Evaluation of Dexmedetomidine-0.5 μg/kg and 1 μg/kg in Blunting the Responses to Laryngoscopy and Intubation

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ABSTRACT

Background: There is an on-going search for an ideal agent to blunt hemodynamic responses pertaining to tracheal intubation.

Objective: To compare the hemodynamic effects of intravenous (IV) dexmedetomidine in a dose of 0.5 μg/kg and 1 μg/kg body weight as premedicant.

Materials and Methods: 90 patients scheduled for various elective surgical procedures under general anesthesia belonging to ASA Class I and II and Mallampatti Grades I and II in the age group of 18 years to 60 years were included in the study. Patients with uncontrolled systemic disorders, difficult airways, and obesity were excluded from the study. The study population was randomly divided into three groups: (1) Group A: 30 Patients, receiving 10 ml of 0.9% saline IV, 10 min before induction. (2) Group B: 30 Patients, receiving 0.5 μg/kg dexmedetomidine IV, 10 min prior to induction (made to 10 ml with normal saline) (3) Group C: 30 Patients receiving 1 μg/kg dexmedetomidine IV 10 min prior to induction (made to 10 ml with normal saline). Patients of all the above-mentioned groups were premedicated with injection ondansetron 0.08 mg/kg IV and injection fentanyl 1.5 μg/kg IV prior to starting of infusion of the study drug.

Result: In our study, both the doses of IV dexmedetomidine blunted hemodynamic responses, however, IV dose of 1 μg/kg body weight was found more optimal with minimal incidence of side effects.

Conclusion: We conclude that dexmedetomidine in a loading dose of 1 μg/kg body weight significantly attenuates response to laryngoscopy and intubation with minimal incidence of side effects as compared with dexmedetomidine in a dose of 0.5 μg/kg which was found insufficient in majority of cases to cause complete attenuation of sympathetic response.

Key words: Intubation Blunting, IV Dexmedetomidine, General anaesthesia & Dexmedetomidine

INTRODUCTION

Laryngoscopy and tracheal intubation are invariably accompanied by an increase in arterial blood pressure and heart rate (HR). The peak rise in blood pressure and HR is usually transient, occurring 30 s after intubation and lasting for <10 min.¹

The magnitude of hemodynamic changes observed may be dependent on various factors such as depth of anesthesia, whether any measures are taken prior to airway manipulation, the anesthetic agent used, the duration of laryngoscopy and intubation. Until date, the exact mechanism of hemodynamic responses to laryngoscopy and intubation has not been clarified. The principle mechanism in hypertension and tachycardia is the sympathetic response²³ which may be the result of increase in catecholamine activity.⁴

The increase in the pulse rate and blood pressure are usually transitory, variable, and unpredictable. Transitory hypertension and tachycardia are probably
of no consequence in healthy individuals but either or both may be hazardous to those with hypertension, myocardial insufficiency or cerebrovascular diseases. This laryngoscopic response in such individuals may predispose them to development of pulmonary edema, myocardial insufficiency, and cerebrovascular accident.

Intravenous (IV) anesthetic induction agents do not adequately or predictably suppress the circulatory responses caused by endotracheal intubation. Hence, before initiating laryngoscopy, additional pharmacological measures such as use of volatile anaesthetics, topical and IV lidocaine, opioids, vasodilators - sodium nitroprusside, nitroglycerine, calcium channel blockers, and β-blockers have been tried by various authors.

None of the drugs mentioned above have been found to be completely effective in attenuating the sympathetic response to intubation.

α-2 agonists have been used for attenuating the sympathetic response and both clonidine and dexmedetomidine appear to fulfill all the above criteria. Both Clonidine and dexmedetomidine have actions on both α-1 and α-2 receptors, but dexmedetomidine is highly specific and selective α-2 adrenoceptor agonist with α2:α1 binding selectivity ratio of 1620:1 compared to 220:1 for clonidine.

Various studies have also found that dexmedetomidine can decrease the hemodynamic response to laryngoscopy and intubation.

The advantages of IV dexmedetomidine as premedicant in anesthesia setting include anxiolysis, analgesia, sedation, improved hemodynamic stability, and no/minimal respiratory depression. These beneficial properties also result in decreased minimum alveolar concentration (MAC) of volatile anesthetics which decreases significantly up to 90% and hence decreases the requirement of anesthetics.

