Effect of low dose dexmedetomidine on hemodynamic response to tracheal extubation and recovery after general anesthesia in patients undergoing septorhinoplastic surgery

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Background

Different drug regimen have been used for attenuating the stress response to intubation, surgery and extubation. Dexmedetomidine is an alpha 2 agonist. The present study was designed to evaluate the effect of intravenous injection of low dose dexmedetomidine on hemodynamic response to tracheal extubation and recovery.

Patients and method: Patients with ASA I and II aged from 20 – 40 years old undergoing septorhinoplastic surgery were randomly divided into two groups: dexmedetomidine group and saline group. General anesthesia were achieved in all patients by the same way. Dexmedetomidine infusion (0.3µg/kg) was started at 15 min before the end of surgery or same volume of normal saline according to grouping. Monitoring included systolic, diastolic blood pressure, heart rate, all were recorded at T 1 = 5 min before injection, T 2 = 5 min after injection, T 3 = before extubation, T 4 = at extubation, T 5 = 5 min after extubation, T 6 = 10 min after extubation, T 7 = 15 min after extubation, T 8 = 30 min after extubation also bispectral index, extubation time, visual analogue scale and sedation score were assessed, time to first analgesic request was recorded.

Results: There were significant decrease of systolic, diastolic blood pressure and heart rate in T3, T4, T5, T6, T7, T8 with P-value (0.000) in dexmedetomidine group with significant decrease in VAS at 1/2 h and 1 h after extubation (3.43±.72 vs. 3.93±.68) and better sedation without affecting extubation and recovery in comparison to saline group.

Conclusion: The present study found that low dose dexmedetomidine before extubation may effectively decrease the hemodynamic response to tracheal extubation and provided analgesic and sedative effects in the early postoperative period without prolonging extubation.

KEY-WORDS: Dexmedetomidine - extubation - stress response

Introduction

Attenuation of the pressor response to laryngoscopy, surgery and extubation has been one of the most important topics in anesthesia practice (1-2). Different drug regimen have been used for attenuating the stress response to intubation and surgery and extubation including opioid, barbiturates, benzodiazepines, beta blockers, calcium channel blockers and vasodilators (3-4).

Dexmedetomidine is an alpha 2 agonist; it decreases the plasma catecholamine level and suppressing its release. Also, dexmedetomidine is a centrally acting alpha 2 agonist which has sedative and analgesic effect after intravenous injection; however, it produces dose dependent decrease in the blood pressure and heart rate (5-6).

The present study was designed to evaluate the effect of intravenous injection of low dose dexmedetomidine at the end of surgery on hemodynamic response to tracheal extubation and recovery after general anesthesia in patients undergoing septorhinoplastic surgery.

Material and method

After obtaining local ethics committee approval and an informed written consent, patients with ASA I and II aged from 20 – 40 years old undergoing elective septorhinoplastic surgery under general anesthesia were randomized divided via sealed envelope assignment into two groups: (16 patients in each) dexmedetomidine group (group D) and saline group (group S). Patients and anesthesiologists were blind to the study protocol. Patients with hepatic, renal, cardiovascular disorder, history of mental disorder, recent use of sedatives, analgesics, beta blockers, digoxin, alpha 2 agonist were excluded. On arrival to the operating theatre, all patients were monitored for ECG, heart rate (HR), noninvasive blood pressure (MAP) and pulse oximetry (Sao2). Induction of general anesthesia was achieved using 1 V fentanyl 2µg/kg, propofol 2 mg/kg and tracheal intubation was facilitated by atracurium 0.5 mg/kg. The lungs were mechanically ventilated to maintain normocapnia, anesthesiawas maintained using sevoflurane 1 MAC in 100% of oxygen and atracurium increments of 0.1-0.2 mg/kg, Bispectral index(BIS) changes and minimum alveolar concentration (MAC) of sevoflurane were continuously monitored throughout the operation with target BIS of 40-50 up to 60 using titration of sevoflurane. Atracurium was stopped and sevoflurane was reduced to 0.5% at 30 min and 15 min before the end of surgery respectively. Dexmedetomidine infusion (0.3µg/kg) was started at 15 min before the end of surgery in (group D), or placebo normal saline in (group S). The prepared solutions were identical, at the end of surgery sevoflurane was stopped and neostigmine (0.04 mg/kg) and atropine (0.02 mg/kg) was injected and extubation was performed when BIS values more than 70%. The monitoring indicators included in the
present study were systolic blood pressure, diastolic blood pressure, heart rate, all were recorded at T 1 = 5 min before injection, T 2 = 5 min after injection, T 3 = before extubation, T 4 = at extubation, T 5 = 5 min after extubation, T 6 = 10 min after extubation, T 7 = 15 min after extubation, T 8 = 30 min after extubation. Also, bispectral index (BIS) changes were monitored at T 1 = 5 min before injection, T 2 = 5 min after injection, T 3 = before extubation. Extubation time was recorded and sedation score was assessed using Ramsay’s sedation scale in which 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. The score was assessed at 15 min and 30 min after extubation. Upon arrival to PACU, visual analogue scale (VAS) for pain (0 = no pain, 10 = worst pain imaginable) were recorded at 1/2 hour and one hour after extubation, also the time to first analgesic request was recorded. The statistical analysis of data done by using excel program for figures and SPSS (SPSS, Inc, Chicago, IL) program statistical package for social science version 17. The description of the data done in form of mean (+/-) standard deviation for quantitative data. The analysis of the data was done to test statistical significant difference between groups. For quantitative data student t-test was used to compared between two groups. Chi square test was used for qualitative data. P is significant if ≤ 0.05 at confidence interval 95%. A priori power analysis of the our pilot study indicated that 14 subjects in each group to detect a 20% difference in the systolic blood pressure values between the placebo and study group, which was assumed to have a clinically significant effect, with a type-I error of 0.05 and a power of 90%. We added 10% more patients for a final sample size of 32 patients to compensate for the dropout during the study.

