Comparison of predicted and real propofol and remifentanil concentrations in plasma and brain tissue during target-controlled infusion

Van Hese, L; Cuypers, E; Theys, T; Absalom, A; Rex, S

Published in:
Anaesthesia

DOI:
10.1111/anae.15452

Correspondence

Comparison of predicted and real propofol and remifentanil concentrations in plasma and brain tissue during target-controlled infusion: a reply

We thank White et al. [1] for their interest in our study [2] and their thoughts on the implications it may have for the clinical use of total intravenous anaesthesia.

Online Supporting information Table S1 provides details of the exact type of surgery and medications of the patients in our study.

When discussing the development of pharmacokinetic models from data, it should be acknowledged that a balance must be sought between model complexity and parsimony. Some very simple models function very well clinically. An example is the Gepts model for sufentanil, which contains no covariates, meaning that for the same target concentration all patients receive the same dose. There is probably a very large number of factors that influence the pharmacokinetics of any one drug. The authors have suggested adding comorbidities and the effect of interacting drugs as covariates. While this may superficially seem simple, it is far from it, as the complexity can become almost infinite. If, for example, one considers adding interacting drugs as a covariate, there are several drugs that can cause PK and PD interactions, and for each there are additional variable factors (such as class of drug, exact drug used, dose of drug, duration of use, route of administration and duration since last dose). Similar complexity applies to comorbidities. Even when a drug has been used and studied in a very large population, and includes large numbers of patients in whom information about the covariables is available, there will always remain pitfalls associated with under-fitting (how would one then accurately model the influence of an interacting drug or comorbidity on PK parameters), but also with over-fitting (adding a covariate to a model structure, having wrongly attributed some of the residual variation to that covariate).

L. Van Hese
University Hospitals Leuven,
Belgium
E. Cuypers
Maastricht University,
Maastricht, The Netherlands
Email: e.cuypers@maastrichtuniversity.nl
T. Theys
University Hospitals Leuven,
Belgium
A. Absalom
University of Groningen,
The Netherlands
S. Rex
University Hospitals Leuven,
Belgium

No competing interests declared.

References

1. White S, Chirvasuta R, Eusuf D. Brain concentrations of anaesthetic agents: the implications of epilepsy surgery. *Anaesthesia* 2020. Epub 10 December. https://doi.org/10.1111/anae.15344.
2. Van Hese L, Theys T, Absalom A, Rex S, Cuypers E. Comparison of predicted and real propofol and remifentanil concentrations in plasma and brain tissue during target-controlled infusion: a prospective observational study. *Anaesthesia* 2020; **75**: 1626–34.

doi:10.1111/anae.15452

Supporting Information

Additional supporting information may be found online via the journal website.

Table S1. Type of surgery and medications of the patients.