Presenting Data versus Predictions as Basic Scientific Information: Target-controlled Infusions versus Microgram per Kilogram per Minutes

To the Editor:

In the August issue of ANESTHESIOLOGY, I found two articles of particular interest regarding propofol administration.\(^1,2\) I was simply confounded by the fact that target-controlled infusion (TCI) “predicted” concentrations have become the basic jargon for scientific papers. In both articles, I never found any TRUE raw data disclosing the actual dose of drug administered to these patients. In addition, the index of anesthesia in the article by Rigouzzo et al.\(^2\) was the bispectral index value (another proprietary, i.e., undisclosed program).

In particular, the article by Rigouzzo et al.\(^2\) demonstrated that true differences exist between the multiple studied TCI models (and probably all others as well). I was confounded for several reasons: (1) TCI is not currently used in the United States and probably will remain withheld from clinical use by the Food and Drug Administration; (2) there apparently are multiple TCI devices with unknown (to any U.S. clinician) validity and deviations in ability/accuracy; and (3) TCI values are predictions and not measured values in any individual study; (4) multiple variables influence actual plasma concentrations in any given patient or patient group; and (5) finally, the actual TCI infusion rates change over time. Our journal (ANESTHESIOLOGY) is a publication of the American Society of Anesthesiologists, where practice remains relevant in terms of microgram per kilogram per minute during propofol infusion. It would seem appropriate to require, at a bare minimum, presentation of this pertinent information to the readership (at least alongside TCI values) for several reasons: (1) microgram per kilogram per minute is the American “frame of reference”; (2) microgram per kilogram per minute is REAL and not proposed/extrapolated scientific information; and (3) TCI devices should/must disclose the instantaneous infusion rate during the relevant study periods.

Although I understand the practicability of “indexing anesthetic depth” to some form of electroencephalogram monitor for studies for total intravenous anesthesia anesthetics, I would hope the journal would also require end-tidal gas concentration disclosure for any inhaled agent mentioned in a manuscript. As a clinical scientist, it is essential to know what is actually being administered to correlate to truly dependent variables such as bispectral index or TCI, especially because no single electroencephalogram monitor or TCI program has been accepted as the standard for scientific studies or even clinical use in the United States. I concluded that I simply came away from both articles without meaningful clinical information—clinical information being why I read this journal. I personally suspect Bandschapp et al.\(^1\) found “analgesic properties of propofol” simply because pain is the conscious perception of noxious stimulation, and impairment of consciousness resulted in these findings (with probably 60 microgram per kilogram per minute of propofol infusing). Perhaps ANESTHESIOLOGY might lead the world’s journals to take on such a basic standard of presenting facts (infusion rates) instead of predictions (TCI/bispectral index) as basic science and in the interests of our readership.

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References


In Reply:

We have read with great interest and also some concern the letter of Dr. Kempen regarding our manuscript.\(^1\) To begin with the last point, the problem of discriminating analgesia from other effect-like sedation is discussed in our article. This is a typical problem when studying pain and has been discussed in a recent article on ketamine, where the euphoric effect of the drug interacted with its analgesic effect.\(^2\)

With regard to Dr. Kempen’s main criticism, he is completely right that dose is basic information that should be given in the article. Therefore, we are glad to have the opportunity to supply this information ex post: the total dosage was 4.4 mg/kg in 45 min with a maintenance infusion rate of approximately 90 µg·kg\(^{-1}\)·min\(^{-1}\). However, we do not agree with Dr. Kempen that the predicted/targeted concentrations are not “real.” Of course, these concentrations are predicted values that will differ from measured concentrations. However, if one looks at these concentrations as “targets,” the view changes a bit: for the user, the target concentration set at the target-controlled infusion system is as “real” as the infusion rate set at a normal infusion pump. If one uses a defined system, that means a commercially available target-controlled infusion system with a defined pharmacokinetic parameter set, the information that a defined concentration was targeted is as definite as the information that a defined infusion rate was chosen. This means that any