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Effectiveness of Dexmedetomidine for Controlled Hypotension in Providing Optimum Surgical Conditions for Functional Endoscopic Sinus Surgeries: A Double-Blinded Randomized Controlled Trial

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Fonksiyonel Endoskopik Sinüs Cerrahilerinde Optimum Cerrahi Koşulları Sağlamada Kontrollü Hipotansiyon için Deksmedetomidinin Etkinliği: Çift Kör Randomize Kontrollü Çalışma

ABSTRACT

Objective: *Bleeding resulting in impaired intraoperative visibility and increased risk of injury to vital structures such as optic nerve and internal carotid artery requires effective control with controlled hypotension during functional endoscopic sinus surgeries. Our aim in this study is to assess the effectiveness of dexmedetomidine in reducing blood loss during functional endoscopic sinus surgeries (FESS) when it is used for controlled hypotension.*
Method: *Ninety-two American Society of Anesthsiologists - ASA class I and II patients of comparable demographic profile, scheduled for elective FESS received either injectable dexmedetomidine (1 µk g hr^{-1}) for the first 10 minutes and then 0.5 µ kg hr^{-1} as infusion (Group A) or equal volume of saline infusion (Group B). The hemodynamic changes, utilization of intraoperative rescue medication, intraoperative blood loss, emergence time, postoperative sedation and pain scores were recorded.*
Results: *Patients in the dexmedetomidine group had a remarkable reduction in blood loss (p=0.000) with lesser intraoperative mean arterial blood pressure, heart rate, better sedation and pain scores postoperatively. The mean intraoperative rescue medication consumption was remarkably higher in patients of group B. Extubation time in group A patients was significantly higher (9.04 minutes) than in group B patients (5.07 minutes) (p=0.000).*
Conclusion: *Dexmedetomidine is an optimal effective agent that reduces blood loss by controlled hypotension during FESS providing ideal surgical field with better sedative and analgesic properties.*

Keywords: *Dexmedetomidine, functional endoscopic sinus surgery, Controlled hypotension, blood loss*

ÖZ

Amaç: *Fonksiyonel endoskopik sinüs cerrahileri sırasında, intraoperatif görüşte azalmaya ve optik sinir ve internal karotid arter gibi vital yapılarda hasar riskinde artmaya neden olan kanama, kontrollü hipotansiyon ile etkin kontrol gerektirir. Bu çalışmada amacımız, fonksiyonel endoskopik sinüs cerrahilerinde (FESS) deksmedetomidinin kontrollü hipotansiyon için kullanıldığında kan kaybını azaltmadaki etkinliğini değerlendirmektir.*
Yöntem: *Elektif FESS planlanan, Amerikan Anesteziyologlar Derneği - ASA sınıf I ve II, demografik özellikler bakımından benzer 92 hasta, deksmedetomidin 1 µ kg sa^{-1} ilk 10 dk, sonrasında 0.5 µ kg sa^{-1} infüzyon (Grup A) veya eşit volümde salin infüzyonu aldı (Grup B). Hemodinamik değişiklikler, intraoperatif kurtarıcı ilaç tüketimi, intraoperatif kan kaybı, derlenme zamanı, postoperatif sedasyon ve ağrı skorları kaydedildi.*
Bulgular: *Deksmedetomidin grubundaki hastalarda, daha düşük intraoperatif ortalama arteriyel kan basıncı, kalp hızı, postoperatif daha iyi sedasyon ve ağrı skorları ile birlikte kan kaybında (p=0.000) belirgin bir azalma vardı. Ortalama intraoperatif kurtarıcı ilaç tüketimi B grubundaki hastalarda belirgin olarak daha yüksekti. A grubundaki hastalarda ekstübasyon süresi (9.04 dk), B grubundaki hastalara göre anlamlı olarak yüksekti (5.07 dk) (p=0.000).*
Sonuç: *Deksmedetomidin, FESS sırasında kontrollü hipotansiyon ile kan kaybını azaltan, daha iyi sedatif ve analjezik özellikler ile ideal cerrahi alan sağlayan optimal etkili bir ajandır.*

Anahtar kelimeler: *Deksmedetomidin, fonksiyonel endoskopik sinüs cerrahisi, kontrollü hipotansiyon, kan kaybı*

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INTRODUCTION

The commonly performed surgery in otorhinolaryngology namely Functional Endoscopic Sinus Surgery (FESS) necessitates reestablishment of ventilation of sinuses and restoring their function. The rich blood supply of sinuses compromises the surgical field due to bleeding resulting in injury to proximal vital structures such as optic nerve, internal carotid artery etc., the successful outcome of FESS depends on oligemic surgical field and stable hemodynamics which are stipulated by anesthetic techniques such as controlled hypotension [(1)].

