The Effect of Sevoflurane and Desflurane on the Early Postoperative Cognitive Functions In Geriatric Patients

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ABSTRACT

Our aim was to compare the effects of desflurane and sevoflurane on cognitive functions of geriatric patients that were planned for elective surgery under general anestesia. After national ethical committee approval, 40 patients (aged 65-75 yr) were enrolled. Patients were allocated to either the desflurane (n=20) or the sevoflurane (n=20) group. In all patients anaesthesia will be induced with propofol and remifentanyl, and maintained with the anaesthetics desflurane, or sevoflurane, and remifentanyl. Emergence times from anaesthesia and Aldrete scores were recorded. Cognitive function will be evaluated with two cognitive test; Blessed Short Orientation Memory Concentration Test (BOMC) and standardized mini mental test (SMMT) preoperatively and postoperatively at 60, and 180 minute after extubation. The mean extubation time, eye opening time and Aldrete scores were similar in the desflurane and sevoflurane groups (p>0,05). There were no significant differences between the desflurane and the sevoflurane groups when the BOMC and MMST scores were compared preoperatively, and postoperatively at 60, and 180 min (p>0,05).The result of this study indicate that there is no difference between effects of desflurane and sevoflurane anesthesia on postoperatif cognitive functions in the elderly.

Key words: *Aged, cognitive disorders, diagnosis, desflurane, sevoflurane*

Yaşlı Hastalarda Erken Postoperatif Kognitif Fonksiyonlarda Sevoflurayin ve Desflurayinin Etkisi

ÖZET

Genel anestezi altında, elektif cerrahi girişim geçirecek geriatrik olgularda desfluran ve sevofluranın erken postoperatif kognitif fonksiyonlar üzerine etkilerini karşılaştırmayı amaçladık. Ulusal etik kurul izni alındıktan sonra, yaşları 65-75 arasında olan 40 hasta çalışmaya dahil edildi. Hastalar desfluran (n=20) ve sevofluran (n=20) olarak iki gruba ayrıldı. Tüm hastaların anestezi indüksiyonunda propofol ve remifantil kullanılırken, anestezi idamesinde remifentanil ile birlikte desfluran veya sevofluran kullanıldı. Anesteziden uyanma zamanları ve Aldrete derlenme skorları kaydedildi. Hastaların kognitif fonksiyonları iki kognitif test; Kısa Blessed Oryantasyon Bellek Konsantrasyon Testi (BOMC) ve Standardize Mini Mental Test (SMMT) ile preoperatif ve postoperatif ekstübasyon sonrası 60. ve 180. dakikalarda değerlendirildi. Ortalama ekstübasyon süreleri, göz açma süreleri ve Aldrete skorları desfluran ve sevofluran grubunda benzerdi (p>0,05). Preoperatif ve postoperatif 60. ile 180. dakikalarda BOMC ve MMST skorları karşılaştırıldığında sevofluran ve desfluran grupları arasında anlamlı fark yoktu (p>0,05). Geriatrik hastalarda desfluran ve sevofluran anestezisinin erken postoperatif kognitif fonksiyonlar üzerine benzer etkilere sahip olduğu sonucuna varıldı.

Anahtar kelimeler: *Yaşlılık, kognitif bozukluklar, tanı, desflurayin, sevoflurayin*

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INTRODUCTION

The postoperative psychomotor disorder is defined as the postoperative cognitive dysfunction (POCD) (1). The psychomotor function disorder may be associated with the anesthetic agents, as well as the physiological changes resulting from the anesthesia (2,3). The knowledge of the factors causing deterioration in cognitive functions, and of the evaluation methods, will ensure the achievement of reliable information about postoperative cognitive dysfunction and will lead to measures to be taken to reduce the frequency and severity of this condition (4). Various psychomotor tests are applied for the evaluation of the cognitive functions (5). However, because the differences in language and culture will affect the test results, the validity and the reliability tests must be done for the specific community. Short Blessed Orientation Memory Concentration Test (BOMC) and Standardized Mini-Mental State Examination (MMSE) are tests with reliability and validity for Turkish people (6). Desflurane and sevoflurane, which are the latest agents for the inhalation anesthesia, have a significantly lower solubility in water, fat and blood compared to the other volatile anesthetics (7). Therefore, with both agents, there is a fast recovery and return of the cognitive functions (8).