The present study, however, was aimed at attenuation of the hemodynamic response to laryngoscopy and intubation in adult patients posted for various surgeries under general anesthesia, with single IV bolus dose of 0.5 mcg/kg and 1 mcg/kg given over 10 min before induction.

**Pharmacology**

**Dexmedetomidine**

Dexmedetomidine is the S-enatiomer (dextroisomer) of medetomidine, a widely used anesthetic in veterinarian practice. Dexmedetomidine was first approved for use in 1999 by the FDA as a short term (<24 h) sedative and analgesic for use in the ICU in patients being mechanically ventilated.

IV/Intramuscular dexmedetomidine causes anxiolysis, sedation, analgesia, and sympatholysis produced with minimal respiratory depression. It is used in ICU setting, as a premedication, as a sole anesthetic agent, in regional anesthesia, and in MAC.

Dose: Dexmedetomidine is initiated as 0.5-1 μg/kg IV over 10 min followed by a maintenance infusion of 0.2-0.7 μg/kg/h for a period not <24 h.

**MATERIALS AND METHODS**

A total of 90 patients scheduled for various elective surgical procedures under general anesthesia belonging to ASA Class I and II and Mallampatti Grades I and II in the age group of 18 years to 60 years were included in the study.

The detailed preanesthetic checkup was done on all patients, and relevant hematological, biochemical, and radiological investigations were carried out for all patients as per surgical requirements.

The study population was randomly divided into three groups:

- **Group A**: 30 Patients, receiving 10 ml of 0.9% saline IV, 10 min before induction.
- **Group B**: 30 Patients, receiving 0.5 μg/kg dexmedetomidine IV, 10 min before induction (made to 10 ml with normal saline).
- **Group C**: 30 Patients receiving 1 μg/kg dexmedetomidine IV 10 min before induction (Made to 10 ml with normal saline).

**Anesthetic Procedure**

Patients of all the above-mentioned groups were premedicated with injection Ondansetron 0.08 mg/kg IV and injection fentanyl 1.5 μg/kg IV prior to starting of infusion of the study drug.

Anesthesia was induced after the administration of the study drug using injection Propofol 2 mg/kg IV and injection Vecuronium 0.02 mg/kg body weight. Further neuromuscular block was maintained by injection Vecuronium 0.02 mg/kg body weight.

The SBP, diastolic blood pressure (DBP), mean arterial blood pressure (MAP), and HR were recorded. All these parameters were recorded as a baseline value,
T = 0 min, 5 min after starting dexmedetomidine infusion, preintubation (T = 10 min), immediately post-intubation, post-intubation 1, 3, 5 min, and at 10 min.

**Adverse Effects**

1. Hypotension was defined as SBP <90 mmHg or a DBP of <60 mmHg or MAP of <50 mmHg on any reading.
2. Bradycardia was defined as HR <50 b/min.
3. Arrhythmia was defined as supraventricular or a ventricular beats >3/min or a rhythm other than sinus.

**Exclusion Criteria**

- Patient refusal
- Patients with ASA Class III and above
- Patients on preoperative beta blockers
- Age <18 years and >60 years
- Pregnant or nursing women
- Any history of drug reactions
- Patients with anticipated difficult intubation
- Patient having hypovolemia, hypotension, and bradycardia
- Duration of laryngoscopy and endotracheal intubation >30 s
- Patients with systemic diseases, obesity.

**DISCUSSION**

**Baseline Comparison of Groups**

**Demographic parameters**

The study included patients in the age group ranging from age 18 to 60 years for all 3 groups. The mean values of the age were 38.33 ± 11.67, 38.30 ± 9.45, and 34.13 ± 11.42 years for Groups A, B, and C, respectively (Table 1). There was no statistical significance difference between the 3 groups with respect to age (P = 0.234).

Distribution of sex was also comparable (Table 2). In our study, Group A, 63.3% were males and 36.7% were females. In Group B, 46.7% were males and 53.3% were females. In Group C, 46.7% were males and 53.3% were females. No statistically significant difference was observed in sex distribution of the cases between the 3 groups (P = 0.328).

