EFFECTS OF ISOFLURANE ON POSTOPERATIVE OLFACTORY MEMORY

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ABSTRACT

Purpose: In this study, we planned to investigate the effects of isoflurane 1.2%, on olfactory memory.

Methods: This is a prospective clinical study conducted over 40 patients aged 18-50 who had elective surgery and American Society of Anesthesiologists (ASA) physical status I-II. The Brief Smell Identification Test (BSIT) was used for interpreting patients’ olfactory memories before and after the surgical procedure. Patients received standard general anesthesia protocol and routine monitoring. For induction, 1.5 mg/kg of fentanyl, 2 mg/kg of propofol, and 0.5 mg/kg of rocuronium bromide were administered. Anesthesia was maintained with the inhalational of anesthetic isoflurane (1.2%). The scores are recorded 30 minute 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 38.4±13.8. Preoperative total correct answer rate to odorous substances was 91.4%, and postoperative rate was 90.8%. Percentage of the odor substance identification by the patients revealed no statistically significant difference when pre and post-operative rates have been compared. (P>0.05)

Conclusion: In conclusion, it is the first time we demonstrate general anesthesia with isoflurane 1.2 % has no significant effect on the olfactory memory. Further studies with larger samples will be required to confirm our findings.

Key words: isoflurane 1.2%, olfactory memory

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Introduction

Halogenated volatile anesthetic agents are usually well tolerated by patients without systemic disease. However, these agents may cause rare complications, including amnesia, taste and odor disorders and olfactory memory impairment. Olfactory memory is important in recognition of foods, the relationship between mother and baby, the perception of harmful odors, and remembering our experiment of the past. Additionally, olfactory impairments may be a prognostic sign of various diseases including such as Parkinson's disease, Alzheimer’s disease, Multiple sclerosis, Huntington's disease(13).

Odor impulses in the brain reach the olfactory cortex by traveling along the course of the bulbus olfactorius, tractus olfactorius, and stria olfactorii (medialis, lateralis, intermedia). The structures involved in olfactory memory are the piriform cortex, amygdala, and the entorhinal cortex(46). In our review of the literature, we could not find any imaging studies that reported general anesthesia to be the cause of olfactory dysfunction by affecting these anatomical structures.

Effects on the olfactory system of anesthetic agents and anesthetic techniques (general anesthesia, regional anesthesia, neuraxial anesthesia) have not been researched in literature excessively.
Demirhan at.al have reported that olfactory memory is not affected after spinal anesthesia\(^{7}\). Kostopanagiotou G at.al. have reported that, olfactory memory is affected after sevoflurane anesthesia\(^{6}\). Volatile anesthetic agents have been blamed for olfactory dysfunction, but these claims could not be proven in clinical trials. However, two cases of anosmia have been reported in the literature following general anesthesia\(^{8,9}\).

Isoflurane is a volatile anesthetic with a pungent odor. Isoflurane has many favourable effects, including analgesia and muscle relaxation. But it has some side effects, such as respiratory depression and amnesia\(^{10}\). There is an experimental study examining the effects of isoflurane on olfactory memory, but clinical trials are not available yet.

In this study, we investigated the effects of isoflurane 1.2% on olfactory memory.

Materials and methods

After receiving institutional ethical committee approval (Clinical Ethical Committee of Abant Izzet Baysal University, Bolu, Turkey, Ethical Committee No: 2012/264), our study included 40 American Society of Anaesthesiologists (ASA) I-II patients aged 18-50 who were scheduled for expected surgery duration of 40 - 120 minutes. Exclusion criteria for this study were patients with upper and lower respiratory tract disease, inflammatory disease in the nose and sinuses, allergic rhinitis, nasal polyps, alcohol and drug addiction, mental retardation, Alzheimer's disease, and psychiatric diseases. In addition, any patient who had undergone nose surgery or had been exposed to head trauma was also excluded from the study. To evaluate the patients' olfactory memories, the Brief Smell Identification Test (BSIT) was used 30 min before surgery. Written consent of all the patients included into the study was obtained after providing adequate information. Participants were asked to read the instructions on the front side of the booklet so they would know how the test would be performed.

This test uses a 12-page booklet. There is one label on every page of this booklet, and four answer choices of smelling substance names are listed as a, b, c, and d. The label was scratched with the aid of a fine-tipped pen, and the patient sniffed the resulting odor. If the odor perceived by the patient was not listed on the page, participants were instructed to select the closest choice instead. These processes were repeated for all 12 pages in the booklet, and the answers given by the participants were recorded. Patients were then taken to the operating room and received standard general anesthesia protocol and routine monitoring (echocardiogram, Spo2, and non-invasive arterial pressure). For induction, 1.5 mg/kg of fentanyl, 2 mg/kg of propofol, and 0.5 mg/kg of rocuronium bromide were administered. Tracheal intubation was performed after obtaining sufficient muscle relaxation. The respiration rate was adjusted so that the mechanical ventilator settings of patients after intubation were as follows: 6-8 ml/kg tidal volume, FiO2: 0.5, end-tidal CO\(_2\) respiration rate: 35-45 mmHg. Anesthesia was maintained with the inhalational of anesthetic isoflurane (1.2%). Patients were taken to the postoperative recovery room after surgery. When the Aldrate Recovery Score reached 10, the BSIT test was repeated to test the olfactory memory of the patients.

Statistical Analysis

Data analysis was performed using the Statistical Package for the Social Sciences (SPSS 15.0) program. Descriptive variables, such as age, height, weight, heart rate (HR), mean arterial pressure (MAP), and duration of surgery, were shown in the form of mean ± standard deviation, and a paired-samples T test was used for their analysis. Goodman and Kruskal tau tests were used for the analysis of BSIT scores. The results were considered statistically significant for p-values <0.05.

