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Research Article

Dexmedetomidine, morphine, propofol vs midazolam, morphine, propofol for conscious sedation in rhinoplasty under local anesthesia. A prospective, randomized study

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KEYWORDS

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Abstract *Background:* Monitored anesthesia care (MAC) has been proposed as one of the suitable techniques for rhinoplasty. In this study our aim was to compare the effects of dexmedetomidine with morphine and propofol vs benzodiazepines with morphine and propofol as adjuncts to local anesthesia – on analgesia, sedation, respiratory and hemodynamics variables and surgeon and patient satisfaction.

Methods: In this prospective, double-blind, comparative study, 60 patients undergoing rhinoplasty by local anesthesia randomly received intravenous sedation of either: dexmedetomidine (Dex group) or midazolam (Mid group) in combination with morphine and propofol. Level of sedation was assessed by using the Observer's Assessment Alertness/Sedation Scale (OAA/S). Pain on local anesthesia injection was assessed by a visual analog scale. Surgeon's satisfaction also can be assessed by using a 3-grades score, the surgeon assessed the quality of surgical bleeding. Mean Arterial Pressure (MAP) and heart rate (HR) were assessed and recorded. Patients' satisfaction, visual analog scale for intraoperative pain, and total amount of propofol used intraoperatively. Adverse effects were also recorded.

Results: In Mid group patients were earlier to reach adequate sedation level than in Dex group, but they felt more pain either on local anesthetic injection or during operation. Intraoperative mean

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arterial blood pressure and heart rate in Dex group were lower than their baseline values and the corresponding values in Mid group. The total amount of propofol needed for Mid group was much higher than in Dex group. Patient satisfaction was higher in Dex group. Time of surgery was longer in Mid group. Both groups were similar in sedation recovery and ward discharge times, as well as, incidence of side effects.

Conclusion: Dexmedetomidine sedation with morphine and propofol in rhinoplasty performed under local anesthesia was associated with shorter surgery time, greater patient and surgeon satisfaction, and lower pain scores with no adverse effects, when compared to midazolam sedation with morphine and propofol.

1. Introduction

Nowadays, rhinoplasty is one of the most common plastic surgery. It can be done to reduce the size of the nose, to change the shape of the tip or nasal bridge, to narrow the opening of the nostrils or all of them [1–3].

According to the exact procedure done and the patient's preference rhinoplasty can be performed under local or general anesthesia. Under local anesthesia patients can be kept asleep (conscious sedation) or awake as desired [4,5].

It may be performed either in a hospital, or an outpatient surgery center [5]. Local anesthesia provides improvement of pain relief, shorter hospital stay, decreased postoperative opioid use, and decreases the incidence of postoperative nausea and vomiting (PONV), time spent in recovery room, and improved patient satisfaction with similar operating conditions comparable to general anesthesia [5,6].

The use of sedative drugs with local anesthesia in rhinoplasty has not been studied well, we found only one article was done by Einstein [7] for cosmetic nose surgery without intubation, the patient is fully monitored for respiratory, heart and cognitive function. The propofol is continuously adjusted with the aid of a computerized pump. He found that, propofol was enough medication was given to eliminate the discomfort of the local anesthesia injections [7].

Dexmedetomidine is a highly selective ∝2-agonist with sedative, sympatholytic, and analgesic-sparing properties, with a favorable safety profile and little effect on respiration compared with benzodiazepines and propofol [8].

Additionally, dexmedetomidine decreases salivary secretion, through sympatholytic and vagomimetic effects [9]. Small-dose infusion of this drug in healthy volunteers provides sedation that can be easily reversed with verbal stimuli [10].

This randomized, double-blind, clinical study was designed to compare the sedative, respiratory and hemodynamic effects together with patients' and surgeon's satisfaction of dexmedetomidine and benzodiazepines in combination with morphine and propofol during rhinoplasty under local anesthesia.