The mean weights of patients were 64.63 ± 10.42 kg, 61.87 ± 10.21 kg, 59.20 ± 10.17 kg in Group A, Group B, and Group C, respectively (Table 3). No statistically significant difference was observed in weight distribution of the cases between the 3 groups (P = 0.128).

**Hemodynamic parameters**

**SBP**

In Group A control, the mean baseline SBP was 124.13 ± 12.66, which decreased by 3.1 mmHg after completion of administration of study drug. Post-intubation, there was a rise in the mean SBP values from the pre-laryngoscopic values (T-10) by 29.64 mmHg immediately after intubation, 22.14 mmHg at 1 min, 15.3 mmHg at 3 min, 6.54 mmHg at 5 min, and 2.37 mmHg at 10 min (Table 4).

In Group B, the mean baseline SBP was 126.03 ± 11.62 which decreased by 6.66 mmHg after completion of administration of study drug. Post-intubation there was a rise in the mean SBP values from the pre-laryngoscopic values (T-10) by 17 mmHg immediately after intubation, 12 mmHg at 1 min, 6.76 mmHg at 3 min, 1.3 mmHg at 5 min and decreased by 0.2 mmHg at 10 min as compared with pre-laryngoscopic values (Table 4).

In Group C, the mean baseline SBP was 126.67 ± 9.01 which decreased by 15.94 mmHg after completion of administration of the study drug. Post-intubation there was a rise in the mean SBP values from the pre-laryngoscopic values (T-10) by 7.87 mmHg immediately after intubation, 7.14 mmHg at 1 min, 1.90 mmHg at 3 min, and decreased by 0.3 mmHg at 5 min and 1.6 mmHg at 10 min as compared with pre-laryngoscopic values. However, at no point of time during the post-intubation period did the mean SBP rise above the Baseline mean SBP value of the study population in this group (Figure 1).

Group C demonstrated a better suppression of the pressor response to intubation compared with other two groups.

**DBP**

In Group A control, the mean baseline DBP was 78.00 ± 8.60, which decreased by 0.4 mmHg after completion of administration of study drug. Post-intubation there was a rise in the mean SBP values from the pre-laryngoscopic values (T-10) by 18.23 mmHg immediately after intubation, 13.77 mmHg at 1 min, 6.87 mmHg at 3 min, and decreased by 0.17 mmHg at 5 min as compared with pre-laryngoscopic values (Table 5). In Group B, the mean baseline DBP was 76.97 ± 8.28 which decreased by 1.2 mmHg after completion of administration of study drug. Post-intubation there was a rise in the mean DBP values from the pre-laryngoscopic values (T-10) by 11.96 mmHg immediately after intubation, 8.43 mmHg at 1 min, 1.66 mmHg at 3 min, and decreased by 0.24 mmHg at 5 min and decreased by 1.54 mmHg at 10 min as compared with pre-laryngoscopic values (Table 5).

In Group C, the mean baseline DBP was 78.87 ± 6.66 which decreased by 9.74 mmHg after completion of administration of study drug. Post-intubation there was a rise in the mean DBP values from the pre-laryngoscopic values (T-10) by 6.04 mmHg immediately after intubation,
4.0 mmHg at 1 min, 0.4 mmHg at 3 min, and decreased by 0.7 mmHg at 5 min and 2.13 mmHg at 10 min as compared with pre-laryngoscopic values (Table 5). However, at no point in time during the post-intubation period did the mean DBP rise above the baseline mean DBP value of the study population in this group (Figure 2).

Group C demonstrated a better suppression of the pressor response to intubation compared to other two groups.

**MAP**
In Group A control, the mean baseline MAP was 93.30 ± 8.76, which decreased by 1.0 mmHg after completion of administration of study drug. Post-intubation there was a rise in the mean MAP values from the pre-laryngoscopic values (T-10) by 21.87 mmHg immediately after intubation, 16.3 mmHg at 1 min, 9.43 mmHg at 3 min, 3.23 mmHg at 5 min, and by 0.5 mmHg at 10 min (Table 6). In Group B, the mean baseline MAP was 92.97 ± 8.15 which decreased by 2.65 mmHg after completion of administration of study drug. Post-intubation there was a rise in the mean MAP values from the pre-laryngoscopic values (T-10) by 12.95 mmHg immediately after intubation, 8.71 mmHg at 1 min, 3.31 mmHg at 3 min, 0.25 mmHg at 5 min, and decreased by 1.11 mmHg at 10 min (Table 6).

