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RESEARCH

A COMPARISON OF RECOVERY CHARACTERISTICS OF SEVOFLURANE AND PROPOFOL–REMIFENTANIL ANESTHESIA IN GERIATRIC PATIENTS

ABSTRACT

Introduction: In this study we aimed to compare the recovery characteristics of propofol/remifentanil and sevofluran/remifentanil anesthesia in 100 geriatric patients undergoing urological procedures.

Materials and Method: The patients were randomized to receive either propofol-remifentanil (group P) or sevoflurane-remifentanil (Group S) anesthesia. Recovery characteristics, the time to post-anesthetic discharge scoring system (PADSS) score and Aldrete score of 9 point, Digit Symbol Substitution Test (DSST) and Trieger Dot Test (TDT)values were compared between two groups.

Results: Extubation time was significantly shorter in group P than in group S (5.3±2.9 min vs 7.8±3.8 min, p=0.038). The times of first eye opening, response to verbal commands and orientation were similar in both groups. The time of Aldrete score of 9 points (grup P: 14.2±3.6 min, group S: 16.3±4.5 min) and PADSS of 9 points (group P: 19.3±5.7 min, group S: 22.1±4.2 min) were also similar (p>0.05). Time to return to the normal value of DSST was significantly shorter in Group P compared with Group S, and TDT was similar in both groups (p>0.05). No significant differences were observed in the incidence of postoperative complications and VAS score (p>0.05).

Conclusion: Both propofol-remifentanil and sevoflurane-remifentanil appears to be an adequate anesthesia in geriatric patients.

Key Words: Sevoflurane; Propofol; Geriatrics; Anesthesia Recovery Period.

ARAŞTIRMA

İLERİ YAŞ HASTALARDA SEVOFLURAN VE PROPOFOL–REMİFENTANİL ANESTEZİSİNİN DERLENME ÖZELLİKLERİNİN KARŞILAŞTIRILMASI

ÖZ

Giriş: Bu çalışmada ürolojik cerrahi girişim geçirecek 100 ileri yaş hastada propofol-remifentanil kullanılarak uygulanan total intravenöz anestezi ile sevofluran-remifentanil anestezisinin derlenme özelliklerinin karşılaştırılması amaçlanmıştır.

Gereç ve Yöntem: Hastalar propofol-remifentanil (grup P) veya sevofluran-remifentanil (grup S) anestezisi verilmek üzere rasgele ayrıldı. Derlenme özellikleri, anestezi sonrası gönderme skor sistemi (PADSS) ve Aldrete derlenme skorunu 9 olma zamanı, Digit Symbol Substitution Test (DSST), Trieger Dot Test sonuçları kaydedildi.

Bulgular: Ekstubasyon zamanı grup P'de grup S'e göre belirgin olarak kısa bulundu (5.3±2.9 dk ve 7.8±3.8dk, p=0.038). İlk göz açma, verbal uyarılara cevap ve oryantasyon gruplar arasında benzerdi. Aldrete skorunun 9 olma zamanı (Grup P: 14.2±3.6 dk, Grup S: 16.3±4.5 dk)ve PADSS'in 9 olma zamanı (Grup P: 19.3±5.7 dk, Grup S: 22.1±4.2 dk) iki grupta benzer bulundu (p>0.05). DSST'in normale dönmesi grup P'de grup S ile karşılaştırıldığınd belirgin olarak hızlı idi (p<0.05) ve TDT iki grupta benzerdi (p>0.05). Bulantı/kusma, titreme, göğüs duvarında sertlik ve VAS ağrı skoru değerlerinde belirgin fark yoktu (p>0.05).

Sonuç: İleri yaş hastalarda, hem propofol-remifentanil hem de sevofluran-remifentanil anestezisi ile yeterli anestezi düzeyi güvenli bir şekilde sağlanabilir.

Anahtar Kelimeler: Sevofluran; Propofol; Geriatri; Anestezi İyileşme Dönemi.

