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Clinical safety and cost analysis of Sevoflurane and Isoflurane in surgical patients

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ABSTRACT

Determining the cost of volatile anesthetic agents is important to buffer the rising cost of healthcare by cost effective use of these drugs. Herein, this paper presented a cost analysis of sevoflurane and isoflurane with considering their effects on hemodynamic stability. In a randomized clinical trial, 52 ASA status I–II patients candidate for aortobifemoral bypass surgery were assigned to receive low-flow sevoflurane anesthesia (n = 26) or low-flow isoflurane (n = 26). Patients were monitored for assessment of hemodynamic parameters and the amount of gas consumption and costs for each patient was also recorded. The mean cost of consumed gas in sevoflurane group was 87807 ± 41261 Iranian rials (currency) and in isoflurane group was 144423 ± 69609 Iranian rials that was considerably higher in isoflurane group (p < 0.001). In line with assessing cost of consumed gas, increased mean arterial blood pressure (> 100 mmHg) was obtained in 80.8% in sevoflurane group and 84.6% in isoflurane group after aortic clamping and also following removal of aortic clamp with no significant differences. Regarding changes in heart rate in sevoflurane and isoflurane groups, after removal of aortic clamp, the overall prevalence of bradycardia was higher in those who received isoflurane compared with another group (97.2% versus 26.8%), while sevoflurane group experienced normal sinus rhythm more than that observed in isoflurane group (30.8% versus 3.8%, p < 0.001). Considering both clinical safety and affordability, Sevoflurane is preferred to isoflurane as anesthetics for surgical patients.

Keywords: Sevoflurane, Isoflurane, cost, hemodynamic

INTRODUCTION

Halogenated gases were created in the 1940s and were safer, more stable, and more potent anesthetic agents(1). In order to meet the growing needs for a rapid acting and dissipating anesthetic agent for surgery, lower solubility volatile anesthetic agents (VAAs) were created that among them, isoflurane (1981) and sevoflurane (1995) have been more applied worldwide(1).

Anesthesia professionals have better control of their anesthetic technique by using these lower solubility agents. Besides of the clinical safety as well as availability of these drugs, cost containment and cost effective use of these agents has also become a priority within healthcare(2).

This has created a challenge for anesthesia providers wanting to deliver high quality healthcare that is safe yet economical. In anesthesia, volatile anesthetic agents may account for up to 20% of total anesthesia costs(3). Sevoflurane is the newest and relatively expensive VAAs used for anesthesia. Sevoflurane is a potent anesthetic that may be ideal for patients undergoing different surgeries and also in patients with reactive airways. Sevoflurane is a versatile sweet smelling VAA that may be used for mask induction and maintenance of anesthesia(4-6). Besides, Isoflurane has been agreed as a safe anesthetic both for patients and for the operating room personnel.

The main advantages of this drug have been expressed to be fast induction and recovery, relative sparing effect on cardiovascular function and cerebral blood flow auto-regulation(7). However, it seems that Isoflurane is not a cost-effective drug and in some cases, costs anywhere from 5-10 times as much as the next highest priced anesthetic agent(8).

The acquisition cost of Sevoflurane and Isoflurane varies per institution, location, and contract. A difficult challenge for hospital pharmacies is budgeting drug cost. Budgeting for intravenous drugs is much simpler than VAA since there is a direct relationship between the amount of drug acquired and administered. Thus, determining the cost of VAAs is important to many institutions attempting to buffer the rising cost of healthcare by cost effective use of drugs and therapies.

This paper presents a cost analysis of Sevoflurane and Isoflurane with considering their effects on hemodynamic stability. On the basis of the present observation, Judgment about more appropriate anesthetics should be based on its both clinical safety and affordability.

