

# Controlled Hypotension With Desflurane Combined With Esmolol or Dexmedetomidine During Tympanoplasty in Adults: A Double-Blind, Randomized, Controlled Trial

Iclal Ozdemir Kol, MD<sup>1</sup>; Kenan Kaygusuz, MD<sup>1</sup>; Altan Yildirim, MD<sup>2</sup>; Mansur Dogan, MD<sup>2</sup>; Sinan Gursoy, MD<sup>1</sup>; Evren Yucel, MD<sup>1</sup>; and Caner Mimaroglu, MD<sup>1</sup>

<sup>1</sup>Department of Anesthesiology, Cumburiet University School of Medicine, Sivas, Turkey; and <sup>2</sup>Department of Otorhinolaryngology, Head and Neck Surgery, Cumburiet University School of Medicine, Sivas, Turkey

## ABSTRACT

**BACKGROUND:** Controlled hypotension is a technique that is used to limit intraoperative blood loss to provide the best possible surgical field during surgery.

**OBJECTIVE:** The aim of this double-blind, randomized, controlled study was to compare the effects of desflurane combined with esmolol or dexmedetomidine on the amount of blood in the surgical field, recovery time, and tolerability in adult patients undergoing tympanoplasty.

**METHODS:** Turkish patients aged 18 to 60 years, classified as American Society of Anesthesiologists physical status I or II, who were scheduled for tympanoplasty were randomly divided into 2 groups: the esmolol group or the dexmedetomidine group. After the anesthesia induction in the esmolol group, a loading dose of esmolol was infused intravenously over 1 minute at 1 mg/kg, followed by a maintenance rate of 0.4 to 0.8 mg/kg/h. In the dexmedetomidine group, a loading dose of dexmedetomidine was infused intravenously over 10 minutes at a rate of 1 µg/kg, followed by a maintenance rate of 0.4 to 0.8 µg/kg/h. The infusion rates were then titrated to maintain mean arterial pressure (MAP) of 65 to 75 mm Hg. General anesthesia was maintained with desflurane 4% to 6%. Heart rate (HR) and MAP were recorded during anesthesia. The following 6-point scale was used to assess the amount of bleeding in the operative field: 0 = no bleeding, a virtually bloodless field; 1 = bleeding that was so mild that it was not a surgical nuisance; 2 = moderate bleeding that was a nuisance but did not interfere with accurate dissection; 3 = moderate bleeding that moderately compromised surgical dissection; 4 = bleeding that was heavy but controllable and that significantly interfered with surgical dissection; and 5 = massive bleeding that was uncontrollable and made dissection impossible. Scores ≤2 were considered to be optimal surgical conditions. The sedation score was determined at 15, 30, and 60 minutes after tracheal extubation using the following scale: 1 = anxious, agitated, or restless;

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2 = cooperative, oriented, and tranquil; 3 = responsive to commands; 4 = asleep, but with brisk response to light, glabellar tap, or loud auditory stimulus; 5 = asleep, sluggish response to glabellar tap or auditory stimulus; and 6 = asleep, no response. Time to extubation and to total recovery from anesthesia (Aldrete score  $\geq 9$  on a scale of 0–10), adverse effects (eg, intraoperative hypotension [blood pressure  $< 65$  mm Hg], bradycardia [HR  $< 50$  beats/min]), intraoperative fentanyl consumption, and postoperative nausea and vomiting were recorded. Arterial blood gas analysis and kidney and liver function tests were conducted. All patients were evaluated by the same attending surgeon and anesthesiologist, both of whom were blinded to the administered study drugs.

**RESULTS:** Fifty-two consecutive white patients undergoing tympanoplasty were identified. Two patients had to be excluded because of hypertension and 2 refused to participate. Forty-eight patients were equally randomized to either the esmolol group ( $n = 24$  [16 women, 8 men]; mean [SD] age, 38.4 [10.5] years) or the dexmedetomidine group ( $n = 24$  [17 women, 7 men]; mean age, 35.5 [14.7] years). Sedation scores were not collected for 1 patient in the esmolol group; therefore, analysis was conducted for 23 patients. The median (range) of the scores for the amount of blood in the surgical field in the esmolol and dexmedetomidine groups was 1 (0–3) and 1 (0–2), respectively ( $P = \text{NS}$ ). Mean intraoperative fentanyl consumption in the esmolol group was significantly higher than in the dexmedetomidine group (50.0 [3.0] vs 25.0 [2.5]  $\mu\text{g}/\text{min}$ ;  $P = 0.002$ ). In the esmolol group, the mean times to extubation and to recovery from anesthesia were significantly shorter than those of the dexmedetomidine group (7.0 [1.4] vs 9.1 [1.9] minutes, respectively; 5.9 [2.1] vs 7.9 [2.3] minutes; both,  $P = 0.001$ ). The mean sedation scores were significantly lower in the esmolol group ( $n = 23$ , because of intent-to-treat analysis) compared with the dexmedetomidine group at 15 minutes (2.5 [0.6] vs 3.6 [0.5];  $P = 0.001$ ) and 30 minutes (2.6 [0.6] vs 3.3 [0.6];  $P = 0.001$ ) postoperatively. No significant differences were found between the study groups in regard to blood urea nitrogen or creatinine concentration, aspartate aminotransferase or alanine aminotransferase activities, pH, partial pressure of carbon dioxide, or bicarbonate, before or after the operation.

