Dexmedetomidine versus Remifentanil for Controlled Hypotensive Anesthesia in Functional Endoscopic Sinus Surgery

Fonksiyonel Endoskopik Sinüs Cerrahisinde Kontrollü Hipotansif Anestezi: Deksmedetomidin ve Remifentalinin Karşılaştırılması

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Objective: During functional endoscopic sinus surgery (FESS), sufficient control of bleeding is essential in order to increase the visibility in the operative field and reduce the risk of injury to the optic nerve or internal carotid artery. However, choosing the ideal agent is still a controversial topic. The aim of this study is to compare the effects and possible side effects of remifentanil and dexmedetomidine for controlled hypotension in FESS.

Methods: Fifty ASA I-II patients, aged between 18-60 years, undergoing elective FESS, were included. Patients were randomly assigned into two groups (n=25) as Group R (remifentanil infusion, 0.25 mcg kg^{-1}h^{-1}) and Group D (dexmedetomidine infusion, 0.2-0.7 mcg kg^{-1} min^{-1}). The duration of anesthesia, surgery and controlled hypotension, total drug doses, dryness of the surgical area, recovery time, side effects, liver and kidney function analyses were recorded.

Results: There was no statistically significant difference between the groups in operation time, duration of anesthesia and controlled hypotension time. Group R and D were similar in average SpO$_2$, dryness, arterial blood pressure, aspartate aminotransferase (AST), alanine aminotransferase (ALT), blood urea nitrogen (BUN) and creatinine at all measurement times. Heart rate was lower in Group D than Group R at the time of extubation and 5, 10, 15, 20, 30. min after extubation (p<0.05). Mean recovery time of Group D was longer than Group R (p<0.001).

Conclusion: Based on the side effect scores, visualisation results of surgical area, liver or renal functions; both dexmedetomidine and remifentanil provided adequate, safe, controlled hypotensive anesthesia. However, dexmedetomidine was associated with significantly longer recovery time period compared with remifentanil.

Key Words: Remifentanil, dexmedetomidine, controlled hypotension

Amaç: Fonksiyonel endoskopik sinüs cerrahisi (FESS) sırasında kanamanın kontrol altına alınması; cerrahi alandaki görüşün artması ile birlikte, optik sinir veya internal karotis arteri gibi önemli yapıların yaralanması riskini de azaltmaktadır. Ancak, bu amaç için ideal ajan seçimi tartışmalı bir konu olmaya devam etmektedir. Bu çalışmada, FESS için kontrollü hipotansiyon uygulamalarında remifentanil ile deksmedetomidinin etkinlikleri ile gelişebilecek yan etkilerinin karşılaştırılmaası amaçlanmıştır.

Yöntemler: Çalışmaya, elektif FESS cerrahisi geçirecek, ASA I-II, 18-60 yaş arasında 50 hasta dahil edildi. Hastalar randomize olarak, Grup R (remifentanil infüzyonu, 0,25 mcg kg^{-1}s^{-1}, n=25) ve Grup D (deksmedetomidin infüzyonu, 0,2-0,7 mcg kg^{-1}dk^{-1}) olarak iki gruba ayrıldı. İlaç enjeksiyonundan, hedeflenen kan basıncının oluşmasına kadar geçen süre, anestezi ve cerrahi süreleri, verilen toplam ilaç miktarı, cerrahi sahanın kuruluğu, derlenme süresi, yan etkiler ile karaciğer ve böbrek işlevlerine ait değerler kaydedildi.

Bulgular: Gruplar arasında anestezi, cerrahi işlem süresi ve kontrollü hipotansiyon süresi bakımından istatistiksel olarak anlamlı fark yoktu. Ortalama periferik oksijen satürasyonu, cerrahi sahanın kuruluğu, kan basınçları, aspartat aminotransferaz (AST), alanin aminotransferaz (ALT), kan üre nitrojeni (BUN) ve kreatinin değerleri karşılaştırıldığında anlamlı bir fark bulunamadı. Kalp atım hızı, ekstübasyon sırasında, ekstübasyondan sonra 5, 10, 15, 20 ve 30. dakikalarda Grup D'de Grup R'den anlamlı olarak düşüktü (p<0,05). Ortalama derlenme süresi ise Grup D'de Grup R'den anlamlı olarak daha uzundu (p<0,001).

