Does Halothane Protect Against Hypoxia?

To the Editor.—Hershenson et al.1 confirmed a previous investigation2 that halothane significantly reduces cardiac output and oxygen consumption in normoxic and hypoxic newborn lambs when compared to paralyzed, ventilated controls. They conclude that halothane reduces oxygen consumption and delivery, and may be protective in hypoxic patients. One must exercise caution in interpreting these results because of two serious design flaws in this study. Hershenson et al.1 used paralyzed newborn lambs that were anesthetized with fentanyl (30 μg·kg⁻¹·hr⁻¹) as their control animals. Fentanyl may not be an “anesthetic” in newborn lambs at ten to 100 times this dose.3 Indeed, the ability of fentanyl to anesthetize other species at this dose has been questioned as well.4 We wonder how this may have affected the author’s conclusions. Were the decreases seen in oxygen consumption and delivery the result of halothane per se, or secondary to the reduction of an artificially elevated oxygen consumption and delivery caused by pain or immobilization stress?5 Perhaps any anesthetic agent would produce the same results.

Secondly, all animals were exposed to progressively lower levels of inspired oxygen (100%, 21%, 15%, 10%) in this study without either an intervening return to normoxia or randomization of the sequence of exposure. Were the decreases in oxygen consumption and delivery at the 10% FIO₂ level unduly influenced or exaggerated by the immediately preceding hypoxic exposure?

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to exhibit tachycardia (240 beats·min⁻¹), have occasional spontaneous movements, and respond to noxious stimuli. We did not, however, observe this in our control animals, in which anesthesia was induced with thiopental, 10 mg·kg⁻¹. Perhaps thiopental has a longer half-life in newborn lambs, or has synergistic effects with fentanyl. Whatever the mechanism, control animals did not suffer from immobilization stress or pain as evidenced by mean heart rate (205 beats·min⁻¹), $O_2$ delivery (29.2 cc·kg⁻¹·min⁻¹), and $O_2$ consumption (12.1 cc·kg⁻¹·min⁻¹), all of which were less than or equal to values obtained in awake newborn lambs. In fact, we have found that fentanyl reduces total-body $O_2$ consumption in succinylcholine-paralyzed lambs by about 20%. These data demonstrate that control animals were, indeed, in an unstressed state, and, therefore, we consider the results of our study to be valid.

With regard to the randomization of exposures to hypoxic gas mixtures, exposure to 10% $O_2$ often caused severe cardiovascular instability or death of the experimental animals. Like Dr. Yaster, we too were concerned that such exposure would influence subsequent measurements, and, therefore, deemed randomization impractical. Instead, as previously stated in the Methods section, animals were exposed to progressively lower levels of inspired oxygen, and ventilated with room air for 30 min between exposure to hypoxic gas mixtures to allow for recovery from hypoxia.

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