2. Patients and methods

After approval of the ethical committee in New Jeddah Clinic Hospital (Saudi Arabia), a written informed consent obtained from a sixty patients of ASA physical status I and II, aged 18–50 years old, who were scheduled for elective rhinoplasty, were enrolled in this randomized, double-blind, clinical study. Exclusion criteria were age < 18 years, a history of drug or alcohol abuse, chronic use of drugs known to alter the anesthetic or analgesic requirements(psycho stimulant drugs, Nefopam), allergy to any of the study medications, second- or third-degree heart block, chronic use of any ∝2-agonists, and a current psychiatric or respiratory disorder. Obese patients with BMI (body mass index) $\geqslant 30$ were also excluded. The local anesthesia procedure was explained to the patient at his consultation visit in anesthesia clinic. Patient selection is important, the patient should be cooperative, understanding and willing for local anesthesia.

On arrival in the operative theater and after the placement of an IV catheter, a baseline measurement of respiratory rate (RR), heart rate (HR), noninvasive mean arterial blood pressure (MAP), and oxygen saturation (SpO_2) were obtained (Datex-Ohmeda; Aisys (GE healthcare). Sedation level was assessed by using the Observer's Assessment Alertness/Sedation Scale (OAA/S) [11], scale: 5 = responds readily to name spoken in normal tone (awake/alert), 4 = lethargic response to name spoken in normal tone, 3 = responds only after name spoken loudly or repeatedly, 2 = responds after mild prodding or shaking and 1 = does not respond to mild prodding or shaking (asleep/unarousable) [11].

Patients were asked to rate the VRS (Verbal Rating Scale; 0 = no pain, 10 = maximal pain). The OAA/S and VAS scores were evaluated by an observer blinded to the patient's group. Patient satisfaction was assessed at the end of the procedure and after 15 min. in the recovery room. Surgeon's satisfaction was assessed and recorded at the end of the procedure.

A nasal oxygen cannula was applied to the mouth and fixed in the chin by tap to supply O_2 at flow rate 3 L/min. Anesthesia was started by Xylocaine spray 4% two puffs in each nostril then wait for three minutes.

A light nasal pack soaked with Xylocaine gel and 5cc Xylocaine 2% with 1:100,000 Adrenaline was used to pack the nasal cavity in a way as to cover the regions of the sphenopalatine ganglion posteriorly, anterior ethmoid nerves under the nasal bones and the pack is made in layers to cover as much of the septum and inferior turbinates. Each pack is sutured to a long silk tie, the tie is fixed with plaster to the cheek.

At this point, patients were randomly assigned by a concealed envelope method into one of two groups (each group was 30 patients); Midazolam (Mid) group, received 0.07 mg/kg Intravenously (total dose not more than 5 mg) of midazolam (Dormicum, Fhoffmann-LaRoche Ltd, Switzerland). The other group is dexmedetomidine (Dex) group (Precedex®, Abbott Laboratories Inc., Abbott Park, IL) (supplied in 2-ml ampoules at a concentration of 100 μg /ml) received 0.75 μg/

kg Intravenously. The calculated dose of midazolam and dexmedetomidine for each patient was prepared in a total volume of 20 ml normal saline and was infused over a period of 10 min. After injection of the study drugs, morphine 0.05–0.1 mg/kg was injected to achieve good analgesia. Patients were assessed for level of sedation using Observer's Assessment Alertness/Sedation Scale (OAA/S) and any patient having a score > 4 received IV propofol 2–4 mg/kg/h very slowly until the score $\leqslant 4$.

For both groups local anesthesia started by injection of lidocaine 2% with 1:200,000 Epinephrine in 10cc syringe and 27 gauge needles is used. Our aim is to eliminate pain and to achieve vasoconstriction, Fig. 1.

In this study, our own technique for nasal block and we named it 11 **points technique:** 3 single (midline injection) and 4 paired (bilateral injection) sites for injection, Fig. 2. A series of Bolus injections and infiltration are administered (0.5–1.00 ml for each point).