**CONCLUSIONS:** Both esmolol and dexmedetomidine, combined with desflurane, provided an effective and well-tolerated method of achieving controlled hypotension to limit the amount of blood in the surgical field in these adult patients undergoing tympanoplasty. Esmolol was associated with significantly shorter extubation and recovery times and significantly less postoperative sedation compared with dexmedetomidine. (*Curr Ther Res Clin Exp.* 2009;70:197–208) © 2009 Excerpta Medica Inc.

**KEY WORDS:** esmolol, dexmedetomidine, desflurane, tympanoplasty, controlled hypotension.

## INTRODUCTION

Controlled hypotension is a technique that is used to limit intraoperative blood loss to provide the best possible field for surgery.<sup>1,2</sup> This technique has been used successfully for tympanoplasty.<sup>3</sup> Various agents (eg, magnesium sulfate,<sup>4</sup> sodium nitroprusside,<sup>2</sup> nicardipine,<sup>5</sup> nitroglycerine,<sup>5</sup> esmolol,<sup>2</sup>  $\alpha_2$ -agonists,<sup>6–8</sup> labetalol,<sup>9</sup> and high doses

of potent inhaled anesthetics [eg, isoflurane<sup>10</sup>]) have been used to achieve controlled hypotension. Some of the disadvantages associated with these drugs include resistance to vasodilators, tachyphylaxis and cyanide toxicity with sodium nitroprusside, the possibility of myocardial depression with esmolol and magnesium sulfate, and a long postanesthetic recovery period with isoflurane. Apart from the adverse effects (AEs) of hypotension on vital organ perfusion, potent hypotensive agents also have their own concentration-dependent AEs that can be reduced by adjuvant treatment.<sup>11</sup> When used alone, inhalational anesthetics require such a high concentration to achieve a significant reduction in bleeding that hepatic or renal injury might occur. Ideally, hypotensive agents should be easy to administer, have a short time to onset, have effects that disappear quickly when administration is discontinued, have rapid elimination without toxic metabolites, have negligible effects on vital organs, and have predictable and dose-dependent effects.<sup>11</sup>

Hemostasis for the middle ear presents special problems for the anesthetist because even minimal bleeding impairs the surgeon's vision and lengthens the time of surgery.<sup>2,5</sup> Esmolol is a short-acting  $\beta_1$ -adrenoceptor antagonist<sup>12</sup> and dexmedetomidine is a selective  $\alpha_2$ -adrenoceptor agonist.<sup>13</sup> The efficacy of dexmedetomidine and esmolol for achieving controlled hypotension has been reported. Boezaart et al<sup>3</sup> found that esmolol provided optimal surgical conditions compared with sodium nitroprusside for endoscopic sinus surgery during general anesthesia. The hypotension caused by a cardioselective  $\beta$ -adrenergic antagonist (esmolol) resulted in increased sympathetic tone of the mucous membrane arterioles that exerted unopposed  $\alpha$ -adrenergic effects on the mucous membrane vasculature, causing capillary vasoconstriction. Durmus et al<sup>8</sup> reported that dexmedetomidine was associated with significantly decreased bleeding and intraoperative anesthetic requirements (both,  $P < 0.05$ ) compared with placebo in patients undergoing tympanoplasty or septorhinoplasty. Richa et al<sup>7</sup> compared the efficacy of dexmedetomidine with that of remifentanyl for achieving controlled hypotension and improving surgical field exposure during tympanoplasty. They found that both remifentanyl and dexmedetomidine administered intraoperatively were effective in decreasing arterial pressure and heart rate (HR) during tympanoplasty. In an experimental study, Lawrence et al<sup>14</sup> found that dexmedetomidine was associated with a significant reduction in bleeding, especially in the skin, compared with baseline ( $P < 0.05$ ). Intraoperative-reduced bleeding may be due to the peripheral vasoconstrictive effects of  $\alpha_2$ -agonists.

Although esmolol is the most frequently used hypotensive agent for tympanoplasty,<sup>2,3</sup> there have been few studies reporting the use of dexmedetomidine<sup>7,8</sup> for this procedure. A review of the literature in MEDLINE was conducted of English-language texts (no year restrictions) using the following terms alone or in combination: *controlled hypotension*, *tympanoplasty*, *esmolol*, *dexmedetomidine*, and *desflurane*. The efficacies of desflurane combined with the  $\beta_1$ -antagonist esmolol or with the  $\alpha_2$ -agonist dexmedetomidine have not been compared previously in tympanoplasty.

