements and additions to the range of monitors are quantifying more and more of these "targets" and improved technology allows delivery systems better match management to these end-points.

The classic example of "target control" uses the response to a nerve stimulator to titrate administration of neuromuscular blockers. In this case the "target" is the desired level of twitch suppression. Much of the basis of current knowledge of pharmacokinetic and pharmacodynamic modelling is based on work with these drugs from nearly 30 years ago. Although the control of muscle relaxation can be automated, for most of us this is a form of manual target control. Another familiar form of manual target control is using changes in gas flow rates and vaporiser setting to achieve a desired end-tidal vapour concentration.

Most anaesthetists are also familiar with the modern concept of "TCI" or target controlled infusion. In TCI a computer controlled pump adjusts the infusion rate of a drug to achieve and then maintain a given level. Initially these levels were blood, or plasma levels based on pharmacokinetic modelling. Newer pumps and algorithms also incorporate pharmacodynamic data to allow control (and therefore targeting) of "effect site" levels.

As with many concepts and devices in anaesthesia we need to know enough to use them intelligently and to understand their limitations. The most straight forward definition of pharmacokinetics and pharmacodynamics is "how much gets there and what does it do?" It is important to realize that pumps are programmed with "population" data, often derived from a very small population!

What do we mean by the "effect site"? It is a totally abstract and slightly circular concept that represents a mythical drug compartment that would explain the effects we see. To define the characteristics of this compartment we need to be able to measure some effect! So in the neuromuscular block example, train-of-four is the effect. By repeatedly measuring drug doses, blood levels and trains-of-four the relationship can be encapsulated into a mathematical model.

The advent of monitors such as BIS has allowed us to "measure" the effect of hypnosis beyond the binary awake or asleep. Effect site calculations for propofol and a wide range of opioids are based on measurement of various EEG effects and the same approach can be applied to other hypnotics including volatile anaesthetic agents.

Now that measures of the actual effect of hypnotic drugs are available in routine clinical practice it is possible to add a third level to "target control". Instead of targeting a given level in blood, or some notional effect site compartment, we can target an actual effect. This also means that instead of searching for more detailed and accurate population based models we can concentration on optimising dosing for the individual patient.

Hypnosis is not the only "target" of anaesthesia delivery. Analgesia and sympathetic stability are also essential. One approach to targeting these is to provide "enough" hypnotic to produce a BIS/entropy value of (say) 50 and then to treat sympathetic activity with opioids. However various "analgesic monitors" are being developed with two quite different approaches being evaluated by Aspect, based on EEG variability and by GE using plethysmographic data. This should mean that we will soon be able to specifically target "analgesia" as an end point.

We "target" many other end points during anaesthesia. We control E_TCO_2 and airway pressure by manipulating ventilator settings and "target" end-tidal volatile concentrations by manipulating fresh gas flow and vaporiser

settings. As overall flow rates decrease and views on appropriate levels of FiO_2 change we are learning new strategies for targeting FiO_2!

One area attracting interest is volume status, especially during bowel surgery, and also in other situations where fluid balance becomes confused. There are several technologies developed initially for minimally invasive cardiac output monitoring that may have value guiding volume replacement. There are suggestions that these indexes, based predominantly around analysis of the pulse waveform outperform traditional measures of volume. They also provide near real time continuous indication of intravascular volume status and allow "volume" to become a target. Point-of-care testing already gives us information on blood composition which can be combined with volume markers to produce an integrated "targeted" approach to fluid therapy.

There is a reasonable amount of data on the interaction between hypnotic and analgesic agents on the response to various stimuli, although this is hard to apply in practice since the interactions are anything but linear. An added complexity is that drugs used in anaesthesia seldom get anywhere near equilibrium. This means that the basic drug kinetics most of us learnt don't explain what is actually going on. We may be able to deal with this for a single drug, especially with the help of TCI pumps, but the situation becomes much more difficult when dealing with multiple drugs and interactions.

Two different approaches are being applied with the relative technologies very close to market. These provide a graphic display of the interactions in a way which allows the user to "drive" the patient through various hypnotic / opioid combinations. A further advantage of these systems is the ability to deal with multiple drugs so that drug substitution is made straight forward. Thus one can use remifentanil for the start and middle of a case, both for the added titratability and to define the specific patient needs and then these systems make it easy to add it an equivalent amount of (say) fentanyl or morphine.

So what is "true target controlled anaesthesia"? That would require the ability to define and measure all the components of anaesthesia management and then to have specific strategies to manage each "target". We still have a long way to go to reach this "target", but we now enough parts of the puzzle to be able to visualize the eventual shape of the picture and an increasing range of tools to improve our aim.