The three single midline injection points are: 1-the nasal tip. 2-subdermal plane in the midline of the columella from tip-defining points to the nasal spine. 3-the mid-point between the two eye brows.

The four paired injection points are: **4 and 5**-Bolus to the alar base at the nasolabial junction. **6 and 7**-Bolus at the frenulum at the midpoint between ala and base of the septum. **8 and 9**-Infraorbital nerve block by advance the needle through the nasal ala to the site of the nerve, **10**–11 Submucously, high under the nasal bones to the region of the anterior ethmoid nerve. Infiltrating along the nasofacial junction. The entry site is intranasally at the pyriform aperture, then the needle is pushed to a midpoint between the medial canthus and the nasion, then pulled while infiltrating. Care should be taken not to enter the angular vein [12].

After 10 min of injection of local anesthesia most of the patients were lethargic and responded to name spoken in normal tone (OAA/S $\geqslant$ 4). The procedure done while the patient was lightly sedated and communicating with the surgeon.

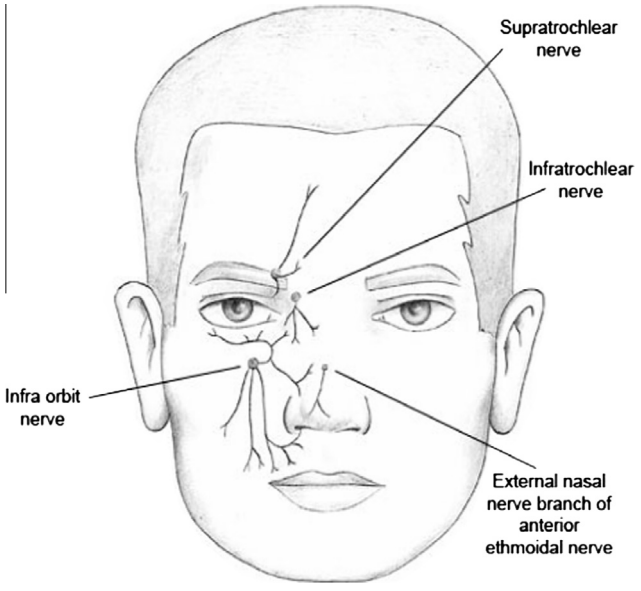

Figure 1 Anatomy of the face with the nerves should be blocked [12].

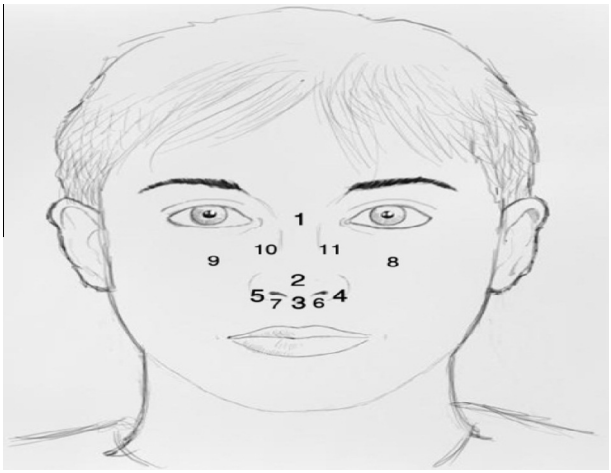

Figure 2 This diagram shows the sites of injection for nasal block (11 points technique).

To achieve adequate sedation during the procedure, in irritable and anxious patients an infusion of propofol 2–4 mg kg^{-1} h^{-1}. If unwanted bradycardia (HR < 50), or hypotension (MAP < 50) were recorded, 0.5 mg atropine was administered, and 200 mL of 0.9% saline was infused, respectively. If apnea (respiratory rate < 6/min) or desaturation (SpO_2 < 90%) occurred patient was encouraged to take deep breath.