Sonuç: Her iki ajanın yan etki skorları, cerrahi saha görüş yeterlilikleri, karaciğer ya da böbrek işlevlerine etkileri değerlendirildiğinde, gerek remifentanilin gerekse de deksmedetomidinin fonksiyonel endoskopik sinüs cerrahilerinde eşit oranda güvenli, kontrollü hipotansiyon oluşturabileceği sonucuna vardık. Ancak deksmedetomidin anlamlı olarak daha uzun derlenme süresiyle ilişkili bulunmuştur.

Anahtar Kelimeler: Remifentanil, deksmedetomidin, kontrollü hipotansiyon

Introduction

Functional endoscopic sinus surgery (FESS) is indicated for the surgical management of acute and chronic sinus pathologies when conservative treatment has failed. This surgical intervention restores the drainage and aeration of the paranasal sinuses. The procedure perpetuates the mucociliary clearance mechanism while conserving the normal non-obstructing anatomic structures (1). Because of decreased surgical invasiveness, this procedure is less painful, and a safe and effective treatment method for paranasal sinus disorders. Because of this, it has been widely used over the past 20 years (2, 3). However, major and minor complications depending on the surgeon's experience and the technique were defined. A series of major complications such as bleeding during surgery, orbital hematoma, cerebrospinal fluid fistula, and intracranial injury were reported (4). As bleeding reduces the visibility in the operative field and increases the risk of injury to the optic nerve, orbita, middle cranial fossa and internal carotid artery, sufficient control of intraoperative bleeding is essential (5). Administration of vasoconstrictors like adrenaline or a beta-blocker to the nasal passages, reverse Trendelenburg position, controlled hypotension or steroid therapy were suggested (6). Controlled hypotensive anesthesia is commonly used in several surgical interventions using different techniques (7,8). Volatile anesthetics, sympathetic antagonists, β adrenoreceptor antagonists, calcium channel blockers, opioids, and direct-acting vasodilators have been used to achieve controlled hypotension. Sodium nitropruside,

nitroglycerine, hydralazine, trimetaphan, adenosine, fenoldopam and α-2 agonists are also employed frequently for this purpose (9-11). However, choosing the ideal agent is still a controversial topic. In the current study, the effects and safety of remifentail, which is an μ opioid receptor agonist and dexmedetomidine, an α-2 agonist; when used for controlled hypotension in FESS, are compared.

Methods

Following the approval of the Health Pharmaceuticals and Pharmacy Ethics Committee of Dr. Lutfi Kirdar Training and Research Hospital, 50 patients aged between 18-60 years, who were at ASA I-II physical status, and who were scheduled for elective functional endoscopic sinus surgery were enrolled in the study. Patients were randomly divided into two groups, as Group R (remifentanil group, n=25) and Group D (dexmedetomidine group, n=25). Patients at ASA III and over; patients receiving β-blockers, opioids and cardiovascular drugs; patients suffering from chronic hypertension or cardiovascular system illness, atrioventricular block, bradycardia (under 55 beats/min), obstructive lung disease, liver disease, kidney disease, diabetes mellitus, morbid obesity, anemia (Hb <%12), coagulation or bleeding problems, were excluded.

Patients received Ringer's lactate through an 18 G intravenous cannula, which was placed on the forearm before entering the operating room. All patients received $0.07 \ mg \ kg^{-1}$ midazolam im and 0.015 $mg \ kg^{-1}$ atropine im for premedication. Monitorization included standard, DII derivation electrocardiography, heart rate (HR), non-invasive blood pressure, and pulse oximetry (CAMS II Comprehensive Anesthesia Monitor). The Modified Allen test was used to assess collateral circulation to the hand. A 20 G cannula was inserted into the radial artery of the non-dominant hand in order to monitor invasive blood pressure.

A correctly sized facemask and 100 % oxygen was used for pre-oxygenation. General anesthesia was induced with iv sodium thiopental $5-7 \ mg \ kg^{-1}$ and fentanyl $2 \ \mu g \ kg^{-1}$. Endotracheal intubation was performed with the aid of iv vecuronium $0.1 \ mg \ kg^{-1}$. Ventilation was controlled with 67% nitrous oxide in oxygen to maintain end-tidal carbon dioxide pressure at 32-36 mmHg. Sevoflurane was used for maintenance. The reverse Trendelenburg position (30° head up) was chosen. Standard dose lidocaine-adrenaline (1% lidocaine 1mL + 1/100 000 adrenaline) infiltration was administered to the nasal passages by the surgeon.