We designed this study to compare the effects of desflurane combined with esmolol or dexmedetomidine on the amount of blood in the surgical field, recovery time, and tolerability in adult patients undergoing tympanoplasty.

## PATIENTS AND METHODS

The study protocol was approved by the Human Ethics Committee of Cumhuriyet University School of Medicine (Sivas, Turkey), and written informed consent was obtained from all study participants prior to study initiation.

Between February 2007 and March 2008, patients aged 18 to 60 years, classified as American Society of Anesthesiologists physical status I or II,<sup>15</sup> who were scheduled for tympanoplasty were enrolled in this double-blind, randomized, controlled clinical study. Patients were excluded from the trial if they had significant dysrhythmia, inadequately controlled hypertension, preexisting coagulation defects, or had been receiving anticoagulant drugs or cardiovascularly active drugs as antiarrhythmic and antihypertensive agents. All patients were hospitalized at the Department of Otorhinolaryngology Head and Neck Surgery, Cumhuriyet University School of Medicine, on the day before surgery and had fasted for  $\geq 8$  hours before surgery. All patients received midazolam 0.07 mg/kg IM for sedation 30 minutes before surgery.

Randomization was achieved using sequentially numbered, opaque, sealed envelopes containing computer-generated random allocations in a ratio of 1:1 in balanced blocks of 8.

On arrival in the operating room, 2 cannulae were inserted at different sites on the same arm, one for the infusion of esmolol or dexmedetomidine and the other for administration of fluids and other drugs. A 22-G catheter was inserted into a radial artery for direct determination of arterial pressure and HR, which were recorded continuously. Before induction of anesthesia, baseline measurements of HR, mean arterial pressure (MAP), and oxygen saturation by pulse oximetry (SpO<sub>2</sub>) were obtained (Criticare System Inc., Waukesha, Wisconsin). A crystalloid solution (5 mL/kg) was administered at the start of the induction period and 100% oxygen was administered by mask for the first 3 minutes. Anesthesia was induced with fentanyl 1  $\mu$ g/kg and propofol 2 mg/kg, and endotracheal intubation was facilitated with IV rocuronium 0.6 mg/kg. Mechanical ventilation was adjusted to provide an end-tidal carbon dioxide (CO<sub>2</sub>) level of 30 to 35 mm Hg and an SpO<sub>2</sub> level  $>95\%$  with 50% air in oxygen. Infusions were initiated to achieve MAP between 65 and 75 mm Hg after tracheal intubation with esmolol or dexmedetomidine. In the esmolol group, a loading dose of esmolol was infused intravenously over 1 minute at 1 mg/kg, followed by a maintenance infusion rate of 0.4 to 0.8 mg/kg/h. In the dexmedetomidine group, a loading dose of dexmedetomidine was infused intravenously over 10 minutes at 1  $\mu$ g/kg, followed by a maintenance infusion rate of 0.4 to 0.8  $\mu$ g/kg/h. The infusion rates were then titrated to maintain MAP between 65 and 75 mm Hg. General anesthesia was maintained with desflurane (end-tidal concentrations of desflurane, 4%–6%).

In both groups, signs of inadequate anesthesia (eg, increases in arterial pressure greater than the targeted MAP) or somatic responses (eg, movement, tearing, or sweating) were treated with additional fentanyl. Nitroglycerine was infused if these target limits could not be achieved with the uppermost dose. The drug infusion rate was then decreased when the targeted MAP was achieved. All study medications were administered by an anesthetist (I.O.K.) who was not involved in patient care or data collection. A second anesthetist (K.K.), who was blinded to treatment group, man-

aged the patients. At the end of surgery, the amount of blood in the surgical field was rated by the same attending surgeon (A.Y.) who was blinded to the treatment groups and who performed all of the surgeries. The following 6-point scale<sup>16</sup> was used to assess the amount of bleeding in the surgical field: 0 = no bleeding, a virtually bloodless field; 1 = bleeding that was so mild that it was not a surgical nuisance; 2 = moderate bleeding that was a nuisance but did not interfere with accurate dissection; 3 = moderate bleeding that moderately compromised surgical dissection; 4 = bleeding that was heavy but controllable and that significantly interfered with surgical dissection; and 5 = massive bleeding that was uncontrollable and made dissection impossible. Scores  $\leq 2$  were considered to be optimal surgical conditions. A local vasoconstrictor was not used to control bleeding at any time during the surgery.