OAA/S score, the respiratory (RR and SpO_2) and hemodynamic variables (MAP and HR) were recorded at 5-min intervals after the baseline measurements until the termination of the procedure. These baseline measurements were obtained just before injection of the studying drug. The OAA/S scores and hemodynamic and respiratory variables were recorded post-operative every 10 min for 1 h in PACU. The VAS scores were recorded at 5-min intervals during the procedure at 10, 15, 20, 25, 30, and 35 min. Patients' satisfaction was recorded post-operatively for all patients. A questionnaire, to rate the overall pain experience for all patients was done (0 = no pain; 1 = mild; 2 = moderate; or 3 = severe) and their degree of overall satisfaction with the management of their pain (0, poor; 1, adequate; 2, good; or 3, excellent) after the procedure. The incidence of nausea and vomiting were also recorded.

After the end of surgery, a surgeon who was blinded to the studying groups was asked to rate his satisfaction by two parameters, the first one was according to bleeding in the surgical field 3-grades score used by Nasreen et al. [13] by the end of operation (Grade I: bloodless field not hampering surgery, Grade II: mild bleeding requiring occasional suctioning, and Grade III: excessive bleeding hampering surgery despite suctioning) [13].The second one was according to movement of the patient and unavoidable talking.

3. Statistical analysis

A total sample size of 60 divided into two equal groups was found to be sufficient to conduct the study. SPSS (statistical program for social science version 12) was used for statistical analysis.

Table 1 Patient characteristics (mean + SD or *n*).

	Dex group (n = 30)	Mid group (n = 30)
Age (years)	25 ± 10.1	26.9 ± 9.3
Gender		
Male	15	17
Female	15	13
Weight (kg)	53 ± 13.2	55.2 ± 9.3
Height (cm)	169 ± 8	170 ± 5
Duration from start of sedation to the end of local anesthesia injection (min)	25.14 ± 4.29	23.45 ± 5.13
Duration of surgery (min)	40.3 ± 5.96	47.61 ± 3.30

Data are expressed as mean ± SD.

