EFFECT OF DEXMEDETOMIDINE AND ESMOLOL IN ATTENUATING THE HAEMODYNAMIC RESPONSES DURING LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION IN ELECTIVE UPPER ABDOMINAL SURGERIES

Subhadeep Chakraborty, Amalendu Bikas Chatterjee, Swarup Dutta

1Specialist Medical Officer, Baruipur Super Speciality Hospital, South 24 Parganas, West Bengal.
2Professor, Department of Anaesthesiology, B. S. Medical College, Bankura, West Bengal.
3Assistant Professor, Department of Anaesthesiology, B. S. Medical College, Bankura, West Bengal.

ABSTRACT

BACKGROUND

Laryngoscopy and endotracheal intubation produces a distinct but transient increase in cardiac workload. In this study, a comparison is made between dexmedetomidine, esmolol and control in their effect in attenuation of pressure response during laryngoscopy and endotracheal intubation.

MATERIALS AND METHODS

With written consent, we studied one hundred and twenty-five (125) adult patients of American Society of Anesthesiologists physical status I and II, aged between 30 to 60 years, of either sex, undergoing elective upper abdominal surgeries. The patients were randomly allocated into three groups: 1) 42 patients in group (D) received Dexmedetomidine (1 μg/kg), 2) 42 patients in group (C) received normal saline 15 ml, and 3) 41 patients in group (E) received Esmolol (2 mg/kg).

All patients received the drugs intravenously over 10 minutes and 3 minutes before induction of general anaesthesia. Premedication, induction and intubation were similar. Heart rate (HR), systemic arterial pressures were recorded at baseline, after study drug infusion, after induction, immediately and 3, 5, 7, 10 minutes after intubation.

Study Design- Prospective, randomized, double blind, controlled study.

Statistical Analysis- Analysis of variance and t-test as appropriate.

RESULTS

The heart rate, systolic arterial pressures and rate-pressure product immediately after intubation and thereafter were significantly lower in Group D (P<0.001) when compared to Group E and Group C. Group E had the same post-intubation parameters reliably (P<0.001) lower than Group C.

CONCLUSION

Dexmedetomidine and esmolol were both effective in attenuating the haemodynamic response to intubation, but dexmedetomidine was more effective than esmolol in lowering the haemodynamic response.

KEYWORDS

Dexmedetomidine, esmolol, normal saline, laryngoscopy, intubation, haemodynamic response.

HOW TO CITE THIS ARTICLE: Chakraborty S, Chatterjee AB, Dutta S. Effect of dexmedetomidine and esmolol in attenuating the haemodynamic responses during laryngoscopy and endotracheal intubation in elective upper abdominal surgeries. J. Evid. Based Med. Healthc. 2018; 5(27), 2065-2073. DOI: 10.18410/jebmh/2018/429

BACKGROUND

Laryngoscopy and endotracheal intubation is a noxious stimulus, which can provoke untoward response in cardiovascular, respiratory and other physiological systems. The effect is transient, occurring immediately after intubation and lasting for 5-10 minutes. Intubation response may be well tolerated by normal, fit, ASA (American Society of Anaesthesiologist) physical status-I patients; but can be deleterious in patients with poor cardiovascular reserve. In patients with coronary artery disease (CAD), hypertension, raised intra-cranial pressure it may be associated with myocardial infarction, arrhythmias, cardiac failure or cerebral haemorrhage.

Methods to attenuate these responses, both pharmacological and physiological, have been extensively studied. Treatment modalities include topical lignocaine spray, deeper planes of anaesthesia by inhalation/intravenous agents or narcotics, calcium channel blockers, α-2 agonists, β-2 blockers, vasodilators such as sodium-nitroprusside, nitroglycerine etc. Although there are several methods, research is still ongoing.

Esmolol is an ultra-short acting, β adrenergic receptor antagonist, with proven efficacy to provide haemodynamic stability during laryngoscopy and tracheal intubation. The peak effect of esmolol is 2 minutes from the time of 

DOI 10.18410/jebmh/2018/429
intravenous administration and is metabolised by esterases resulting in short duration of action (10-15 minutes). These characteristics make esmolol a useful drug to blunt the response.

Dexmedetomidine, a highly selective alpha-2 receptor agonist, decreases systemic noradrenalin release results in attenuation of sympathoadrenal responses and maintain haemodynamic stability during laryngoscopy and tracheal intubation.

This background study guided us to perform this randomized, prospective double blind study.