In group R; 5 mg remifentanil was diluted with 50 ml 0.9 % saline, and patients received $1 \ mcg \ kg^{-1}$ iv loading dose of remifentanil over a period of 60 seconds. Later, an infusion (Braun pump) was started at the rate of $0.25 \ mcg \ kg^{-1} \ h^{-1}$. The infusion rate was adjusted according to the patient's response, to achieve a mean arterial pressure between 65 and 75 mmHg. In group D, 2 mL of 200 mcg dexmedetomidine was diluted with 48 ml 0.9% saline and patients received a $1 \ mcg \ kg^{-1}$ loading dosage of dexmedetomidine within 10 min and later, infusion was started at the rate of $0.2-0.7 \ mcg \ kg^{-1} min^{-1}$. The infusions began immediately after tracheal intubation in both groups. For 5 minutes, no interventions were allowed in the subjects to assess target blood pressure.

Mean arterial blood pressure, HR, SpO_2 were recorded every 10 min, from the beginning of anesthesia. Perioperative hypotension and bradycardia were defined as mean arterial blood pressure < 90 mmHg or 50 beat/min respectively. Atropine 0.5 mg was adminis-

tered intravenously for the treatment of bradycardia. In hypotension, the infusion dose was reduced to half of its basal value, if MAP <60 mmHg for more than 60 sec. If no increase could be obtained, the infusion of the study drug was discontinued, and the patient was excluded from the study.

The time needed to reach the target blood pressure, durations of surgery and anesthesia, the duration of controlled hypotension, and total drug doses (pentothal, remifentanil, dexmedetomidine, vecuronium) were recorded.

During surgery, the surgeon, who was blinded to the study drug, evaluated the dryness of the surgical area every ten minutes. A four-point quality scale (0=no bleeding-no suction needed, 1=unimportant bleeding-no suction of blood required, 2=moderate bleeding-frequent suction required, 3= severe bleeding-constant suction needed) was used to evaluate the visibility in the surgical field.

Patients received 10 mg metoclopramide and $1mg \ kg^{-1}$ tramadol intravenously 5 minutes before the cessation of infusion. All infusions were stopped 5 min before the end of surgery. When spontaneous breathing movements began, muscle paralysis was reversed with 1.5 mg neostigmine and 0.5 mg atropine.

Recovery time was recorded in the postoperative period. An anesthetist employing the Modified Aldrete Scoring System assessed recovery. Patients with an Alderete Score of 12 or higher were discharged from the recovery room. In the recovery room, adverse effects such as nausea, vomiting, agitation, bradycardia, coughing, shivering, reflex tachycardia and rebound hypertension were recorded. Aspartate aminotransferase (AST), alanine aminotransferase (ALT), blood urea nitrogen (BUN) and creatinine were analyzed 1 day before surgery, at the second hour and on the 3rd day of the postoperative period.

Statistical Analysis

For statistical analysis, NCSS 2007 software was used. The data is presented as mean and standard deviation. One-way analysis of variance was used to compare the groups, chi square test to compare qualitative data, and unpaired t-test was used to compare dual groups. Values of $p<0.05$ were accepted as statistically significant.

Results

There was no significant difference between the demographic characteristics of the groups (Table 1). There were no statistically significant differences between the groups in the duration of operation, anesthesia and controlled hypotension (Table 2).

Mean arterial pressure values were similar in both groups (Figure 1). Heart rates were higher in group R than group D at the time of extubation and 5, 10, 15, 20, and 30th min.s after extubation (Figure 2). Mean

Table 1. Patient demographics

		Group R (n=25)	Group D (n=25)	p
Gender°	Male	11 (40%)	16 (61.5%)	0.210
	Female	14 (60%)	9 (38.5%)	
Age (years)*		33.08±9.97	36.92±12.67	0.236
Weight (kg)*		71.04±9.68	76.77±14.1	0.098

Group R: Remifentanil infusion group, Group D: Dexmedetomidine infusion group
°Chi square test, *Unpaired t-test

Table 2. Duration of anesthesia, surgery and controlled hypotension (mean±SD)

	Group R (n=25)	Group D (n=25)	p
Duration of anesthesia (min)*	97.19±53.08	105.23±29.50	0.54
Duration of surgery (min)*	80.95±46.01	91.3±37.09	0.41
Duration of controlled hypotension (min)*	84.52±48.09	91.96±32.15	0.54