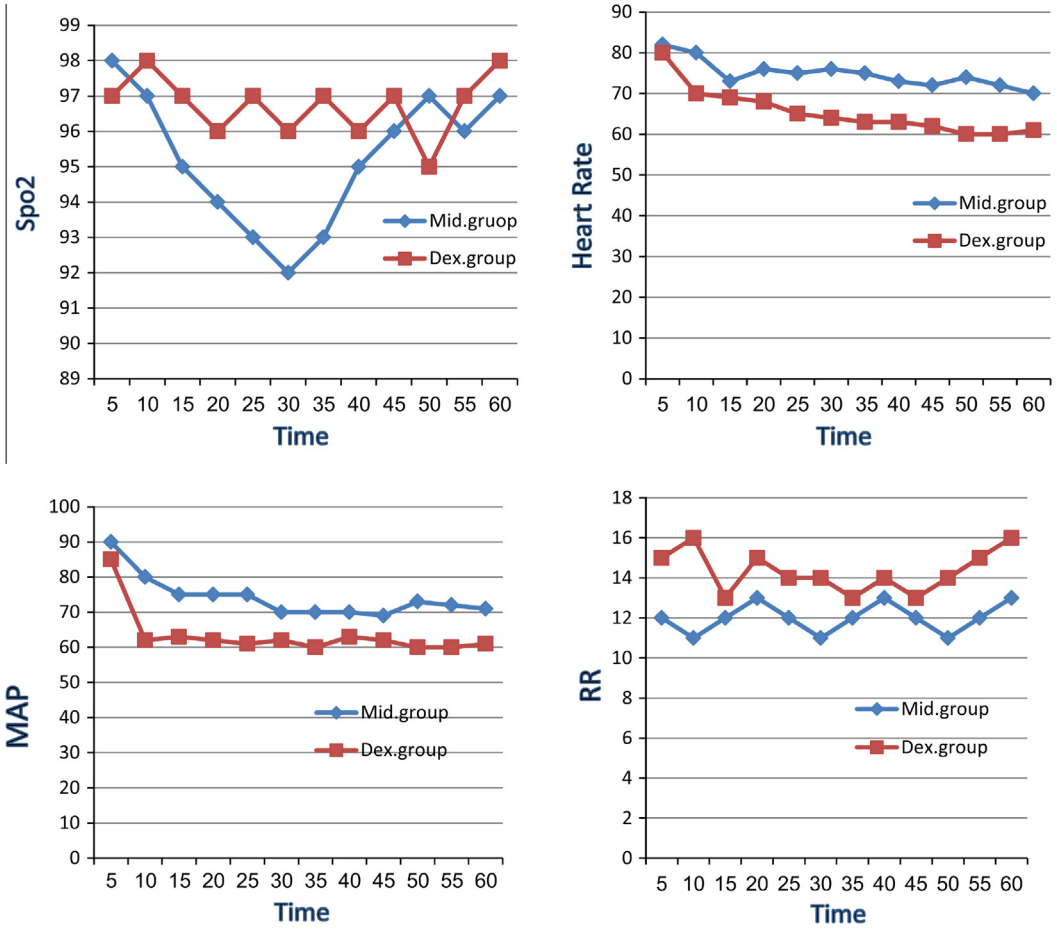

Figure 3 Shows the mean values of hemoglobin oxygen saturation (SpO_2), heart rate (HR), mean arterial blood pressure (MAP) and respiratory rate (RR) determined over the course of the procedure (total 60 min).

Data were presented as mean ± SD, number and percentage within the same group. Demographics were compared with *t*-test. The proportions of men/women, dose of propofol given to achieve adequate sedation, nausea, vomiting, overall pain experience scores 2 and 3, and overall satisfaction scores 0 and 1 of the study groups were compared with $\chi 2$ test. RR, SpO_2, MAP, HR, and VAS were compared with repeated measures analysis of variance (ANOVA) with post hoc Tukey test. OAA/S was analyzed with Friedman's nonparametric repeated measures ANOVA with post hoc Tukey test. A p value of <0.05 was considered significant.

4. Results

Sixty patients were recruited for this study (30 in each group). Two patients were excluded in the MID group from the study and were shifted to general anesthesia with endotracheal intubation due to poor tolerance to local anesthesia and too much movement. There were no statistically significant differences between the two groups regarding to age, gender, height and body weight, as well as duration of anesthesia and duration of surgery (Table 1).

Table 2 Patient satisfaction score, pain scores and total propofol given.

	Dex group (n = 30)	Mid group (n = 28)
Onset of sedation	17.1 ± 4.54**	6.7 ± 2.64
Patient satisfaction score		
Excellent	23 (76.6%)**	2 (7.1%)
Good	6 (20%)	6 (21.4%)
Fair	1 (3.3%)	14 (50%)*
Poor	0 (0%)	6 (21.4%)
VAS on LA injection	1.5 ± 0.25	3.6 ± 0.90**
VAS intraoperative	1 ± 0.21	2.9 ± 0.30**
Baseline OAA/S, n (%)		
5	29	24
4	1	2
3	0	1
2	0	1
1	0	0
Total propofol given	80 mg	200 mg**
Surgeon's satisfaction score		
Grade I	20 (66.6%)**	3 (10.7%)
Grade II	9 (30%)	19 (63.3%)*
Grade III	1 (3.3%)	6 (21.4%)

Data were expressed as mean ± SD, or numbers (%).
* $p < 0.05$; statistically significant.
** $p < 0.01$; statistically highly significant.

In Dex group the HR values started to be lower than the baseline at 5 min, while MAP started to be lower than the baseline at 10 min from the start of sedation. This significant reduction in hemodynamics in Dex group continued till the end of surgery and showed significant difference from those values recorded in Mid group that showed more stable hemodynamics with little change from the baseline ($p < 0.05$) (Fig. 3).