**MATERIALS AND METHODS**

After written informed consent of each patient and clearance from Institutional ethical committee a study was conducted at B. S. Medical College, Bankura. One hundred and twenty five (125) normotensive, ASA physical status I and II patients of either sex, aged 30-60 years, who were scheduled for elective upper abdominal surgeries under general anaesthesia (GA) requiring endotracheal (ET) intubation, were included in this study. Pre-anaesthetic checkup were done for all patients. Patients were excluded as per our exclusion criteria. On the night before surgery, patients were given 0.5mg alprazolam orally.

Pre-operative baseline vital parameters of patients including pulse rate (PR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MBP) and oxygen saturation (SpO2) were recorded. In operation theatre, Ringer’s lactate was infused (6 ml/kg). Routine standard monitors such as pulse oximetry, electrocardiography (ECG) and non-invasive blood pressure were applied, and monitoring started. Premedication done with intravenous ondansetron 0.08 mg/kg and glycopyrrolate 0.004 mg/kg, midazolam 0.02 mg/kg 10 min before induction. The study drugs were premixed to a volume of 15 ml and were presented as coded syringes. The anaesthesiologists who prepared and who administered the medications were different. The patients were blinded to the anaesthesiologists who prepared and who administered the study drugs.

The en operating theatre, anaesthesia was induced with Thiopentone sodium 5 mg/kg and intubated after succinylcholine 2 mg/kg. After confirming the position and fixing the endotracheal tube anaesthesia was maintained with, 66% N2O in 33% oxygen and 1% sevoflurane in 6 l of fresh gas flow and vecuronium 0.08 mg/kg bolus followed by intermittent dose of 0.02 mg/kg. At the end of the surgery all patients were reversed with appropriate dose of neostigmine and glycopyrrolate. Patients were extubated after adequate recovery and then shifted to anaesthesia recovery room.

Vital parameters such as PR, SBP, DBP and MBP were recorded at baseline, after study drug infusion, after induction, immediately and 3, 5, 7 and 10 min after intubation. No surgical intervention was allowed throughout the study period of 10 min.

**RESULTS**

Sample size was calculated based on primary objective of difference of mean arterial blood pressure (MBP) of 20 mmHg (SD 15) immediately after intubation between dexmedetomidine and esmolol group. Considering the type I error and power of the study as 5% and 90% respectively a total of 41 patients in each of the three groups was optimum sample size, expecting a dropout of 5%. All raw data were entered into a predesigned excel spreadsheet and analysed using standard statistical software SPSS-16. Chi square test was used to compare the three groups in terms of gender and one -way Analysis of variance (ANOVA) was used to compare them based on their age and body weight. The baseline parameter and the change of that parameter before and after intubation at different time intervals were compared between the three study groups by Analysis of Variance (ANOVA). Also, the parameters at different time intervals between any two among the three study groups were analysed by unpaired student's t test. A P value of less than 0.05 was considered statistically significant.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Dexmedetomidine</th>
<th>Esmolol</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean ± SD) in years</td>
<td>45.71 ± 9.354</td>
<td>46.19 ± 7.649</td>
<td>45.95 ± 7.774</td>
</tr>
<tr>
<td>Body weight (mean ± SD) in kilograms</td>
<td>57.93 ± 9.295</td>
<td>58.66 ± 8.880</td>
<td>58.71 ± 4.836</td>
</tr>
<tr>
<td>Gender ratio (M:F)</td>
<td>22:20</td>
<td>21:20</td>
<td>20:22</td>
</tr>
</tbody>
</table>

**Table 1. Mean Age, Body Weight and Gender Ratio of the Study**

The table 1 shows the comparison of age, body weight and gender ratio between the three groups. There was statistically no significant difference in these demographic parameters between these three groups (p ≥0.05). Age of the study subjects range from 30 to 60 years. Body weight of the subjects range from 40-75 kg.
Comparison of Pulse Rate (PR)