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Introduction

Rapid emergence from anesthesia and postoperative recovery of cognitive function are important requirements of modern anesthetics. Generally, both propofol and sevoflurane meet these criteria (1).

The elderly comprise an ever-growing proportion of the population, particularly in developed countries. A common definition of "old age" encompasses people older than 65 years. Factors such as autonomic dysfunction, cardiac and respiratory problems and concomitant medications limit the choice of anesthetic agents and methods in elderly patients (2).

Comparison of emergence and recovery after propofol and sevoflurane anesthesia has produced different results depending on patient status, surgical procedures and use of analgesics (3). The pharmacokinetics of remifentanil allows easy titration to change intraoperative conditions and swift and, predictable emergence from anesthesia.

A total IV anesthesia regimen with remifentanil and propofol is an ideal anesthetic technique to control response to tracheal intubation effectively and intense surgical stimulation, while allowing for rapid emergence from anesthesia without prolonged respiratory depression.

The low blood/gas ratio and tissue partition coefficients of sevoflurane provide a rapid uptake during the induction of anesthesia, rapid changes in depth of anesthesia, and also rapid elimination (4).

The aim of this study was to compare the clinical properties of these two anesthetics with regard to recovery from anesthesia and postoperative cognitive function.

Materials and Method

After approval by the institutional review board and written informed consent, 100 patients with ASA physical status I-III, aged 65-80, and scheduled for elective urological surgery estimated to last > 1.5 hours, were enrolled in the study. Exclusion criteria were routine use of sedative drugs, requirement of dialysis, emergent surgery, cardiac and respiratory failure.

All patients were pre-medicated with 0.06 $mg.kg^{-1}$ midazolam 45 min before the procedure.

One hour before induction of anesthesia, cognitive function were assessed using the Trieger Dot Test (TDT) and Digit Symbol Substitution Test (DSST) (5,6). For the TDT, patients connected printed dots on a paper sheet within 1 min; missed dots were noted (7). For the DSST, patients were asked to replace digits with appropriate symbol located in a legend at the top of the page within 1 min.

After arrival in the operating room, two peripheral intravenous (IV) catheters were inserted, and standard monitors (electrocardiography, heart rate, non invasive blood pressure, end-tidal carbondioxide_concentration and arteriel oxygen saturation) were applied. Prior to induction, all patients received 5 $ml.kg^{-1}$ of IV fluid (e.g., Ringers's solution). The anesthesia induction started with a bolus dose of 1$\mu g.kg^{-1}$ of remifentanil (injected over 30 to 60 sec), and a continuous infusion of remifentanil was added simultaneously at a delivery rate 0.5 $\mu g.kg^{-1}.min^{-1}$ in two groups. Then propofol was given for hypnosis at a starting dose of 0.5 $mg.kg^{-1}$ and titrated thereafter at 10 mg every 10 seconds until the patients were unresponsive to verbal command in all subjects. After anesthesia induction, tracheal intubation was facilitated with 0.6 $mg.kg^{-1}$ rocuronium. After tracheal intubation, the remifentanil infusion was initially adjusted to 0.25 $\mu g.kg^{-1}$ min^{-1} in both groups and the patients were divided randomly into two groups.

Anesthesia was maintained and adjusted according to physiological parameters. For the group P, the propofol infusion rates were within the range 2-8 $mg.kg^{-1}.h^{-1}$ and, end expiratory sevoflurane levels and MAC values were within the range of 0-4% and 0.5-1, respectively.

During the maintenance of anesthesia, patients were ventilated with a fresh gas flow with 4 $l.min^{-1}$ of oxygen 35% in air by using a semiclosed circle system.

Anesthetic concentrations were adjusted according to the depth of anesthesia. The hemodynamic reactions were used while determining the depth of anestesia. The anesthetics (remifentanil, propofol, sevoflurane) were increased to control the hemodynamic responses to surgical stimulation, assigned by MAP>20% of the preinduction baseline values and heart rate or/and clinical signs of light anesthesia (patient movement, eye opening, swallowing, grimacing, lacrimation, or sweating). The concentrations of anethesics were decreased when the MAP and heart rate values were <20 % of baseline. The vasopressor and/or fluid replacement were planned to use whether the hypotension epizode persisted despite of decreasing the anestetic concentration and, atropine_was designed to use for bradycardia (Bradycardia was defined as heart rate < 50 bpm).

