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Costs of Inhaled Anesthetics: IV

To the Editor:—Although as a proponent of liquid injection–closed circuit anesthesia I admire and appreciate Weiskopf and Eger's insights into the pharmacokinetics and costs of desflurane *versus* isoflurane,[1] I cannot help but worry that their comparison might be misinterpreted and misquoted.

In the Results section of their abstract, Weiskopf and Eger say that "the relative cost of administering . . . desflurane can be less than, greater than, or the same as the cost of administering isoflurane, depending on the background gas inflow rate selected." Anesthesiologists not quantitatively inclined who skim over the text may not realize that desflurane is less expensive only when delivered in fresh gas flows less than or equal to 1 l/min from the moment of induction. Yet many clinicians justifiably will not use such low flows in the absence of an agent analyzer and the presence of a complex, heated vaporizer of revolutionary design. Eger himself[2] has suggested fresh gas flows during desflurane administration in the absence of an agent analyzer of 4–6 l/min for 10–20 min, followed by 2 l/min for the next 1–2 h, after which flows might be reduced. At these flows, Weiskopf and Eger's data[1] show desflurane to be more expensive than isoflurane. Furthermore, upgrading to desflurane agent analysis adds at least $1,000 in capital and maintenance costs.

In the Discussion section of their report, Weiskopf and Eger contend that "the need for analysis is decreased in the case of poorly soluble anesthetics (*e.g.*, desflurane)."[1] Though agreeing on this point as a theoretical matter, I do not administer desflurane without agent analysis. I cannot help but worry about the long-term reliability of the Tec 6 vaporizer, with its numerous active electrical components. Until this vaporizer has an established track record, I believe my patients deserve real-time measurement to alert me to a malfunction. Desflurane's vaunted insolubility suggests a very rapid progression to cardiovascular collapse in the event that the Tec 6 vaporizer accidentally delivers an overdose.

The prices that Weiskopf and Eger use in their calculations (close to what we in Chicago pay) suggest either that isoflurane is overpriced or that the manufacturer of desflurane is temporarily sacrificing to gain market share for its new proprietary anesthetic. Why should desflurane cost only $0.29 per milliliter, when it is synthesized from isoflurane,[2] which sells for $0.71 per milliliter? Recall that desflurane comes in a more expensive bottle and that its sales must amortize the cost of all the $9,500 Tec 6 vaporizers that the manufacturer is supplying at no additional charge to encourage anesthesiologists to start using desflurane.

From a broader perspective, I agree with those who hold that because pharmaceutical agents constitute a small percentage of perioperative costs, it may well be worth spending more for a demonstrably superior agent. Had desflurane been *proven* to result in less serious morbidity or mortality; earlier discharge or return to activity; less nausea and vomiting; less postoperative pain; or lower perioperative costs, I would be enthusiastic about the drug, even if it cost more. In reality, though, introduced after so many anesthesiologists had learned to provide safe, rapid-emergence general anesthesia with drugs already available, desflurane's release and acceptance may be far more important to the manufacturer than to our profession and our patients.

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Costs of Inhaled Anesthetics: V

To the Editor:—Weiskopf and Eger[1] state that the amount of anesthetic needed to load the patient's lungs and the circuit is "relatively small and will be ignored in the present analysis." I wish to expand on this small point.

Lowe and Ernst have previously termed this amount of anesthetic (equal to MAC times the sum of volume of the anesthetic system plus the patient's functional residual capacity) the "ventilatory prime."[2] With a conservative estimate of 6 l for the functional residual capacity plus circuit volume, the formula for the ventilatory prime in milliliters of vapor would be 6,000 ml times MAC. This equals 69 ml isoflurane vapor or 360 ml desflurane vapor. Using the conversions of 1 ml isoflurane liquid to 196.1 ml isoflurane vapor and of 1 ml desflurane liquid to 210.6 ml desflurane vapor,[3] one arrives at the need for 0.35 ml isoflurane liquid or 1.71 ml desflurane liquid to achieve this prime. Converted to dollars (at the prices given by Weiskopf and Eger[1]), roughly $0.25 is required to prime the circuit–patient unit with isoflurane, and twice as much ($0.50) is required for desflurane. Although these amounts seem small they are a significant fraction of the total cost for 30 min of anesthesia. At the lowest flows practical[1] for isoflurane and desflurane (1 l/min), the cost of the prime is 4.7% ($5.30) of the isoflurane cost and 10.8% ($4.62) of the desflurane cost.