The observations were recorded at baseline (PRb), after study drug infusion (PRI), after induction (PR2), immediately (PR3) and 3, 5, 7 and 10 minutes after intubation (PR4-7 respectively). The median values (ordinate) of the pulse rate are compared for each treatment group using linear charts for eight different time points (abscissa) – (PRb-PR7). The error bars represent 95% confidence internal to each median data point.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group E (N=41) (Mean ± SD)</th>
<th>Group D (N=42) (Mean ± SD)</th>
<th>t-value</th>
<th>P-value</th>
<th>Significance of difference*</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRb</td>
<td>83.73 ± 8.59</td>
<td>83.45 ± 6.55</td>
<td>-0.127</td>
<td>0.868</td>
<td>Not Significant</td>
</tr>
<tr>
<td>PR1</td>
<td>71.46 ± 7.90</td>
<td>74.43 ± 7.13</td>
<td>1.796</td>
<td>0.076</td>
<td>Not Significant</td>
</tr>
<tr>
<td>PR2</td>
<td>70.02 ± 7.52</td>
<td>71.79 ± 6.71</td>
<td>1.126</td>
<td>0.263</td>
<td>Not Significant</td>
</tr>
<tr>
<td>PR3</td>
<td>85.00 ± 9.19</td>
<td>72.88 ± 6.77</td>
<td>-6.852</td>
<td>&lt;0.001*</td>
<td>Significant</td>
</tr>
<tr>
<td>PR4</td>
<td>88.29 ± 9.49</td>
<td>73.93 ± 6.69</td>
<td>-8.100</td>
<td>&lt;0.001*</td>
<td>Significant</td>
</tr>
<tr>
<td>PR5</td>
<td>85.56 ± 7.92</td>
<td>72.33 ± 6.61</td>
<td>-8.272</td>
<td>&lt;0.001*</td>
<td>Significant</td>
</tr>
<tr>
<td>PR6</td>
<td>80.63 ± 5.89</td>
<td>72.90 ± 6.35</td>
<td>-5.696</td>
<td>&lt;0.001*</td>
<td>Significant</td>
</tr>
<tr>
<td>PR7</td>
<td>78.51 ± 6.05</td>
<td>73.88 ± 5.98</td>
<td>-3.484</td>
<td>0.001*</td>
<td>Significant</td>
</tr>
</tbody>
</table>

Table 2. Comparison of Pulse Rate between Group E & Group D

Table 2. Comparison of means of the pulse rate at different stages between the patients receiving Esmolol (Group E) and the patients receiving Dexmedetomidine (Group D). (* Statistical significance of difference is considered at a confidence interval of 95%).
Figure 3. Comparison of Pulse Rate

**Pulse Rate**

For both Group D & E the mean pulse rate decreased below baseline after study drug infusion. Both the groups were also comparable after study drug infusion and after induction. They developed a significant difference among themselves only on/after intubation. The mean pulse rate of Group D never rose above baseline during the entire period of observation. In group E the highest rise was seen 3 minutes post intubation (5.8% of baseline) and ended below baseline after 7 minutes of intubation.

Esmolol was significantly effective than control in minimizing the pulse rate response though not as effective as dexmedetomidine, in the aforesaid dosage.

**Comparison of Systolic Blood Pressure (SBP)**

Figure 4- The median values (ordinate) of the SBP are compared for each treatment group using linear charts for eight different time points (abscissa) – (PRb-PR7). The error bars represent 95% confidence internal to each median data point.
<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group E (N=41) (Mean ± SD)</th>
<th>Group D (N=42) (Mean ± SD)</th>
<th>t-value</th>
<th>P-value</th>
<th>Significance of difference*</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBPb</td>
<td>135.34 ± 11.79</td>
<td>132.83 ± 9.61</td>
<td>-1.063</td>
<td>.291</td>
<td>Not Significant</td>
</tr>
<tr>
<td>SBP1</td>
<td>121.95 ± 10.97</td>
<td>121.45 ± 7.00</td>
<td>-.248</td>
<td>.805</td>
<td>Not Significant</td>
</tr>
<tr>
<td>SBP2</td>
<td>113.17 ± 11.48</td>
<td>113.69 ± 8.05</td>
<td>.239</td>
<td>.811</td>
<td>Not Significant</td>
</tr>
<tr>
<td>SBP3</td>
<td>128.46 ± 11.66</td>
<td>114.48 ± 7.82</td>
<td>-6.428</td>
<td>&lt;0.001*</td>
<td>Significant</td>
</tr>
<tr>
<td>SBP4</td>
<td>135.46 ± 12.86</td>
<td>116.05 ± 8.26</td>
<td>-8.084</td>
<td>&lt;0.001*</td>
<td>Significant</td>
</tr>
<tr>
<td>SBP5</td>
<td>120.59 ± 11.16</td>
<td>115.90 ± 7.88</td>
<td>2.269</td>
<td>.026*</td>
<td>Significant</td>
</tr>
<tr>
<td>SBP6</td>
<td>118.80 ± 9.48</td>
<td>113.60 ± 7.24</td>
<td>-2.934</td>
<td>.004*</td>
<td>Significant</td>
</tr>
<tr>
<td>SBP7</td>
<td>118.02 ± 6.40</td>
<td>111.38 ± 7.24</td>
<td>-4.502</td>
<td>&lt;0.001*</td>
<td>Significant</td>
</tr>
</tbody>
</table>

Table 3. Comparison of SBP between Group E & Group D

Table 3 shows the comparison of means of the SBP at different stages between the patients receiving Esmolol (Group E) and the patients receiving Dexmedetomidine (Group D). (* Statistical significance of difference is considered at a confidence interval of 95%).