At the end of the surgery, all anesthetics were discontinued simultaneously without previous tapering, and ventilation was controlled 6 $L.min^{-1}$ of oxygen until the return of

spontaneous ventilation. The trachea was extubated when adequate spontanous ventilation (tidal volume > 4 ml.kg^{-1}), and patient response to verbal commands were established.

Tramadol 2mg.kg^{-1} was administered to all patients for the hyperalgesia induced by remifentanyl approximately 30 min before the surgery was finished.

After the extubation, the patients were transferred to the postanesthesia care unit and standard monitoring was recorded every 10 min. The patients were sended to the ward when they were stable. All patients were assessed in the recovery area by the same investigator who was blinded to the anesthetic technique used. The times of ability to independent maintenance of first eye opening, response to verbal commands, time of extubation and orientation (patient able to correctly state their names and ages) were noted. Postoperative pain (visual analoque scale=VAS), postoperative nausea/vomiting, shivering and rigidity of chestwall were recorded. The time at which the patient scored in Aldrete score of 9 points (8) and post-anesthetic discharge scoring system (PADSS) of 9 points (9) were noted.

Postoperative pain (VAS>4) was treated with tramadol, intravenously. DSST and TDT were repeated at 30, 60 and 90 min after discontinuation of anesthesia by the same observer who was blinded to the anesthesia received by the patient.

Student's t-test was performed for continuous variables and paired Student's t-test was used to compare the intragroup difference. Categorical data were analysed by X^2 test or Fisher's exact test. All tests were two sided and a value of $p<0.05$ was considered statically significant.

RESULTS

There were no significant differences between the two groups with regard to demographic characteristics, duration of operation and anesthesia (p>0.05) (Table 1).

Baseline and intraoperative blood pressure, heart rate, arterial oxygen saturation and end-tidal CO_2 pressure were also similar between two groups (p>0.05).

Both total dose of remifentanil (7.1±2.8 mg in the group P and 11.1±4.5 mg in the group S) and remifentanil infusion rates (0.38±0.15 μg.kg^{-1}.min^{-1}in the group P, 0.51±0.18 μg.kg^{-1}.min^{-1}in the group S) did not differ significantly (p>0.05) (Table 1).

Extubation time was significantly shorter in group P than that of group S (5.3±2.9 min vs 7.8±3.8 min, p=0.038) (Table 2). The times of first eye opening (5.5±2.1 min in the group P and 6.8±3.1 min in the group S, p>0.05), response to verbal commands (9.6±2.3 min in the group P and 10.8±3.2 min in the group S, p>0.05), time of orientation (patient able to correctly state their name, age) (10.6±2.6 min in the group P and 11.4±3.3 min in the group S p>0.05) were similar (Table 2).

The time of Aldrete score of 9 points (Group P: 14.2±3.6 min, Group S: 16.3±4.5 min), the time of PADSS of 9 points (19.3±5.7 min in the group P and 22.1±4.2 min in the group S) and the time of discharge from postanesthetic care unit

Table 1— Demographic Data, Characteristics of Surgery and Anesthesia

Characteristics	Group P (n=50)	Group S (n=50)
Age (years)	69.2±4.8	69.8±3.9
Gender (F:M)	12/38	14/36
Weight (kg)	75.8±6.7	72.8±6.3
Body mass index (kg.m^{-2})	25.2±2.7	26.6±3.1
ASA physical status 1:2:3 (n)	18/24/8	18/25/7
Type of surgery (n)		
Prostatectomy	22	23
Nephrectomy	17	19
Bladder Ca operation	11	8
Duration of surgery (min)	162.6±21.2	170.9±18.6
Duration of anesthesia (min)	176.4±10.4	179.5±11.5
Propofol infusion (mg.kg^{-1}.h^{-1})	3.62±0.6	–
Remifentanil infusion (μg.kg^{-1}.min^{-1})	0.38±0.15	0.51±0.18
Total remifentanil dose (mg)	7.1±2.8	11.1±4.5
MAC	–	0.65±0.12