The respiratory variables (RR and SpO_2) were different in Dex group than in Mid group. RR and SpO_2 were significantly lower in Mid group than Dex group started after the first 5 min of injection till the end of the procedure and it showed significant difference from those values recorded in Dex group ($p < 0.05$) (Fig. 3).

Patients in Mid group felt more pain on local anesthesia injection than those in Dex group (VAS: 3.6 ± 0.9 vs 1.5 ± 0.25, respectively). Also, intraoperative pain was more in Mid group compared to Dex group (VAS: 2.9 ± 0.3 vs 1 ± 0.21, respectively) $p < 0.001$ (Table 2).

Total amount of propofol injected in Mid group during the study was significantly higher than in Dex group.

Patients, satisfaction was better in Dex group (Table 2). The method of sedation was described as excellent in most of patients in Dex group (76.6%) vs (7.1%) of patients in Mid group ($p < 0.001$). Poor satisfaction was not reported in Dex group, while reported in 26.6% of patients in Mid group.

Patients in Mid group achieved adequate sedation level earlier than those in Dex group (6.7 ± 2.64 vs 17.1 ± 4.54, respectively), ($p < 0.001$) (Table 2).

The times taken for recovery from sedation and discharge from PACU were equal in both groups (Table 2).

Comparing Dex group to Mid group regarding surgeon's satisfaction about surgical field bleeding Grades I, II, and III were 20 (66.6%) ** vs 3 (10.7) with $p < 0.001$, 9 (30%) vs 19 (63.3%) ** with $p < 0.001$ and 1 (3.3%) vs 6 (21.4%) respectively (Table 2). According to these results, surgical field bleeding Grade I (no bleeding) was significantly better in Dex group compared to Mid group ($p < 0.001$) and in Grade II (moderate bleeding was significantly higher in Mid group than in Dex group ($p < 0.001$).

Table 3 Intraoperative and postoperative adverse effects.

	Dex group (n = 30)	Mid group (n = 28)
Apnea (respiratory rate < 6)	1 (3.3%)	8 (28.5%)
Desaturation SpO_2 < 90%	1 (3.3%)	9 (32.1%)
Nausea	0	0
Vomiting	0	0
Bradycardia (HR < 50)	48 ± 4.3	55 ± 2.3
Hypotension (MAP < 50)	55 ± 3.2	62 ± 1.4

Data were expressed as mean ± SD, or numbers (%).

The intraoperative and postoperative adverse effects were reported in both groups but it was insignificant and easily managed (Table 3).

5. Discussion

The primary outcome of this study was to compare VAS and OAA/S between dexmedetomidine and midazolam in sedation and analgesia in combination with morphine and propofol during rhinoplasty under local anesthesia. The secondary outcome was Respiratory and hemodynamic variables. RR was more slowly and SpO_2 was less with midazolam than dexmedetomidine. Study drugs were comparable with regard to sedation, MAP, HR, overall pain experience and satisfaction scores.

Our results demonstrated that Dex sedation for rhinoplasty was associated with significantly lower HR and MAP values when compared to midazolam sedation. While midazolam group was earlier to achieve sedation, Dex group was associated with less operation time, higher patient satisfaction, and lower pain scores. Both methods of sedation were equal in the incidence of adverse effects, time for sedation recovery and PACU discharge.

Dexmedetomidine was used in many settings to provide sedation for operations performed under local anesthesia. For aesthetic facial surgery under local anesthesia, Taghinia et al. [14] compared the addition of dexmedetomidine infusion to the usual sedative protocol (propofol, midazolam, fentanyl, and ketamine), and they reported lower blood pressure values. They also found that dexmedetomidine improved the sedation safety as evidenced by the reported fewer incidences of oxygen desaturation, and the reduced need for the use of narcotics, and antiemetics [14].

When dexmedetomidine was compared to midazolam to provide monitored anesthesia care for cataract surgery, Alhashemi [15] found significantly better patient satisfaction scores in Dex group. Although he reported lower HR and MAP values in Dex group, he did not find any difference in the incidence of hypotension, bradycardia or desaturation between both groups [15].