Group R: Remifentanil infusion group, Group D: Dexmedetomidine infusion group
*Unpaired t-test

Table 3. Postoperative values for AST, ALT, BUN and creatinine (mean±SD)

	Group R (n=25)	Group D (n=25)
AST*	T1: 18.4±3.46	20.38±4.74
	T2: 18.32±4.55	19.76±3.55
	T3: 16.56±3.33	18.33±3.48
ALT*	T1: 18.16±6.45	21.42±8.02
	T2: 19.16±4.99	21.24±8.15
	T3: 17±3.71	19.8±6.96
BUN*	T1: 14±4.33	15.56±7.55
	T2: 13.56±4.02	14.01±6.14
	T3: 13. 12±3.92	13.29±6.26
Creatinine*	T1: 0.77±0.14	0.82±0.18
	T2: 0.75±0.11	0.77±0.16
	T3: 0.71±0.1	0.73±0.13

T1: one day before surgery, T2: postoperative 2nd h, T3: postoperative 3rd day Group R: Remifentanil infusion group, Group D: Dexmedetomidine infusion group, AST: aspartate amino transferase, ALT: alanine amino transferase, BUN: blood urea nitrogen
*Unpaired t-test, p>0.05

SpO_2 values were similar in Group R and Group D at all measurement times (Figure 3). Mean dryness score of the surgical area did not differ statistically between the groups (Figure 4).

There were no significant differences between AST, ALT, BUN and creatinine values before surgery, at the end of the second hour and on the 3th day of the postoperative period (Table 3). Nausea and vomiting, agitation, bradycardia, coughing, shivering, reflex tachycardia and rebound hypertension time were similar in both groups (p=0.554). In Group R, 2 patients had sinus bradycardia (8%), 6 patients had nausea (24%), 2 patients had vomiting (8%), 2 patients had agitation (8%), 1 patient had shivering (4%), 2 patients had coughing (8%) and 3 patients had rebound hypertension (12%). In Group D, 1 patient had nausea (4%), 1 patient had agitation (4%), 6 had bradycardia (24%) and 3 patients had coughing (12%). There was no significant difference between the groups regarding the side effects. The mean recovery time of Group D was longer than Group R (p<0.001) (Figure 5).

Discussion

Previous studies showed that, although different opioids had similar effects on achieving a bloodless surgical area, the clearance of remifentanil was the most rapid. Remifentanil also maintained hemodynamic stability better than the other opioids, like fentanyl or alfentanil (12, 13). Reducing blood flow to the middle ear with sevoflurane and 0.25 µg kg^{-1}min^{-1} remifentanil combination provided a drier surgical site than sodium nitroprusside and 0.5 µg kg^{-1}min^{-1} alfentanil infusion (14). In this study, the remifentanil dose was the same as the previous studies in group R. With this dose, a clear operative field had been obtained, and no other hypotensive agent was needed to reduce blood flow. Hemodynamic stability was good in both groups.

