

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

Hugo Vereecke, MD, PhD¹; JH Proost, PhD²; Michele Struys, MD, PhD³

UMCG, Groningen, The Netherlands¹, Hamamatsu University School of Medicine, Hamamatsu, Japan², Bern University Hospital, Bern, Switzerland³

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