In Group C, the mean baseline MAP was 94.53 ± 6.66 which decreased by 11.66 mmHg after completion of administration of the study drug. Post-intubation there was a rise in the mean MAP values from the pre-laryngoscopic values (T-10) by 6.83 mmHg immediately after intubation, 5.26 mmHg at 1 min, 1.1 mmHg at 3 min, and decreased by 0.24 mmHg at 5 min and 1.97 mmHg at 10 min as compared with pre-laryngoscopic values (Table 6). However, at no point in time during the post-intubation period did the mean MAP rise above the Baseline mean MAP value of the study population in this group (Figure 3). Group C demonstrated a better suppression of the pressor response to intubation compared to other two groups.

**HR**
In Group A control, the mean baseline HR was 79.8 ± 11.06, which remained the same after completion of administration of study drug. Post-intubation there was a rise in the mean HR values from the pre-laryngoscopic values (T-10) by 28.37 beats/min immediately after intubation, 21.67 beats/min at 1 min, 16.9 beats/min at 3 min, 9.07 beats/min at 5 min, and by 3.54 beats/min at 10 min (Table 7).

In Group B, the mean baseline HR was 80.73 ± 10.65 which decreased by 7.36 beats/min after completion of administration of study drug. Post-intubation there was a rise in the mean HR values from the Pre-laryngoscopic values (T-10) by 4.0 mmHg at 1 min, 0.4 mmHg at 3 min, and decreased by 0.7 mmHg at 5 min and 2.13 mmHg at 10 min as compared with pre-laryngoscopic values (Table 5). However, at no point in time during the post-intubation period did the mean DBP rise above the baseline mean DBP value of the study population in this group (Figure 2).

Group C demonstrated a better suppression of the pressor response to intubation compared to other two groups.

**Table 1: Age distribution of patients studied**

<table>
<thead>
<tr>
<th>Age groups (years)</th>
<th>Group A</th>
<th>Group B</th>
<th>Group C</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-30</td>
<td>11 (36.7)</td>
<td>7 (23.3)</td>
<td>12 (40.0)</td>
<td></td>
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<tr>
<td>31-40</td>
<td>8 (26.7)</td>
<td>12 (40.0)</td>
<td>11 (36.7)</td>
<td></td>
</tr>
<tr>
<td>41-50</td>
<td>7 (23.3)</td>
<td>10 (33.3)</td>
<td>5 (16.7)</td>
<td></td>
</tr>
<tr>
<td>51-60</td>
<td>4 (13.3)</td>
<td>1 (3.3)</td>
<td>2 (6.7)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>30 (100)</td>
<td>30 (100)</td>
<td>30 (100)</td>
<td></td>
</tr>
<tr>
<td>Mean±SD</td>
<td>38.33±11.67</td>
<td>38.30±9.45</td>
<td>34.13±11.42</td>
<td>0.234</td>
</tr>
</tbody>
</table>

**Table 2: Gender distribution of patients studied**

<table>
<thead>
<tr>
<th>Sex</th>
<th>Frequency (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>19 (63.3)</td>
<td>14 (46.7)</td>
</tr>
<tr>
<td>Female</td>
<td>11 (36.7)</td>
<td>16 (53.3)</td>
</tr>
<tr>
<td>Total</td>
<td>30 (100)</td>
<td>30 (100)</td>
</tr>
</tbody>
</table>

**Table 3: Distribution of weight in three groups of patients studied**

<table>
<thead>
<tr>
<th>Weight (in Kgs)</th>
<th>Mean±SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>64.63±10.42</td>
<td>61.87±10.21</td>
</tr>
</tbody>
</table>

