CORRESPONDENCE

References

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In Reply:—We appreciate the suggestions of Overdyk and Roy and agree that the essential point of our manuscript was to validate the context-sensitive half-time (CSHT) predicted by the pharmacokinetics previously programmed into our Computer Assisted Continuous Infusion device. This was done, and the modeled CSHT from our measured data was not significantly different from CSHT calculated from historical pharmacokinetic parameters. For alfentanil, the "historical CSHT" was published previously and is reported in the first paragraph of the discussion section as 59.4 min. The measured alfentanil CSHT was reported in table 3 as 51.9 ± 12.3 min (mean $\pm$ SD) and represents a validation of the "historical" calculation of CSHT. The same is true for remifentanil. In hindsight, we may have presented confusing nomenclature by using the terms "modeled" and "measured" CSHT (table 3). These terms would probably have been better called "measured CSHT: entire data" and "measured CSHT: terminal data", respectively, to indicate that they both represent measured CSHTs, but that each was based on different parts of the same data set. We used the exponential functions simply because one cannot directly measure the precise time for a 50% decrease in concentration with intermittent (discrete) blood samples. Instead, one has to develop a continuous function, fit to the data, from which the time to a 50% decrease can be interpolated accurately.

As Overdyk and Roy correctly observe, the essential point is that no matter how the measured CSHT was calculated, it should (and does) confirm the previously published *a priori* expectation of CSHT. We appreciate the opportunity to clarify this portion of the article.

As for their concern of the pharmacodynamic CSHT regarding the "usually . . . sigmoidal relationship between effect site concentration and the effect," we simply re-state that we have reasonable assurance that we were measuring ventilation effects over the middle range of the sigmoidal curve, where the change in effect site concentration and effect is nearly linear. Therefore, we do not require a sigmoidal curve to define our change in minute ventilation because we did not seek to measure a 50% change in minute ventilation from maximal effect (E_{max}) to no effect (E_o), but rather a 50% change in the measured effect over the linear portion of the curve, as exhibited in our study population.

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