Along with non-pharmacological measures like head elevation, controlled hypotension is utilized to prevent bleeding in FESS. Various inhalational and intravenous anesthtics, sympatholytics, opioids, and vasodilators have been evaluated as for controlled hypotension. Delayed recovery, tachyphylaxis, toxicity (such as cyanide toxicity from nitroprusside), the need for unambiguous hemodynamic monitoring, hyperalgesia (with remifentanil) are some of the complications that necessitate a search for an ideal agent for controlled hypotension [(2)].

Dexmedetomidine is a highly selective alpha-2 specific agonist with sedative, anesthetic, and analgesic-sparing properties that help reduce blood loss and also perioperative anesthetic requirements [(3)]. The activated alpha-2 adrenoceptors result in decreased sympathetic tone, via reducing hemodynamic and neuroendocrine responses to surgical nociception. The stable hemodynamics of heart rate and blood pressure during FESS provided by dexmedetomidine creates a controlled hypotensive environment through reducing blood loss and enhancing intraoperative visualisation of the surgical field.

The objective of our study is to assess the effectiveness of dexmedetomidine in decreasing intraoperative blood loss during FESS when used for controlled hypotension.

MATERIALS and METHODS

After Institutional ethics committee approval and written informed consent of American Society of Anesthsiologists class I and II of 92 patients of both genders,aged 18-60 years were obtained for elective FESS, the patients were enrolled in our prospective double-blinded randomized controlled study to be performed in a tertiary care teaching hospital. All patients were assessed by clinical examination, basic laboratory investigations, chest radiography, and electrocardiography. Patients of ASA III and above, with a history of cardiorespiratory disorders, infective etiology, re-do surgeries, bleeding diathesis, patients receiving beta-blockers, sedatives, opioids, and cardiovascular medications were excluded.

Power analysis was done to calculate the sample size. With an alpha error of 5% and a power of 80, the sample size obtained was 92. A computer-generated random number table was used to allow allocation of patients into two equal comparable groups of 46 each. Group A patients received dexmedetomidine 1 μ kg^{-1} as loading dose over 10 minutes, followed by 0.5 μ kg^{-1} hr^{-1} infusion. Group B patients received an identical amount of normal saline solution. The entire operating room staff including anesthesiologists, surgeons, nurses, and recovery room nurses were blinded to the study protocol.

On arrival into the operating room, the patients' heart rates, blood pressures, and oxygen saturation levels were monitored using lead II, V5 of the electrocardiogram, noninvasive blood pressure monitor, and pulse oximeter, respectively. Ringer's lactate solution was administered after an intravenous line is secured. All patients were pre-oxygenated with 100% oxygen, and induction of anesthesia was performed with IV. propofol 2 mg kg^{-1}, fentanyl 2 μ kg^{-1} and vecuronium 0.1 mg kg^{-1}. After induction, the patient's head was elevated to 30° before surgery is started. As per the group assigned, the study drug was started at a dose of 1 μ kg^{-1} for 10 minutes and then continued with 0.5 μ kg^{-1} hr^{-1}. Anesthesia was maintained with delivery of oxygen (1L min^{-1}), nitrous oxide (2L min^{-1}), and 1 MAC of sevoflurane. The end-tidal CO_2 was maintained between 30-35 mm Hg. In both groups, the infusion of the study drug was stopped 30 minutes before the end of surgery. All patients were extubated at the end of procedure following adequate reversal of neuromuscular blockade with neostigmine (0.05 mg kg^{-1}) and glycopyrrolate (0.01 mg kg^{-1}).

