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Original Article

Investigating sevoflurane, remifentanil, and propofol effects on recovery of patients with movement disorders under general anesthesia

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ABSTRACT

The present randomized double-blind clinical trial compared the effects of two drug regimens of sevoflurane and remifentanil plus propofol on recovery conditions in adult patients with movement disorders for dental treatments under general anesthesia. Thirty patients were selected among the adult patients who had movement disorders and underwent general anesthesia in the operating room to perform dental procedures. Then, each patient was allocated to one of the control or case groups using a table of random numbers. Anesthesia was induced similarly in both groups using 5 mg/kg sodium thiopental, 1 µg/kg fentanyl, and 0.8 µg/kg atracurium. Then, the first group received sevoflurane with MAC: 1.85 and the Second one received remifentanil plus propofol (propofol 3mg/kg/min and then remifentanil 1µg/kg/min) to maintain anesthesia. The mean score of delirium in recovery was analyzed using the Cox regression test. After the patient entered recovery, the delirium level was evaluated at 5, 10, 15, 30, and 60 minutes using the Nu-DESC checklist. The results revealed that there was no significant difference between the two groups regarding the variables of age, gender, underlying disease, the drugs used by the patient, level of physical ability, the severity of movement disorder, the total number of dental procedures, recovery time, anesthesia time, and mental problems (P value=0.260) and also delirium rate was similar in both.

Keywords: Sevoflurane, Remifentanil, Propofol, Recovery period after anesthesia, Movement disorders, Delirium

Introduction

Patients suffering from movement disorders or dyskinesia move involuntarily, too much, or too little. Dyskinesia patients can be a complicating factor in managing dental problems, such as the problem of stabilizing the patient's head [1]. Patients with intensive care needs are at higher risk of oral and dental diseases. Parental anxiety about the problems of patients with intensive care needs often delays dental treatment, so it causes serious oral diseases in the patients. In such cases, if the patient does not cooperate, the dentist will consider other alternatives such as protective maintainers and general anesthesia to perform the necessary dental treatments. One advantage of general anesthesia is to provide efficient and more appropriate treatment, which is performed in a safer environment in only one session with minimum discomfort, and mental and physical stress [2]. Safe recovery without delirium and extubation is critical for patients with movement disorders since restlessness and involuntary movements during recovery can harm these patients. Sevoflurane is an inhaled anesthetic with a minimum of 1.85 alveolar concentrations. It is exclusively halogenated with fluoride. Thus, it has less dissolution in the blood and tissues and allows faster recovery for the patient. The time required to reduce sevoflurane concentrations by 50% is less than 5 minutes.

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It does not increase significantly with the increase in the anesthesia duration [3].

General anesthesia is primarily considered for dental treatments due to less damage during treatment and the problems of patients with movement disorders. Faster recovery and safe extubation are crucial in these patients owing to the movement problems. A drug that can create a faster and more complete recovery and cause fewer side effects can provide a faster discharge and higher safety. Propofol is an intravenous anesthetic used extensively in anesthesia and sedation [4]. Propofol has more pharmacological advantages than other anesthetic drugs, including faster and short effects, fewer side effects, and anti-nausea [5]. However, this drug has no analgesic effect. Remifentanil is also a short-acting narcotic that has a very fast onset and end effect. The extremely high clearance of remifentanil by plasma esterases makes it an appropriate drug for high cumulative doses and fast titration [6, 7].

Nishikawa *et al*. examined and compared two groups of anesthesia induction and maintenance with propofol and anesthesia maintenance with sevoflurane in laparoscopic surgery that lasted three hours. In the mentioned study postoperative pain was controlled with continuous epidural analgesia. It was revealed that the eye-opening time, extubation, response to commands, and consciousness were significantly higher in the sevoflurane group than in the propofol group. Immediate onset (eye-opening and leaving anesthesia) was significantly faster after sevoflurane ($P < 0.05$). No significant difference was observed between the two groups regarding the delirium rate in the first 3 days after the operation. Delirium was significantly higher in the propofol group than in the sevoflurane group two and three days after the operation ($P < 0.01$) [8].