MATERIALS AND METHODS

Fifty two consecutive patients with ASA status I–II candidated for aortobifemoral bypass surgery were entered into this double-blinded randomized controlled trial at Sina hospital in Tehran. The study protocol was approved by the research and ethics committee at the Tehran University of Medical Sciences and written informed consent was provided from the participants. none of the subjects had history of hepatic or renal disease, hypertension or diabetes mellitus, history of consuming substance or alcohol, or treated with clonidine, beta-blockers, calcium-blockers, digitalis, tricyclic antidepressants, or any analgesic drugs. None of the groups received premedication before entering surgical ward, using block randomization method, patients were assigned to receive sevoflurane or isoflurane by a research unaware of group characteristics. After setting two peripheral venous access routes and hydrating with Ringer solution (7 ml/kg) and setting an arterial line, all patients were monitored on standard protocol using ECG monitoring, invasive assessment of blood pressure by Dynascope 3300 (Fukuda Denshi Ltd Co., Tokyo, Japan) as well as pulse oxymetry monitoring and capnography by CO2SMO-Capnograph/Pulse Oxymeter (Novamaterix, Wallingford, USA). Before anesthesia induction, ensuring the safety of anesthesia machine (Drager, Germany), lack of leaking from semi-closed system, to full vaporizers of evaporative anesthetics, and also calibration of anesthetic gas analyzer and replacement of Sodalime Canister was taken. For controlling postoperative pain, and reducing the need for analgesic medication after surgery, patients received Bupivacaine 0.5% (10 ml) through epidural anesthesia from L3-L4 or L4-L5 spaces.

Then, the patients were premedicated with midazolam (0.04 mg/kg) and fentanyl (1.0 µg/kg) and were preoxygenated with 100% oxygen(6 L/min for 3 minutes). Anesthesia was then induced with thiopental (5 mg/kg) and Atracurium (0.5 mg/kg) and then patients were ventilated with mask. all subjects were intubated and then mechanically ventilated with tidal volume 6 ml/kg and frequency of 10 respiratory rate per min that the EtCO2 was maintained in the range of 35 to 40 mmHg.

After assignment of patients into two study groups and along with mechanical ventilation, 100% oxygen (250 mL/min) was used in sevoflurane group and inlet gas flow was adjusted such that a negative pressure was not appeared and SPO2 was set lower than 95%. In this state, FGF was also set in the range of 250 to 300 ml/min. sevoflurane level was maintained at 3%. Fentanyl (1.0 µg/kg) was administered every 45 min if required. Isoflurane with the volume of 1. MAC was also administered with considering FGF 2.5 L/min along with administration of oxygen and N2O equally.

Patients were also monitored for assessment of: (1) Inspiratory and expiratory concentrations of sevoflurane and isoflurane every minute for 30 minutes and then every 5 min until the end of surgery; and (2) blood pressure and heart rate every 3 minutes for 30 minutes and then every 5 min until the end. The amount of gas consumption and costs for each patient were recorded.

Results were reported as mean ± standard deviation (SD) for quantitative variables and percentages for categorical variables. The groups were compared using the Student's t-test for continuous variables and the chi-square test or Fisher's exact test if required for categorical variables. P- values of 0.05 or less were considered statistically significant. All the statistical analyses were performed using SPSS version -19.

RESULTS

The average age of patients who received sevoflurane and isoflurane was 65.1 ± 7.6 years and68.3 ± 7.7 years respectively with no different statistically (p = 0.142). also two groups have not significant different according sex parameter(p=0.275) (table-1).

Table 1. Comparison of demographic factors between the two study groups

Sex		Age			Groups
Male	Female	Standard deviation	Mean	Number	
12	14	7.7	68.3	26	isofluran
15	11	7.6	65.1	26	sevofluran
0.275		0.142			p-value
Chi-square		Independent sample T-test			test

The mean cost of consumed gas in sevoflurane group was 87807 ± 41261 Iranian rials (currency) and in isoflurane group was 144423 ± 69609 Iranian rials that was considerably higher in isoflurane group (p <0.001). In line with assessing cost of consumed gas, the changes in hemodynamic status was also assessed and showed that increased mean arterial blood pressure (> 100 mmHg) was obtained in80.8% in sevoflurane group and 84.6% in isoflurane group after aortic clamping with no significant difference (p = 0.714). Also, following removing aortic clamp, the elevated mean arterial blood pressure in the two groups reached in 61.5% and 53.8% respective lt with no significant difference (p = 0.575). Regarding changes in heart rate in sevoflurane and isoflurane groups, after setting aortic clamp, bradycardia was found in 34.6% and 46.2% respectively with no difference (p = 0.538).Moreover after removal of aortic clamp, the overall prevalence of bradycardia was higher in those who received isoflurane compared with another group (97.2% versus 26.8%), while sevoflurane group experienced normal sinus rhythm more than that observed in isoflurane group (30.8% versus 3.8%, p < 0.001)(table-2).