Systolic Blood Pressure (SBP)

![Comparison of SBP: Group E & Group D](image)

![Comparison of SBP: Group C&Group D](image)

![Comparison of SBP: Group C&Group E](image)
Systolic Blood Pressure (SBP)

For both Group D & E the mean SBP decreased below baseline after study drug infusion and further after induction. Both the groups were comparable after study drug infusion and after induction other than at baseline. They developed a significant difference among themselves only on/after intubation. The mean SBP of Group D never rose above baseline during the entire period of observation. The mean SBP of Group E was highest 3 minutes post intubation, and decreased significantly thereafter. The mean SBP in both Group E & D were significantly lower than the SBP values of Group C in all observations other than baseline.

Therefore, although both Esmolol and Dexmedetomidine are effective in neutralizing the surge in SBP, the study here shows that Dexmedetomidine was significantly more effective than Esmolol in attenuating the reflex response to intubation, in the aforesaid dosage for SBP.

### Table 4. Comparison of RPP between Group E & Group D

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group E (N=41) (Mean ± SD)</th>
<th>Group D (N=42) (Mean ± SD)</th>
<th>t-value</th>
<th>P-value</th>
<th>Significance of difference*</th>
</tr>
</thead>
<tbody>
<tr>
<td>RPPb</td>
<td>11257.32 ± 778.61</td>
<td>11101.67 ± 1339.23</td>
<td>-0.156</td>
<td>.876</td>
<td>Not Significant</td>
</tr>
<tr>
<td>RPP1</td>
<td>8646.38 ± 532.37</td>
<td>9039.38 ± 997.53</td>
<td>2.23</td>
<td>.028</td>
<td>Significant</td>
</tr>
<tr>
<td>RPP2</td>
<td>7863.41 ± 597.78</td>
<td>8167.24 ± 993.11</td>
<td>1.684</td>
<td>.096</td>
<td>Not Significant</td>
</tr>
<tr>
<td>RPP3</td>
<td>10848.88 ± 864.83</td>
<td>8353.93 ± 1059.80</td>
<td>11.73</td>
<td>&lt;.001</td>
<td>Significant</td>
</tr>
<tr>
<td>RPP4</td>
<td>11865.59 ± 789.51</td>
<td>8590.69 ± 1104.97</td>
<td>-15.313</td>
<td>&lt;.001</td>
<td>Significant</td>
</tr>
<tr>
<td>RPP5</td>
<td>10257.17 ± 736.75</td>
<td>8394.48 ± 1063.63</td>
<td>-9.296</td>
<td>&lt;.001</td>
<td>Significant</td>
</tr>
<tr>
<td>RPP6</td>
<td>9538.85 ± 523.16</td>
<td>8287.57 ± 958.39</td>
<td>-7.396</td>
<td>&lt;.001</td>
<td>Significant</td>
</tr>
<tr>
<td>RPP7</td>
<td>9237.98 ± 460.44</td>
<td>8232.24 ± 891.97</td>
<td>-6.549</td>
<td>&lt;.001</td>
<td>Significant</td>
</tr>
</tbody>
</table>

* Statistical significance of difference is considered at a confidence interval of 95%.

Figure 6 shows the median values (ordinate) of the RPP are compared for each treatment group using linear charts for eight different time points (abscissa) – (RPPb-RPP7). The error bars represent 95% confidence internal to each median data point.
Rate Pressure Product (RPP)

For both Group D & E the RPP decreased below baseline after study drug infusion and further after induction. Both the groups were comparable after induction other than at baseline. They developed a significant difference among themselves thereafter.

There was a 37% after induction rise in RPP on attempt/during intubation in Group E. The RPP was highest in Group E; 3 minutes post intubation (rise by 5% of baseline). The RPP in Group E decreased thereafter and ended below baseline 5 minutes post intubation.

In contrast the mean RPP of Group D never rose above baseline during the entire period of observation and also the rise was only 2.2% during intubation from post induction values. The mean RPP in both Group E & D were significantly lower than the RPP values of Group C in all observations other than baseline.

Therefore, although both Esmolol and Dexmedetomidine were effective in neutralizing the surge in RPP, the study here shows that Dexmedetomidine was significantly more effective than Esmolol in attenuating the reflex response to intubation, in the aforesaid dosage.

