A randomized controlled study of intravenous dexmedetomidine to attenuate the cardiovascular responses to laryngoscopy and endotracheal intubation

Ninad Deepak Chodankar and Bhagyashree Shivde

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Abstract

**Design:** Prospective, Randomized, controlled study.

**Aims:** Objective is to compare the efficacy of intravenous Dexmedetomidine in attenuating the cardiovascular response to laryngoscopy and endotracheal intubation.

**Method:** Study was done on 60 adults, ASA grade I or II normotensive patients, undergoing elective surgery under general anaesthesia and willing to participate. These patients were be randomly allocated in to either group C (Control), or D (Dexmedetomidine). Group ‘C’ Control group. Group ‘D’, patients were given intravenous Dexmedetomidine infusion 1 mcg/kg over 10 minutes, 3 minutes before start of laryngoscopy. All patients were premedicated, induced and intubated using Thiopentone and Succinyl Choline as per the protocol. Heart rate (HR), SBP, DBP and MAP were recorded at baseline (taken half an hour prior to anaesthesia), Before sedation, After induction but before intubation, Immediately after endotracheal intubation and Thereafter at 1, 2, 3, 4, 5 and 10 minutes.

**Results:** There was statistically significant rise in Heart rate after intubation in Group C compared to Group D, and difference was significant. After intubation, Heart rate continued to decrease and was significantly lower in Group D. There was statistically significant rise in MAP immediately after intubation in Group C compared to Group D.

**Conclusion:** We conclude that intravenous Dexmedetomidine 1 ug/kg is adequate to attenuate hemodynamic response to laryngoscopy and intubation.

**Keywords:** laryngoscopy, intubation, Dexmedetomidine, hemodynamic, response

**Introduction**

Laryngoscopy and endotracheal intubation is long standing basic requirement for general anaesthesia. It is often accompanied with significant increases in heart rate and arterial blood pressure, often leading to adverse outcome. These pressor responses are transient occurring 30 seconds after intubation and lasting less than 10 minutes. This happens due to sympathetic system activation and can lead to cardiac rhythm abnormalities. These responses are most often of short duration and of little consequence in healthy individuals, serious complications can occur in patients with underlying coronary artery disease reactive airways. These reflexes are mediated by the cardioaccelerator nerves and sympathetic system. This response includes wide-spread release of norepinephrine from adrenergic nerve terminals and secretion of epinephrine from the adrenal medulla.

**Dexmedetomidine** is an imidazole derivative and highly selective central alpha2 adrenergic receptor agonist. Alpha-2 agonists produce hyperpolarization of noradrenergic neurons and suppression of neuronal firing in the locus coeruleus leads to decreased systemic noradrenaline release results in attenuation of sympathoadrenal responses. Dexmedetomidine has been shown to provide hemodynamic stability during laryngoscopy and tracheal intubation.

**Method**

Study period was from May 2015 to May 2016.
Study Population: 60 adult ASA grade I or II normotensive patients, undergoing elective surgery under general anaesthesia and willing to participate were the study population.

Study Design: It is a prospective randomized study. The approval for the study was obtained from the Institutional Ethics Committee.

Inclusion Criteria
Male and female of age group between 25 to 65 years. Undergoing elective surgery under general anaesthesia. Weight 40 kg to 90kg. Resting systolic blood pressure less than 140 mmHg and diastolic pressure less than 90 mmHg. American Society of Anaesthesiologist Grade I and II.

Exclusion Criteria
Ischemic heart diseases or ECG abnormalities indicating ischemic heart diseases. Patients with any overt cardiac, renal, pulmonary and liver diseases. Hypertensive patients. Any Patients with history of dyspnoea on exertion of grade III or more as per NYHA guidelines. Obesity (weight more than 90kg). Pregnancy. ASA grade III or IV patients. Anticipated difficult intubation. Any contraindication of Dexmedetomidine.