König *et al*. showed no significant difference between the rates of delirium in the two groups of anesthesia maintenance with propofol and anesthesia maintenance with sevoflurane in children's candidates for dental procedures. However, using sevoflurane significantly reduced post-operative nausea and vomiting. Leaving the anesthesia occurred 10 minutes earlier in the sevoflurane group than in the propofol group. Parental satisfaction was at the same level and high in the two groups [9].

Joe *et al*. examined and compared two groups of anesthesia maintenance with remifentanil hydrochloride plus propofol and anesthesia maintenance with sevoflurane plus nitrous oxide. They showed that delirium was less in the propofol group than in the sevoflurane group in open rhinoplasty, septoplasty, turbinoplasty, endoscopic sinus surgery, and endoscopic nasal surgery [10]. Examining and comparing two groups of anesthesia maintenance with sevoflurane and anesthesia maintenance with propofol plus remifentanil in strabismus surgery, Chandler *et al*. showed that the delirium rate was lower in the propofol group than in the sevoflurane group [11].

Fung and Zavalishina *et al*. revealed no significant differences in the recovery time of the patients in the two groups of anesthesia maintenance with propofol and anesthesia maintenance with sevoflurane, who were candidates for craniotomy surgery. The recovery time was short in both groups. They also revealed that the need for vasoactive, soporific, and analgesic drugs during recovery was less in the sevoflurane group than in the propofol group. It seems that the combined one-hour costs of analgesic, soporific, and vasoactive drugs in the patients of the sevoflurane group are lower than the patients of the propofol group [12, 13].

Watson and Shah examined two groups of anesthesia maintenance with propofol plus alfentanil and anesthesia maintenance with sevoflurane plus nitrous oxide and alfentanil in adult patients who were candidates for spinal surgery. They showed that postoperative nausea, vomiting, and pain in both groups when leaving the anesthesia were not affected by the anesthetic method. However, the time needed to leave anesthesia was more predictable in the sevoflurane group. Cardiovascular stability was good and comparable in both groups. Both methods were acceptable to most patients. They selected the same anesthesia again. Induction and maintenance in the propofol group were much cheaper compared to the sevoflurane group [14].

Sneyd and Bahri *et al*. examined and compared the patients of the two groups of anesthesia maintenance with propofol plus remifentanil and anesthesia maintenance with sevoflurane plus remifentanil who were candidates for spinal surgeries. They found that stopping anesthesia time, eye-opening time (5.2 vs. 16.5 minutes), and movement time (5.5 vs. 17.4 minutes) were faster in the sevoflurane group. Evaluating the neurological function after anesthesia with sevoflurane was facilitated more quickly [15, 16].

Dashfield *et al*. examined and compared two groups of anesthesia induction with propofol and anesthesia induction with sevoflurane and anesthesia maintenance with 8% sevoflurane in nitrous oxide and oxygen. They showed that the induction time to the start of spontaneous ventilation was less in the sevoflurane group than in the propofol group. There was no significant difference between the two groups in terms of heart rate, and arterial blood pressure immediately before induction, and 10 minutes after induction. There was no significant difference between the two groups regarding the rate of airway complications in the two groups [17, 18]. Kim *et al*. compared two groups of anesthesia maintenance with propofol plus remifentanil and anesthesia maintenance with sevoflurane plus remifentanil in female patients who were candidates for thyroidectomy surgery. They found that the wake-up and extubating times were significantly shorter in the propofol group (4.7 minutes and 6.1 minutes, respectively) than in the sevoflurane group (7.9 minutes and 8.9 minutes, respectively) [19].

