Effects of Sevoflurane and Desflurane on Some Biochemical Parameters

Mustafa Yontem*[1], Aydın Akkaya[2], Suleyman Kaleli[3], Fatih Erci[1], Fatma Emel Kocak[4]
[1]Necmettin Erbakan University, Faculty of Science, Department of Biotechnology, Konya, Turkey
[2]Dumlupinar University, Faculty of Science, Department of Biology, Kutahya, Turkey
[3]Sakarya University, Faculty of Medicine, Department of Medical Biology, Sakarya, Turkey
[4]Dumlupınar University, Faculty of Medicine, Department of Medical Biochemistry, Kutahya, Turkey

Research Article

Article Info

Recived on:24/03/2015
Accepted on: 07/04/2015
Published on: 25/04/2015

QR Code for mobile

Literati

Open Access

ABSTRACT :

General anesthesia is the administration of certain anesthetics that enable a patient to tolerate surgical conditions. This study was aimed to better explain effects of sevoflurane, and desflurane, inhaled anesthetics, on liver and kidney functions by determining postoperative changes of some biochemical parameters. In this study, 35 patients suited physical status of American Society of Anesthesiologists (ASA) I-II groups were included. Patients with normal renal and hepatic functions were randomly allocated into two groups according to the inhalation agents used. These groups are group of sevoflurane (group S) and group of desflurane (group D). In all groups, general anesthesia was induced with thiopentone and cisatracurium and maintained with 50 % N2O - 50 % oxygen and one of the two volatile agents (desflurane, and sevoflurane). Levels of serum BUN, Urea, Creatinine, AST, ALT were determined in blood samples. Levels of AST in group S and group D increased in post-operation. While there was no significant difference in group D, there was statistically significant difference in group S. The primary effects of volatile anesthetics were on the biochemical parameters of liver postoperatively. Especially, in people with liver disease, it may be considered that desflurane can be a good alternative to sevoflurane in general anesthesia.

Keywords: Anesthetics, Sevoflurane, Desflurane, Biochemical parameters.

INTRODUCTION:

Clinically, general anesthesia is primarily implemented to supply convenient surgical conditions creating temporary amnesia, analgesia, areflexia, and muscle relaxation without causing any change in the patient's vital functions. General anesthetics provide both analgesic, and anesthetic effects. In fact, analgesia occurs prior to anesthesia, but it is unimportant in practice[1, 2].

The question of whether or not a patient is suitable to be applied anesthesia is faced often. The patients are divided into 5 groups in terms of the risks of anesthesia according to the evaluation established by the American Society of Anesthesiologists (ASA), and accepted internationally. These are ASA I, ASA II, ASA III, ASA IV, and ASA V [1, 3].

Sevoflurane, fluoromethyl 2, 2, 2-trilloro-1-(trifluoromethyl) ethyl ether, is chemically fluorinated derivative of methyl isopropyl ether. Sevoflurane is a clear, colorless liquid that does not contain any additives or chemical stabilizers. Five percent of absorbed sevoflurane is metabolized. It is metabolized to hexalloroisopropanol (HFIP) by cytochrome P450 2E1, conjugated with glucuronic acid, and excreted by the kidneys. Inorganic fluoride, and carbon dioxide are also released. It slightly reduces renal, and hepatic blood flow. The nephrotoxicity that can be caused by fluoride is not a clinical troublesome. However, its use should be avoided in the patients having renal dysfunction. The metabolism of sevoflurane can be accelerated by well-known factors triggering cytochrome P450 2E1 [4].

The chemical structure of desflurane resembles isoflurane. Fluorine atom replaces chlorine in desflurane, and it is a member of the halogenated methylethy-

doi: 10.15272/ajbps.v5i43.678

**Corresponding author:*
Mustafa Yöntem
Address: Necmettin Erbakan University, Faculty of Science, Department of Biotechnology, Konya, Turkey
E-mail: myontem42@hotmail.com, **Tel**: +903323605954 Fax : +903323238245

Conflict of interest: Authors reported none

lether family that small change results in significant physical alterations. Dose-dependent hypotension, respiratory depression, increase in cerebral pressure, abnormal cardiac rhythm, and myocardial ischemia may occur. Particularly in children, increased secretion of saliva, cough, laryngeal, and bronchial spasms, nausea, vomiting, and hepatitis may be seen independently of the dose. It has been reported that like other halogenated anesthetics, desflurane reacts with dry carbon dioxide absorbents, and generates carbon monoxide. At high concentrations, heart rate, central venous pressure, and pulmonary artery pressure increases [2, 5 – 9].

