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Evaluation of olfactory memory after sevoflurane anesthesia: is really short-term memory influenced?

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Abstract

Objective: Olfactory disorders can negatively effect the quality of life. Few clinical studies and case reports have investigated the relationship between anesthesia and olfactory dysfunction. The aim of this study was to investigate the effect of sevoflurane on olfactory memory with Brief-Smell Identification Test™ in patients used sevoflurane.

Patients and Methods: This, prospective, clinical study was performed on 60 ASA physical status I-II patients, between 18-65 years of age who were scheduled for expected surgery duration of 40-120 minutes. All patients were preoperatively informed about Brief-Smell Identification Test. For induction 2 mg.kg^{-1}propofol, 0.5 mg.kg^{-1} rocuronium and 1 μg.kg^{-1} iv fentanyl were administered. Anesthesia was maintained with the inhalational of anesthetic sevoflurane (2%). Brief-Smell Identification Test scores are recorded 30 minutes before the surgery and when the Aldrate Recovery Score reached 10 in the postoperative period. Preoperative and postoperative results were compared and p-values<0.05 were considered statistically significant.

Results: The patients mean age were 47.1 ± 13.8. There was no statistically significant difference between the mean preoperative and intraoperative HR and MAP values. Preoperative total correct answer rate to odorous substances was 85.4%, and postoperative rate was 84.5%. Percentage of the odor identification by the patients revealed no statistically significant difference when pre and post-operative rates were compared (P>0.05).

Key words:

Sevoflurane, Olfactory, Memory.

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Introduction

Although the olfactory disorders are often seen in general population and have a negative impact on the quality of life, these disorders may be ignored by both patients and clinicians. The sense of smell works as a first warning system against harmful objects and odors. Also it has a role in the stimulation of gastric secretion in normal digestive physiology [1-3]. Aging and smoking have been reported to be the most important causes of smell dysfunction [1,4]. The other etiological factors of olfactory disorders include head trauma, upper respiratory infections, systemic disorders, nasal disorders (eg, sinusitis, nasal polyps), neurodegenerative diseases and medical drugs [1,5,6]. In animal studies adverse effects of anesthetic agents on smell function have been investigated for several times [5,7]. Besides this, few clinical trials and case reports about the association between anesthesia and olfactory dysfunction are present in the literature [5,8-11]. As far as we know only one study investigated the effect of sevoflurane on olfactory memory [12,13]. They used the University of Pennsylvania Smell Identification Test (UPSIT) and their results showed that sevoflurane have an effect on olfactory memory. Additionally they studied the effects of sevoflurane on plasma melatonin levels and showed that the ratios of melatonin change significantly decreased and melatonin levels significantly correlated to the UPSIT scores in patients used sevoflurane. However in another study which was conducted to investigate the effect of sevoflurane on melatonin plasma levels, authors concluded that sevoflurane did not influence significantly plasma melatonin levels [14]. Therefore, we aimed to investigate the effect of sevoflurane on olfactory memory with Brief-Smell Identification Test™ (B-SIT) in a greater number of patients used sevoflurane.

Materials and Methods

This study was conducted at the Department of Anaesthesiology of the Abant Izzet Baysal University Hospital. Ethical approval for this study was granted by the Clinical Research Ethical Committee of Abant Izzet Baysal University, Turkey (Ethical Committee No: 2015/92). Our prospective clinical study included 60 American Society of Anaesthesiologists (ASA) I-II patients aged 18-65 who were scheduled for expected surgery duration of 40 - 120 minutes. Written consent was obtained from each patient.

Exclusion criteria included patients with upper and lower respiratory tract disease, smokers, structural and infectious diseases in nose (eg, polyp, deviation, and rhinitis), inflammatory disease in the sinuses and nose drug and alcohol addiction, mental retardation, Alzheimer's disease, and psychiatric diseases, neurological symptoms (such as diplopia hearing, loss). Additionally, any patient who had undergone nose surgery or had been exposed to head trauma was also excluded from the study.

Olfactory function was evaluated using the Brief-Smell Identification TestTM (B-SIT). This test consists of a small book which includes 12 different odorants that are released when scratched with the tip of a pencil. The patient sniffed the resulting odor after scratching. For each odor, the patient is given four different choices with only one correct answer. If the odor perceived by the patient was not identified on the page, participants were instructed to select the closest choice instead. These processes were repeated for all 12 pages in the booklet. The smell diskette odors used in this test included mint, honey, banana, lemon, garlic, clove, lilac, leather, strawberry, coffee, grapes, black pepper, melon, watermelon, peanut, soap, baby powder, chewing gum, chocolate, pine, vanilla, peach, fume (smoggy), cinnamon, soot, grass, peaches, rose, and pineapple. All patients were informed about B-SIT and the method of application of the test during the obtaining of written consent. One hour before the surgery, the patients were brought into the recovery room and B-SIT (Turkish version) was applied to each patient and the scores were recorded.