Results

Forty patients were included in the study. The demographic data of the patients are shown in the table (Table 1). (P>0.05). The patients' average pre-operative and intraoperative heart rates were 84.1 ± 18.8 and 78.3 ± 16.0, respectively (p>0.05) while the mean preoperative and intraoperative arterial pressures were 94.5 ± 20.5 and 84.4 ± 16.4, respectively (p>0.05).

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 evaluation duration became 10. When we compared the percentage of identification of odors by the patients, there was no statistically significant difference between the pre and the postoperative periods. (P>0.05) (Table 2). Preoperatively, the rate of correct answers of patients to the BSIT test was found as 91.4%, this rate was 90.8% after the operation.
Patients experienced difficulty in recognizing the smell of Leather. In preoperative period, the ratio was 77.5% and post-operatively 77.5%.

**Table 1:** The demographic characteristics of patients and the mean values (Mean±SD,n).

<table>
<thead>
<tr>
<th>Item No</th>
<th>Odor</th>
<th>Preoperative n(%)</th>
<th>Postoperative Aldrete scores 10 n(%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Mint</td>
<td>38(95)</td>
<td>9(97.5)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Banana</td>
<td>38(95)</td>
<td>37(92.5)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Clove</td>
<td>39(97.5)</td>
<td>37(92.5)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Leather</td>
<td>31(77.5)</td>
<td>31(77.5)</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Strawberry</td>
<td>33(82.5)</td>
<td>34(85)</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Pine</td>
<td>39(97.5)</td>
<td>38(95)</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Cinnamon</td>
<td>35(87.5)</td>
<td>35(87.5)</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Soot</td>
<td>39(97.5)</td>
<td>39(97.5)</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Lemon</td>
<td>36(90)</td>
<td>37(92.5)</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Soap</td>
<td>40(100)</td>
<td>39(97.5)</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Baby powder</td>
<td>35(95)</td>
<td>39(97.5)</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Rose</td>
<td>33(82.5)</td>
<td>31(77.5)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>Correct identification</td>
<td>439 (91.4)</td>
<td>436(90.8)</td>
<td></td>
</tr>
</tbody>
</table>

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

\( n(\%) \): The number of patients’ correct answers to odorous substances (n) and the percentage of correct answers(%).

Discussion

The perception of odor impulses and olfactory memory are important for people. A decrease in one’s sense of odor (hyposmia), the complete absence of a sense of odor (anosmia), or not being able to distinguish odours (dysosmia) affects the quality of life\(^{(11)}\). Anosmia cases have been reported after general anesthesia\(^{(8, 9)}\). The authors of that study used fentanyl, propofol, and sevoflurane to maintain general anesthesia\(^{(8, 9)}\).

It is known that, volatile anesthetics affect memory and learning functions. Volatile anesthetics have shown their effects via the gamma-aminobutyric acidergic (GABAergic), glutamatergic, and adrenergic neurotransmitter system\(^{(12, 13)}\). In particular, it has been reported that, GABAergic system is related with learning and olfactory memory\(^{(14)}\).

Isoflurane is an inhalation agent commonly used in general anesthesia. Isoflurane has been blamed for the development of neurodegeneration in human neuroglioma cells when used at a concentration of 2%\(^{(15)}\). It has been reported that isoflurane affected the levels of acetylcholine in brain tissue and also impaired learning and memory functions when used in high doses\(^{(16, 17)}\).

In our study, we investigated the short-term olfactory memory. All patients have reached the value of 10 in Aldrete Score before 24th hours postoperatively, and we have repeated BSIT test at that time. It has been reported that isoflurane may affect olfactory memory in animal studies, but we could not find any clinical studies on this issue in our literature review. In an animal study conducted by Jugovac et al. the electroencephalographic effect of four anesthetic agents infused intracerebro ventricularly (pentobarbital, propofol, fentanyl, and midazolam) were examined. The study reported that fentanyl and propofol depressed olfactory response\(^{(19)}\).

In our study, we used propofol and fentanyl for induction, but our study showed that these agents did not affect olfactory memory. Demirhan et al. evaluated olfactory memory, using Turkish version of BSIT test after spinal anesthesia and reported that it does not affect olfactory memory\(^{(20)}\).

In a randomized clinical trial\(^{(21)}\), the olfactory memories of three groups were compared after epidural anesthesia, total intravenous anesthesia with propofol, and anesthesia induced with sevoflurane. Minor cases whose operation duration was expected to last from 40 to 120 minutes were included in the study. Olfactory memory was evaluated 30 minutes and 3 hours after the operation, and was impaired in
the group for which sevoflurane was used was both 30 minutes and 3 hours postoperatively. In their study, the University of Pennsylvania Smell Identification Test (UPSIT) was used\(^{(6)}\). Another commonly used test to evaluate olfactory function is the BSIT\(^{(20)}\). This test, which includes 12 different odors, is called as “the Cross-Cultural Smell Identification Test” (CC-SIT). This test is different for each culture, and it contains local odors\(^{(20,21)}\).

In a previous study, the sensitivity and specificity of the BSIT was reported to be 82%\(^{(22)}\). In our study, we used the Turkish version of the BSIT.

Main limitations of our study are the use of only one concentration of isoflurane (1.2%), untested long-term olfactory memory, and relatively small sample size.

In conclusion, we demonstrated for the first time in the literature that general anesthesia using isoflurane (1.2%) did not affect short-term olfactory memory. Further studies with larger sample size will be necessary to confirm our findings.

References