CURRENT THERAPEUTIC RESEARCH
VOLUME 68, NUMBER 2, MARCH/APRIL 2007

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

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ABSTRACT

Background: Monitored anesthesia care (MAC) may be applied for septoplasty or endoscopic sinus surgery in which an adequate sedation and analgesia without respiratory depression are desired for comfort of both the patient and the surgeon. Several combinations with different agents have been used for this purpose in these patients. However, analgesic properties for these agents have not been reported.

Objective: The aim of this study was to investigate the analgesic and sedative effects of dexmedetomidine or midazolam infusion combined with tramadol that was used via patient-controlled analgesia (PCA), and to document the effects of these drugs on early cognitive functions.

Methods: This prospective, randomized, double-blind, clinical study enrolled patients undergoing septoplasty or endoscopic sinus surgery at the Abant Izzet Baysal University Hospital, Bolu, Turkey, between February and September 2006. Patients were randomly allocated in a 1:1 ratio into 1 of 2 groups: the dexmedetomidine group (group D) patients received IV dexmedetomidine 1 μg/kg for 10 minutes followed by continuous infusion of 0.5 $\mu g/kg \cdot h^{-1}$; and the midazolam group (group M) patients were administered a loading dose of IV midazolam 40 μg/kg for 10 minutes followed by infusion at the rate of 50 $\mu g/kg \cdot h^{-1}$. A 1-minute bolus dose of IV tramadol (1.5 mg/kg) was administered in both groups 10 minutes after the administration of the primary drug, and continued via infusion using a PCA device. After baseline measurements, systolic arterial pressure (SAP), diastolic arterial pressure (DAP), mean arterial

Accepted for publication February 20, 2007.
doi:10.1016/j.curtheres.2007.04.001
0011-393X/$32.00

pressure (MAP), heart rate (HR), oxygen saturation, and rate of respiration were recorded after the loading dose of study drug, after the bolus tramadol dose, at 10-minute intervals during the operation, and twice in the recovery rooms; 5 minutes after arrival and 5 minutes before discharge. Verbal rating score (VRS) and Ramsay sedation score were determined at baseline (after surgery was started), every 10 minutes thereafter until the end of the operation, and 2 times during recovery. All patients were assessed with the Wechsler Memory Scale–Revised at baseline (preoperatively) and 4 hours after the operation.

Results: Seventy patients were enrolled in the study and randomly assigned to 1 of 2 groups: group D (sex, male/female, 23/12; mean [SEM] age, 32.53 [2.07] years; mean [SEM] weight, 73.03 [2.41] kg) or group M (sex, male/female, 21/14; mean [SEM] age, 34.43 [1.83] years; mean [SEM] weight, 67.90 [2.32] kg). All hemodynamic parameters (SAP, DAP, MAP, HR) were significantly higher in group M compared with group D from the onset of the surgery to discharge time ($P < 0.05$). Pain and sedation scores were similar in both groups, but the amount of PCA-administered rescue tramadol was significantly higher in group M ($P = 0.001$). A higher, though not statistically significant, prevalence of adverse events (ie, hypotension, bradycardia, and perioperative nausea and vomiting) were observed in group D. Postoperative logical verbal memory and digit span values were significantly higher in group D when compared with group M ($P < 0.05$). Postoperative digit span and visual reproduction scores were significantly higher than preoperative values in group D ($P < 0.05$). Postoperative personality functioning scores were significantly higher than preoperative values in group M ($P < 0.05$).

Conclusions: Based on VRS, Ramsay sedation scores, and surgeon and anesthesiologist satisfaction scores, dexmedetomidine or midazolam combined with tramadol PCA provided adequate analgesia and sedation in these adult patients undergoing septoplasty or endoscopic sinus surgery with MAC. A significantly larger amount of rescue tramadol was used by group M, suggesting that a better analgesic effect was achieved with dexmedetomidine. (*Curr Ther Res Clin Exp*. 2007;68:69–81)

Key words: dexmedetomidine, midazolam, sedoanalgesia, cognitive function.