**Table 4: Comparison SBP mmHg in three groups of patients studied**

<table>
<thead>
<tr>
<th>SBP</th>
<th>Group A</th>
<th>Group B</th>
<th>Group C</th>
<th>Group A vs. Group B</th>
<th>Group A vs. Group C</th>
<th>Group B vs. Group C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>124.13±12.66</td>
<td>126.03±11.62</td>
<td>126.67±9.01</td>
<td>0.789</td>
<td>0.657</td>
<td>0.974</td>
</tr>
<tr>
<td>T0</td>
<td>128.83±11.07</td>
<td>131.00±10.53</td>
<td>130.87±9.53</td>
<td>0.699</td>
<td>0.730</td>
<td>0.999</td>
</tr>
<tr>
<td>T5</td>
<td>124.40±10.18</td>
<td>124.20±12.66</td>
<td>117.30±11.43</td>
<td>0.997</td>
<td>0.048</td>
<td>0.057</td>
</tr>
<tr>
<td>T10</td>
<td>121.03±9.58</td>
<td>119.37±15.39</td>
<td>110.73±12.25</td>
<td>0.866</td>
<td>0.006</td>
<td>0.026</td>
</tr>
<tr>
<td>TP1</td>
<td>150.67±11.14</td>
<td>136.37±15.49</td>
<td>118.60±10.78</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>T1</td>
<td>143.17±12.21</td>
<td>131.37±13.73</td>
<td>117.87±11.71</td>
<td>0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>T3</td>
<td>136.33±11.24</td>
<td>126.13±12.03</td>
<td>112.63±10.76</td>
<td>0.002</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>T5</td>
<td>127.57±12.26</td>
<td>120.67±11.41</td>
<td>110.43±10.04</td>
<td>0.052</td>
<td>0.002</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>T10</td>
<td>123.40±12.88</td>
<td>119.17±11.43</td>
<td>109.13±9.51</td>
<td>0.323</td>
<td>&lt;0.001</td>
<td>0.003</td>
</tr>
</tbody>
</table>

SD: Standard deviation, SBP: Systolic blood pressure
values (T-10) by 20.23 beats/min immediately after intubation, 15.03 beats/min at 1 min, 12.53 beats/min at 3 min, 9.36 beats/min at 5 min, and 6.4 beats/min at 10 min (Table 7).

In Group C, the mean baseline HR was 83.73 ± 12.15 which decreased by 15.23 beats/min after administration of the study drug. Post-intubation there was a rise in the mean HR values from the pre-laryngoscopic values (T-10) by 6.6 beats/min immediately after intubation, 6.67 beats/min at 1 min, 4.43 beats/min at 5 min and 1.33 beats/min at 10 min (Table 7). However, at no point of time during the post-intubation period did the mean HR rise above the T0 min mean HR value of the study population in this group (Figure 4).
Group C demonstrated a better suppression of the pressor response to intubation compared to other two groups.

Side effects
Group A, Group B, and Group C were statistically comparable in terms of side effects ($P = 0.351$). There were 2 cases of bradycardia (HR < 50/min) in Group B, and 2 cases of bradycardia (HR < 50/min) in Group C, respectively. There were no other cases with hypotension or arrhythmias in terms of side effects (Table 8).

Comparison with Other Studies
In the study by Menda et al.,\textsuperscript{18} they found that the SBP, DBP, MAP, HR values were below the baseline values in the dexmedetomidine group at all measurement times,\textsuperscript{18} which was in accordance with our results.

Esra et al.\textsuperscript{22} observed in their study using dexmedetomidine 1 μg/kg that the mean SBP, DBP, MAP, and HR values were significantly lower at post-induction and 5 min after intubation compared to baseline values which were similar to the results of our study.

Our study results also concurred with the results of Keniya et al.\textsuperscript{23} who observed an 8% increase in SBP and 11% for DBP, 7% for HR when compared with pre-laryngoscopic values in dexmedetomidine 1 mcg/kg group.

CONCLUSION
• Dexmedetomidine in a dose of 0.5 mcg/kg:
  o Is insufficient to cause complete blunting of the hemodynamic response to laryngoscopy and intubation for 10 min in majority of cases.
• Dexmedetomidine in a dose of 1 mcg/kg:
  o Significantly attenuates the hemodynamic response to laryngoscopy and intubation for 10 min.
  o Side effects observed were not statistically significant and comparable with side effects present in Group B.

No arrhythmias were seen during/after administration of study drug.

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6. Dalton B, Guiney T. Myocardial ischemia from tachycardia and


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