Infusion of the study drugs was stopped 5 minutes before the anticipated end of surgery, and desflurane was stopped after skin closure. At the end of surgery, any residual neuromuscular blockade was antagonized with neostigmine and atropine. Extubation time and time to total recovery from anesthesia were recorded (Aldrete score  $\geq 9$  on a scale of 0–10. Each variable was scored on a 3-point scale—consciousness [2 = fully awake; 1 = able to be roused on calling; 0 = not responding], activity [able to move voluntarily or on command: 2 = 4 extremities; 1 = 2 extremities; 0 = 0 extremities], respiration [2 = able to breathe deeply and cough freely; 1 = dyspnea, shallow or limited breathing; 0 = apneic], circulation [2 = blood pressure (BP)  $\pm < 20$  mm of preanesthetic level; 1 = BP  $\pm 20$ –50 mm of preanesthetic level; 0 = BP  $\pm > 50$  mm of preanesthetic level], and SpO<sub>2</sub> [2 =  $> 92\%$  on room air; 1 = needs oxygen inhalation to maintain SpO<sub>2</sub>  $> 90\%$ ; 0 = SpO<sub>2</sub>  $< 90\%$  even with oxygen supplementation]—with a maximum achievable score of 10).<sup>17</sup> After total recovery from anesthesia, patients were transferred to the recovery room. AEs (eg, intraoperative hypotension [BP  $< 65$  mm Hg], bradycardia [HR  $< 50$  beats/min]), intraoperative fentanyl consumption, and postoperative nausea and vomiting were recorded. Requirements for an additional hypotensive agent (nitroglycerine) were also recorded. Arterial blood gas analysis was used to determine changes in pH, partial pressure of CO<sub>2</sub> (PaCO<sub>2</sub>), and bicarbonate (HCO<sub>3</sub>). Blood samples were drawn immediately before surgery in the operating room to determine the baseline value and at 1 hour postoperatively in the recovery room. Blood samples were also drawn for blood urea nitrogen (BUN) and creatinine concentrations, and for aspartate aminotransferase (AST) and alanine aminotransaminase (ALT). The sedation score<sup>18</sup> was measured using the following scale at 15, 30, and 60 minutes after tracheal extubation: 1 = anxious, agitated, or restless; 2 = cooperative, oriented, and tranquil; 3 = responsive to commands; 4 = asleep, but with brisk response to light, glabellar tap, or loud auditory stimulus; 5 = asleep, sluggish response to glabellar tap or auditory stimulus; and 6 = asleep, no response.

#### STATISTICAL ANALYSIS

The number of patients enrolled in this study was determined based on our preliminary analysis and a desired power of 80% to detect a between-group difference of 20% in the scale used to assess the amount of blood in the surgical field with a sig-

nificance level of 5%. Forty-four patients (22 in each arm of the study) would be needed for the study. Assuming a dropout rate of 15%, a total of 52 patients would need to be enrolled.

Data are mean (SD), median, or percentage. Statistical analyses were performed using Statistica software version 7.0 (Statsoft Inc., Tulsa, Oklahoma). Age, weight, duration of anesthesia and surgery, extubation time, time to complete recovery from anesthesia, BUN and creatinine concentrations, AST and ALT activities, pH, PaCO<sub>2</sub>, and HCO<sub>3</sub> were compared using *t* tests. Sedation score, the amount of blood in the surgical field, and intraoperative fentanyl consumption were compared using the Mann-Whitney *U* test. Sex, the presence of a hypotensive agent, hypotension, bradycardia, and nausea and vomiting were compared in the 2 groups using the  $\chi^2$  test or Fisher exact test. MAP and HR were compared using repeated-measures analysis of variance. All post hoc comparisons were performed using Tukey tests. *P* < 0.05 was considered statistically significant.

## RESULTS

Fifty-two consecutive white patients undergoing tympanoplasty were identified. Two patients had to be excluded because of hypertension and 2 refused to participate. Forty-eight patients were equally randomized to either the esmolol group (*n* = 24 [16 women, 8 men]; mean [SD] age, 38.4 [10.5] years) or the dexmedetomidine group (*n* = 24; [17 women, 7 men]; mean [SD] age, 35.5 [14.7] years). Sedation scores were not collected in 1 patient in the esmolol group; therefore, analysis was conducted for 23 patients. The durations of anesthesia and of surgery were similar in the esmolol and dexmedetomidine groups (Table I).

Of these 48 patients, 1 in the esmolol group was excluded from data analysis because the sedation scores were not properly recorded. Intent-to-treat analyses were carried out on all outcomes based on the original randomization.

Scores for a bloodless surgical field were low in both groups; there was no significant difference in the between-group scores. The median (range) of the scores was

**Table I. Demographic and clinical characteristics in adults undergoing tympanoplasty (N = 48).**

Characteristic	Esmolol Group ( <i>n</i> = 24)	Dexmedetomidine Group ( <i>n</i> = 24)	<i>P</i>
Age, mean (SD), y	38.4 (10.5)	35.5 (14.7)	0.112
Sex, no. (%)			0.680
Female	16 (66.7)	17 (70.8)	
Male	8 (33.3)	7 (29.2)	
Weight, mean (SD), kg	72.9 (14.8)	68.8 (14.1)	0.993
Duration of anesthesia, mean (SD), min	84.8 (21.5)	82.3 (20.9)	0.796
Duration of surgery, mean (SD), min	73.3 (21.5)	72.1 (21.0)	0.834



1 (0–3) in the esmolol group and 1 (0–2) in the dexmedetomidine group. The scores were  $\leq 2$  throughout the study, except that 1 patient in the esmolol group had a score of 3.