INTRODUCTION

Monitored anesthesia care (MAC) may be applied for endoscopic sinus or septoplasty surgery in which an adequate sedation and analgesia without respiratory depression are desired for comfort of both the patient and the surgeon.[1] Several agents (eg, alfentanil, sufentanil, remifentanil-propofol, dexmedetomidine-morphine, midazolam) with different combinations have been used for this purpose in these types of patients.[1–4] Midazolam has been reported to be well tolerated when used in MAC.[4,5] Dexmedetomidine, a highly selective α_2-adrenoceptor agonist, is an agent (approved in 1999 by the US Food and Drug Administration) that possesses both sedative and mild analgesic properties, yet no respiratory

depressant effects have been reported. It also has been reported to be helpful in patients requiring sedoanalgesia.[4,6] A search of the literature on MEDLINE using the key terms *analgesia* and *dexmedetomidine* found that the analgesic properties of these agents have not been clearly reported. Cognitive effects of these drugs in these patients have not been reported in large samples either. Tramadol provides significant analgesia but minimal sedation.[7]

The aim of this study was to examine and compare the effects of either dexmedetomidine or midazolam combined with tramadol patient-controlled analgesia (PCA), on perioperative hemodynamic properties, sedation, analgesia, and early cognitive functions in patients undergoing endoscopic sinus or nasal septoplasty surgery.

METHODS

Following the approval of the institutional ethics committee of the Abant Izzet Baysal University Hospital, Bolu, Turkey, male and female adult American Society of Anesthesiologists physical status classification I or II[8] patients scheduled for nasal septoplasty or endoscopic sinus surgery with monitored anesthesia care, aged between 18 and 50 years, signed a written informed consent to participate in this prospective, randomized, double-blind, clinical trial.

Exclusion criteria included the following: pregnancy, currently breastfeeding women, history of serious adverse reaction or allergy to any drug, patients with a body weight >25% larger than the ideal based on body mass index, a history of sleep apnea or asthma, patients on psychotropic medication, an abnormal electrocardiogram, and use of α_2-agonists or -antagonists.

After randomization by sealed-envelope method, patients were allocated into 1 of 2 groups. The dexmedetomidine group (group D) received IV dexmedetomidine* 1 μg/kg over 10 minutes followed by continuous infusion of 0.5 $\mu g/kg \cdot h^{-1}$. The midazolam group (group M) were administered a loading dose of midazolam† 40 μg/kg over 10 minutes followed by infusion at the rate of 50 $\mu g/kg \cdot h^{-1}$. Intravenous tramadol‡ 1.5 mg/kg was administered slowly (over 1 minute) as a bolus dose in both groups 10 minutes after the administration of the primary drug, and continued with infusion using a PCA device (Abbott Pain Manager, Abbott Laboratories Inc., Abbott Park, Illinois) (20-mg/h basal rate, 20-mg PCA dose, 10-minute lockout time). In both groups surgery was started after the injection of the loading dose of study medication, and infusions of all study drugs were stopped at the end of the operation. Local anesthesia was performed with 5 mL of prilocaine 1% in all patients just after the onset of tramadol infusion.

*Trademark: Precedex® (Abbott Laboratories Inc., Abbott Park, Illinois).
†Trademark: Dormicum® (Roche Müstahzarlari Sanayi A.S., Istanbul, Turkey).
‡Trademark: Contramal® (Abdi Ibrahim Ilaç San. Tic. A.S., Istanbul, Turkey, licensed by Grunenthal GmbH, Germany).

The primary end point of the study was to investigate the analgesic and sedative effects of dexmedetomidine. The secondary end point was to document the effects of this drug on early cognitive functions.

Efficacy

Cardiorespiratory monitoring included the following: systolic arterial pressure (SAP), diastolic arterial pressure (DAP), mean arterial pressure (MAP), heart rate (HR), oxygen saturation (SaO_2), and rate of respiration (RR). After baseline measurements (t_0), SAP, DAP, MAP, HR, SaO_2, and RR were recorded after the loading dose of the study drug (t_1), after the bolus tramadol dose (t_2), at 10-minute intervals during the operation (t_3, t_4, t_5), and twice in the recovery room; 5 minutes after arrival at the recovery room (t_{reca}) and 5 minutes before discharge (t_{recd}).