In our literature review, we did not find a study investigating the postoperative cognitive functions in the geriatric patients, using the appropriate tests for Turkish people. The hypothesis of the study is that, in geriatric patients, desflurane, which has a lower blood / gas solubility compared to sevoflurane, can provide an early recovery of cognitive functions (9). For this purpose, we aimed to compare desflurane and sevoflurane inhalation anesthesia in geriatric patients, with respect to the hemodynamics, the early postoperative recovery and the effects on the cognitive function by applying BOMC and MMSE cognitive function tests.

MATERIALS AND METHODS

After approval by the Clinical Drug Trials Ethics Advisory Board of the Ministry of Health (No. 15; dated 24.09.2010), between 01.10.2010-30.06.2011, 40 patients of ASA I-III, who were scheduled for grade 2 elective surgery, as defined by the application guide of the Turkish Society of Anesthesiology (TARD), 65 years and older, at least literate were included for the study. The study was carried out to investigate the effects of the desflurane and sevoflurane anesthesia on early postoperative cognitive functions. All patients were informed and a written informed consent was obtained from each subject. The patients with a history of neurological or psychiatric disease that influence the cognitive functions and the CNS, drug use affecting the CNS, alcohol use two or more times a week or any addiction, and sleep disorders were excluded. The patients were randomly divided into two groups by the method of sealed envelopes, one day before surgery the BOMC and the SMMT were done, and the normal levels of cognitive function of the patients were determined (6) (Appendix 1-2). In the operation room, an 18 or 20 gauge cannula was inserted in a peripheral vein and 0.9% NaCl solution infusion was started. Electrocardiogram (ECG), peripheral oxygen saturation (SpO2) and non-invasive arterial pressure monitoring (Datex-Ohmeda S/5 ADU, SWEDEN) were performed. The heart rate (HR), the mean arterial pressure (MAP), and the SpO_2 were measured and recorded before the induction, during the induction, after the extubation, and 5 minutes after the extubation. Every 15 minutes until the end of the operation, MAP, HR, SpO2, $ETCO_2$, end-tidal volatile anesthetic drug concentrations were measured (Datex, Capnomac ® SWEDEN) and recorded.

Throughout the operation, the anesthetic and the analgesic requirement was set to maintain the MAP and the HR values at ± 20% of the baseline value right before the induction. A 20% increase in the value of the OAB and / or >90 beats / min were considered to be superficial anesthesia, and the remifentanyl (Ultiva™ GlaxoSmithKline) dose was increased by 25%. A 20% reduction in the value of MAP and / or HR <50 beats / min was considered as deep anesthesia in the remifentanyl dose was reduced by 25%. In the operation room, before the induction, preoxygenation with 100% O2 was performed for 5 minutes. In Group I, 0.5 µg/kg/min remifentanyl infusion was started intravenously for the induction of anesthesia, together with 1-2 mg/kg propofol (Propofol ®, Fresenius Kabi). As the spontaneous respiration disappeared, 0.5 mg / kg atracurium (Tracrium ® GlaxoSmithKline) was administered for muscle relaxation, and three minutes later, the patient was intubated orotracheally and the mechanical ventilation support (Datex-Ohmeda anesthetic machine with S/5TM) was started. The anesthesia was maintained with 50% O_2+50% air, and 0.5-1 minimal alveolar concentration (MAC) desflurane and 0.25 to 0.5 µg/kg/