As remifentanil is the drug with most rapid onset of action and shortest duration, the recovery time was shorter. Although remifentanil provided a dry surgical field, it caused some adverse effects such as nausea, vomiting, respiratory depression, pruritus, headache, vertigo, hypotension, and sinus bradycardia via vagal stimulation (15, 16). Nausea was
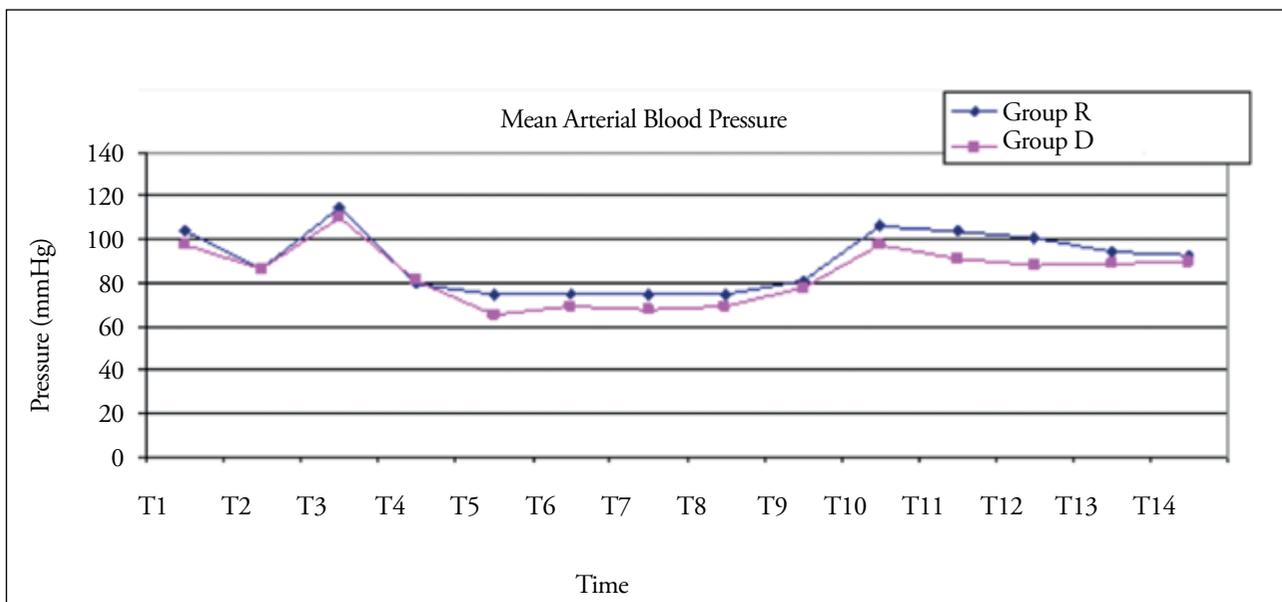
Figure 1. Mean arterial blood pressure (mean±SD)
Group R: Remifentanil infusion group, Group D: Dexmedetomidine infusion group, T1: before induction, T2: after induction, T3: after intubation, T4: after bolus drug administration, T5: 10. min of operation, T6: 20. min of operation, T7: 30. min of operation, T8: 40. min of operation, T9: after surgery, T10: during extubation, T11: 5 min after extubation, T12: 10 min after extubation, T13: 20 min after extubation, T14: 30 min after extubation
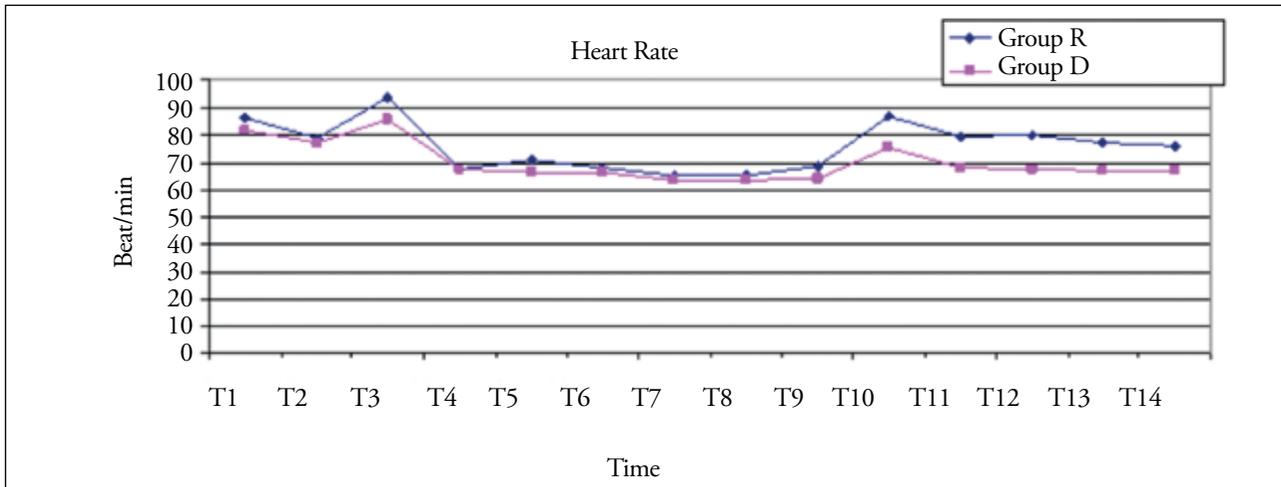
Figure 2. Heart Rate (mean±SD)