Table 2. Comparison of variables between the two study groups

mean cost of consumed gas	increased mean arterial blood pressure (> 100 mmHg)		bradycardia		normal sinus rhythm	
	Aortic clamp	Removal of aortic clamp	Aortic clamp	Removal of aortic clamp		Groups
144423 ± 69609	84.6%	53.8%	46.2%	97.2%	3.8%,	isofluran
87807 ± 41261	80.8%	61.5%	34.6%	26.8%	30.8%	sevofluran
< 0.001	0.714	0.575	0.538	< 0.001	< 0.001	p-value
Independent sample T-test	Chi-square					

DISCUSSION

The current literature supports the use of low flow anesthesia, regardless of VAA in reducing anesthetic cost. Hence, this clinical investigation was designed to compare the clinical effects as well as cost-effectiveness of sevoflurane and isoflurane for anesthesia in surgical patients.

In this study, the cost of each inhalant was calculated by multiplying the mean amount of inhalant used by its retail cost. Our study revealed more affordability and also more clinical safety of sevoflurane regarding hemodynamic status in comparison with isoflurane. According to study findings and considering day rate of exchange, the mean cost of consumed gas in sevoflurane group was estimated 7.2 $ versus the mean cost of consumed gas in isoflurane group as 11.7 $, indicating more affordability in the first groups. Furthermore, the overall prevalence of arrhythmia was also lower in former group. In fact, considering both clinical effectiveness concummitantly with its cost is necessary to select proper anesthetic agents.

Because of the use of low-flow rate, selecting sevoflurane in this flow situation is more preferred. The majority of the literature supports sevoflurane as the most cost effective agent using similar flow rates(9-14).

Several articles advocate the use of low flow gas rates, however only one makes a case for comparing each agent at lowest allowable flow rates(12,13,14,18). Currently in the United States the FDA recommends FGF no less than 1 L/min for cases less than 2 MAC hours and FGF 2 L/min for cases longer than 2 MAC hours for sevoflurane(15). However, in some regions, possible disadvantages of sevoflurane over isoflurane expressed to be the possibility of nephrotoxicity and higher cost. On the other hand, sevoflurane cost seven times that of isoflurane per Ml(16).

Ries et al. also showed that volatile consumption and cost were greater for sevoflurane compared with isoflurane(17). Conclusions that one drug is more or less cost effective than another can rarely be translated from one region to another because of the variability in drug acquisition cost and availability of generic formulations of sevoflurane. Therefore in some institutions sevoflurane may be less expensive than isoflurane and in others the opposite may hold true. It seems that anesthesia professionals are able to decrease cost of any VAA agent by using low FGF.

The cost of a VAA may be determined using the market price, potency, amount of vapor produced, and the fresh gas flow rate(18). In 1992 in a letter to the editor Dr. Peter Dion stated a formula for directly measuring the cost of inhaled anesthetic incorporating ideal gas law the cost of an anesthetic agent can be calculated from the concentration of gas delivered, FGF, duration of inhaled anesthetic delivery, and even molecular weight and density (19).

According to several affecting factors on estimating cost, the cost of anesthesia using these agents can be minimized by limiting waste of the gas; making sure there aren't leaks in the machine, breathing circuit or leaks around the cuff of the endotracheal tube. Premedication with sedatives or analgesics will help decrease the MAC-value needed for maintenance, which will help reduce the cost.

Determining cost of VAA is a difficult task, made even more challenging by the various methods available to determine cost. Of the methods discovered in the literature, most of them were found to be either impractical or inaccurate. Weighing vapors is impossible to replicate in a busy operating room setting(20). The computer data log method and four compartment model methods do not disclose cost calculation, making it difficult to determine accuracy(21).

A simple comparison of MAC does not factor in important variables such as FGF and differences in VAA properties. Using the volume percent calculation is inaccurate since it is based on a dialed concentration and not an actual concentration determined by a gas analyzer(22).

According to in accessibility of an acceptable tool for determining cost, identifying different affecting factors on anesthetic agents and anesthesia procedures for presenting a valid formula with consider to stabilizing hemodynamic stability should be the main goal.

In conclusion, because of this fact the clinical safety of sevoflurane regarding hemodynamic stability as well as its affordability in our region, the use of this anesthetic instead of isoflurane is preferred.

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