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.

James Szocik, M.D.
Lecturer
Department of Anesthesiology
University of Michigan Medical Center
1500 East Medical Center Drive
UH-1G323, Box 0048
Ann Arbor, Michigan 48109-0048

References

1. Weiskopf RB, Eger EI: Comparing the costs of inhaled anesthetics. ANESTHESIOLOGY 79:1413–1418, 1993
2. Lowe HJ, Ernst EA: The quantitative practice of anesthesia: Use of the closed circuit. Baltimore, Williams & Wilkins, 1981, p 58
3. Eger EI: Desflurane (suprane): A compendium and reference. Rutherford, Healthpress Publishing Group, Inc., 1993, p 89

(Accepted for publication March 9, 1994.)

Anesthesiology
80:1407–1408, 1994
© 1994 American Society of Anesthesiologists, Inc.
J. B. Lippincott Company, Philadelphia

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.

Downloaded from http://asa2.silverchair.com/anesthesiology/article-pdf/80/6/1408/327596/0000542-199406000-00041.pdf by guest on 21 February 2024

failure. Thus, he argues that such an analyzer is essential and would not rely on the setting of the vaporizer to indicate effective concentration. However, we remember that anesthesia was given successfully 20 yr ago, when analyzers were not in common use and the danger of overdose was far greater with the more soluble anesthetics. Two additional observations come to mind. First, any failure that might occur almost certainly would lead to an underdose rather than an overdose, because the vaporizer would shut off. Second, warning signs of overdosing should emanate from not only the analyzer (a signal, presuming limits had been set to detect such an event) but also from the patient (increased pulse rate and decreased blood pressure).

We accept Szocik's suggestion that we include the cost of loading the anesthetic circuit and patient's lungs, a cost that favors isoflurane. Even the small additional amount of $0.25 for the first 30 min of desflurane probably should not be ignored.

Johnstone correctly notes that both desflurane and isoflurane are considerably more expensive than halothane. Similarly, Abajian and Viscomi ask why we did not include halothane and enflurane in our discussion. Given the current medicolegal concerns regarding the administration of halothane to adults, is halothane a viable alternative? We compared only desflurane and isoflurane because the use of halothane for adults has virtually disappeared in the United States. Also, the use of enflurane has decreased so markedly that it, too, is of limited interest.

Johnstone, Abajian and Viscomi, Macario, and Meyer believe that marketing issues, such as the pricing of a drug before *versus* after expiration of its patent, would limit our analysis. Generic competition might further lower the price of isoflurane, and patent protection may allow an increase in the price of desflurane. Either change would increase the relative cost of adopting desflurane as part of one's practice. However, figure 2 in our report can be used to compare cost at any new price that might be set. The concern regarding future price changes implies that there is a danger to the acceptance of desflurane—that one might become "addicted" to its use. This concern ignores the modular nature of modern anesthetic machines and underestimates the assertiveness of most anesthetists. Ohmeda has made a "revolutionary" vaporizer that can be substituted for other Tec-type vaporizers. However, such a substitution can be immediately reversed by the anesthetist who does not become "addicted" to the use of desflurane and who concludes that the benefit does not justify the cost.

Thus, we are not as pessimistic as some of the correspondents appear to be concerning the cost of desflurane *versus* the cost of isoflurane. Desflurane can be *more* or *less* costly to use than isoflurane. Reducing the cost of desflurane requires an understanding of pharmacokinetic principles. Applying those principles may be slightly more complicated than the approach suggested, for example, by Johnstone. It is, however, more rational.

Richard B. Weiskopf, M.D.
Professor

Edmond I. Eger II, M.D.
Professor

Department of Anesthesia
University of California, San Francisco
521 Parnassus Avenue, C450
San Francisco, California 94143-0648

(Accepted for publication March 9, 1994.)

Anesthesiology
80:1408–1409, 1994
© 1994 American Society of Anesthesiologists, Inc.
J. B. Lippincott Company, Philadelphia

Digoxinlike Immunoreactive Substance in Critically Ill Patients

To the Editor:—A digoxinlike immunoreactive substance (DLIS) has been detected in the absence of treatment with cardiac glycosides in the serum of patients with renal or liver failure, in newborn infants, and in third-trimester pregnant women.[1,2] The structure and physiologic function of DLIS are unknown. DLIS is produced principally by the adrenal gland.[3] It inhibits Na^+/K^+–adenosine triphosphatase and may produce natriuresis. For this reason it has been proposed that DLIS is produced in conditions of volume overloading.[4] We therefore have examined the occurrence of DLIS in patients of an intensive care unit.

The sera of 135 randomly selected patients were analyzed on the day of admission by fluorescence polarization immunoassay (FPIA). This method is used most widely for digoxin monitoring but also has a high sensitivity to DLIS.[5] All digoxin determinations were done in the Abbott TDx® autoanalyzer with FPIA reagents (Digoxin II reagent pack, Abbott Diagnostics, North Chicago, IL). The digoxin antiserum (rabbit) does not cross-react with other drugs except digitoxin. FPIA digoxin immunoreactivity was extrapolated from fluorescence polarization data stored in the autoanalyzer and consisting of analytic digoxin standards (Abbott Diagnostics). Before digoxin measurement by FPIA, the serum protein was precipitated, in accordance with the manufacturer's recommendations. None of the patients had been treated with a cardiac glycoside. We also determined the patients' Acute Physiology and Chronic Health Evaluation II (APACHE II) score, which has been found to correlate with the subsequent risk of hospital death.[6]

Of the 135 patients tested, 101 had nonmeasurable DLIS concentrations; 6 had DLIS concentrations less than the lower detection limit of 0.2 ng/ml (for a total of 107 DLIS-negative patients); and 28 (21%) had DLIS concentrations greater than 0.2 ng/ml (28 DLIS-positive patients). Of the 28 DLIS-positive patients, only 6 showed signs of liver or renal impairment. The DLIS-positive group consisted of patients with head injury (4), liver failure (3), rupturing abdominal aneurysm (1), coronary bypass surgery (2), acute heart transplant

Downloaded from http://asa2.silverchair.com/anesthesiology/article-pdf/80/6/1408/327596/0000542-199406000-00041.pdf by guest on 21 February 2024