min remifentanyl infusion. The ventilation was achieved with a tidal volume of 8-10 mL/kg and a respiratory rate of 10-14 / minute. In Group II, 0.5 µg/kg/min remifentanyl infusion was started intravenously for the induction of anesthesia, together with 1-2 mg/kg propofol. As the spontaneous respiration disappeared, 0.5 mg/kg atracurium was administered for muscle relaxation, and three minutes later, the patient was intubated orotracheally and the mechanical ventilation support was started. The anesthesia was maintained with 50% O_2+50% air, and 0.5-1 MAC sevoflurane and 0.25 to 0.5 µg/kg/min remifentanyl infusion. The ventilation was achieved with a tidal volume of 8-10 mL/kg and a respiratory rate of 10-14/minute. The inhalation anesthetics were ceased as soon as the skin closure initiated, and the remifentanil infusion was terminated as soon as the skin was completely closed. Neuromuscular blockade was antagonized by 0.01 mg/kg atropine and 0.03 mg/kg neostigmine, and the patients were extubated after spontaneous respiration. In both groups, for postoperative analgesia, tramadol HCl (Abdi Ibrahim Contramal ®) 1 mg/kg was administered intravenously if there was no contraindication. Extubation time (the re-establishment of the swallowing reflexes after the discontinuation of anesthetics, stabilization of the vital functions and regular spontaneous breathing movements), eye-opening time (the time to open the eyes after discontinuation of anesthetics), and the Aldrete Recovery Score at the 2nd and the 5th minutes after extubation were recorded. When the Aldrete Recovery Score was ≥9, the patients were brought to the postoperative care room. After the recovery from the anesthesia, at postoperative 60 and 180 minutes, the cognitive functions were evaluated using the BOMC, and the MMSE (6). The data was analyzed using the SPSS 16.0 package program. The descriptive statistics were shown in tables and graphics. Between-group comparisons were performed with the Kruskal-Wallis analysis of variance. The binary comparison of the parameters in terms of the differences between the groups was done with the Mann-Whitney U test with a Post-hoc Bonferroni Correction. Gender and ASA differences between the two groups were compared by the chi-square test. The repeated measurements within groups were compared using the Friedman test. The significant results were compared with the Bonferroni-corrected Wilcoxon Signed Ranks test. The significance level was taken as 0.05. The power of the study to show that there is no difference between the groups was calculated as 0.95, with the current cognitive tests, a difference of 0.7 and within a standard deviation of ± 0.1, when 20 patients were included in both groups.

RESULTS

Forty patients were included In ASA I-III risk group, scheduled for elective surgery under general anesthesia. The patients were divided into two groups as desflurane group (Group I) and the sevoflurane group (Group II). Age, weight, height, sex, operative and anesthesia times were similar in two groups (p>0.05) (Table 1). There was no statistical difference between the groups with respect to the total doses of remifentanyl used intraoperatively (p> 0.05) (Table 2). The average used end-tidal (ET) sevoflurane and desflurane concentration values are shown in Table 2. The first 75 minutes of hemodynamic parameters were evaluated statistically. The both groups of patients in the study, were found to have similar hemodynamical features. In both groups there was a decrease in MAP after the induction of the anesthesia (Figure 1). There was statistically no significant difference between the desflurane and the sevoflurane group in terms of extubation and eye-opening time (p>0.05). No statistical difference was found between the groups with respect to Aldrete Recovery Scores at the end of the operation and at 2 and 5 minutes (p>0.05) (Table 3). BOMC was assessed over 28 points. The comparison of the preoperative values and postoperative values of the 60th minutes and the 180th minutes revealed no statistically significant results (p>0.05) (Table 4). MMSE score was evaluated out of 30 points. When the preoperative values and the values at the postoperative 60th minutes and 180 minutes were compared, there was no statistically significant difference between the groups (p>0.05) (Table 4).

DISCUSSION

This study, conducted in 40 elderly patients, was carried out to compare the effects of desflurane and sevoflurane anesthesia on cognitive functions, in the early postoperative period. The cognitive functions were evaluated with the BOMC and the MMSE tests. Both tests were performed preoperatively and postoperatively at 60 and 180 minutes. After the induction of anesthesia, both groups were hemodynamically stable. Extubation and eye opening time, and the Aldrete recovery Scores

Table 1. *Characteristics of the study*

	Group I (n:20)	Group II (n:20)
Age (years)	68.9±4.5	68.9± 5.7
Weight (kg)	75.1±8.6	71.9±10.8
Height (cm)	169.7±5.9	166.1± 6.4
Gender (Female/Male)	5/15	7/13
Inguinal Hernia	17	15
Incisional Hernia	3	5
Operating time (min)	76.1±10.6	77.9±10.3
Anesthesia time (min)	83.1±10.4	84.6±11.9