Ku *et al*. compared two groups of anesthesia maintenance with propofol plus alfentanil and anesthesia maintenance with sevoflurane plus nitrous oxide and alfentanil in adult patients who were candidates for scoliosis surgery. They found that the recovery was faster in the sevoflurane group than in the propofol group. The patients who received sevoflurane had a shorter recovery time regarding eye-opening (mean of 5.1 vs. 20.6 minutes, $P = 0.09$) and toe movement (mean of 7.9 vs. 15.7

minutes, P = 0.22). The patients who received sevoflurane had clearer communication and better cooperation in recovery [20].

Chen *et al*. compared two groups of anesthesia maintenance with propofol plus remifentanil and anesthesia maintenance with sevoflurane in bronchoscopy in children aged one to three years. They found that the hemodynamic variables and stress hormone levels were higher in the sevoflurane group than in the propofol group. Irritation and cough also occurred frequently in the propofol group. Moreover, the physician satisfaction level was higher in the propofol group. The results revealed that propofol plus remifentanil is superior to sevoflurane alone for children undergoing flexible fiberoptic bronchoscopy [21].

Smith and Thwaites compared two groups of anesthesia maintenance with propofol and anesthesia maintenance with sevoflurane in day-case patients. They found that leaving anesthesia was faster in the sevoflurane group (2.2 vs.3.7 minutes). However, it was associated with more nausea and vomiting. Patient satisfaction was high with both methods. Thus, both methods had advantages and disadvantages for anesthesia in day-case patients [22]. Due to a lack of evidence on the effect of sevoflurane drug on the recovery conditions in adult patients with movement disorders compared to remifentanil plus propofol, the present study compared the effects of two drug regimens of sevoflurane and remifentanil plus propofol on the recovery conditions in adult patients with movement disorders underwent dental treatments under general anesthesia.

Materials and Methods

The present study is a double-blind and randomized clinical trial with a control group and parallel groups. A table of random numbers was used for randomization. The study subjects were selected among the adult patients who suffered from movement disorders and were referred to the operating room of the Faculty of Dentistry of Isfahan University of Medical Sciences to perform dental procedures under general anesthesia.

The inclusion criteria included a willingness to participate in the study, and patients over 18 years of age with movement disorders, who received dental procedures under general anesthesia. The non-inclusion criteria included people who had an allergy to eggs or soy and known allergies, and chronic diseases, including heart diseases, bleeding disorders, liver diseases, and kidney diseases. The exclusion criteria included non-cooperation of the patient in any of the stages of the study. The samples were divided into two groups using a convenience random sampling method using a table of random numbers. Fifteen samples were included in each group (30 samples in total). There is a difference of at least 5 minutes between the means of the two methods at a significance level of 0.05 with a probability of 0.80.

After recovery, restlessness was assessed at 5, 10, 15, 30, and 60 minutes using the Nu-DESC checklist [23]. This checklist includes 5 variables that examine delirium. It is scored from 0 to 2, (0 indicates no symptom, 1 indicates moderate symptom, and 2 indicates severe symptom). It was completed by the nurse for two minutes. it examined lack of insight, inappropriate behavior, inappropriate communication, delirium, and movement and cognitive delay. A score greater than or equal to two means having delirium [24]. Analgesics or sedatives were injected if needed based on clinical judgment. The patient was under care in recovery until the end of recovery was determined based on the Post Anesthesia Discharge Scoring System (PADS). The validity and reliability of this checklist had been assessed in previous articles [25]. The anesthesia was induced in two groups similarly using sodium thiopental 5mg/kg, fentanyl 1µg/kg, and atracurium 0.8 µg/kg. Then, the tracheal intubation was performed nasally. The patient was connected to an anesthesia machine with a breathing volume of 10 cc/kg and a breathing rate of 12. The breathing volume and rate were controlled based on the capnograph. Then, the first group received sevoflurane with MAC: 1/85(1) to maintain anesthesia and the second group received remifentanil plus propofol (propofol: 3 mg/kg of body weight and then remifentanil: 1 µg/kg of the body weight per minute) [6]. More drugs (remifentanil: 0.5 µg/kg of body weight or propofol 0.5-1 mg/ kg of body weight) were injected depending on whether the patient was shaking or showing signs of consciousness in response to the situation [26].