Mean (SD) intraoperative fentanyl consumption in the esmolol group was significantly higher than in the dexmedetomidine group (50.0 [3.0] vs 25.0 [2.5]  $\mu\text{g}/\text{min}$ ;  $P = 0.002$ ). The mean time to extubation was significantly shorter in the esmolol group than in the dexmedetomidine group (7.0 [1.4] vs 9.1 [1.9] min;  $P = 0.001$ ), as was the time to total recovery from anesthesia (Aldrete score  $\geq 9$ ) (5.9 [2.1] vs 7.9 [2.3] min;  $P = 0.001$ ). The mean postoperative sedation scores were significantly lower in the esmolol group ( $n = 23$  because of intent-to-treat analysis) than in the dexmedetomidine group at 15 minutes (2.5 [0.6] vs 3.6 [0.5] min;  $P = 0.001$ ) and 30 minutes (2.6 [0.6] vs 3.3 [0.6] min;  $P = 0.001$ ). There was no significant between-group difference in the postoperative sedation score at 60 minutes (Table II).

There were no significant between-group differences in MAP (Figure 1) or HR (Figure 2) at baseline, after induction, or during the hypotensive period. MAP at the end of surgery was significantly higher in the esmolol group than in the dexmedetomidine group ( $P = 0.002$ ). MAP and HR during the hypotensive period were significantly lower than at baseline, after induction, and at the end of surgery in both groups (all,  $P < 0.05$ ).

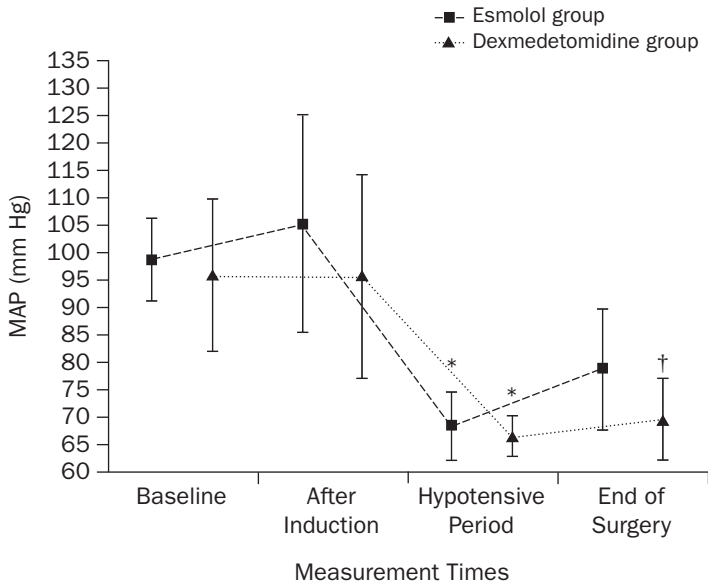
There were no significant differences between the study groups in regard to BUN and creatinine clearance concentrations, AST and ALT activities, pH,  $\text{PaCO}_2$ , and  $\text{HCO}_3^-$  at

**Table II. Fentanyl requirements, recovery characteristics, and sedation scores by study group in adult patients undergoing tympanoplasty (N = 48). Data are mean (SD).**

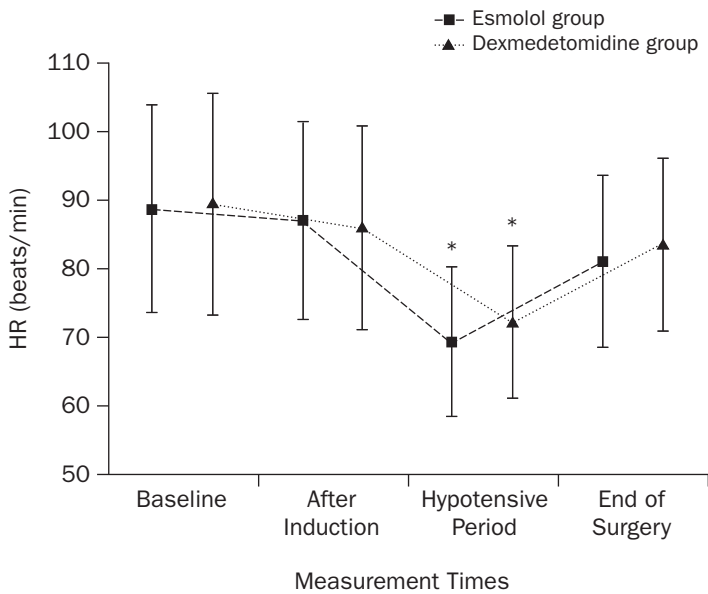
Variable	Esmolol Group (n = 24)	Dexmedetomidine Group (n = 24)	P
Intraoperative fentanyl consumption, $\mu\text{g}$	50.0 (3.0)	25.0 (2.5)	0.002
Time to extubation, min	7.0 (1.4)	9.1 (1.9)	0.001
Time to Aldrete score $\geq 9$ , min*	5.9 (2.1)	7.9 (2.3)	0.001
Sedation score 15 minutes after surgery <sup>†</sup>	2.5 (0.6)	3.6 (0.5)	0.001
Sedation score 30 minutes after surgery <sup>†</sup>	2.6 (0.6)	3.3 (0.6)	0.001
Sedation score 60 minutes after surgery <sup>†</sup>	2.0 (0.2)	2.1 (0.4)	0.176