The aim of this study was to ascertain the effects of sevoflurane, and desflurane, recently available inhalation anesthetic agents, on liver, and kidney functions.

MATERIALS AND METHODS

Subjects

The study was conducted in Dumlupinar University Evliya Celebi Research, and Education Hospital among the patients with age range of 25-65 years whose physical statuses were consistent with ASA I-II group, and who were planned to have elective surgeries because of different diagnoses, and decided to be eligible for general anesthesia by specialist physicians. Evliya Celebi Research and Education Hospital has 750 bed capacity, and 40 medical departments. Our study was conducted with blood specimens collected from totally 35 patients (11 men, 24 women). The patients who had problems during surgery or those who required additional medical agents were excluded from the study. The patients were randomly divided into two groups according to the inhalation agent used. The Group S was consisted of 18 individuals (6 male patients, and 12 female patients), and the Group D was consisted of 17 individuals [5 male patients, and 12 female patients). The study was carried out in accordance with Declaration of Helsinki. Ethical committe approval was received from the local Human Research Ethics Committee. Written informed consent was obtained from the all subjects.

Methods

All patients were examined before, and prepared to the surgery with determination of the premedication. The patients were given premedication intramuscularly with 0.15 mg/kg dose of diazepam, and 0.5 mg of atropine sulfate 30 minutes before the surgery. The induction of anesthesia was done in all patients with the injections of 4-7 mg/kg of thiopental sodium, and 0.15-0.20 mg/kg of cisatracurium, in that order. The concentrations of volatile agents were adjusted to be between 1 to 2% in the sevoflurane group, and between 6 to 8% in the desflurane group. The patients were given preoperatively 3-5 mg/kg of crystalloid serum infusion. Blood specimens were collected at both preoperative, and postoperative 24 h.

For each donor, preoperative, and postoperative venous blood samples were collected into an evacuated serum seperator clot activator tubes (Vacuette®, Greiner Bio-One, Kremsmunster, Austria). The venous blood samples were centrifuged at 3500 rpm for 10 minutes at room temperature, and serum samples were separated. Serum blood urea nitrogen (BUN), urea, creatinine, aspartate aminotranspherase (AST), and alanine aminotranspherase (ALT) levels were measured on Roche Cobas c501 analyzer (Roche Diagnostics GmbH, Mannheim, Germany) with original reagents. Controls for both groups were designated within each group.

Statistical analysis

Statistical analyses were performed using SPSS software (version 13.0 for Windows; SPSS, Inc, Chicago, IL, USA). Mean values for all variables were compared between study groups using paired t test, and two-tailed distribution analysis. For all statistical tests, $P \leq 0.05$ was considered statistically significant.

RESULTS

The levels of serum BUN, urea, creatinine, AST, and ALT determined in the preoperative and postoperative venous blood samples obtained from the desflu-

	Groups	N	Mean ± SD
BUN (mg/dl)	Pre-operation	17	11,8±2,53
	Post-operation	17	11,1±4,12
Urea (mg/dl)	Pre-operation	17	25,1±5,24
	Post-operation	17	23,9±8,93
Creatinine (mg/dl)	Pre-operation	17	0,89±0,12
	Post-operation	17	0,91±0,10
AST (U/L)	Pre-operation	17	16,2±3,82
	Post-operation	17	20,1±8,21
ALT (U/L)	Pre-operation	17	23,0±11,56
	Post-operation	17	19,2±8,18

Results were expressed as mean ± standard deviation

Table 1. The levels of serum BUN, urea, creatinine, AST and ALT in the desflurane group.