Value are mean±SD or number.
MAC: Minimum alveolar anesthetic concentration

Table 2— Emergence and Clinical Recovery

Recovery Variable (min)	Group P (n=50)	Group S (n=50)
Time to extubation	5.3±2.9	7.8±3.8*
Time to first eye opening	5.5±2.1	6.8±3.1
Time to response to verbal commands	9.6±2.3	10.8±3.2
Time to orientation	10.6±2.6	11.4±3.3
Time to Aldrete score of 9 points	14.2±3.6	16.3±4.5
Time to PADSS of 9 points	19.3±5.7	22.1±4.2

Value are mean±SD
*p<0.05 Group P versus Grup S

Table 3— Trieger Dot Test and Digit Symbol Substitution Test

	TDT (number of missed dots)		DSST (% located symbols)	
	Group P	Group S	Group P	Group S
Preoperative value	6.1±1.6	5.8±2.2	98.2±1.3	98.4±1.2
30 min	14.3±2.6*	17.3±3.6*	83.6±3.2*#	62.8±4.5*
60 min	10.3±3.1*	14.3±3.4*	88.6±4.5	86.4±3.2
90 min	7.9±2.3	8.7±3.3	94.3±2.6	91.8±3.5

Value are mean±SD
TDT: Trieger Dot Test, DSST: Digit Symbol Substitution Test
*p<0.05 value versus preoperative value, #p<0.05 Group P versus Group S

(PACU) (20.4±2.7 min in the group P and 24.2±3.8 in the group S) were shorter in group P than in group S but a statistical significant difference was not obtained (p>0.05) (Table 2).

In the group P, the patients showed a tendency of less error responses on the TDT than patients after sevoflurane anesthesia administration but there were no statistical differences between two groups (p>0.05) (Table 3).

At the 30 min after termination of anesthesia, the patients in group P gave more correct responses on the DSST than in group S (p=0.032), whereas no statistical difference was obtanied on this test among the two groups after 60 min and 90 min anesthesia administration, (p>0.05) (Table 3).

There was no difference with regard to pain scores in group P and group S at any time (30, 60, 90, 120 min) (p>0.05) (Table 4). Group P had lower incidence of nausea and vomiting when compared with group S. However, these differences did not reach statistical significance (p>0.05) (Table 4). The incidence of shivering and rigidity of chestwall were similar between both groups (p>0.05) (Table 4).

Table 4— Postoperative Pain, Analgesic Demands, Adverse Effects

	Group P (n=50)	Group S (n=50)
Patients requiring additional analgesic in the PACU (n)	43	40
VAS for analgesia		
30 min after extubation	6.4±2.3	5.1±2.2
60 min after extubation	3.6±2.5	3.1±1.4
90 min after extubation	6.9±2.6	4.8±2.8
120 min after extubation	3.5±2.1	2.8±1.8
Nausea/vomiting (n)	8/5	16/9
Shivering (n)	23	20
Rigidity of chestwall (n)	8	10

Value are mean±SD or number.

Discussion

Our study showed that both propofol and sevoflurane anesthesia supplemented with remifentanil were suitable for elderly patients because they have comparable hemodynamic stability and postoperative recovery. Additionally extubation time and recovery of DSST were slightly shorter in group P, but discharge time from PACU was not shorter.

There are several anesthetic agents in anesthesia practice and the recovery profiles of these agents are different. It was shown that the early recovery time was shorter after desflurane or sevoflurane administration in adults or children when compared with isoflurane or halothane administration in many previous studies (10-12) and it's also shown that desflurane administration have better effects than sevoflurane for the aspect of recovery time in ambulatory adult or pediatric patients (13,14).