\*Aldrete scale<sup>17</sup>: Aldrete score  $\geq 9$  on a scale of 0 to 10. Each variable was scored on a 3-point scale—consciousness (2 = fully awake; 1 = able to be roused on calling; 0 = not responding), activity (able to move voluntarily or on command: 2 = 4 extremities; 1 = 2 extremities; 0 = 0 extremities), respiration (2 = able to breathe deeply and cough freely; 1 = dyspnea, shallow or limited breathing; 0 = apneic), circulation (2 = blood pressure [BP]  $\pm < 20$  mm of preanesthetic level; 1 = BP  $\pm 20$ –50 mm of preanesthetic level; 0 = BP  $\pm > 50$  mm of preanesthetic level), and Oxygen ( $\text{O}_2$ ) saturation ( $\text{SpO}_2$ ) (2 =  $> 92\%$  on room air; 1 = needs  $\text{O}_2$  inhalation to maintain  $\text{SpO}_2 > 90\%$ ; 0 =  $\text{SpO}_2 < 90\%$  even with  $\text{O}_2$  supplementation)—with a maximum achievable score of 10.

<sup>†</sup>Sedation score<sup>18</sup>: 1 = anxious, agitated, or restless; 2 = cooperative, oriented, and tranquil; 3 = responsive to commands; 4 = asleep, but with brisk response to light, glabellar tap, or loud auditory stimulus; 5 = asleep, sluggish response to glabellar tap or auditory stimulus; 6 = asleep, no response. Sedation scores were not collected in 1 patient in the esmolol group and analyzed for 23 patients.



**Figure 1. Mean arterial pressure (MAP) by study group in adult patients undergoing tympanoplasty. Data are mean (SD). \*P < 0.05 versus all other time points. †P = 0.002 versus the esmolol group.**



**Figure 2. Heart rate (HR) by study group in adult patients undergoing tympanoplasty. Data are mean (SD). \*P < 0.05 versus all other time points.**



preoperative and postoperative measurements (Table III). During the study, there were no episodes of hypotension or bradycardia and there was no need to use nitroglycerine as an additional hypotensive agent. No major AEs were observed in the study groups.

## DISCUSSION

The present study found that esmolol or dexmedetomidine, when used in combination with desflurane, provided a comparably optimal surgical field. Both drugs were effective in reaching MAP of 65 to 75 mm Hg and ensured good surgical conditions. This study is the first to compare the effects of esmolol or dexmedetomidine combined with desflurane in providing controlled hypotension and improving surgical field exposure during tympanoplasty. Both agents demonstrated similar hemodynamic

**Table III. Kidney and liver function tests and arterial blood gas analysis by study group in adult patients undergoing tympanoplasty (N = 48). Data are mean (SD).**

Variable	Normal	Esmolol Group (n = 24)	Dexmedetomidine Group (n = 24)	P
BUN, mg/dL	8.0–20.0			
Preoperative		10.4 (3.4)	12.4 (4.1)	0.288
Postoperative		11.0 (3.1)	12.6 (4.8)	0.358
Creatinine clearance, mg/dL	0.7–1.2			
Preoperative		0.8 (0.2)	0.8 (0.2)	0.221
Postoperative		0.8 (0.2)	0.8 (0.3)	0.763
AST, IU/L	15.0–41.0			
Preoperative		21.5 (9.4)	19.5 (5.8)	0.654
Postoperative		19.6 (4.6)	19.0 (5.4)	0.335
ALT, IU/L	17.0–63.0			
Preoperative		20.2 (9.1)	20.6 (12.6)	0.806
Postoperative		19.7 (10.9)	19.5 (13.4)	0.983
pH	7.35–7.45			
Preoperative		7.4 (0.1)	7.4 (0.1)	0.747
Postoperative		7.4 (0.1)	7.4 (0.1)	0.747
PaCO <sub>2</sub> , mm Hg	35.0–45.0			
Preoperative		34.5 (5.8)	33.8 (5.8)	0.135
Postoperative		32.3 (5.7)	30.2 (5.7)	0.097
HCO <sub>3</sub> <sup>-</sup> , mol/L	21.0–28.0			
Preoperative		22.1 (3.7)	21.6 (3.5)	0.674
Postoperative		22.1 (3.7)	21.6 (3.5)	0.674

BUN = blood urea nitrogen; AST = aspartate aminotransferase; ALT = alanine aminotransferase; PaCO<sub>2</sub> = arterial partial pressure of carbon dioxide; HCO<sub>3</sub><sup>-</sup> = bicarbonate.

effects during tympanoplasty. The fentanyl requirement was significantly less with dexmedetomidine than with esmolol; however, dexmedetomidine was associated with significantly longer times to extubation and to total recovery from anesthesia, and significantly increased postoperative sedation scores. The clinical significance of these differences remains to be determined.