	Groups	N	Mean ± SD
BUN (mg/dl)	Pre-operation	18	12,8±3,30*
	Post-operation	18	11,2±3,04
Urea (mg/dl)	Pre-operation	18	27,4±7,41
	Post-operation	18	24,1±6,79
Creatinine (mg/dl)	Pre-operation	18	0,86±0,16
	Post-operation	18	0,84±0,13
AST (U/L)	Pre-operation	18	17,6±5,14[a]
	Post-operation	18	23,2±8,95[b]
ALT (U/L)	Pre-operation	18	16,6±5,68
	Post-operation	18	17,5± 7,59

Results were expressed as mean ± standard deviation.
*: Superscript letters in the same column (a - b) indicate significant differences (p<0.05).
Table 2. The levels of BUN, urea, creatinine, AST and ALT in the sevoflurane group.

rane group (Group D) are shown in Table 1. As shown in Table 1, no statistically significant differences were found for serum BUN, urea, creatinine, and ALT levels. Although there was an increase in serum AST levels, it was not found to be statistically significant.

The levels of serum BUN, urea, creatinine, AST, and ALT determined in the preoperative and postoperative venous blood samples obtained from the sevoflurane group (Group S) are shown in Table 2. As shown in Table 2, no statistically significant differences were found for serum creatinine, and ALT levels. Although there was a decrease in BUN, and urea levels, that decrease was not found to be statistically significant. But the increase in AST level was found to be statistically significant (p≤0.05).

The changes in preoperative and postoperative serum AST levels in both groups were shown in Table 1. Serum AST levels increased arithmetically in both groups. The increase in the Group S was higher than the group D, and was found to be statistically significant (p≤0.05). There was no statistically significant difference between the groups in terms of the increases in AST levels.

DISCUSSION

The goal of anesthesia is to ensure a rapid and comfortable anesthetic induction in the patient without any hemodynamic changes, maintenance of preoperative hemodynamic stability, a rapid wake up without undesirable effects and early mobilization [1, 10-13]. Bedi, and Fee denoted that sevoflurane, and desflurane were more advantageous than isoflurane, and halothane [5]. It is disadvantageous that sevoflurane, and desflurane react with soda lime to generate compound A, and CO, and that the patients inhale these products; however, it has been denoted that it was not clear whether these degradation products led to significant problems for the patients [5]. None of the inhalation anesthetics being used today is directly nephrotoxic. However, their metabolites (inorganic fluoride) may cause to renal injury because of their directly nephrotoxic effects. With halothane, desflurane, and isoflurane, the level of fluorine does not reach to danger limit even in the situations in which their metabolisms are accelerated; in contrast, with enflurane and sevoflurane, fluorine levels may increase after prolonged anesthesia [1, 4, 8, 9, 14]. It is known that sevoflurane generates compound A reacting with CO2 absorbents. The compound A is toxic; its toxic effect on the liver and particularly on the kidneys has been shown in the studies performed with rats. The formation of compound A enhances especially in the situations in which fresh gas flow reduces (low flow), and the temperature increases; and that causes to the formation of compound B and other degradation products [2, 4, 7, 9, 15- 17].

In the light of the above data, we planned to ascertain the effects of sevoflurane, and desflurane, volatile anesthetic agents recently become available in our country, on the liver and kidney functions. When we statistically analyzed the results achieved, the change in AST parameter in the Group S was found to be statistically significant (p≤0.05), however, clinically that change was in normal ranges. In the Group D, the change in AST level was not statistically significant (p>0.05). When the changes in ALT parameter were analyzed statistically, there was not any significant difference between the groups, and in in-group comparisons. That in the Group S ALT level tended to increase in comparison with the Group D, although it was not statistically significant, and that in the Group S there was a statistically significant difference in AST made us think that this agent might have a greater impact on the liver.

When the changes in serum BUN, urea, and creatinine values were analyzed statistically, the changes in all three parameters were not statistically significant; however, the change in BUN level was remarkable.