DISCUSSION

The pressor response to laryngoscopy and endotracheal intubation though transient, may be potentially hazardous due to reflex sympathetic discharge caused by pharyngeal stimulation. Transient hypertension and tachycardia are probably of no consequence in healthy individuals but either or both may be hazardous to those with hypertension, myocardial insufficiency and cerebrovascular disease. These changes are the maximal at 1 minute after intubation and last for 5-10 minutes. Prophylaxis include topical lignocaine sprays, deeper planes of anaesthesia by inhalational agents; narcotics, calcium channel blockers, vasodilators such as sodium nitroprusside; nitroglycerin etc, but they have got side effects such as sedation, respiratory depression, hypotension and bradycardia.

The analgesic, sedation, anxiolytic, sympatholytic and blunting of exaggerated haemodynamic responses by administration of dexmedetomidine are being extensively studied and are mainly mediated by the activation of α-2 receptors located in the postsynaptic terminals in the central nervous system (CNS), which causes decreased neuronal activity and augmentation of the vagal activity.

Esmolol is a water soluble, rapid onset, ultra-short-acting, selective beta-adrenergic receptor antagonist with proven efficacy to provide haemodynamic stability during laryngoscopy and tracheal intubation. It has a half-life of nine minutes and without severe side effects. Esmolol seems to be an appropriate selection for attenuating the haemodynamic response to laryngoscopy and tracheal intubation, because of its cardioselectivity, rapid onset of action and short elimination half-life.

Miller et al. reported that 100 mg of single bolus dose of esmolol was effective for controlling the haemodynamic response to tracheal intubation. In another study, Liu et al. who used esmolol infusion to control haemodynamic responses associated with intubation, found significant decreases in PR and SBP, in the esmolol treated patients compared to the placebo group. Oxorn et al. concluded that esmolol in bolus doses of 100 mg and 200 mg affects solely the chronotropic response in a significant manner. Kindler et al. reported that esmolol administration before laryngoscopy was sufficient to control PR after intubation, but it did not affect sbp. Similar to the above studies in our study Esmolol was significantly more effective than normal saline in obtunding the surge in PR and blood pressure.

Scheinin et al. studied that 0.6 μg/kg dexmedetomidine decreased, but not totally suppressed, the haemodynamic response to tracheal intubation in healthy individuals. Keniya et al. stated that the pre-treatment with dexmedetomidine 1.0 μg/kg attenuated, but not totally obtund the cardiovascular response to tracheal intubation after induction of anaesthesia. In this study, the percentage rise in PR and other haemodynamic parameters between induction and post intubation were minimal in the dexmedetomidine group compared to Control and Esmolol.

Bradycardia and hypotension have been reported in some studies pertaining to the effect of dexmedetomidine administration. But in our study, neither bradycardia nor hypotension was observed in the patients. Dexmedetomidine has been used IV in doses ranging from 0.1 to 10 μg/kg/h but higher doses have been associated with a significant increase in incidence of bradycardia and hypotension. Rapid administration of dexmedetomidine might produce tachycardia, bradycardia and hypertension followed by hypotension. We administered dexmedetomidine, 1.0 μg/kg slowly, over 10 mins.

Yallapragada SV et al. studied on the efficacy of dexmedetomidine with that of esmolol in attenuating...
laryngoscopic and intubation response after rapid sequence induction. In their study they concluded that dexmedetomidine is superior to esmolol in attenuating the haemodynamic response to laryngoscopy and tracheal intubation. Subsequently, Reddy SV et al.,22 again studied dexmedetomidine versus esmolol to attenuate the haemodynamic response. Similar to this study, they found that the suppression in cardiovascular responses was greater with dexmedetomidine 1.0 μg/kg than that resulted from infusion of esmolol 2.0 mg/kg.

Monitoring of PR and ECG has shown no evidence of myocardial insult in any of the patient in any group in our study.

In our study infusion of dexmedetomidine 1.0 μg/kg prior to induction of anaesthesia suppressed the haemodynamic response to tracheal intubation in normotensive patients. This suppression in cardiovascular responses was found to be greater with dexmedetomidine infusion than with esmolol. In the present study the haemodynamic response to laryngoscopy and intubation were studied for a period of 10 minutes as this is the average period for which haemodynamic changes are believed to last. It was found that with this dose dexmedetomidine had better control over PR, SBP, DBP and MBP. On comparison between the two groups, the heart rate, blood pressure and rate pressure product was better controlled with dexmedetomidine than esmolol.

**CONCLUSION**

In this study, infusion of dexmedetomidine 1.0 μg/kg prior to induction of anaesthesia suppressed the haemodynamic response to tracheal intubation in normotensive patients. This suppression in cardiovascular responses was found to be greater with dexmedetomidine than that resulted from infusion of esmolol 2.0 mg/kg.

**REFERENCES**