A verbal rating score (VRS) to determine pain (0 = no pain and 10 = the worst pain the patient had ever experienced) was recorded by a different anesthesiologist who was blinded to the drug being infused to the patient after surgery had been started (baseline), every 10 minutes thereafter until the end of the operation, and 2 times in the recovery unit. Sedation was assessed at the same time as the VRS assessment using the Ramsay sedation scale[9,10] (1 = patient is anxious and agitated or restless, or both; 2 = patient is cooperative, oriented, and tranquil; 3 = patient responds to commands only; 4 = patient exhibits brisk response to light glabellar tap or loud auditory stimulus; 5 = patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus; 6 = patient exhibits no response). Rescue medication in the form of IV tramadol 50 mg was administered to the patient in both groups if the VRS score was ≥5. The study drug dose was then repeated 10 minutes after the rescue dose if the response did not change. Additive amounts of tramadol were also recorded.

All patients were assessed with the Wechsler Memory Scale–Revised[11,12] preoperatively (baseline) and 4 hours after the operation. Four primary tests and 6 subtests were used for this purpose: (1) personality functioning—questionnaire-related subject or environment (maximum of 6 points); (2) orientation—evaluation of place and time adaptation (maximum of 5 points); (3) attention and concentration—(a) mental control, repetition of a familiar series of numbers or letters (maximum of 9 points) and (b) digit span, repetition of number sequences, forward and backward trials (maximum of 15 points); and (4) memory—(a) logical verbal memory, immediate recall of story paragraphs (maximum of 23 points) and (b) visual memory, visual reproductions, drawing of 4 different designs immediately after exposure (maximum of 8 points).

Tolerability

Any occurrence of hypertension (SAP >140 mm Hg, DAP >90 mm Hg) during the operation was to be treated with the infusion of nitroglycerin (1–10 μg/kg · min^{-1}); hypotension (a 30% decrease of baseline values in SAP or DAP) with

ephedrine 5 mg IV; and bradycardia (HR <40 bpm) with IV atropine 0.5 mg. Nausea and vomiting, when observed, were to be treated with IV metoclopramide 10 mg.

Satisfaction with regard to the sedation, analgesia, and patient comfort was assessed by both the anesthesiologist and the surgeon using a 10-point scale (1 = extremely dissatisfied to 10 = extremely satisfied). All of the operations were performed by the same surgeon (F.Y.) and were sedated and followed up by the same anesthesiologist (K.K.). Patients' discharge time from the recovery room, and adverse events (AEs) such as nausea and vomiting, bradycardia, and hypotension were recorded.

Statistical Analysis

The analysis of power was determined using NCSS 2001 software (NCSS, Kaysville, Utah). Based on the results for a 2-sample *t* test, subgroup sample sizes of 35 were found to achieve ~100% power. Based on the χ^2 test power analysis, a total sample size of 70 would achieve 90% power. Data were analyzed using SPSS software version 9.0 (SPSS Inc., Chicago, Illinois). The Mann-Whitney *U* test was used for continuous variables. Categoric data were compared using the χ^2 test or the Fisher exact test. *P* values <0.05 were considered statistically significant.

RESULTS

Seventy patients were enrolled and randomized into 2 groups: 35 patients were assigned to group D (sex, male/female, 23/12; mean [SEM] age, 32.53 [2.07] years; mean [SEM] height, 169.33 [1.24] cm; mean [SEM] weight, 73.03 [2.41] kg) and 35 patients were assigned to group M (sex, male/female, 21/14; mean [SEM] age, 34.43 [1.83] years; mean [SEM] height, 165.47 [1.39] cm; mean [SEM] weight, 67.90 [2.32] kg). The 2 groups were comparable in terms of demographic characteristics and surgical duration (**Table I**).

Efficacy

There were no significant differences in the amount of tramadol used in PCA between the 2 groups, but group M reported a significantly greater mean (SD) amount of added rescue tramadol (26.67 [7.48] vs 13.33 [4.11]; $P = 0.001$) and total tramadol used (61.99 [9.01] vs 45.78 [6.25]; $P = 0.03$). Satisfaction scores of both the surgeon and anesthesiologist about sedation and analgesia were >8, and were similar (**Table II**).