Methodology
Pre-Operative Investigations and Assessment:
A preoperative evaluation was carried out in all patients with demographic data like age, gender, weight and detailed clinical history, physical examination including, associated medical co-morbidities, and current medications. Blood pressure was measured at three occasions at least 1 hour apart to confirm that it fulfils the selection criteria. All routine and relevant investigations such as complete blood count, renal function test (serum electrolytes, serum creatinine, and blood urea levels), urine routine and microscopy, electrocardiogram, chest X-ray were carried out for all patients. The factors indicating difficult intubation on clinical examination were ruled out.

Pre-Operative Management:
All patients received Tablet Pantoprazole 40 mg at night before surgery and 3 hours before surgery and Tablet Alprazolam 0.5 mg was given night before surgery. A 20G intravenous cannula was secured on non-dominant hand in appropriate vein in wards and intravenous fluid Ringers. Thiopentone 5mg/kg body weight given slowly till loss of eyelash reflex is seen. Then intravenous Succinylcholine was given in dose of 2 mg/kg. Then facemask ventilation was done till twitches disappears and adequate relaxation obtained. Direct laryngoscopy was conducted by the same anaesthesia consultant for all cases, using standard McIntosh blade and an appropriate size cuffed endotracheal tube lubricated with non-anaesthetic jelly and was inserted in single attempt and cuff will be immediately inflated with air to a pressure of 25 cm of water.

After confirming bilateral equality of air entry in lungs by auscultation, the endotracheal tube was secured with the adhesive tape. Ventilation was done by IPPV on ventilator. Ventilator setting was set to provide tidal volume of 8-10 ml/kg and respiratory rate 14/minute for 10 minutes. No noxious stimulus or surgical incision was applied over 10 minutes after intubation. Supine position was maintained. Anaesthesia was maintained using 50% nitrous oxide and 50% oxygen with Isoflurane (MAC-1.0). Hemodynamic parameters were monitored as follows: Heart rate (HR), Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Mean Arterial Pressure (MAP) by non-invasive technique.

The intervals for these measurements were:
1. Baseline (taken half an hour prior to anaesthesia)
2. Before sedation
3. After induction but before intubation
4. Immediately after intubation
5. Therelater at 1, 2, 3, 4, 5 and 10 minutes.

After this monitoring for 10 minutes post-intubation, further operative and anaesthetic procedure were continued as per plan.

Statistical methods
- Statistical analysis was carried out with the help of SPSS (version 20) for Windows package (SPSS Science, Chicago, IL, USA). The description of the data was done in form of mean +/- SD for quantitative data while in the form of % proportion for qualitative (categorical) data. P-values of < 0.05 will be considered significant.
- For quantitative data, Unpaired Student’s t-test was used to test statistical significance of difference between two independent group means.
- For comparison of categorical variables chi-square test was used.

Results
Comparison of patient variables such as age, gender and weight shows that there is no statistically significant
demographical difference between group C and D. (Table 1). Heart rate was lower in Group D as compared to Group C. There was no statistically significant difference at “baseline”, “before sedation” or “after induction”. Thereafter heart rate was statistically significant lower in Group D from “immediately after intubation” till “10 minutes after intubation”. (Table 2).

SBP was lower in Group D as compared to Group C. There was no statistically significant difference at “baseline”, “before sedation” or “after induction”. Thereafter SBP was statistically significant lower in Group D from “immediately after intubation” till “10 minutes after intubation”. (Table 3).

DBP was lower in Group D as compared to Group C. There was no statistically significant difference at “baseline” or “before sedation”. Thereafter DBP was statistically significant lower in Group D from “after induction” till “10 minutes after intubation”. (Table 4).

