Sevoflurane Cost Comparisons Questioned

To the editor: The article “Sevoflurane induction procedure: cost comparison between fixed 8% versus incremental techniques in pediatric patients” was an interesting study that shared several findings that we would like to discuss. The assumption asserted by the authors that a typical incremental sevoflurane induction (a smooth induction) is clinically comparable to 8% sevo/N2O induction (a rapid induction) is not valid. Rapid induction with an 8% sevo/N2O primed circuit is often used for the uncooperative child, those in whom sedation is not desired or ineffective, and those that may require a fast induction for a multitude of other reasons. In short, the study compares separate techniques often used for very different clinical rationale and unlikely chosen interchangeably for typical inductions. More relevant to clinical decision-making and cost analysis would be a comparison of two types of smooth induction (incremental sevo compared to 8% sevo initiated at time of administration without priming).

Had the authors compared two types of smooth mask induction, the difference in sevoflurane consumption would be negligible, 0.42 mL per induction procedure. If the authors’ finding of 2.62 mL sevoflurane consumed by priming the circuit with 8% sevoflurane/N2O were subtracted from the amount of sevoflurane consumed with circuit priming, the result would be the amount that would be consumed by using a smooth mask induction at 8% sevoflurane without priming (3.51 mL).

An argument could be made that these cost savings are still important to consider given the authors stated sevoflurane costs of $6.00/mL; however, this is not the typical cost. Typical cost of sevoflurane is less than $1.00/mL ($0.4-0.65/mL). At $6.00/mL a 240 mL bottle of generic sevoflurane would cost $1,440.00. This cost is astronomical considering the US generic sevoflurane cost is as low as $10.00/bottle. This raises the question why the disparity between India and the US for cost of generic sevoflurane? Also questioned are the apparent contradictory price disclosures between this article and the same authors’ very similar article “Pharmacoeconomics: Minute-based cost of sevoflurane in pediatric short procedures and its relation to demographic variables” in which the stated open market price of sevoflurane in India is 5,500 Rupees (Rs) which converts at current exchange rate of 1 Rs = 0.016 $ (5 year exchange rate range 0.0190-0.0225) to $88.67 US per bottle. The authors specifically state “the cost per milliliter was calculated to be Rs. 22/mL.” Rupee to dollar conversion equals 35 cents/mL not $6.00/mL cost as stated by the authors. Thus, the mean cost savings per induction in the study is approximately $1.07 (mean difference in sevoflurane consumption 3.04 mL [6.13 – 3.09 mL = 3.04 mL]. It appears likely that the 5,500 Rs cost of generic sevoflurane was incorrectly converted to US dollars and thus all data in this study fatally flawed.

The comparison of sevoflurane consumptive cost is appropriate when exploring an area of potential savings. Once a volatile anesthetic agent leaves a vaporizer it is not recoverable for reuse (except during low-flow rebreathing for that particular patient) and therefore the purchaser has realized absolute cost. Interest in the cost analysis of clinical scenarios using different volatile anesthetic agents at different concentrations, carrier flow rates, and durations spurred the development of an anesthesia iApp, CRNA Volatile Anesthetic Agent Cost Calculator, to address this clinical concern of cost effectiveness. The use of this iApp may clarify actual costs and questions that remain unanswered in the literature.

REFERENCES


Mark Welliver, CRNA, DNP, ARNP
Dawn Dalpé Welliver, CRNA, DNP, ARNP
Fort Worth, Texas

DISCLOSURE
Authors have no conflict of interest or financial involvement in the subject material.

Response: We thank Welliver et al for their critical comments on our study “Sevoflurane induction procedure: cost comparison between fixed 8% versus incremental techniques in pediatric patients.” It is such critical analysis that helps to improve the scientific literature. There are several points in the interpretation of our study results/methodology on which we disagree to assumptions made by Welliver and colleagues.