There were no significant differences between the 2 groups in regard to RR, VRS, and Ramsay sedation scores (**Table III**). In all perioperative measurements, mean HR of group D was significantly lower than those of group M ($P < 0.05$). DAP at the t_1 and t_3 measurements was significantly lower than that of group M ($P < 0.05$). SAP, DAP, and MAP at the t_4, t_5, t_{reca}, and t_{recd} measuring points were also significantly lower in group D than those of group M ($P < 0.05$).

Table I. Demographic characteristics of adult patients undergoing septoplasty or endoscopic sinus surgery with monitored anesthesia care. All data are reported as mean (SEM) unless otherwise noted.

Variable	Group	
	Dexmedetomidine (n = 35)	Midazolam (n = 35)
Sex, no. (%)		
Male	23 (65.7)	21 (60.0)
Female	12 (34.3)	14 (40.0)
Age, y	32.53 (2.07)	34.43 (1.83)
Height, cm	169.33 (1.24)	165.47 (1.39)
Weight, kg	73.03 (2.41)	67.90 (2.32)
Duration of surgery, min	28.67 (1.27)	30.67 (1.33)

Mean (SEM) SaO_2 was significantly lower in group M at the t_2 measurement (94.13% [0.48%] vs 96.43% [0.32%], respectively; $P < 0.05$). HR was significantly lower in group D at the t_4, t_{reca}, and t_{recd} measurements compared with t_0 values (all, $P < 0.05$). In group M, HR was significantly higher at all time measurements compared with t_0 values (all, $P < 0.05$). SAP, MAP, and DAP were found to be signifi-

Table II. Perioperative tramadol consumption and satisfaction scores in adult patients undergoing endoscopic nasal surgery with dexmedetomidine or midazolam for monitored anesthesia care combined with tramadol administered via patient-controlled analgesia (PCA) (N = 70).

Variable	Group		*P*
	Dexmedetomidine (n = 35)	Midazolam (n = 35)	
Tramadol, mean (SD), mg			
PCA	32.45 (2.81)	35.32 (2.25)	0.27
Added	13.33 (4.11)	26.67 (7.48)	<0.001
Total	45.78 (6.25)	61.99 (9.01)	0.03
Satisfaction score, median (SEM)			
Surgeon	8.80 (0.31)	8.43 (0.33)	0.48
Anesthesiologist	8.40 (0.32)	8.07 (0.33)	0.94
Reported adverse events, no. (%)			
Perioperative nausea and vomiting	7 (20.0)	2 (5.7)	0.25
Intraoperative hypotension	5 (14.3)	1 (2.9)	0.13
Intraoperative bradycardia	4 (11.4)	0	0.23

Table III. Hemodynamic changes, verbal rating score (VRS), and Ramsay sedation scores from adults undergoing endoscopic nasal surgery with dexmedetomidine or midazolam for monitored anesthesia care combined with tramadol administered via patient-controlled anesthesia. Data are reported as mean (SEM) for hemodynamic parameters, and median (SEM) for VRS and Ramsay sedation score.