Table 3. *Postoperative recovery values (mean ± SD).*

	Grup I (n:20)	Grup II (n:20)
Extubation time (min)	7.4±2.4	7.3±1.8
Eye opening time (dk)	8.4±2.7	8.4±2.2
Aldrete Score at the 2nd min.	9.3±0.4	9.2±0.4
Aldrete Score at the 5th min.	10.0±0.0	10.0±0.0

at the 2nd and 5th minutes after the surgery were similar in two groups. as The early postoperative cognitive functions, measured by BOMC and MMSE tests, showed similar features in both groups. In general anesthesia, the new inhalation anesthetics are often preferred for reasons such as easy adjustment of the depth of the intraoperative anesthesia, minimal postoperative side effects, and a quick and full recovery (10). Sevoflurane and desflurane are widely used due to their low solubility, and their hemodynamics, recovery and side effects are compared in various studies. Dupont et al. have evaluated the hemodynamic parameters during anesthesia with desflurane (at a concentration of 3.4%), sevoflurane (1.4%) and isoflorane (0.7%), and reported similar blood pressure and heart throughout the anesthesia rate (11). Similarly, in the study of Ebert et al. comparing the desflurane and the sevoflurane anesthesia, no significant change in heart rate was observed at 0.83 MAC in both groups. They have identified a dose-dependent decrease in the OAB in both groups, and reported that the hemodynamic effects of sevoflurane and desflurane were similar (12). In our study, in both groups, the HR was within the normal limits in all periods. Statistically non-significant decreases were observed in the mean arterial pressure, compared to the preoperative values. These changes were thought to be associated with the depression on the cardiovascular system caused by the anesthetic agents.

Gauthier et al. have investigated the effects of sevoflurane and isoflurane on the recovery, in 60 patients between the ages of 18-70, undergoing neurosurgery, found that, the recovery of sevoflurane group was not only faster, but the postoperative neurological examination could be done in a shorter time (13). Fredman et al. have compared the sevoflurane and the propofol anesthesia in patients undergoing ambulatory surgery, and used propofol for the induction and the maintenance of the anesthesia in group I, whereas in group II, anesthesia was induced with propofol, and maintained with sevoflurane (1-2% in Et), and in group III both the induction of and the maintenance was done with sevoflurane (1-4% in Et). The ability to respond to simple verbal commands and to open the eyes was evaluated at 15 to 30 second intervals after the discontinuation of the anesthetics. Spontaneous eye opening, verbal response to commands, the extubation time, and the recovery time until the ability to tell the name, age, date of birth was similar in all three treatment groups. The authors have concluded that sevufluran can be an alternative to propofol to start and maintain the general anesthesia in ambulatory surgery (14). Juvin et al. have observed effects of desflurane and sevoflurane on postoperative recovery in the morbidly obese patients, and reported that the recovery in the desflurane group was faster and more comfortable. The extubation, the eye-opening and the orientation time was shorter in the desflurane group (15). Larsen et al. have compared the recovery and the cognitive functions in remifentanyl - propofol, desflurane and sevoflurane anesthesia. They have attributed the more rapid recovery in the remifentanyl – propofol group to the more rapid elimination of these drugs compared to the sevoflurane and desflurane. In addition, they have reported a possible residual effect of fentanyl on the recovery, since it was used in all the groups (16). Dupont et al. have found that a significantly shorter recovery, eye opening and extubation time in

Table 2. *Total drug doses (mean ± SD).*

	Grup I (n=20)	Grup II (n=20)
Total remifentanyl(μg)	585.9±231.5	547.7±242.8
Average ET desflurane(%)	2.6±0.90	-
Average ET sevoflurane(%)	-	0.6 ± 0.50

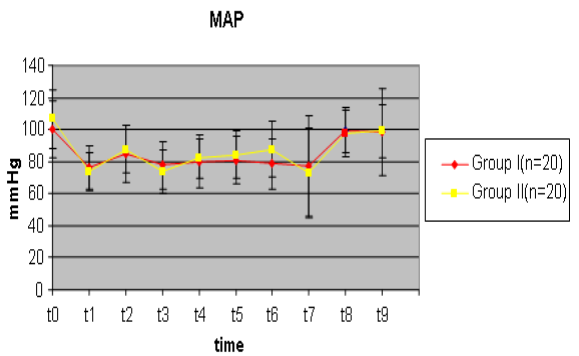
ET: End Tidal

Table 4. *BOMC and MMSE results (mean ± SD).*

	Grup I (n.20)	*Grup II (n:20)*	*p value*
Preop. BOMC	*7.1±5.1*	*5.2±5.1*	*0.249*
Postop. 60th min BOMC	*7.2±5.6*	*6.0±4.3*	*0.471*
Postop. 180th min BOMC	*6.3±5.3*	*4.6±4.5*	*0.276*
Preop. MMSE	*27.8±2.2*	*27.0±2.1*	*0.277*
Postop. 60th min MMSE	*27.1±1.9*	*25.9±1.4*	*0.310*
Postop. 180th min MMSE	*27.9±2.2*	*27.2±1.6*	*0.264*