The drugs were injected in 10 to 15 seconds. This study was a double-blind clinical trial. Two different people were used to inject the drugs and evaluate the recovery conditions. For this purpose, a person outside the study was used to evaluate the recovery conditions. The person assessing the recovery conditions did not know about the drug used for anesthesia. The ethical considerations of the study were approved after the necessary examinations by the Ethical Council of Isfahan University of Medical Sciences. It was conducted after obtaining the code of ethics of IR.MUI.RESEARCH.REC.1398.756. The data of each group were entered into SPSS software and statistically analyzed using the Cox regression test.

Results and Discussion

The participants of the study in the sevoflurane group had a minimum age of 18 years and a maximum age of 39 years, and a mean age of 24 years (±5.593). The participants of the propofol group had a minimum age of 18 years and a maximum age of 45 years, and a mean age of 31.53 years (±9.485). The t-test showed a significant difference between the two groups (p=0.014). The effect of age was controlled by Cox regression analysis. There were 9 female and 6 male subjects in the sevoflurane group. Also, there were 8 female and 7 male subjects in the propofol group. The Chi-Square test showed no significant difference between the two groups (p=0.073). Regarding the disease, 11 people were healthy and 4 people had epilepsy in the sevoflurane group. Also, 12 people were healthy and 3 people had epilepsy in the propofol group. Fisher's exact test showed no significant difference between the two groups (p=1). Regarding drug use, 12 people did not use any drug and 3 people used drugs

in the sevoflurane group. Also, 13 people did not use any drug and 2 people used drugs in the propofol group. Fisher's exact test showed no significant difference between the two groups (p=1). Two people in the sevoflurane group and 3 people in the propofol group received analgesics or sedatives during recovery. Regarding physical ability, 13 people were able to walk with aid and 2 people were disabled in the sevoflurane group and11 people were able to walk with aid and 4 people were disabled in the propofol group. Mann-Whitney test showed no significant difference between the two groups (p=0.510). Mann-Whitney test showed no significant difference between the two groups regarding the severity of movement disorder in the two groups (p=0.369). Regarding mental ability, 7 people were normal, 5 people were mentally retarded, and 3 people were mentally disabled in the sevoflurane group. Also, 4 people were normal, 8 people were mentally retarded, and 3 people were mentally disabled in the propofol group. Mann-Whitney test showed no significant difference between the two groups (p=0.421).

Table 1. Mean number of dental procedures in two groups

Groups	Extraction	Endo	Restoration	Total
Sevoflurane	2.53	2.20	6.40	11.53
Propofol	1.53	1.60	6.20	9.93
The sum of the two groups	2.03	1.90	6.30	10.73

Mann-Whitney test showed no significant difference between the two groups regarding the total number of dental procedures (p=0.270). Also, there was no significant difference between the two groups regarding extraction (p=0.221), endo (p=0.296), and restoration (p=0.706) using the Mann-Whitney test **(Table 1)**.

The mean anesthesia time was 96.67 minutes in the sevoflurane group and 98 minutes in the propofol group. The t-test showed no significant difference between the two groups (p=0.937). The mean recovery time was 84 minutes in the sevoflurane group and 78 minutes in the propofol group. The t-test showed no significant difference between the two groups (p=0.648).

Table 2. Mean score of delirium in recovery in two groups

Groups	Delirium (minute 5)	Delirium (minute 10)	Delirium (minute 15)	Delirium (minute 30)	Delirium (minute 60)
Sevoflurane	3.40	3.13	1.60	1.13	0.53
Propofol	3.53	2.80	1.40	1.00	0.40
The sum of the two groups	3.47	2.97	1.50	1.07	0.47

The mean scores of delirium in 5, 10, 15, 30, and 60 minutes were not significantly different between the two groups (P value =0.260) **(Table 2, Figure 1)** using Cox regression analysis and by controlling the effect of the variables of age (P value=0.522), gender (P value=0.918), disease (P value=0.957), drugs taken by the patient (P value=0.981), physical ability (P value=0.210), movement disorder severity (P value=0.730), the total number of dental procedures (P value=0.410), recovery time (P value=0.801), anesthesia time (P value=0.094), and mental ability (P value=0.150).