Group/ Time	SAP, mm Hg	DAP, mm Hg	MAP, mm Hg	HR, bpm	SaO_2, %	VRS	Ramsay Sedation Score
D/t_0	128.63 (2.62)	76.43 (1.96)	92.53 (2.03)	78.53 (1.98)	97.87 (0.25)	–	–
M/t_0	127.43 (2.01)	79.87 (1.70)	96.97 (1.61)	80.10 (2.65)*	97.27 (0.32)*	–	–
D/t_1	127.70 (2.87)	76.20 (2.28)†	93.97 (2.20)	74.47 (1.59)*†	96.37 (0.36)*†	–	–
M/t_1	124.37 (1.83)	82.80 (1.54)	96.70 (1.34)	84.30 (2.76)*	95.20 (0.42)*	–	–
D/t_2	126.70 (2.59)	77.63 (2.04)†	95.70 (1.92)	75.90 (2.20)†	96.43 (0.32)*†	0.63 (0.29)	2.03 (0.11)
M/t_2	126.77 (2.27)	83.27 (1.78)*	99.60 (2.01)*	87.57 (3.24)*	94.13 (0.48)*	0.63 (0.26)	2.20 (0.07)
D/t_3	118.63 (3.04)*†	70.77 (2.46)*†	87.47 (2.49)†	76.27 (2.11)†	95.07 (0.48)*	1.00 (0.30)	2.17 (0.10)
M/t_3	127.77 (2.76)	80.70 (2.44)	96.83 (2.43)	87.33 (2.69)*	94.33 (0.53)*	1.40 (0.49)	2.33 (0.12)
D/t_4	117.83 (3.59)*†	69.20 (2.45)*†	86.50 (2.64)†	73.33 (2.11)*†	95.00 (0.45)*	1.00 (0.30)	2.17 (0.10)
M/t_4	128.90 (2.82)	84.57 (2.05)*	101.20 (2.21)	91.83 (3.05)*	94.37 (0.47)*	1.43 (0.43)	2.07 (0.08)
D/t_5	118.10 (3.03)*†	68.17 (2.76)*†	84.80 (2.64)*†	74.67 (1.93)†	94.37 (0.45)*	0.73 (0.29)	2.10 (0.11)
M/t_5	127.70 (3.07)	83.63 (2.55)	100.43 (2.58)*	90.97 (3.50)*	93.60 (0.52)*	1.37 (0.54)	2.10 (0.11)
D/t_{reca}	115.57 (2.23)*	67.97 (2.01)*†	84.63 (1.92)*†	73.47 (2.16)*†	94.50 (0.75)*	1.37 (0.31)	1.97 (0.08)
M/t_{reca}	124.00 (2.29)	79.03 (1.56)	91.70 (1.84)*	82.27 (2.11)	94.07 (0.48)*	1.00 (0.38)	1.93 (0.05)*
D/t_{recd}	113.83 (1.85)*†	67.93 (1.75)*†	83.37 (1.58)*†	69.40 (1.90)*†	96.03 (0.27)*	0.97 (0.23)	1.97 (0.06)
M/t_{recd}	122.03 (1.69)	76.87 (1.74)	90.93 (1.93)*	81.20 (2.14)	95.23 (0.43)*	0.67 (0.29)	2.00 (0.00)*

SAP = systolic arterial pressure; DAP = diastolic arterial pressure; MAP = mean arterial pressure; HR = heart rate; SaO_2 = oxygen saturation; D = dexmedetomidine group; t_0 = baseline measurements; M = midazolam group; t_1 = after the loading dose; t_2 = after bolus tramadol dose; t_3 = first 10-minute interval during operation; t_4 = second 10-minute interval during operation; t_5 = third 10-minute interval during operation; t_{reca} = 5 minutes after arrival to the recovery room; t_{recd} = 5 minutes before discharge from the recovery room.
*$P < 0.05$ compared with baseline within groups.
†$P < 0.05$ between groups.

cantly decreased at t_5, t_{reca}, and t_{recd} measurements in group D compared with t_0 values (all, $P < 0.05$). In group M, DAP was significantly higher than the t_0 value at the t_2 and t_4 measurements, and MAP was significantly higher at the t_2 and t_5 measurements (all, $P < 0.05$). SaO_2 was significantly lower in both groups in all measurements compared with t_0 values, although the value never decreased below 90% (all, $P < 0.05$).

Tolerability

None of the patients experienced respiratory depression. However, desaturation was observed in both groups in all measurements compared with baseline (all, $P < 0.05$). This difference was not significant between the groups except at the t_1 measurement point, in which oxygen saturation was lower in group M than group D (95.20 [0.42] vs 96.37 [0.36]; $P < 0.05$) (**Table III**).

Although not statistically significant, the prevalence of AEs was higher in group D compared with group M: nausea and vomiting (7 vs 2, respectively), hypotension (5 vs 1), and bradycardia (4 vs 0) ($P > 0.05$) (**Table II**). None of the patients in any group needed nitroglycerin.

Wechsler Memory Test scores revealed several significant differences between the 2 groups (**Table IV**). In group D, median (SEM) postoperative digit span (9.93 [0.87] vs 7.63 [0.70]) and visual reproduction (6.76 [0.26] vs 6.26 [0.32]) scores were significantly higher than preoperative values (both, $P < 0.05$). In group M, postoperative personality functioning scores were significantly higher than preoperative values (5.70 [0.09] vs 5.23 [0.21]; $P < 0.05$). Postoperative digit span and logical verbal memory scores were significantly higher in group D when compared with group M (both, $P = 0.01$). All other cognitive properties were numerically higher in group D, although these differences were not statistically significant. In group M, preoperative logical verbal memory, digit span, and mental control scores were numerically lower than postoperative values, but the difference was not statistically significant.

