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Opioids and Cerebral Blood Flow Velocity

To the Editor:—The study by Trindel *et al.* on the effects of fentanyl and sufentanil¹ on cerebral blood flow velocity is interesting and raises some important questions. As the authors indicated, opioids, at least as far as we know, do not uncouple cerebral blood flow and metabolism. The demonstration of significant depression in cortical electrical activity with concomitant increase in cerebral blood flow velocity simply is puzzling. Moreover, as discussed by the authors, this is inconsistent with previous observations.^{2*} Although there is no doubt that the observed increase in flow velocity is real, this finding may have been caused by an increase in Pa_{CO₂} and not necessarily by a direct action of the opioids. The investigators were successful in maintaining the end-tidal carbon dioxide constant and performed a validation study in four additional patients to defend the use of end-tidal carbon dioxide. However, we believe the possibility of flow velocity increase secondary to Pa_{CO₂} increase has not been eliminated in the study.

First, although there is generally a good correlation between end-tidal and arterial carbon dioxide, this relationship is consistent only when the tidal volume as well as the alveolar dead space are relatively constant, be it during spontaneous breathing in an awake individual or during mechanical ventilation in an anesthetized patient. During the transition from spontaneous breathing to assisted ventilation by mask (as occurred in this study), one cannot be certain that these variables remained unchanged. Considering the large doses of fentanyl and sufentanil that were given, it is conceivable that the total chest wall compliance was affected, even though chest wall rigidity was not clinically evident.

Second, opioids may decrease pulmonary artery pressure and, coupled with the increase in alveolar pressure from positive pressure ventilation, will lead to an increased alveolar dead space, with a corresponding increase in arterial to end-tidal carbon dioxide gradient.

Finally, the authors' validation attempt in four patients casts some doubt on their assessment that Pa_{CO₂} was unchanged. The mean change

in end-tidal and arterial carbon dioxide was indeed small (only 0.37 mmHg for the former and 1.9 mmHg for the latter), leading to their conclusion that the change in Pa_{CO₂} in the study patients could not be more than 2.0 mmHg. However, the standard deviation (3.57 mmHg) was 10 times that of the mean for end-tidal carbon dioxide and 2.6 times (4.9 mmHg) that of the mean for Pa_{CO₂}. Such large standard deviations detract the usefulness of the mean values and put the authors' contention that Pa_{CO₂} did not change appreciably during the course of the study on shaky grounds. Considering that flow velocity changes approximately 3% per mmHg change in Pa_{CO₂},³ the results could be explained by an increase of Pa_{CO₂} of 7–8 mmHg, a possibility, we believe, that has not been ruled out by their validation study. It is clear that the influence of opioids on cerebral blood flow remains controversial. We hope Trindel *et al.*'s work will stimulate further research to clarify this issue, and if indeed their observations are confirmed, the mechanism for this flow-metabolism uncoupling warrants delineation and clarification.

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