The patients were assessed intraoperatively and for 1 hour postoperatively. The physiological measures assessed intraoperatively were baseline heart rate, blood pressure, O_2 saturation, at the start of infusion (during intubation), and every 5 minutes for 15 minutes and then every 15 minutes till the end of surgery. Intraoperative blood loss was calculated by substracting the weights of the soaked gauze, patty, cotton balls from those of dry gauze/patty/cotton balls and measuring the volume of collected blood from suction bottles.

Intraoperatively patients were monitored for adverse effects like bradycardia, and hypotension. Bradycardia was defined as heart rate of <50 bpm and hypotension as mean arterial pressure of <55 mmHg and these conditions were treated with atropine (0.6 mg) and ephedrine (3 mg), respectively. If BP was >30% of baseline, a bolus dose of nitroglycerine (5 µg) was used. Postoperatively heart rate, blood pressure, O_2 saturation, sedation and pain scores were assessed every 15 minutes for 60 minutes in PACU. Sedation was assessed using Ramsay sedation scale.

Pain assessment was done by using Visual Analog Pain Scale. Duration of surgery was noted in both groups. Requirement of rescue medication, time of stopping the infusion and the time to extubation was noted in both groups. The time from the end of surgical procedure to extubation is taken as 'Time to extubation'.

Statistical Analysis:

The data obtained are presented in a table format and expressed as mean ± standard deviation or as numbers. Statistical analysis was done using SPSS software (IBM Corp. Released 2010. IBM SPSS Statistics for Windows, Version 19.0. Armonk, NY: IBM Corp.). The demographic data for categorical variables were compared using the chi-square test. Statistical significance of time-related variables was determined using student t-test. A p value of less than 0.05 was considered statistically significant.

RESULTS

Our study was successfully completed with 92 adult patients and data of all patients were included for analysis. The effectiveness and safety of intravenous dexmedetomidine for controlled hypotension in reducing blood loss was evaluated in this study.

The demographic data like age, gender, ASA physical status and duration of surgery were comparable between both groups (Table I).

Table I. Demographic characteristics

Parameters	Group A	Group B
N	46	46
Age (years)	35±13.5	33.76±9.8
Gender (male/female)	28/18	26/20
ASA Status I/II	36/10	27/19

There was a statistically significant difference between blood loss in Group A (145.22 mL) compared to Group B (233.26 mL) (p<0.001) (Table II, Figure 1). Baseline values of mean heart rate were comparable between both groups, but intraoperatively a statistically significant reduction (p<0.05) in the mean heart rate in Group A patients was observed when compared with those in Group B after 5, 20, 25, 30, 45, 60, 75, 90 minutes of infusion (Figure 2).

Table II. Comparison of surgery duration, blood loss and time to extubation between Group A and B:

		N (% within Groups)			
Parameters		**Group A**	**Group B**	**95% CI of the difference**	**P - value**
Surgery duration (min)		76.63± 20.52	79.35 ± 22.92	-11.73 to +6.29	0.551
Blood loss (mL)		145.22 ± 42.73	223.26 ± 73.34	-102.91 to -53.18	<0.001
Time to extubation (min)		9.04 ± 1.80	5.07 ± 1.79	+3.23 to +4.72	<0.001
		N (% within Groups)			
Rescue medication	Atropine	4 (8.7)	0 (0)		0.058
	Nitroglycerine	2 (4.3)	8 (17.4)		0.064
	Ephedrine	6 (13)	2 (4.3)		0.090

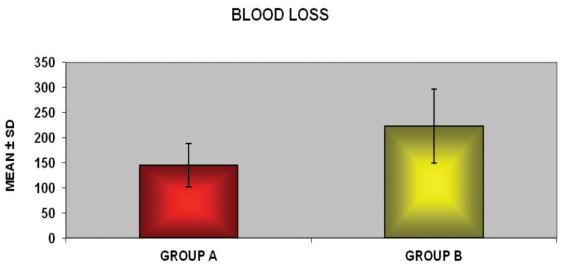

Figure 1. Comparison of blood loss (in mL) between Groups A&B.