DISCUSSION

The results from this clinical trial suggest that patients using dexmedetomidine infusion used significantly less rescue tramadol when compared with midazolam infusion when both drugs were combined with tramadol PCA in sedoanalgesia of the patients undergoing endoscopic sinus surgery and nasal septoplasty. Surgeon and anesthesiologist satisfaction scores were adequate and similar in both groups. Although desaturation was observed in both groups in all measurements, as determined by SaO_2, oxygen saturation was found to be significantly lower in group M at 1 measurement. These findings support those of the Alhashemi study,[4] in which 44 cataract surgery patients were randomly administered either dexmedetomidine or midazolam alone, which determined that respiratory dysfunction may be observed with both study drugs. However, this effect was more markedly observed with midazolam in our study. Changes

Table IV. Preoperative and postoperative Wechsler Memory Scale–Revised[12] cognitive functioning scores for adults undergoing endoscopic nasal surgery or septoplasty with dexmedetomidine or midazolam for monitored anesthesia care combined with tramadol administered via patient-controlled anesthesia. Data are reported as median (SEM).

	Group		
Test	Dexmedetomidine (n = 35)	Midazolam (n = 35)	*P*
Personality functioning			
Preoperative	5.26 (0.18)	5.23 (0.21)	0.90
Postoperative	5.36 (0.18)	5.70 (0.09)*	0.27
Orientation			
Preoperative	4.63 (0.16)	4.83 (0.11)	0.15
Postoperative	4.63 (0.16)	4.90 (0.05)	0.26
Mental control			
Preoperative	7.60 (0.21)	8.10 (0.18)	0.10
Postoperative	7.53 (0.28)	7.60 (0.26)	0.96
Digit span			
Preoperative	7.63 (0.70)	7.53 (0.52)	0.90
Postoperative	9.93 (0.87)*	6.96 (0.74)	0.01
Logical verbal memory			
Preoperative	9.53 (0.61)	8.00 (0.69)	0.10
Postoperative	9.63 (0.61)	7.50 (0.53)	0.01
Visual memory			
Preoperative	6.26 (0.32)	6.56 (0.17)	0.95
Postoperative	6.76 (0.26)*	6.96 (0.22)	0.59

*$P < 0.05$ compared with preoperative value within groups.

in cardiovascular properties in response to surgical stress, such as increase in blood pressure (BP) and HR, were significantly higher in group M. The results of the memory test performed at postoperative hour 4 suggested that memory functions of patients were not badly affected by either study drug.

The interest in the use of α_2-adrenoceptor agonists as sedatives is growing because of their favorable properties: relatively short half-life, analgesic effects, cardiorespiratory stabilization, and rapidly reversible sedation.[13] These properties may prove dexmedetomidine to be a useful agent for intraoperative sedation. Arain and Ebert,[14] in their randomized study of 40 elective surgery patients, observed that patients receiving dexmedetomidine used significantly less postoperative morphine sulfate and significantly higher levels of sedation score throughout the recovery period compared with the propofol-treated

group. The placebo-controlled, double-blind, randomized study of 12 healthy subjects by Angst et al[15] found that systemically administered dexmedetomidine produced mild to moderate sedation in human volunteers without unconsciousness, and did not suggest any analgesic effect in models of acute pain (heat or electrical pain). The pilot study of 7 healthy volunteers by Hall et al[6] documented that 2 infusions of dexmedetomidine at the doses of 0.2 and 0.6 $\mu g/kg \cdot h^{-1}$ produced significant analgesia and sedation that resolved 2 hours after terminating the infusion. Alhashemi and Kaki,[16] in their randomized, double-blind, clinical study of 60 patients undergoing extracorporeal shock wave lithotripsy for urinary calculi, reported that dexmedetomidine in combination with morphine PCA provided better analgesia and was associated with higher patient and urologist satisfaction when compared with a midazolam/tramadol PCA combination. However, 2 different combinations with 4 different drugs were compared in that study, and it might not correctly represent the sedative and analgesic properties of dexmedetomidine. In our study we compared 2 different combinations, with 1 of the drugs (tramadol) being common in both groups; that might have reflected the analgesic and sedative effects of dexmedetomidine more accurately.

