THE INTERACTION BETWEEN NITROUS OXIDE, SEVOFLURANE AND OPIOIDS: A RESPONSE SURFACE APPROACH

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Background: The interaction of sevoflurane and opioids can be described by response surface modeling using the Hierarchical model.1,2 We expanded this model with the co-administration of nitrous oxide (N2O), using data from Katoh et al 3 on sevoflurane MAC and MAC-BAR reduction by fentanyl with and without 66% N2O.

Methods: Using the Hierarchical model for sevoflurane and opioids, four potential actions of N2O were postulated: (1) N2O is equivalent to X vol.% of sevoflurane (additive interaction); (2) N2O reduces C50 of sevoflurane by a factor Y; (3) N2O is equivalent to P ng/ml of fentanyl (additive interaction); (4) N2O reduces C50 of fentanyl by a factor Q. Each of these four actions, and any combination of them, was tested to the data using NONMEM, assuming identical interaction parameters (X,Y,P,Q) for movement and sympathetic responses.

Results: The influence of 66% N2O was best described by a combination of an additive effect corresponding to 0.54 vol.% sevoflurane (X) and an additive effect corresponding to 0.27 ng/ml fentanyl (P). Including the parameters Y and Q did not further improve the fit.

Conclusion: With this simple extension the effect of N2O can be incorporated in the Hierarchical interaction model and the response surface and the probability of movement and sympathetic responses can be estimated with any combination of sevoflurane, opioids, and N2O.

References:

1. Heyse et al: Anesthesiology 2011: under revision
2. Bouillon et al.: Anesthesiology 2004;100;1353-72
3. Katoh et al.: Anesthesiology 1999;90:398-405