Granted, the relative cost of priming decreases as anesthetic time or flows increase. However, priming the patient's lungs and circuit with desflurane still costs twice as much as isoflurane and is 10% of the cost of a 30-min desflurane anesthetic. The priming cost estimated here is conservative, because it assumes an instantaneous increase in anesthetic concentration of the initial patient–circuit volumes. In reality, this increase must be accomplished by washing in the anesthetic at high concentrations and flows with a concomitant increase in waste. In addition, a prime volume of only 6 l was used in the calculations, as opposed to 10 l as assumed by Lowe and Ernst.[2] The priming cost should be included in any cost analysis and not ignored as trivial.

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In Reply:—Abajian and Viscomi and Johnstone correctly take us to task for failing to state our paid consultant relationship to Ohmeda (Madison, WI), the manufacturer of desflurane. The potential bias that such a relationship entails should have been brought to the attention of the reader. Indeed, to do so is our normal practice, and the omission is an embarrassment.

Johnstone's letter does not acknowledge the overall concept of our cost analysis, partly because his approach circumvents consideration of basic pharmacodynamic and kinetic principles. One problem is a focus on 0.2-l/min inflow rates when, at current pricing, the meaningful point is 1 l/min. That is, at flows of less than 1 l/min (not simply 0.2 l/min), desflurane currently is less expensive than isoflurane for the 1st h of anesthesia. At higher rates of flow, desflurane is more expensive, as we presented in figure 2.

Johnstone errs in using 5 l/min as an example. Currently, the average flow used is not 5 l/min but approximately 3.7 l/min (as determined by Ohmeda in an audit of 6,400 anesthetics in 128 institutions across the nation*). The lower the flow rate, the closer the costs of desflurane and isoflurane.

Most important, Johnstone suggests that no account need be taken of the effect of differences in solubility on the effectiveness of a given inspired or delivered concentration. His cost analysis gives all anesthetics at a vaporizer setting (delivered concentration) of 1 MAC. However, if the effect produced by a delivered concentration of 1 MAC halothane is just right, then a dose of desflurane also delivered at 1 MAC would be an overdose of at least 50% at high inflow rates (*i.e.*, as a MAC multiple, the concentration of desflurane in the alveoli would be 50% greater than the concentration of halothane) and an overdose of much more than 50% at low inflow rates.

Again to the point of setting the vaporizer at a fixed multiple of MAC: anesthesiologists who have agent-specific monitors need not rely on the vaporizer setting to determine and control the alveolar concentration of anesthetic. The solubility of desflurane is sufficiently low that after the initial wash-in of anesthetic, the vaporizer setting may be used to gauge the alveolar concentration, particularly at inflow rates of 1 l/min or greater. This advantage does not apply to more soluble agents such as isoflurane and halothane. The cost for anesthetic delivery may increase, in part because of a perception that one needs to purchase a device to monitor the concentration of anesthetic.

Johnstone and Macario believe that higher inflow rates are the norm and that they continue to be used by all anesthesiologists. One possibility regarding less soluble anesthetics is that they enable use of low-flow systems more effectively than do more soluble agents. Our practice is to maintain anesthesia with desflurane at an inflow rate of 1 l/min or less. As argued in our article, these low inflow rates permit greater precision in the control of anesthesia (*i.e.*, a smaller difference between delivered and alveolar concentrations, both as MAC multiples) than do higher inflow rates used with more soluble anesthetics. For example, desflurane delivered at an inflow rate of 2 l/min is currently considerably less expensive than isoflurane delivered at a rate of 4 l/min.

Meyer points to the additional cost of equipment needed to analyze a new anesthetic such as desflurane. He remains unconvinced that the multiple fail-safe devices controlling the output of the Tec-6 vaporizer preclude the potential for overdose in the event of vaporizer

* Ohmeda: Unpublished data.