Ebert and Arain [18] researched the effects of desflurane, sevoflurane, and propofol on the liver and kidney functions and similar to our study, they showed that the changes in ALT and total bilirubin levels

were insignificant in the groups of sevoflurane and desflurane; that the change in AST level was found to be significant and although the change was higher in the sevoflurane group, there was no statistically significant difference between the groups. In terms of kidney function tests, similar to our study, the authors found the change in serum creatinine levels to be insignificant in the groups; they showed that the decrease in BUN levels was significant in all groups but clinically within normal ranges. Eger *et al*.[19], in a similar study with sevoflurane and desflurane, found that the change in serum creatinine levels was not significant in both groups; that serum fluoride level was significantly increased with sevoflurane ($p<0.001$), while there was no significant increase in serum fluoride level with desflurane; the authors demonstrated that there was a significant change in urinary albumin excretion with sevoflurane, that α-GST (α-glutathione-S-transferase) was increased only at the hour 8 in the sevoflurane group, otherwise it was normal and that there were no significant changes in ALT and total bilirubin levels from liver function tests.

Obata et al. researched the effects of high-flow sevoflurane, low-flow sevoflurane and low-flow isoflurane anesthesia on the liver and kidney functions and eventually the authors demonstrated that there were no significant changes in BUN and creatinine levels, as in our study. Similar to our study, among liver function tests, AST and ALT levels were found to be increased and the authors demonstrated that although the increase in AST level was statistically significant, there was no difference between the groups and there was no correlation with the compound A. They found a significant increase in total bilirubin level in all groups, however, the authors demonstrated that there was no difference between the groups and the changes in LDH and ALP levels were insignificant. The authors highlighted that the effects of sevoflurane on the kidneys and on the liver were remarkable in low-flow anesthesia practices in which the fresh gas flow reduced [16]. Goldberg et al. demonstrated that low-flow sevoflurane anesthesia led to a significant increase in urinary albumin, glucose, α-GST and compound A excretion [14]. In a similar study, Conzen *et al*. achieved similar results about the effect of low-flow sevoflurane and isoflurane anesthesia on the kidney functions, and the authors demonstrated that the change in the serum fluoride levels was significant in the sevoflurane group [20]. The same study was done by Abdel-Latif *et al*. and they also achieved similar results [21]. In another study, Story *et al*. researched the effects of sevoflurane, isoflurane and propofol on the creatinine levels among the patients with cardiac disorders and they demonstrated that the increase in the sevoflurane group was higher than all other groups although there were small differences between the groups [22].

Kharasch et al. studied the effects of isoflurane and sevoflurane on the liver and kidney functions and similarly they demonstrated that the changes in AST, ALT and renal function tests were statistically insignificant and there was no correlation between the change and the increase in the level of compound A [15].

Iyer et al., in a study with rats, denoted that the urinary glucose and urea levels were significantly increased when the compound A level exceeded 150 ppm, and similarly statistically significant changes in BUN levels were observed [23].

In a study with 51 patients with known renal disorders, Litz et al. researched the effects of desflurane and isoflurane on the renal response. They demonstrated that desflurane and isoflurane did not result in statistically significant changes in BUN, creatinine and creatinine clearance in the patients with renal dysfunction [24]. In a study, Bauer et al. demonstrated that under desflurane and isoflurane anesthesia at 0.75 MAC for 1 hour, the liver microcirculation was not affected in comparison with pentobarbital [25].

Demirel *et al*. researched the histopathologic effects of inhalation anesthetics on the liver in the mice and they found liver damage in 3 mice from the control group (n=20), in the sevoflurane group (n=20), in 17 mice from the isoflurane group (n=20) and in 20 mice from the halothane group (n=20). They reported that sevoflurane was safer than isoflurane and halothane, nevertheless liver damage was observed [26].

In conclusion, in the light of the data that we achieved, we think that volatile anesthetic agents affect the functions of the liver and the kidney, that desflurane, which is less metabolized, should be preferred particularly for the patients with liver disorders and that it is necessary for patients' safety to disclose thoroughly the effects of the inhalation anesthetics with further studies about this issue.

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Cite this article as:
Mustafa Yontem, Aydın Akkaya, Suleyman Kaleli, Fatih Erci, Fatma Emel Kocak. Effects of Sevoflurane and Desflurane on Some Biochemical Parameters.Asian Journal of Biomedical and Pharmacutical Sciences, 5(43), 2015, 01-05.