Group R: Remifentanil infusion group, Group D: Dexmedetomidine infusion group, T1: before induction, T2: after induction, T3: after intubation, T4: after bolus drug administration, T5: 10. min of operation, T6: 20. min of operation, T7: 30. min of operation, T8: 40. min of operation, T9: after surgery, T10: during extubation, T11: 5 min after extubation, T12: 10 min after extubation, T13: 20 min after extubation, T14: 30 min after extubation
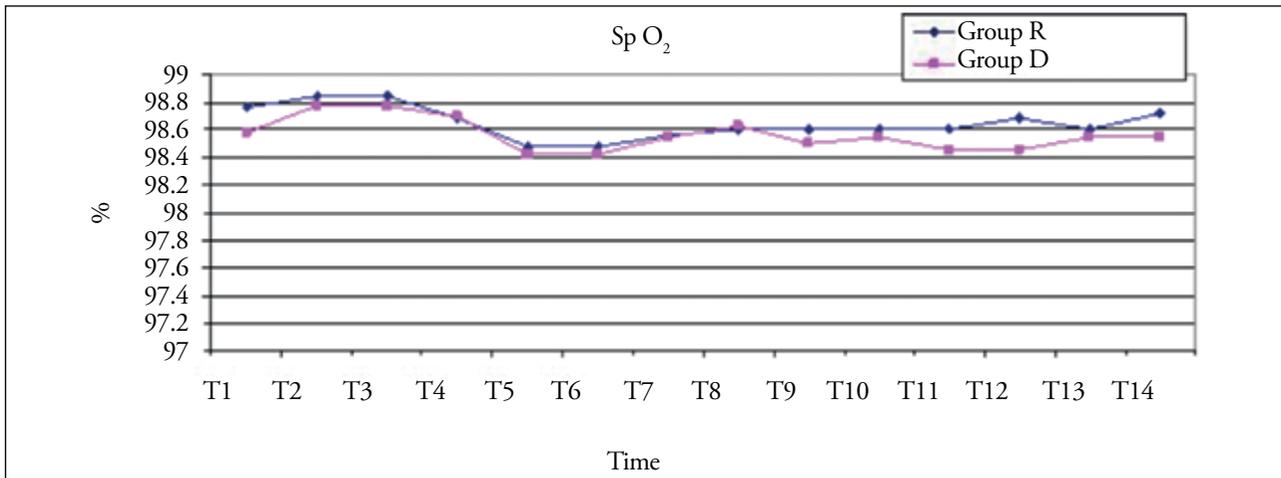
Figure 3. Peripheral oxygen saturation (mean±SD)
Group R: Remifentanil infusion group, Group D: Dexmedetomidine infusion group, T1: before induction, T2: after induction, T3: after intubation, T4: after bolus drug administration, T5: 10. min of operation, T6: 20. min of operation, T7: 30. min of operation, T8: 40. min of operation, T9: after surgery, T10: during extubation, T11: 5 min after extubation, T12: 10 min after extubation, T13: 20 min after extubation, T14: 30 min after extubation
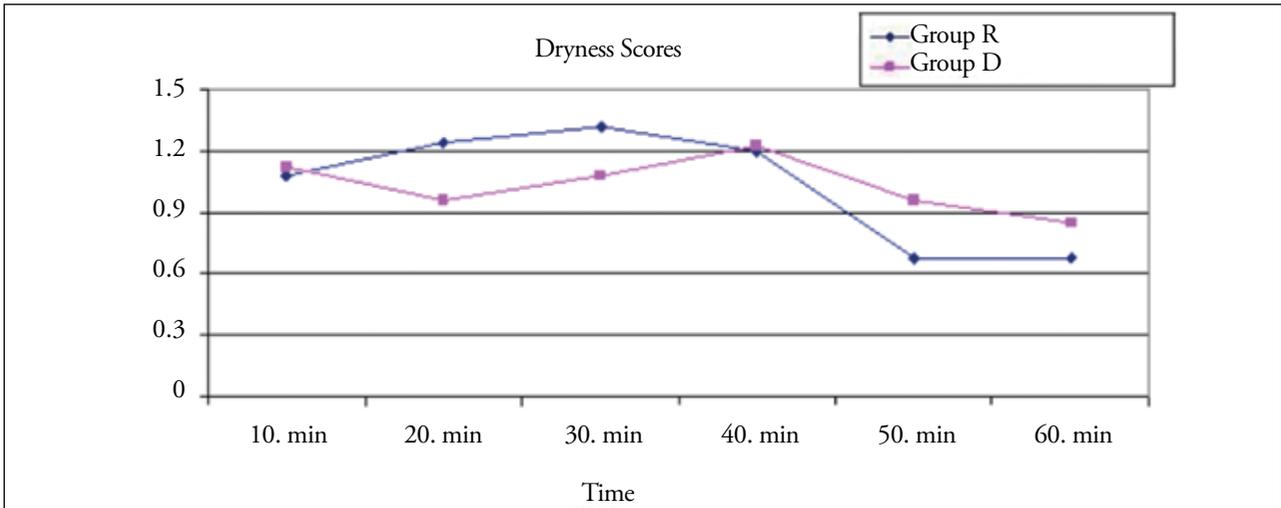
Figure 4. Dryness Scores (mean±SD)
Group R: Remifentanil infusion group, Group D: Dexmedetomidine infusion group