MAP was lower in Group D as compared to Group C. There was no statistically significant difference at “baseline” or “before sedation”. Thereafter MAP was statistically significant lower in Group D from “after induction” till “10 minutes after intubation”. (Table 5).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group C</th>
<th>Group D</th>
<th>p-Value</th>
</tr>
</thead>
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<td>Age</td>
<td>36.03 ± 9.219</td>
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<td>Weight</td>
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<td>65.4 ± 9.103</td>
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<tr>
<td>Gender</td>
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<tr>
<td>Male</td>
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<tr>
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<td>11</td>
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<td>Baseline</td>
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<td>84.60 ± 11.171</td>
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<td>After Induction</td>
<td>84.77 ± 10.513</td>
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<td>99.10 ± 11.514</td>
<td>82.53 ± 9.365</td>
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</tr>
<tr>
<td>2 mins</td>
<td>96.10 ± 11.400</td>
<td>80.87 ± 9.566</td>
<td>0.000*</td>
</tr>
<tr>
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<td>93.73 ± 11.453</td>
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<tr>
<td>4 mins</td>
<td>90.13 ± 11.658</td>
<td>78.13 ± 9.213</td>
<td>0.001*</td>
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<tr>
<td>5 mins</td>
<td>85.93 ± 11.310</td>
<td>76.97 ± 9.427</td>
<td>0.006*</td>
</tr>
<tr>
<td>10 mins</td>
<td>83.63 ± 11.731</td>
<td>75.23 ± 9.957</td>
<td>0.015*</td>
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*statistically significant

<table>
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<th>Variables</th>
<th>Group C</th>
<th>Group D</th>
<th>p-Value</th>
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<td>Baseline</td>
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<tr>
<td>Before Sedation</td>
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<td>After Induction</td>
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<td>1 min</td>
<td>151.10 ± 10.114</td>
<td>121.43 ± 8.912</td>
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<tr>
<td>2 mins</td>
<td>142.93 ± 7.428</td>
<td>118.33 ± 8.636</td>
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<tr>
<td>3 mins</td>
<td>137.67 ± 7.950</td>
<td>117.10 ± 8.385</td>
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<td>4 mins</td>
<td>132.83 ± 7.410</td>
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<td>5 mins</td>
<td>127.90 ± 8.168</td>
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<tr>
<td>10 mins</td>
<td>124.37 ± 9.046</td>
<td>111.30 ± 8.567</td>
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*statistically significant

<table>
<thead>
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<th>Variables</th>
<th>Group C</th>
<th>Group D</th>
<th>p-Value</th>
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<td>Baseline</td>
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<td>After Induction</td>
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<td>1 min</td>
<td>88.57 ± 7.463</td>
<td>79.03 ± 7.712</td>
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<td>2 mins</td>
<td>86.57 ± 6.590</td>
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<tr>
<td>3 mins</td>
<td>83.87 ± 6.202</td>
<td>75.47 ± 7.628</td>
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<tr>
<td>4 mins</td>
<td>82.40 ± 6.344</td>
<td>73.60 ± 7.686</td>
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<tr>
<td>5 mins</td>
<td>79.33 ± 4.908</td>
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<tr>
<td>10 mins</td>
<td>77.27 ± 5.382</td>
<td>69.73 ± 8.292</td>
<td>0.000*</td>
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</tbody>
</table>

*statistically significant

Table 1: Comparison of Patient variables

Table 2: Intergroup Comparison of mean Heart Rate between Group C and D

Table 3: Intergroup Comparison of mean Systolic Blood Pressure between Group C and D

Table 4: Intergroup Comparison of mean Diastolic Blood Pressure between Group C and D
Table 5: Intergroup Comparison of mean MAP between Group C and D

<table>
<thead>
<tr>
<th>Time</th>
<th>Group C</th>
<th>Group D</th>
<th>p-Value</th>
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<tr>
<td>Baseline</td>
<td>90.90 ± 8.057</td>
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<tr>
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<td>1 min</td>
<td>112.73 ± 10.945</td>
<td>95.83 ± 9.706</td>
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<td>2 mins</td>
<td>108.47 ± 9.899</td>
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<tr>
<td>3 mins</td>
<td>103.57 ± 9.555</td>
<td>90.67 ± 9.185</td>
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<td>4 mins</td>
<td>99.93 ± 8.706</td>
<td>89.00 ± 9.620</td>
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<td>5 mins</td>
<td>95.00 ± 7.344</td>
<td>87.03 ± 9.301</td>
<td>0.000*</td>
</tr>
<tr>
<td>10 mins</td>
<td>90.93 ± 7.148</td>
<td>85.63 ± 9.338</td>
<td>0.005*</td>
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</tbody>
</table>