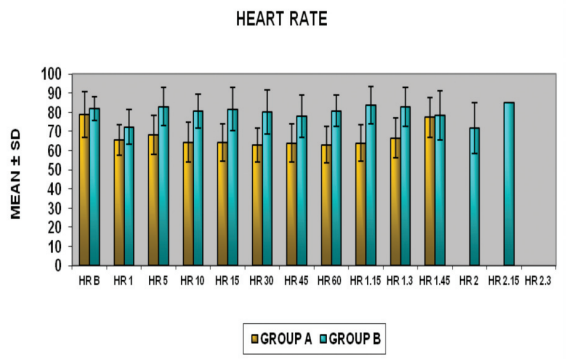

Figure 2. Intraoperative comparison of heart rate (beats per minute) between groups A&B.

The requirement of rescue medications - atropine and ephedrine were higher in Group A without any statistically significant difference (p=0.123), however, the requirement of nitroglycerin was lesser in Group A than in group B (Table III).

Table 3. Comparison of sedation scores between Groups A and B:

	Mean±Standard deviation			
Time (min)	Group A	Group B	95% CI	P-Value
0	2.78±0.59	2.04±0.63	0.48 to 0.99	<0.001
15	2.54±0.50	2.09±0.41	0.27 to 0.65	<0.001
30	2.26±0.44	2.04±0.21	0.07 to 0.36	<0.001
45	2.09±0.29	2.00±0.00	0.004 to 0.17	0.04

There was no significant difference in mean arterial pressure before and at the start of infusion but was highly significant with lower blood pressure in Group A within 5 minutes of the start of study drug infusion till the end of surgery (Figure 3). Time to extubation was significantly higher in Group A (9.04 minutes) than in Group B (5.07 minutes) (p<0.001). Postoperatively after extubation, heart rate and blood pressure remained at statistically significantly lower levels in Group A (p<0.05). Group A patients were found to have statistically significantly better sedation scores and lower pain scores in postoperative period compared to Group B patients (p<0.05) (Table III, Figure 4).

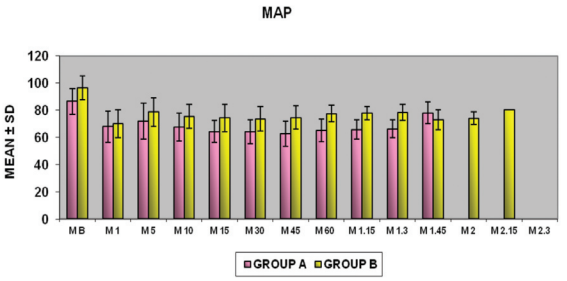

Figure 3. Intraoperative comparison of mean blood pressure (in mmHg) between groups A&B.

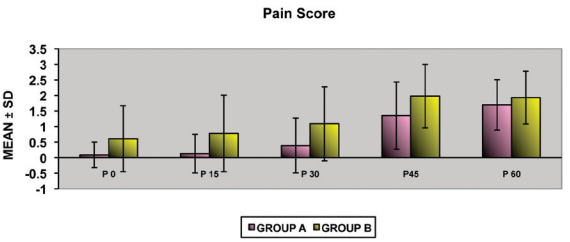

Figure 4. Comparison of visual analog pain scale between Groups A and B.

DISCUSSION

Functional endoscopic sinus surgery aims at restoring sinus ventilation and improving its function. It necessitates controlled hypotension intraoperatively for reduction of blood loss, for better surgical field visualisation and to prevent complications such as trauma to the optic nerve, and internal carotid artery etc. Our aim in this study is to assess the effectiveness of dexmedetomidine in reducing blood loss during FESS when used for controlled hypotension.

Earlier studies demonstrated that opioids, nitroglycerin, inhalational agents, beta-blockers achieved oligemic surgical field at the cost of nausea, vomiting, respiratory depression, pruritis, sinus bradycardia or reflex tachycardia, hypotension and hyperalgesia. Preoperative steroid administrations in nasal polyps provide better visibility because of their anti-inflammatory and anti-edema properties. Topical vasoconstrictors decrease congestion of mucosa and bleeding at the cost of tachycardia and hypertension. Controlled hypotension with various

drugs has been studied with varied satisfactory effects on the surgical field and blood loss [4]. Most studies reported varied results for the effects of dexmedetomidine during FESS though they have emphasized the reduction of maintenance drugs for anesthesia.