**Results**

Patients demographic data (age, gender, weight) and duration of surgery showed that there was no significant difference between dexmedetomidine group and saline group (table 1). Basal values, values during T 1 (5 min before injection) and values during T 2 (5 min after injection) of systolic blood pressure, diastolic blood pressure and heart rate, showed no significant differences between dexmedetomidine group and saline group, but their values during T 3, T 4 (at extubation), T 5 (5 min after extubation), T 6 (10 min after extubation), T 7 (15 min after extubation) and T 8 (30 min after extubation) showed significant decrease in the dexmedetomidine group in comparison to the saline group with the p-value (0.000) [graph 1, 2, 3]. BIS values at T 1 (5 min before injection), T 2 (5 min after injection) and T 3 (before extubation) showed no statistically significant differences between both dexmedetomidine group and saline group (table 2). Also MAC of sevoflurane and O2 saturations showed no statistically significant differences during the whole surgery. Extubation time showed no statistically significant differences between both dexmedetomidine group and saline group (table 3). VAS at 1/2 hour, 1 hour after extubation showed significant decrease in dexmedetomidine group in comparison to the saline group with the p-value (0.000) and the time to first analgesic request was prolonged (53.75±14.31 in the dexmedetomidine group versus 34.37±5.12 in saline group) (table 3). Also sedation scores at 15 min, 30 min showed statistically significant increase in the dexmedetomidine group in comparison to saline group with the p-value (0.000) (table 3). There were no cases that showed any respiratory or cardiovascular complications.

Table (1): Demographic data (age, sex, weight) and duration of surgery. Data are expressed as mean ± standard deviation, P is significant if ≤ 0.05 at confidence interval 95%.

No significant differences between group D and group S.
Table (2): BIS (bispectral index, Data are expressed as mean ± standard deviation), P is significant if ≤ 0.05 at confidence interval 95%.

BIS T 1 = 5 min before injection
BIS T 2 = 5 min after injection
BIS T 3= before extubation.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group D (N=16)</th>
<th>Group S (N=16)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BIS T1</td>
<td>55.02±2.4</td>
<td>54.58±2.6</td>
<td>0.62</td>
</tr>
<tr>
<td>BIS T2</td>
<td>66.69±3.2</td>
<td>66.49±3.2</td>
<td>0.86</td>
</tr>
<tr>
<td>BIS T3</td>
<td>79.38±3.1</td>
<td>78.89±3.1</td>
<td>0.65</td>
</tr>
</tbody>
</table>

No significant differences between group D and group S.

Table (3): VAS (visual analog score), sedation score, extubation time (min) first analgesic request (min) after extubation. Data are expressed as mean ± standard deviation, P is significant if ≤ 0.05 at confidence interval 95%.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group D (N=16)</th>
<th>Group S (N=16)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>VAS at 1/2 hour after extubation</td>
<td>3.43±.72</td>
<td>4.43±.51</td>
<td>.000 *</td>
</tr>
<tr>
<td>VAS at 1 hour after extubation</td>
<td>3.93±.68</td>
<td>5.31±.47</td>
<td>.000 *</td>
</tr>
<tr>
<td>sedation score at 15 min after extubation</td>
<td>3.12±.34</td>
<td>2.12±.34</td>
<td>.000 *</td>
</tr>
<tr>
<td>sedation score at 30min after extubation</td>
<td>3.68±.47</td>
<td>2.56±.51</td>
<td>.000 *</td>
</tr>
<tr>
<td>extubation time (min)</td>
<td>13.00 ± .73</td>
<td>12.62 ± .71</td>
<td>.154</td>
</tr>
<tr>
<td>first analgesic request (min) after extubation</td>
<td>53.75±14.31</td>
<td>34.37±5.12</td>
<td>.000 *</td>
</tr>
</tbody>
</table>

