Science vs supposition: the case of target-controlled propofol infusion

Editor—I continue to be confounded by the use of target-controlled propofol infusion (TCI) dosing paradigm as an accepted basis for presenting the scientific study in anaesthesia journals without specific documentation of instantaneous and total dose infusion rates, in conjunction with body weight and duration of infusion at the study point. Although TCI may be utilitarian in the clinical administration of drug for clinical anaesthesia, the recent study by Yufune and colleagues\(^1\) clearly documented a real and important departure from scientific measured blood levels using the ‘black box’ technology of TCI. This non-clinical study was also undertaken in patients removed from surgical stimulation: surgery imparts typically significant sympathetic responses which change haemodynamics and, expectantly, drug kinetics. Although bispectral index (BIS) ranged between 25 and 50 with the average BIS near 35–40, in spite of TCI set for induction at 6 s then at 90 s reduced for the study period to 4 \(\mu\text{g m}^{-1}\), this BIS indicates significant overdose, as the ‘Target/desired’ BIS level for minimizing cant overdose, as the ‘Target/desired’ BIS level for minimizing anaesthesia is to reduce hypnotic doses, inhibit spinal reflexes, and to offset haemodynamic effects of surgical stimulation. The effects on anaesthetic depth in the non-stimulated anaesthetic state on BIS, as the haemodynamic effects of preparatory (i.e. ‘surgical’) stimuli of intubation, etc. spontaneously decline, something quite commonly noted clinically. BIS is known to vary directly to the surgical stimulation, exhibit extinction/regression phenomenon over time after termination of surgical stimulation, and is not specific to the depth of anaesthesia in all instances. The utility of narcotic administration during clinical anaesthesia is to reduce hypnotic doses, inhibit spinal reflexes, and to offset haemodynamic effects of surgical stimulation. The effects on anaesthetic depth in the absence of surgery would be expected to be quite different than in this non-surgical setting. The authors also presumed to study if: ‘remifentanil may decrease the blood flow at propofol clearance sites and increase the \(C_p\) during constant propofol infusion’, but TCI by definition is not a constant infusion rate and specifically varies to maintain a projected (and apparently erroneous, as documented here) plasma concentration.

I would like to simply plea that internationally, TCI presentation in scientific journals no longer be acceptable without presenting drug administration rates, total doses, and duration times, including BMI, body weight, or both, to allow documentation of scientific vs supposition data, especially as multiple TCI paradigms exist worldwide and are not always readily accessible to or can be translated into drug administration rates by the readership. Thankfully, the remifentanil dosing was scientifically dosed in \(\mu\text{g kg}^{-1}\ \text{min}^{-1}\), and not in TCI ‘supposition units’. Why should propofol be exempt from the standard scientific System International units?

Conflict of interest

None declared.

P. M. Kempen*
Cleveland, USA
*E-mail: kmnpnm@yahoo.com


doi:10.1093/bja/aer043

Reply from the authors

Editor—We thank Dr Kempen for his comments regarding our article.\(^1\) Propofol target-controlled infusion (TCI) is used during general anaesthesia. Although propofol TCI is set by \(\mu\text{g m}^{-1}\), which is also the unit used to represent plasma propofol concentration, the target plasma concentration is not the same as the actual plasma propofol concentration. Furthermore, many factors (co-administered drugs, surgical stimulation, haemodynamic instability, etc.) may affect the discrepancy between the target and actual plasma propofol concentration. When a TCI system is used, the operator should know how these factors affect the actual propofol concentration during propofol TCI. In this study, we investigated the effect of remifentanil, which is commonly used with propofol anaesthesia, on the plasma propofol concentration in the absence of other factors (before surgical stimulation) during propofol TCI.

The propofol infusion rate is not constant even when the predicted plasma/effect site propofol concentration is constant. We agree that the sentence ‘remifentanil may decrease the blood flow at propofol clearance sites and increase the \(C_p\) during constant propofol infusion’ in the Introduction section is confusing: ‘during constant propofol infusion’ should be changed to ‘during propofol TCI’.

To investigate the effect of remifentanil on plasma propofol concentration, the target plasma concentration of propofol was constant during the data-sampling period in our study. When TCI was set at 2.5 \(\mu\text{g m}^{-1}\) in a preliminary study, the bispectral index (BIS) was over 60 before the data-sampling period (during the 15 min maintenance period) in some patients; therefore, we set TCI to 3 \(\mu\text{g m}^{-1}\) in this study. Please note that, after tracheal intubation,