Patients were then transported to the operating theatre and they were monitored with non-invasive blood pressure, pulse oximetry and electrocardiogram. None of the patients were premedicated. After establishing vascular access, anaesthesia induction was conducted with 2 $mg.kg^{-1}$ propofol, 1 $\mu g.kg^{-1}$ Fentanyl and 0.5 $mg.kg^{-1}$ rocuronium. After induction, orotracheal intubation was performed following adequate muscle relaxation. Anesthesia was maintained with sevoflurane 2 % in a mixture of 60 % N_2O/O_2. Controlled mechanical ventilation was adjusted to maintain $ETCO_2$ pressure between 35-45 mmHg with a respiratory rate of 8-10 breaths min-1 and a tidal volume of 6-7 $mL.kg^{-1}$. Neuromuscular block was reversed with a combination of neostigmine (40 $mcg.kg^{-1}$) and atropine sulfate (0.015 $mg.kg^{-1}$). The patients were extubated when adequate spontaneous ventilation was established and then patients were taken to the postoperative recovery room. B-SIT was reapplied to all patients when the Aldrete Recovery score was attained 10 points.

Heart rate (HR), Mean Arterial Pressure (MAP) for each patient were noted at 5 and 10 minutes of intubation, and certain intervals until the end of the surgery.

Statistical analysis

Data analysis was performed using the Statistical Package for the Social Sciences (SPSS 18.0) program. Descriptive variables such as age, height, weight, HR, MAP were shown in the form of mean ± standard deviation and a paired samples T test was used for their analysis.

Goodman and Kruskaltau were tested with analysis of BSIT scores. The results were considered statistically significant for p values <0.05.

Results

Data of 60 patients (41 females and 19 males) with a mean age of 47.1 years were collected for the study. ASA physical status classification system was assessed for all patients; 29 were ASA 1, and 31 ASA 2.

The demographic data and clinical characteristics are demonstrated in Table 1. The patients' preoperative baseline heart rates and heart rates obtained during the intraoperative period were 83.0 ± 14.7 and 81.1 ± 14.6, respectively ($p>0.05$).

There was no statistically significant difference between the mean preoperative and intraoperative MAP values (94.5 ± 20.5 and 84.4 ± 16.4, respectively) ($p>0.05$).

Table I. Demographics and clinical characteristics of the patients.

Number of patients	60
Age	47.1 ± 12.8
Height	166.5 ± 8.2
Weight	76.28 ± 12.3
Gender (Male/Female)	19/41
Duration of Surgery	80.0 ± 22.7

In the evaluation of olfactory memory, BSIT scores measured before surgery were considered as a baseline, and compared with the BSIT scores measured when the postoperative Aldrete recovery score became 10.

No statistically significant difference was observed in the correct odor answer ratio between the preoperative and postoperative BSIT scores ($p>0.05$) (Table 2).

The rate of correct answers of patients to the BSIT test was found as 85.4 % before operation, this rate was 84.5% after the operation.

Patients experienced difficulty in recognizing the smell of "leather". The ratio was 56.7% in preoperative period and post-operatively 55%.

Table 2. *Preoperative BSIT score and postoperative BSIT score when it reaches 10 of Aldrete score.*

Item No	Odor	Preoperative n (%)	Postoperative n (%)	p value
1	Mint	55 (91.7)	54 (90)	p>0.05
2	Banana	58 (96.7)	56 (93.3)	
3	Clove	55 (91.7)	55 (91.7)	
4	Leather	34 (56.7)	33 (55)	
5	Strawberry	50 (83.3)	52 (86.7)	
6	Pine	55 (91.7)	53 (88.3)	
7	Cinnamon	53 (88.3)	55 (91.7)	
8	Soot	49 (81.7)	46 (76.7)	
9	Lemon	45 (75)	46 (76.7)	
10	Soap	59 (98.3)	58 (96.7)	
11	Babypowder	60 (100)	60 (100)	
12	Rose	42 (70)	41 (68.3)	
Total	Correctidentification	615 (85.4)	609 (84.5)	