Our choice of targeted MAP was 65 to 75 mm Hg, which is considered moderate controlled hypotension.<sup>19,20</sup> Controlled hypotension is associated with morbidity and mortality; ischemic organ failure resulting in death was found to be 0.02% to 0.06% in surgery involving controlled hypotension.<sup>21</sup> Accordingly, we avoided profound controlled hypotension (MAP = 50 mm Hg). Intraoperative blood pressure and bleeding at the surgical site are not necessarily correlated.

Decreasing MAP below 70 mm Hg may increase intraoperative bleeding due to local vasodilatation.<sup>3,22</sup> In the present study, all patients except 1 had scores that indicated good surgical conditions (0–2) during tympanoplasty. Fukusaki et al<sup>23</sup> investigated the effects of controlled hypotension with nitroglycerine on hepatic function (MAP ~60 mm Hg). They reported that controlled hypotension was associated with an increase in AST and lactate dehydrogenase activities, although these values remained within the normal range. In our study, normal liver and kidney functions were found in both groups, probably because MAP was maintained at >65 mm Hg in all patients. Using a high dose of inhalational anesthetics to decrease blood pressure is likely to be associated with prolonged recovery from anesthesia, delayed patient discharge, and metabolic AEs.<sup>24</sup> This use may also be associated with increased bleeding because of the peripheral vasodilating effects of inhaled anesthetics.

In our study, fentanyl consumption was significantly lower in the dexmedetomidine group compared with the esmolol group. Several studies have found that perioperative use of dexmedetomidine was associated with a significant decrease in the consumption of inhalational agents ( $P < 0.05$ ),<sup>25</sup> fentanyl ( $P < 0.05$ ),<sup>26</sup> and analgesics ( $P < 0.05$ )<sup>27</sup> in a dose-dependent manner.<sup>25</sup> We found that patients in the dexmedetomidine group had significantly higher postoperative sedation scores than those in the esmolol group. Dexmedetomidine has sedative and analgesia-sparing effects via central actions in the locus coeruleus and in the dorsal horn of the spinal cord, respectively.<sup>28,29</sup> Similar to our study, Richa et al<sup>7</sup> reported that extubation time was significantly slower in patients receiving dexmedetomidine compared with those receiving remifentanyl for controlled hypotension ( $P < 0.001$ ).

#### LIMITATIONS

For bloodless surgical field data, post hoc power analysis suggested a power of 39%. For sedation score data, post hoc power analysis suggested a power of 100%. The numbers of patients in the study groups did not provide the expected power value for bleeding in surgical field data. Consequently, a type II error might have occurred due to low statistical power. Nonetheless, despite the low sample size, the present study indicated that esmolol and dexmedetomidine might be associated with similar success rates of controlled hypotension during tympanoplasty. Larger prospective, controlled studies are necessary to draw definitive conclusions about the effects of these drugs.

## CONCLUSIONS

Both esmolol and dexmedetomidine, combined with desflurane, provided an effective and well-tolerated method for achieving a bloodless surgical field with controlled hypotension in these patients undergoing tympanoplasty. Esmolol was associated with significantly shorter extubation and recovery times and significantly less postoperative sedation compared with dexmedetomidine.