the desflurane group compared to the sevoflurane group (11). There are several tests used to evaluate the restoration of the cognitive functions after anesthesia in the elderly. Geriatric Mental State Examination, Digit Symbol Substitution Test (DSST), Trieger Dot Test (TDT), BOMC, and the MMSE are some of these. Heavner et al. have used the scoring method DSST as the postoperative recovery score, and found similar DSST scores in the desflurane and the sevoflurane groups which they have compared (17). Tarazi et al. have also used the DDST scoring system to compare the desflurane and sevoflurane anesthesia, and have found higher DSST scores at all periods, with a significant difference at the 30th minute (18). Nathanson et al. have evaluated the effects of anesthesia with sevoflurane and desflurane at the ambulatory surgery on the cognitive functions, and measured with the DDST scoring system preoperatively and at the postoperative 30th, 60th, 90th and 120th minutes. Their findings were in accordance with our results, the restoration of the cognitive functions in this study were similar in both groups (19). Wandel et al. have compared the characteristics of the sevoflurane or propofol anesthesia in adults undergoing ambulatory surgery. In this study, preoperative cognitive functions were measured by DSST. The cognitive functions were restored significantly faster after sevoflurane anesthesia (20). Chen et al. have compared the cognitive functions in patients over 65 years of age, after desflurane or sevoflurane anesthesia, using the Mini Mental Test (MMT), and reported that there were no statistically significant difference between the groups with respect to the MMT values preoperatively and postoperatively at 1,3,6 and 24 hours (21). The tests used to measure the cognitive impairment in the early postoperative period, give different results depending on the anesthetic procedures (22). Furthermore, the neuropsychological tests are also affected by the differences in language and culture (6). Therefore, the validity and reliability studies must be made for the community before implementing the tests. In this study, the fact that the BOMC and the MMSE results were better at 180 minutes after the operation than the preoperative values, suggests that repeated applications may be effective for learning. The inclusion of the patients who smoke to the study is a limitation of this study. Smoking can have a negative effect on the cognitive functions by increasing the low-density lipoprotein (22).

There were no complications during the operation and at the recovery room, all cases were sent to the wards uneventfully. In conclusion, desflurane and sevoflurane anesthesia in geriatric patients were shown to have similar characteristics with respect to the hemodynamic stability, the early postoperative cognitive functions, and the recovery.



after the extubation., t9:5 min. after the extubation.

Figure 1. *The change of the MAP values over time.*

Appendix 1. Short Blessed Orientation-Memory-Concentration Test (BOMC)

Question	Fault	Score	Weight??
1 Which year is this?	1	….	x 4 = …….
2 Which month is this?	1	….	x 3 = …….

Remember this address:

Emine Keskin Fırın Sokak No:42 BARTIN

3 How late is it now? (within one hour) 1 ….x 3 = …….

4 Count backwards from twenty one at a time 2 ….x2 = …….

5 Count down the months. 2 …. x 2 = …….

6 Repeat the address I've told 5 …… x 2 = …….

TOTAL = …….

Appendix 2. Standardized Mini-Mental State Examination (MMSE)

Questions	Points
1. Which year is this?	1
2. Which season is this?	1
3. Which month is this?	1
4. What is the date?	1
5. Which day is this?	1
6. In which country do we live?	1
7. In which city are you now?	1
8. In which district are you now?	1
9. In which building are you now?	1
10. In which floor of the building are you now?	1
11. Repeat these three nouns after me (table, flag, dress)	3
12. Go backwards from 100 by subtracting 7	5
13. Do you remember the three words I have just said?	3
14. What is the name of these objects? (watch, pen, etc.).	2
15. Repeat the sentence (if and but if I do not want)	1
16. Take the paper on the table, fold it with both hands, and put it back	3
17. I will give you a sentence, read it and do what it says	1
18. I will give you a piece of paper, write a meaningful sentence	1
19. Draw the shape I'll show you (Two rhombuses, one inside the other, for the educated subjects a circle in a triangle)	1
Total	30

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