*significant differences between the Group D and Group S

VAS = visual analog score

Systolic blood pressure (mmhg)
Figure (1): Systolic blood pressure basal (mmHg), systolic blood pressure at $T_1 = 5$ min before injection, $T_2 = 5$ min after injection, $T_3 = 15$ min before extubation, $T_4 = 10$ min after extubation, $T_5 = 5$ min after extubation, $T_6 = 10$ min after extubation, $T_7 = 15$ min after extubation, $T_8 = 30$ min after extubation. Data are expressed as mean ± standard deviation. There were significant decrease in group D at $T_3, T_4, T_5, T_6, T_7, T_8$ in comparison to group S.

![Systolic Blood Pressure Graph](image)

Figure (2): Diastolic blood pressure basal (mmHg), diastolic blood pressure at $T_1 = 5$ min before injection, $T_2 = 5$ min after injection, $T_3 = 15$ min before extubation, $T_4 = 10$ min after extubation, $T_5 = 5$ min after extubation, $T_6 = 10$ min after extubation, $T_7 = 15$ min after extubation, $T_8 = 30$ min after extubation. Data are expressed as mean ± standard deviation. There were significant decrease in group D at $T_3, T_4, T_5, T_6, T_7, T_8$ in comparison to group S.

![Diastolic Blood Pressure Graph](image)
Heart rate (beat /min)

Figure (3): Heart rate basal(beat /min), heart rate at T 1 = 5 min before injection , T 2 = 5 min after injection , T 3= before extubation , T 4 = at extubation , T 5 = 5 min after extubation, T 6= 10 min after extubation , T 7= 15 min after extubation , T 8 = 30 min after extubation, Data are expressed as mean ± standard deviation , there were significant decrease in group D at T3, T4, T5, T6, T7, T8 in comparison to group S.

Discussion
The present study showed that intravenous infusion of low dose dexmedetomidine 0.3µg/kg before the end of surgery may attenuate the hemodynamic stress response to tracheal extubation and provide analgesic and sedative effects in the early postoperative period without any adverse effects on the hemodynamics or affecting the recovery and extubation. Attenuation of hemodynamic stress response during intubation, surgery and extubation considered one of the most researched topics in anesthesia practice (9).

Different analgesic and anesthetic drugs have been used, dexmedetomidine is a potent and more selective α2adrenergic agonist and exhibit a wide range of sedative, analgesic and sympatholytic properties (10-11). The role of α2adrenergic agonist in regulating the autonomic and cardiovascular responses is well understood (12). Whereby they inhibit the release of catecholamine (nor-epinephrine) from the nerve terminals by augmentation of vasoconstrictive effects (13-14).

There are a number of reasons for the use of α2adrenergic agonist, may be due to the availability of the drug with the short half-life, and also may be that there are favorable effects of dexmedetomidine as analgesic and maintain cardiorespiratory function (15).

CONCLUSION
The present study found that intravenous infusion of low dose dexmedetomidine before extubation may effectively decrease the hemodynamic response to tracheal extubation and provided analgesic and sedative effects in the early postoperative period without any adverse effects on the hemodynamics or affecting the recovery and extubation. Attenuation of hemodynamic stress response during intubation, surgery and extubation considered one of the most researched topics in anesthesia practice (9).

Guler et al. in a placebo controlled study concluded that dexmedetomidine 0.5µg/kg five minutes before the end of surgery attenuated the air way reflexes during extubation (16).

Aksu et al. proved in a comparative study between dexmedetomidine and fentanyl, they concluded that dexmedetomidine 0.5µg/kg administered before extubation was more effective in attenuating air way reflexes to tracheal extubation and maintain hemodynamic stability without prolonging recovery compared with fentanyl 1µg/kg (17) and this parallel with the present study. Similarly to the results of the present study Turan et al. Found that dexmedetomidine 0.5 µg/kg one minute before extubation is effective agent for optimal hemodynamic stability and good recovery and extubation than the administration of dexmedetomidine 1 µg/kg (18).

Sudheesh and Harsoor found that doses in the range of 0.5 µg/kg not only blunted the extubation response but also reduced the emergence reaction and analgesic requirements to extubation following rhinoplasty and neurosurgery. Also there was no delay in recovery or prolonged sedation when boluses were administered before induction or before extubation, and this supports the present study (19).
The effects in the early postoperative period without any cardiovascular, respiratory complications or prolonging the extubation time in patients undergoing septorhinoplastic surgery.