Results of previous studies indicated that early recovery from remifentanil based anesthesia even might be accelerated by combining remifentanil with an inhaled anesthetic in small concentrations instead of propofol due to faster and more predictable elimination of the inhaled anesthetic when compared with propofol (15,16). We found that these were associated with shorter extubation time in the propofol group compared with sevoflurane group in geriatric patients but there were no differences in the times of spontane eye opening, response to verbal commands, orientation, and Aldrete score of 9 points and PADSS of 9 points.

Previous studies comparing propofol and sevoflurane anesthesia in children and adolescents also demonstrated reduced time to extubation for propofol, which did not result with earlier discharge from the postanesthesia care unit (3,17).

When discussing our results, we should point out some potential shortcomings. The first problem was the question of equipotency of the doses of the anesthetics given for hypnosis. The dosage regimen of propofol and sevoflurane used in the present study was comparable to other remifentanil-based anesthesia studies, and had also an empiric basis that proved to be clinically suitable. Nowadays, it would be possible to use an electroencephalographically (EEG) derived parameter (e.g., the bispectral index) to titrate anesthetic agents for an equivalent level of hypnosis. However, from a clinical standpoint, when these EEG parameters are not available, our dosage regimen may closely reflect daily routine practice. Therefore, the results should be eveluated with these conditions.

The fact that all patients had equivalent depth of anesthesia as the starting point in the different groups was a major cocern of measuring the recovery in our study. Because of EEG or other monitoring device of anesthetic depth was not available to ensure for beginning of the patients' recovery from comparable levels of anesthesia, the anesthesia provider was forced to rely on standard clinical indicators to titrate the maintenance anesthetics as described in methods. However, all anesthesia was provided by the same experienced anesthesiologist and the doses of the anesthetics applied were comparable to those used in other studies to achieve a state of surgical anesthesia judged clinically or by EEG monitoring or its modifications (18,19).

In previous studies during EEG or BIS-monitored anesthesia, shorter extubation times for propofol-remifentanil were observed compared to sevoflurane-remifentanil, but did not result into earlier discharge from the postanesthesia care unit (3,17). In other previous studies, total intravenous anesthesia with propofol-opioid was compared inhalational agent, and these studies reported similar recovery characteristics. However, in these studies, different opioid agents and N_2O were used (2,20). Loop et al.(1) reported the combination of remifentanil infusion with small-dose desflurane, sevoflurane and propofol was characterized by predictably rapid and early recovery.

In anesthesia practice, Mini Mental Test (MMT), TDT and DSST have been widely used for the assessment of the intermediate and late recovery of cognitive function in the postanesthesia recovery unit (7, 20-24). These studies have shown that DSST appears to be the most sensitive tests for residual cortical depression by anesthetics, particularly impairment of information processing performance and the ability to concentrate.

In the present study, the patients in the group P showed a tendency toward less error responses on the TDT, and the patients in the group P gave more correct responses on the DSST than in the group S.

In a previous study, Hocker et al (17) reported similar TDT and DSST results in propofol and sevoflurane anesthesia. Differently, BIS was used in this study. Larsen et al (7) reported that the patients given propofol-remifentanil had a better performance for TDT and DSST than desfluran and sevoflurane, but they added fentanyl to sevoflurane and desfluran. Özünlü et al (23) showed that cognitive functions were similar between desflurane and propofol anesthesia but MMT was used for cognitive function in this study.

In our study, DSST was more rapidly restored after propofol-remifentanil anesthesia administration compared with sevoflurane-remifentanil but we did not used EEG or BIS for anesthetic depth. We reported similar postoperative complication (nausea, vomiting, shivering, e.g.) in the group P and the group S.

We have concluded that in geriatric patients undergoing urological surgery, the choice of anesthetic agent might have an influence on the postoperative recovery process. The propofol-remifentanil anesthesia was associated with a faster recovery of cognitive function and shorter extubation time than sevoflurane-remifentanil anesthesia. However, propofol-remifentanil and sevoflurane-remifentanil groups were found similar with respect to recovery profile.

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