*statistically significant

Graph 1: Comparison of Mean HR in Group C, D and E

Graph 2: Comparison of Mean SBP in Group C, D and E
Discussion

The cardiovascular response which leads to hemodynamic pressor changes characterized by tachycardia and hypertension to manipulation in the area of the larynx, by means of laryngoscopy and intubation, is well-recognized. Stimulation of mechanoreceptors in the pharyngeal wall, epiglottis and vocal cords, is thought to be the cause for this hemodynamic response. Cardiovascular pressor response following laryngoscopy and tracheal intubation has been investigated extensively since the early days of anaesthesia [9].

Myocardial ischemia might occur during the induction-intubation sequence in patients with coronary artery disease. Intraoperative ischemia has been associated with a high rate of perioperative myocardial infarction [9]. During procedure like direct laryngoscopy involving severe sympathetic stimuli prevention of tachycardia, hypertension and rise in total oxygen consumption may prove beneficial in patients with limited cardiac reserve [11].

Dexmedetomidine is a highly selective and specific alpha-two adrenergic agonist which produces its action by decreasing the catecholamine release from locus coeruleus in the brain. It decreases the cerebral blood flow (CBF) while preserving the CBF-cerebral metabolic rate coupling, decreases intracranial pressure [12, 13]. It also decreases sympathetic tone and their preoperative use has been shown to blunt the hemodynamic responses to laryngoscopy and intubation [14].

Sagiroglu et al. [15] concluded that the overall control of hemodynamic responses to tracheal intubation were better with Dexmedetomidine 1 $\mu$g/kg as compared to Dexmedetomidine 0.5 $\mu$g/kg. Laha et al. [16] in their study compared Dexmedetomidine 1 $\mu$g/kg with control and concluded that Dexmedetomidine effectively blunted the hemodynamic responses during laryngoscopy, and reduced anaesthetic requirements.

Kunisawa et al. [17] reported that an injection of Dexmedetomidine inhibits a decrease in blood pressure caused by the anaesthetic agent, and so postulated that it may be the result of vasoconstriction caused by the alpha-2 receptor in the vascular smooth muscle. The report stated that blood pressure temporarily increases one minute after an injection with a loading dose of Dexmedetomidine, and
reaches its peak at 3 min. When Dexmedetomidine is used in a combination with anaesthetics, it reportedly prevents further drops in blood pressure and rather inhibits it [18]. Sulaifman et al. [19] studied efficacy of intravenous Dexmedetomidine for attenuation of cardiovascular responses to laryngoscopy and endotracheal intubation in patients with coronary artery disease. They observed that Dexmedetomidine at a dose of 0.5 mcg/kg as 10-min infusion administered prior to induction of general anaesthesia was effective to attenuate the sympathetic response to laryngoscopy and intubation in patients undergoing myocardial revascularization.

In another study comparing Lignocaine and Dexmedetomidine [20] they observed that hemodynamic stress response was seen following laryngoscopy and tracheal intubation was significantly attenuated in dexmedetomidine group. Our study demonstrated that the use of Dexmedetomidine was effective in decreasing the hypertensive response to laryngoscopy and intubation.

Conclusion
In Normotensive patients requiring general anaesthesia with intubation, after induction with Fentanyl and Thiopentone, and Succinylcholine as muscle relaxant, we found that intravenous Dexmedetomidine 1ug/kg is effective to attenuate hemodynamic response to laryngoscopy and intubation.

Acknowledgements
I express my sincere thanks to all my patients who made my research possible and meaningful.

References