Figure 5. Recovery Time (mean±SD)
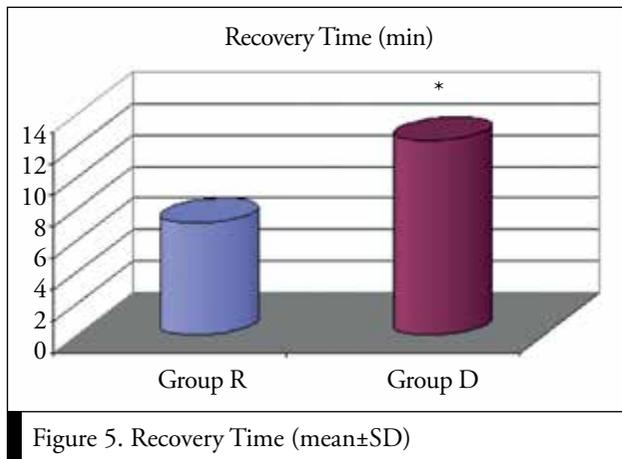
the most common side effect in the remifentanil group (24%). Bradycardia was the most frequent adverse effect in the dexmedetomidine group (24%). However, there was no significant difference between the groups regarding the side effects.

Because dexmedetomidine reduced HR and MAP, it was thought that it could be a beneficial agent for controlled hypotension. It was useful because it did not cause reflex tachycardia and it blocked the sympathetic system. In a case report, dexmedetomidine had been administered to achieve controlled hypotension in a spinal fusion operation of a 14-year-old patient. The infusion rate of dexmedetomidine was adjusted between 0.5-0.7 $\mu g\ kg^{-1}hr^{-1}$ to achieve a mean arterial pressure between 55 and 65 mmHg. Although HR was decreased from 90-100 beat/min to 70-80 beat/min and MAP was reduced from 75-80 mmHg to 55-60 mmHg with an infusion of dexmedetomidine, there had not been a reflex tachycardia (17). In the current study, there was no need to increase the infusion rate of dexmedetomidine, because it was sufficient to achieve a moderate controlled hypotension. No reflex tachycardia was observed, but one patient experienced rebound hypertension in dexmedetomidine group.

In a study by Ülger et al. (18) dexmedetomidine was compared with nitroglycerine to achieve controlled hypotension in forty ASA I adult patients scheduled for tympanomastoidectomy or tympanoplasty. The infusion rates of drugs were titrated to maintain a mean arterial pressure between 65 to 75 mmHg. In this study dexmedetomidine was found to be better in maintaining hemodynamic stability, drier surgical field and devoid of reflex tachycardia or rebound hypertension. Liver and renal functions were not affected by dexmedetomidine.

In cardiovascular surgery, clonidine, dexmedetomidine or mivazerol were administered in the preoperative, intraoperative or postoperative periods and the rates for mortality, myocardial infarction, ischemia or supraventricular tachycardia were evaluated. The α_2 adrenergic agonists were found to decrease ischemia and ischemia dependent mortality in vascular surgery (19).

In this study, there was no need to use additional hypotensive agents in both groups, during controlled hypotension.

Conclusion

Based on the side effect scores, dryness scores of surgical area, liver or renal functions, both dexmedetomidine and remifentanil provided safe, controlled hypotensive anesthesia in patients undergoing functional endoscopic sinus surgery. However, dexmedetomidine was associated with a significantly longer recovery time compared with remifentanil.

Conflict of Interest
No conflicts of interest were declared by the authors.

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