Multiple studies from time to time have shown that high concentration sevoflurane induction is equally safe when compared to incremental induction in contrast to similar induction techniques used with halothane (only other agent validated for inhalation induction). Trials have not reported any significant adverse effects with high concentration sevoflurane induction. Thus safety and acceptability concerns make a comparison possible unlike halothane. Additionally, the assumption made by Welliver et al that incremental induction is “smoother” may not be entirely correct, on the contrary Hall et al showed that high concentration induction shortens the second stage of anesthesia (stage associated with excitatory phenomena) and actual induction may be smoother than low concentration. Thus from experience and literary evidence we suggest that high concentration induction is equally smooth (if not better) than incremental or low concentration techniques. Other important reason that actually caused the introduction of high concentration technique into clinical practice is possibility to achieve rapid of induction by using higher MAC equivalents (concentration multiples of MAC). The reason that rapidity of induction remains a priority is because it is not comfortable for awake or even partially sedated child to have mask applied tightly to the face even with a slight awareness for a longer duration. Additionally, oral sedation in day care settings does not assure complete alleviation of anxiety as well. Thus in our study we adopted techniques (circuit priming) to simulate actual settings. In high turnover centers, like many others and our center large number of children undergo ocular examination under anesthesia on day care basis (setting in which our study was conducted) and sedation is known to be not completely adequate always.

Welliver et al have subtracted the sevoflurane consumed during priming of circuit (ie, 2.62 mL) from the 8% induction group and state that sevoflurane consumed in both the groups is nearly equivalent, which is an incorrect oversimplification and deviates from actual clinical settings. We impress upon the fact that by eliminating priming one loses the rapidity of induction, which is very important in this age group. The filling up of circle system and eventual building up of concentration of sevoflurane in the circuit is a first order kinetic process and is related to a number of time constants allowed for priming. If the mask is applied to the child for induction without priming (with 8% sevoflurane) the concentration that child inhales gradually builds up in comparison to situation where it is done after circuit priming where the child actually gets high concentration right from the application of the mask. So, eliminating priming gas flow would prolong the duration of induction (defined as duration from mask application to end point of clinical induction) thus sevoflurane at 8% post priming would run for much longer duration to induce anesthesia. So, assuming that subtracting 2.62 mL (priming volume of sevoflurane) would not affect the subsequent phase and thus consumption would remain the same (as of value in present finding) is not actually true. There is a gross flaw in understanding the concept of pharmacokinetics of anesthesia circuit (circle system) in such an oversimplification.

Welliver and colleagues suggest from our study in the Indian subcontinent that the cost of sevoflurane used in India is Rs 22/mL and thus is only 35 US cents, which should probably be extrapolated to this study as well. However, in actual setting such a cost evaluation of drug/medical services by simple currency conversion across borders can never be correct. Drug costs are regulated by various authorities within a country and generally with values being significantly lower in low-income countries. Thus, drug costs cannot be equated between India and USA directly (as the values in the study represent expected costs in the USA). We however agree to the comment that sevoflurane cost shows significant variations within USA itself. Costs
of drugs also show marked variation within the same region with time as well; a drug extremely expensive may become very cheap in a few years span. Generic drugs can be significantly cheaper.

Also, costs used at one time point are likely to show significant variations both geographically and chronologically. AANA Journal is an international journal archived online for years. Thus our study not only targets readers of the present time in the USA alone but also internationally even for future reference as well. Keeping this in mind the conclusion of our study clearly states that the cost of high concentration induction is nearly twice the incremental method of induction. Such a cost ratio is not limited by country or year in which the study is read/interpreted. Thus, we suggest avoiding only isolated cost values interpretation of our study conclusion without considering factors that actually govern these costs.

REFERENCES


Preet Mohinder Singh, MD, DNB, MNAMS
Anuradha Borle, MD, DNB, MNAMS
Anjan Trikha, MD
New Delhi, India

DISCLOSURE

Authors have no conflict of interest or financial involvement in the subject material.