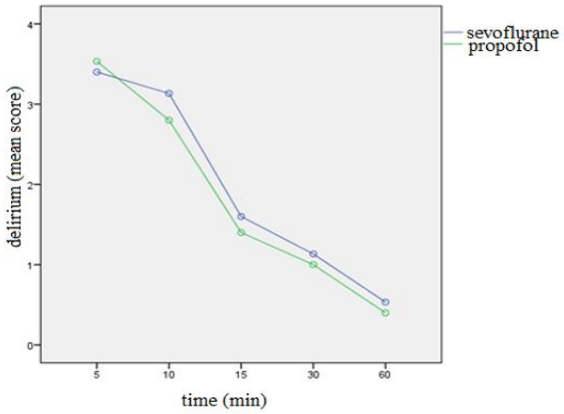

Figure 1. Mean score of delirium in two groups

The Pearson test showed no significant relationship between the recovery time and the age of people in the sevoflurane group (p=0.715, r=0.103). It also showed no significant relationship between the recovery time and the people's age in the propofol group (p=0.897, r=-0.037). The Pearson test showed no significant relationship between the recovery time and the number of dental procedures in the sevoflurane group (p=0.152, r=0.389). It showed a significant relationship between the recovery time and the number of dental procedures in the propofol group (p=0.018, r=0.600). In the propofol group, the recovery time was prolonged with increasing the number of dental procedures.

The Spearman test showed no significant relationship between recovery time and mental ability in the sevoflurane group (p=0.194, r=0.355). It showed no significant relationship between the recovery time and mental ability in the propofol group (p =0.534, r=-0.175). The Spearman test showed no significant relationship between recovery time and physical ability in the sevoflurane group (p=0.126, r=0.413). It also showed no significant relationship between recovery time and physical ability in the propofol group (p= 0.172, r=0.372). The Spearman test showed no significant relationship between the recovery time and the movement disorder severity in the sevoflurane group (p=0.767, r=0.084). It also showed no significant relationship between the recovery time and the movement disorder severity in the propofol group (p=0.459, r=-0.207). The Pearson test showed no significant relationship between recovery time and anesthesia time in the sevoflurane group (p=0.443, r=0.214). It showed a significant relationship between the recovery time and anesthesia time in the propofol group (p =0.030, r=0.559). In the propofol group, the recovery time was prolonged by increasing the anesthesia time.

Patients with intensive needs often suffer from mental disabilities such as reduced cognitive skills, impaired cooperation, and reduced quality of life. Tooth decay is a common disease in these patients. The pain of tooth decay may cause eating problems and they may affect daily activities. They also may lead to life-

threatening complications resulting from an untreated oral infection. However, it is difficult for patients to receive dental services in an ordinary dental clinic. General anesthesia is often demanded to do the dental treatment [27]. The present study examined patients with intensive needs of movement disorders. Among them, 63.33% had the problem of mental disability, indicating the high prevalence of mental disability in this disorder. An average of 10.73 dental procedures were performed under general anesthesia for each patient, indicating high dental decay and inadequate care.

Nishikawa *et al*. compared the two groups of anesthesia induction and maintenance with propofol and anesthesia maintenance with sevoflurane in laparoscopic surgery that lasted three hours. They showed that postoperative pain was controlled with continuous epidural analgesia and the delirium 2 and 3 days after the operation was significantly higher in the propofol group than in the sevoflurane group. This study was conducted on 50 healthy patients over 65 years of age [8, 28]. The present study showed no difference between the two groups regarding delirium. This discrepancy in the results of the two studies might be due to the reason that delirium was examined from the beginning of recovery until minute 60 in the present study. However, delirium was examined in the first 2 and 3 days in the above-mentioned article.

