

Effect site concentrations and volatile anesthetics?

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The concept of target controlled infusion (TCI) is familiar to most anaesthetists. Commercial TCI systems initially supported only propofol plasma levels. Over recent years "open TCI" pumps have made TCI possible for an increasing range of drugs and also control of either plasma or "effect site" levels of most of these drugs. There is a reasonable amount of evidence that using effect site targeting does allow better titration of drug delivery(1).

We have been applying many of the principles of TCI to the delivery of inhalational agents for several years and have deployed tools to guide inhalational delivery in our hospital (2).

It is frequently stated that end-tidal levels give a good indication of inhalation effect site concentrations. However the delay between end-tidal and effect site for inhaled agents is similar to that between plasma and effect for propofol or remifentanyl, with half times between 2 and 4 minutes. This means that a change in end-tidal concentration will take 5-10 minutes to be fully reflected at the effect site. A variety of factors mean the time from a change in vaporizer setting until the full effect is seen will be much longer, and we have attempted to overcome these delays without needing to resort to high gas flow rates(3). We have been able to demonstrate that estimates of effect site levels required for various stimuli correspond to the "MAC" values which are determined allowing time for equilibrium (4,5).

Many drugs, including volatile anaesthetics, have more than one effect. Since these probably occur at different locations we should not be surprised that these "effects" may require different effect site concentrations(6,7). For instance the hypnotic effect of volatile agents, which is what BIS measures, is a cortical effect, while responses to nociception occur in the spinal cord. Less obvious is that the half times for these various effects also differ. Although this concept of a whole range of different effect sites may sound confusing, it does have the potential to allow us to more closely match drug levels to requirements at different stages of anaesthesia especially when coupled with estimates of effect site concentrations.

Estimates of volatile anesthetic effect site levels use measured end-tidal concentrations and would therefore appear more accurate than those for IV agents for which there is no real-time measurement. However all estimates of effect site concentrations are based on models and assumptions, and "required" levels, such as MAC values, are derived from populations. This means that we still need to adjust delivery to the requirements of the individual patient. We have access to devices that measure the degree of hypnosis and monitors of the nociceptive component of anaesthesia are under development. Devices that model of the combined effect of multiple drugs on these two "dimensions" of anaesthesia are available in some markets.

Once these various devices are validated, the way in which we control drug administration to match the needs of the individual patient and stage of the

procedure may change significantly. An understanding of effect site volatile levels and tools to control them will help understand the information from these devices and monitors and will continue to be of value as long as these agents continue to be widely used.

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