Discussion

Patients with olfactory disorder have severe impairment in quality of life. It was reported that patients with smell disorder have also serious problem in safety, eating and personal hygiene [15,16]. Olfactory dysfunction occurs approximately 5% in the general population [5]. Determination of the cause of olfactory loss is very important for clinicians. The underlying causes of olfactory disorders may be various. The primary causes of olfactory dysfunction include aging, smoking, head trauma, infections, rhinosinusitis, neuropsychiatric and neurodegenerative disorders and drugs. Defining a definite relationship between drug use and olfactory dysfunction may be difficult, and it is hard to determine with accuracy the role of an agent in the occurrance of olfactory disorder [15]. Numerous agents have been reported in the literature. Common examples include chemotherapy agents, intranasal medications (zinc gluconate), antihypertensive drugs (diuretics, angiotensin-converting enzyme inhibitors), antimicrobials (macrolides, penicillins, tetracyclines), antidepressants, and anticonvulsants [15]. However effects of anesthetic agents and anesthesia methods on the olfactory system have not been investigated in literature excessively.

In a case report, authors discussed a patient with smell dysfunction after propofol and sevoflurane anesthesia. They concluded that the causative function of each anaesthetic agent used has remained unclear and they offered experimental researches for assessing the influence of certain anaesthetic agents on olfaction [5]. Demirhan et al. [8] have reported that olfactory memory is not affected after spinal anesthesia. In a prospective clinical study it was demonstrated that general anesthesia with isoflurane 1.2 % has no significant effect on the olfactory memory [9]. In an animal study, authors reported that infusion intracerebroventricularly of fentanyl and propofol reduce the olfactory response [7]. To our knowledge, only one clinical study exist in the literature investigated the effect of sevoflurane on olfaction. In that study conducted by Kostopanagiotou et al. showed that olfactory memory was affected by sevoflurane and also they reported that melatonin change ratios significantly decreased and melatonin levels significantly correlated to the UPSIT scores in patients used sevoflurane. However in the present study, we have found that the olfactory memory is not significantly affected by sevoflurane. In our study we used Turkish version of the BSIT which was developed as a quick instrument to measure odor identification deficits and derived from the UPSIT [17]. It has been prepared and used taking into consideration cultural differences and the sensitivity and specificity of the BSIT was reported to be 82% [8].

Halogenated volatile anesthetic agents are widely used in anesthesia and also well tolerated by patients without systemic disease. Sevoflurane, isoflurane and desflurane now constitute the fundamental halogenated volatile anaesthetics used in developed countries [18]. Sevoflurane is advantageous both in adults and children for induction and also maintenance of anesthesia. The pharmacokinetics (low blood/gas partition coefficient), non-pungent odour, lack of irritation to airway passages and minimal effect on cerebral blood flow make the sevoflurane as an ideal and safe inhalational agent [19]. However adverse effects of the sevoflurane have been reported with a low incidence such as agitation, laryngospasm, apnea, arrhythmias, hypotension, and increased salivation. Besides this, sevoflurane has been blamed for the development of anosmia and diminished sense of taste in case reports [5,11]. In these case reports, authors tried to establish a relationship between gamma-aminobutyric acidergic (GABAergic) neurotransmitter system and olfactory system by the citation of clinical researches that have demonstrated that sevoflurane influence GABA receptor. They claimed that any agent that has an impact on the GABA dependant pathways could probably affect the central components of the olfactory system [5,13]. Additionally in a clinical study it was reported that sevoflurane has an effect of on olfactory memory. They also mentioned that sevoflurane anaesthesia decreased plasma melatonin levels, which could show an underlying humoral mechanism [12]. On the other hand, in a prospective clinical study it was reported that sevoflurane did not influence significantly melatonin plasma levels [14]. In our study, in none of the patients anosmia was observed in the short-term and we have found that the use of sevoflurane at clinical doses (2% MAC) has not any effect on olfactory memory during the early postoperative period. Therefore we have encountered various results and conclusions. We also thought that the number patients enrolled in Kostopanagiotou et al. study may be inadequate to determine the certain relation between olfaction and

sevoflurane. Moreover in most of the studies mentioned above, authors concluded that defining the certain relationship between anesthesia or anesthetic agent and the olfactory system needs additional investigation with well-designed experimental and controlled clinical studies. Primary limitations of our study are lack of investigation of various concentrations of sevoflurane for longer periods and also their postoperative long-term effects and relatively small sample size.

Conclusion:

We concluded that sevoflurane (2%) did not affect short-term olfactory memory. Further studies with larger sample size will be necessary to confirm our findings.

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