König *et al*. showed no difference between the two groups of anesthesia maintenance with propofol and anesthesia maintenance with sevoflurane in children's candidates for the dental procedure regarding the delirium rate. This study was conducted on 179 healthy pediatric patients [9]. The present study also showed that there was no difference between the two groups regarding the delirium rate. Joe *et al*. compared two groups of anesthesia maintenance with remifentanil hydrochloride plus propofol and anesthesia maintenance with sevoflurane and nitrous oxide in open rhinoplasty surgery, septoplasty, turbinoplasty, endoscopic sinus surgery, and endoscopic nose surgery. They found that delirium in the propofol group was lower than in the sevoflurane group. This study was conducted on 80 patients [10]. This result is inconsistent with the result of the present study. One of the reasons is probably the larger number of samples in Joe's article. The results of the present study might have been consistent with results of the Joe's article if it used a larger number of samples. Another reason might be the use of two different checklists in two studies. Joe used RASS and SAS checklists in his study. In the RASS checklist, the criteria for performing risky behaviors, very agitated, agitated, restless, alert and calm, drowsy, light sedation, moderate sedation, heavy sedation, and unconscious are checked by the nurse. In the SAS checklist, the criteria for risk behaviors, very agitated, restless, calm and cooperative, drowsy, heavy sedation, and anesthesia are checked by the nurse. If a supplementary checklist was used in the present study, the results might have been similar to Joe's study. Another reason for the discrepancy might be the type of surgery and the physical ability and health of the patients. Joe's study was conducted on healthy patients with nose surgery. However, the present study was conducted on people with skeletal problems who were candidates for the dental procedure, and more than them had mental disabilities.

Chandler *et al*. examined and compared the two groups of anesthesia maintenance with sevoflurane and anesthesia maintenance with propofol plus remifentanil in strabismus repair surgery. They found that the delirium rate was lower in the propofol group than in the sevoflurane group. This study was conducted on 112 healthy children aged 6 years and older [11]. Their results were inconsistent with the results of the present study. One of the reasons might be that the present study was conducted on adults and Chandler's study was conducted on children. If the present study was conducted on children, its results might have been similar to the results of Chandler's study. Another reason for this discrepancy in the results of the two studies might be the number of people studied. Chandler investigated 112 children, but the present study investigated 30 patients. If more samples were used in the present study, its results might have been similar to the results of Chandler's study. Another reason for the discrepancy in the results might be the use of different criteria to measure delirium. In Chandler's study, the PAED checklist was used, which examines eye contact, purposeful actions, awareness of the surrounding environment, and the restlessness of children.

Sneyd *et al*. showed no significant differences between the two groups of anesthesia maintenance with propofol and anesthesia maintenance with sevoflurane in patients who were candidates for craniotomy surgery regarding the recovery time. This study was conducted on 50 patients [15]. The present study also showed no significant difference between the two groups regarding recovery time. Watson and Shah examined and compared two groups of anesthesia maintenance with propofol plus alfentanil and anesthesia maintenance with sevoflurane plus nitrous oxide and alfentanil in adult patients who were candidates for spinal surgery. They found that anesthesia induction and maintenance in the propofol group was much cheaper compared to the sevoflurane group [14]. They concluded that the combined costs of one-hour soporific, analgesic, and vasoactive drugs in patients maintained with sevoflurane are lower than propofol [15]. In the present study, the cost of maintaining anesthesia in the propofol group was much cheaper than in the sevoflurane group.

Conclusion

The delirium rate was similar in both groups in this study. The results of the present study and other studies suggest that the delirium rate is similar in the sevoflurane and propofol drugs in patients with movement disorders. Delirium is crucial for them in recovery. Sevoflurane can be a good alternative if propofol cannot be used.

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Ethics statement: This study has been approved by the ethics committee of Isfahan University of Medical Sciences (Code: IR.MUI.RESEARCH.REC.1398.756.) and all subjects had been informed regarding the details of the study and have all signed a consent.

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