In our study, dexmedetomidine infusion significantly reduced intraoperative heart rate, blood pressure and surgical bleeding due to its alpha-2 effects causing central sympatholysis leading to hypotension. The effectiveness of intraoperative use of dexmedetomidine for an ideal surgical field has been extensively reported for middle ear [5,6] and maxillo-facial surgeries. The optimal anesthetic technique of relative bradycardia and associated hypotension found by Ulger et al. [7] compared dexmedetomidine with nitroglycerin to achieve controlled hypotension for middle ear surgeries. They found that dexmedetomidine maintains hemodynamic stability and better surgical visibility. In our study, we found that dexmedetomidine provided excellent controlled hypotension that assured surgical visibility with minimal bleeding. Contrary to administration of nitroglycerin any reflex tachycardia or rebound hypertension was not observed.

In their study Solimon R et al. [8] elucidated that dexmedetomidine is associated with lower blood loss and better-operating conditions in trans sphenoidal pituitary resection when compared to magnesium. We have found similar results in our study in that dexmedetomidine, by virtue of controlled hypotension, provided better operating conditions and reduced blood loss.

Goksu et al. [9] reported moderate controlled hypotension, lesser pain scores, better surgical visibility, and lesser side effects when dexmedetomidine was administered for FESS under local anesthesia. In their study, Gousheh SMR et al. [10] investigated the efficacy of dexmedetomidine on bleeding during FESS and found that dexmedetomidine not only reduces bleeding significantly but also decreases the intraoperative requirement for drugs used in the maintenance of anesthesia. In our study, the efficacy of dexmedetomidine in reducing intraoperative surgical site bleeding was examined. There was a remarkable enhancement in quality of the surgical field and an ideal surgical field was achieved in 86% of patients of Group A with minimal bleeding that did not hamper the surgical procedure.

The arousal time and time to total recovery from anesthesia was obscurely prolonged with dexmedetomidine. Richa et al. [5] reported a slower extubation time when patients received dexmedetomidine compared with those who received remifentanil for controlled hypotension. In our study, patients who received dexmedetomidine had slower but smooth emergence from anesthesia compared with the control group.

In our study, awakening time increased marginally but the intraoperative bleeding, requirement for nitroglycerin for hypotension showed a significant reduction. Karabayirli et al. [11] found no significant differences between dexmedetomidine and remifentanil in terms of surgical field visibility, and intraoperative bleeding in FESS, but recovery from anesthesia was delayed with dexmedetomidine. This could be possible, because all drugs in both groups were standardized for induction and maintenance of anesthesia except dexmedetomidine.

Bajwa et al. [12] showed that dexmedetomidine achieved desired mean arterial pressure, slightly higher sedation score and prolonged recovery time when compared with nitroglycerine and esmolol. Also, the request for analgesia was delayed in postoperative period (time of first analgesic request) in the dexmedetomidine group similar to our study, signifying the analgesic effects of dexmedetomidine.

Shams T et al. [13] Durmus et al. [14] and Karabayirli S et al. [11] in their independent studies found that dexmedetomidine is a better alternative to other drugs for controlled hypotension, blood loss, and better surgical visibility. Also, they found, dexmedetomidine has analgesic and anesthetic properties that help reducing perioperative analgesic and anesthetic requirements. We found similar results in our study with dexmedetomidine providing controlled hypotension, reduced blood loss, stable hemodynamics with better sedation and pain scores.

In their review, Snidvongs K et al. [15] found that the

quality of operative field for FESS was greatly improved when dexmedetomidine was used as an adjuvant which is consistent with our study findings. Similarly, in their study Gupta K et al. [16] also substantiated that dexmedetomidine provides an ideal oligemic surgical field for FESS similar to the findings of our study.

We believe that dexmedetomidine is an effective agent to reduce blood loss when used for controlled hypotension by providing hemodynamic stability and reducing perioperative anesthetic and analgesic requirements.

CONCLUSION

Dexmedetomidine effectively decreases blood loss by providing optimal controlled hypotension and better surgical field. With better hemodynamic stability and analgesic properties, it reduces intraoperative anesthetic and postoperative analgesic requirements. We have concluded that dexmedetomidine is effective in providing controlled hypotension and thus reducing blood loss in FESS.

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