In this study, we reported lower HR and MAP in Dex group, which provide controlled hypotensive anesthesia for

better surgical field exposure and it was preferred by surgeon in this group than in Mid group.

Mizuno et al. [16] observed that sedation with intravenous midazolam during upper gastrointestinal endoscopy was useful to control the cardiovascular responses, and to induce amnesia. However, they suggested that decreases in the SpO_2 should be monitored carefully. In the midazolam group, they observed apnea in one patient and decreased SpO_2 in two patients. No deterioration in respiratory and cardiovascular parameters was observed in the dexmedetomidine group and this previous results match well with the results of our study.

A combination of propofol, meperidine/fentanyl and midazolam was used in 100 adult patients by Cohen et al. [17]. Their study showed that endoscopy could be performed at a moderate level of sedation by combining a low dose of propofol with a narcotic agent and/or benzodiazepine, and that the use of a small dose of a narcotic agent and midazolam in combination with propofol does not prolong patient recovery. However, Vargo et al. [18] reported that propofol led to significantly improved recovery to baseline activity compared with a combination of midazolam/meperidine. Additionally, they discovered 54 episodes of apnea/disordered respiration in 28 patients receiving a combination of midazolam/meperidine (mean duration 70.8 s). This idea and the concept of Cohen et al. (to reduce the side effects of drugs by administration of small doses of other drugs) and it was the same way of thinking in this study.

Durmus et al. [19] reported that dexmedetomidine was associated with less bleeding, lower anesthetic requirements, and more hemodynamic stability in response to anesthesia and surgery in patients undergoing septorhinoplasty and tympanoplasty under general anesthesia [19]. This previous results match well with the results of our study and it was one of the important points that augment the surgeon's satisfaction but they studied the hypotensive effect of dexmedetomidine with general anesthesia. On the other hand, Dogan et al. [20]. evaluated the surgical bleeding in septoplasty operations, and found that those performed under local anesthesia with Dex sedation were associated with significantly less bleeding when compared to those performed under general anesthesia [20].

In this study, we observed that the sneezing episode during nasal block which is common during injection of local anesthesia in the nose was much lower in Dex group than in Mid group. This observation may be due to the deep sedative and analgesic action of dexmedetomidine or through its sympatholytic and vagomimetic effects that will leads to decreases salivary and nasal secretion [9].

Cooper et al. [22], he and his colleagues found in their study. Dexmedetomidine-treated patients were significantly more satisfied with their anesthetic than patients in the Mid group. Higher satisfaction scores for dexmedetomidine compared with midazolam have been reported in other trials as well. In addition, anesthesiologists indicated that the ease of achieving and maintaining the targeted sedation level was significantly better in dexmedetomidine group compared with the group using midazolam [21,22].

In another study, McCutcheon et al. [23] found that dexmedetomidine, when compared with midazolam and fentanyl in carotid surgery patients was associated with fewer interventions for hypertension and tachycardia. The effect of reducing HR and arterial blood pressure could be beneficial for patients at risk for cardiac morbidity because perioperative tachycardia and hypertension are associated with adverse cardiac outcomes in the postoperative period [24].

The use of sedative drugs with local anesthesia in rhinoplasty has not been studied well, we found only one article was done by Einstein [7] for cosmetic nose surgery without intubation, the patient is fully monitored for respiratory, heart and cognitive function. The propofol is continuously adjusted with the aid of a computerized pump. He found that, propofol was enough medication was given to eliminate the discomfort of the local anesthesia injections [7].

In conclusion, dexmedetomidine with morphine and propofol at the doses studied well-tolerated, safe with lower incidence of clinically relevant respiratory depression, better patient's satisfaction and effective primary sedative alternative to midazolam in patients undergoing MAC for rhinoplasty despite a significant lower mean arterial blood pressure and HR.

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