Angst et al[15] reported that administration of dexmedetomidine significantly decreased the speed of cognitive performance in a plasma-concentration–dependent manner. Hall et al[6] suggested that psychomotor performance was impaired and persisted for ≥1 hour after terminating the dexmedetomidine infusion. In that study, there was no difference in the degree of performance impairment between the different infusion doses of dexmedetomidine. Arain and Ebert[14] suggested that patients sedated with either dexmedetomidine or propofol experienced similar effects on the psychomotor functions. Our findings revealed significant changes in psychomotor functions which do not fit the findings of that study. In the present study, we did not observe any cognitive dysfunction in the early postoperative period. Postoperative logical verbal memory and visual reproduction scores were significantly higher than preoperative values in group D. However we observed numerical, though not statistically significant, decreases in logical verbal memory, digit span, and mental control in group M.

Hypotension and bradycardia are recognized as 2 major AEs associated with α_2-agonist agents. It has been suggested that these effects are mediated by activation of α_2-adrenoceptors, imidazoline-preferring receptors, or both in the ventrolateral medulla and especially in the solitarius nucleus tract.[17,18] Rare cases of sinus arrest or vasovagal collapse have been reported in adult human volunteers administered dexmedetomidine.[19,20] A 1 μg/kg bolus of dexmedetomidine has been associated with a biphasic cardiovascular response; a transient increase in BP and a reflex decrease in HR which was attributed to the α_2-adrenoceptor stimulation of vascular smooth muscle.[21] One minute after the bolus administration, a decrease in BP was observed which was attributed to the inhibition of sympathetic outflow.[21,22] Arain and Ebert[14] reported that, in

patients receiving dexmedetomidine, MAP was significantly reduced during the intraoperative period, and the reduction was significantly smaller than that observed with propofol. The results from the study by Talke et al[23] of 41 vascular surgery patients suggested that HR and BP did not increase significantly in response to intubation, skin incision, extubation, or during emergence; however, HR decreased significantly intraoperatively with no change in BP. The double-blind, randomized, placebo-controlled study by Taittonen et al[19] found that, in 10 patients premedicated with dexmedetomidine (2.5 μg/kg), HR during the operation, and SAP, MAP, and DAP after the operation were significantly lower than that of placebo. Hall et al[6] documented that dexmedetomidine did not significantly impair cardiorespiratory variables in healthy volunteers who received 50-minute IV infusions of 0.2 or 0.6 μg/kg after a 10-minute initial dose of dexmedetomidine 6 μg/kg. In the present study, we observed no increase in HR, and arterial BP values were more stable in group D. In group M, HR and arterial BP were found to be higher during the operation in subsequent measurements compared with both baseline values and group D. These findings suggest that dexmedetomidine has clinical advantages over midazolam with regard to controlling hemodynamic variabilities.

Dexmedetomidine did not affect RR or SaO_2, although ventilatory pattern has been reported to become irregular,[15] and short episodes of apnea have been reported after bolus administration of IV dexmedetomidine at the dose of 1 to 2 μg/kg.[24] Hall et al[6] determined that small and moderate doses of dexmedetomidine maintained respiratory function well, and there were no dose-dependent effects on respiratory rate or end tidal carbon dioxide. Arain and Ebert[14] suggested that dexmedetomidine was not associated with respiratory depression despite the profound levels of sedation. In our study, we did not observe such complications in any group.

In the present study, the observed complications such as hypotension, preoperative nausea and vomiting, and bradycardia were numerically higher, though not statistically different in either group. Although it is not statistically significant, it is clinically important and should be kept in mind when using dexmedetomidine in these patients. The nonsignificance might have been due to the small sample size of this study. Further studies with larger sample sizes may be helpful to document the characteristics of complications in this application.

CONCLUSIONS

Based on VRS, Ramsay sedation scores, and surgeon and anesthesiologist satisfaction scores, dexmedetomidine or midazolam combined with tramadol PCA provided adequate analgesia and sedation in these adult patients undergoing septoplasty or endoscopic sinus surgery with MAC. However, a significantly larger amount of rescue tramadol was used by the midazolam group, suggesting a better analgesic effect was achieved with dexmedetomidine.

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