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## REFERENCES

1. Tobias JD. Controlled hypotension in children: A critical review of available agents. *Paediatr Drugs*. 2002;4:439–453.
2. Degoute CS, Ray MJ, Manchon M, et al. Remifentanyl and controlled hypotension; comparison with nitroprusside or esmolol during tympanoplasty. *Can J Anaesth*. 2001;48:20–27.
3. Boezaart AP, van der Merwe J, Coetzee A. Comparison of sodium nitroprusside- and esmolol-induced controlled hypotension for functional endoscopic sinus surgery. *Can J Anaesth*. 1995;42:373–376.
4. Elsharnouby NM, Elsharnouby MM. Magnesium sulphate as a technique of hypotensive anesthesia. *Br J Anaesth*. 2006;96:727–731.
5. Degoute CS, Dubreuil C, Ray MJ, et al. Effects of posture, hypotension and locally applied vasoconstriction on the middle ear microcirculation in anaesthetized humans. *Eur J Appl Physiol Occup Physiol*. 1994;69:414–420.
6. Lee J, Lovell AT, Parry MG, et al. I.v. clonidine: Does it work as a hypotensive agent with inhalation anesthesia? *Br J Anaesth*. 1999;82:639–640.
7. Richa F, Yazigi A, Sleilaty G, Yazbeck P. Comparison between dexmedetomidine and remifentanyl for controlled hypotension during tympanoplasty. *Eur J Anaesthesiol*. 2008;25:369–374.
8. Durmus M, But AK, Dogan Z, et al. Effect of dexmedetomidine on bleeding during tympanoplasty or septorhinoplasty. *Eur J Anaesthesiol*. 2007;24:447–453.
9. Saarnivaara L, Klemola UM, Lindgren L. Labetolol as a hypotensive agent for middle ear microsurgery. *Acta Anaesthesiol Scand*. 1987;31:196–201.
10. Pavlin JD, Colley PS, Weymuller EA, et al. Propofol versus isoflurane for endoscopic sinus surgery. *Am J Otolaryngol*. 1999;20:96–101.
11. Degoute CS. Controlled hypotension: A guide to drug choice. *Drugs*. 2007;67:1053–1076.
12. Blowey DL. Antihypertensive agents: Mechanisms of action, safety profiles, and current uses in children. *Curr Ther Res Clin Exp*. 2001;62:298–313.
13. Karaaslan K, Yilmaz F, Gulcu N, et al. Comparison of dexmedetomidine and midazolam for monitored anesthesia care combined with tramadol via patient-controlled analgesia in endoscopic nasal surgery: A prospective, randomized, double-blind, clinical study. *Curr Ther Res Clin Exp*. 2007;68:69–81.
14. Lawrence CJ, Prinzen FW, de Lange S. Effect of dexmedetomidine on nutrient organ blood flow. *Anesth Analg*. 1996;83:1160–1165.

15. American Society of Anesthesiologists (ASA). ASA Physical Status Classification System. <http://www.asahq.org/clinical/physicalstatus.htm>. Accessed May 24, 2009.
16. Fromme GA, MacKenzie RA, Gould AB Jr, et al. Controlled hypotension for orthognathic surgery. *Anesth Analg*. 1986;65:683–686.
17. Aldrete JA. The post-anesthesia recovery score revisited. *J Clin Anesth*. 1995;7:89–91.
18. Ramsay M, Savege T, Simpson BR, Goodwin R. Controlled sedation with alphaxolone-alphadolone. *Br Med J*. 1974;2:656–659.
19. Kaygusuz K, Yildirim A, Kol IO, et al. Hypotensive anesthesia with remifentanil combined with desflurane or isoflurane in tympanoplasty or endoscopic sinus surgery: A randomised, controlled trial. *J Laryngol Otol*. 2008;122:691–695.
20. Jacobi KE, Böhm BE, Rickauer AJ, et al. Moderate controlled hypotension with sodium nitroprusside does not improve surgical conditions or decrease blood loss in endoscopic sinus surgery. *J Clin Anesth*. 2000;12:202–207.
21. Leigh JM. The history of controlled hypotension. *Br J Anaesth*. 1975;47:745–749.
22. Lim YJ, Kim CS, Bahk JH, et al. Clinical trial of esmolol-induced controlled hypotension with or without acute normovolemic hemodilution in spinal surgery. *Acta Anaesthesiol Scand*. 2003;47:74–78.
23. Fukusaki M, Miyako M, Hara T, et al. Effects of controlled hypotension with sevoflurane anesthesia on hepatic function of surgical patients. *Eur J Anaesthesiol*. 1999;16:111–116.
24. Simpson P. Perioperative blood loss and its reduction: The role of the anaesthetist. *Br J Anaesth*. 1992;69:498–507.
25. Aantaa R, Jaakola ML, Kallio A, Kanto J. Reduction of the minimum alveolar concentration of isoflurane by dexmedetomidine. *Anesthbesiology*. 1997;86:1055–1060.
26. Scheinin H, Jaakola ML, Sjövall S, et al. Intramuscular dexmedetomidine as premedication for general anesthesia. A comparative multicenter study. *Anesthbesiology*. 1993;78:1065–1075.
27. Ebert TJ, Hall JE, Barney JA, et al. The effects of increasing plasma concentrations of dexmedetomidine in humans. *Anesthbesiology*. 2000;93:382–394.
28. Maze M, Segal IS, Bloor BC. Clonidine and other alpha2 adrenergic agonists: Strategies for the rational use of these novel anesthetic agents. *J Clin Anesth*. 1988;1:146–157.
29. Guo TZ, Jiang JY, Buttermann AE, Maze M. Dexmedetomidine injection into the locus coeruleus produces antinociception. *Anesthbesiology*. 1996;84:873–881.

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**ADDRESS CORRESPONDENCE TO:** Iclal Ozdemir Kol, MD, Department of Anesthesiology, Cumhuriyet University School of Medicine, 58140 Sivas, Turkey. E-mail: driclal@gmail.com