Attenuation of hemodynamic responses to endotracheal intubation: Comparison of Clonidine, Esmolol, Lignocaine and Placebo

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Abstract—This prospective randomized study was designed to evaluate the efficacy of intravenous clonidine, esmolol, lidocaine and placebo in suppressing the hemodynamic changes during endotracheal intubation. A total of one hundred and twenty patients belonging to ASA 1 and 2 were randomly divided into four groups. Patients in group A received clonidine 2 mcg/kg, in group B received Esmolol 1mg/kg, in group C received lidocaine 1.5 mg/kg and in group D received normal saline two minutes prior to induction. Patients in group A showed the maximum attenuation of both heart rate and blood pressure following endotracheal intubation. Patients in group B showed a significant attenuation of heart rate as effective as group A but attenuation of blood pressure (though effective than groups C and D) was not as effective as group A. Patients in group C showed no significant difference from group P in attenuating circulatory responses and both lignocaine and placebo were ineffective. All the patients were recovered well from anesthesia and none of them developed complications like severe Bradycardia (HR< 50/min) or profound hypotension (SBP<80mmHg).
Keywords---clonidine, hemodynamic response, lignocaine, neurosurgery

Introduction

The induction of anaesthesia in cases of laryngoscopy, tracheal intubation and surgical stimulation often evoke cardiovascular responses characterised by alteration in systemic arterial blood pressure, heart rate and cardiac rhythm\(^1\). Its response following laryngoscopy and intubation take at the peaks in 1.2 minutes and it return to baseline within 5 to 10 minutes\(^2\). There are various systemic as well as topical agents have been used for reducing hemodynamic reposes while performing laryngoscopy. The commonest strategies adopted are narcotics, calcium channel blockers, β-blockers, lignocaine, clonidine. Since clonidine, lignocaine and esmolol have been known to dull sympathetic responses to intubation, their efficacy can be compared with control (placebo)\(^3\).

Clonidine

It is derivate of imidazoline and act as alpha adrenergic with antihypertensive activity. It binds with and stimulates central alpha 2 adrenergic receptors they reduce the amount of norepinephrine release and it decreasing sympathetic outflow of heart kidney and peripheral region. Due to reduction in sympathetic flow, it will decrease blood pressure. It also bind with imidazoline receptor subtype 1 it also help in lowering the blood pressure\(^4\).

Esmolol

Esmolol act as the rapid onset which have a half-life of 9 min β-1 adrenergic receptor antagonist and proved to be an efficient agent to provide hemodynamic stability during laryngoscopy and intubation\(^5\).

Lidocaine

It is a local anaesthetic which is a type amino amide. It can also use to treat ventricular tachycardia. When it is used as local anaesthesia or given a nerve block, it is working within several minutes and it lasts for half an hour to 3 hours. It can also apply direct on skin or mucosa membranes for numbs the local area. It can also use with mixed with a small amount of adrenaline which provide a long local effect and it decrease bleeding\(^6\).

Placebo

It's is sugar like pills inert injections by mixing with saline for injecting purpose and use in sham surgery, or in other procedures. It is also used for pain relieving\(^7\).
Materials And Methods

The present study was carried out on 100 subjects in GSVM medical college during July 2021 to March 2022 Department of Anesthesiology. Patients belonging to age group 15 to 60 years of both the sexes were included. It is a prospective randomized controlled study.

Inclusion criteria

- Patients with airway with modified mallam patti grade class1 or 2
- Age group 15 to 60 years of both sexes.

Exclusion criteria

- Patients with full stomach
- Patients posted for emergency surgery
- Patients with difficult airway

Materials

Following Material Are Needed Injection Thiopentone 2.5% Solution, Injection Suxamethonium, Injection Glycopyrrolate, Injection Fentanyl, Injection Esmolol Hydrochloride (Esocard) 100mg/10ml Vial, Injection Lignocaine 2% (Preservative Free), Injection Clonidine 0.15mg/ Ml Ampoule, Normal Saline, Disposable 10 Ml Syringe, Laryngoscope with Blades 3 and 4, Endotracheal Tubes of Various Sizes.

Method

Preanaesthetic Preparations

All the patients were admitted and they underwent routine investigations like: Hemogram, Blood urea and sugar, Serum creatinine and electrolytes, Chest X-ray, Electrocardiogram. Other investigations were obtained on the basis of the condition of the patient.

Anaesthetic protocol

Pre-operative visit was done to allay anxiety and good rapport was established with the patients. All the patients were given pre operative night sedation with tab. diazepam 10mg orally.

Interventions

Induction of anaesthesia was standardised for all patients. Monitors used were NIBP, ECG, Etco2 and pulse oximetry.
Method

All 100 patients were divided into 4 group according to drug given to these patients.

- Group A (Clonidine 2 mcg/kg) – 25 patients were given intravenous clonidine 2mcg/kg2minutesbeforeinduction.
- Group B (Esmolol 1mg/kg) -- 25 patients were given intravenous clonidine 1mg/kg2minutesbeforeinduction.
- Group C (lignocaine 1.5mg/kg) – 25 patients were given intravenous lignocaine1.5mg/kg 2minutes before induction
- Group D (Placebo- normal saline) – 25 patients were given normal saline 2minutes before induction.

Premedication

Patients are shifted to OT table. The following parameter were recorded Blood pressure, Pulse rate Spo2. There were premeditated with injected glycopyrollate4 mcg/kg. Body weight intravenously and injection fentanyl 2mcg/kg body weight intravenously.

Statistical Analysis

All the parameters of two groups were analysed for mean and standard aviation. The results were expressed as Mean ± standard deviation. Data was analysed by statistical software SPSS Version 22.0.

Observation and Results

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>30.25±2.15</td>
<td>31.20±6.25</td>
<td>34.25±3.25</td>
<td>32.21±5.41</td>
</tr>
<tr>
<td>Sex</td>
<td>Male 15</td>
<td>10</td>
<td>12</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>Female 10</td>
<td>15</td>
<td>17</td>
<td>13</td>
</tr>
<tr>
<td>Weight (kgs)</td>
<td>38.45±5.12</td>
<td>40.45±2.35</td>
<td>45.25±6.14</td>
<td>48.45±6.25</td>
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<tr>
<td>Basal heart rate</td>
<td>90.67±16.68</td>
<td>97.20±14.85</td>
<td>89.23±15.88</td>
<td>87.60±7.99</td>
</tr>
<tr>
<td>Basal systolic blood pressure (mmHg)</td>
<td>122.00±8.45</td>
<td>124.80±10.77</td>
<td>120.35±4.25</td>
<td>120.25±4.24</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>84.15±4.5</td>
<td>82.45</td>
<td>80.14±2.25</td>
<td>78.45±1.14</td>
</tr>
<tr>
<td>Basal mean arterial pressure (mmHg)</td>
<td>95.73±4.52</td>
<td>94.47±6.69</td>
<td>94.70±5.41</td>
<td>91.36±6.25</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group</th>
<th>Group-A</th>
<th>Group-B</th>
<th>Group-C</th>
<th>Group-D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>90.67±16.68</td>
<td>97.20±14.85</td>
<td>89.23±15.88</td>
<td>87.60±7.99</td>
</tr>
</tbody>
</table>
Table 3
Showing the mean systolic blood pressure changes in all group as showing in the table give below

<table>
<thead>
<tr>
<th>Group</th>
<th>Group-A</th>
<th>Group-B</th>
<th>Group-C</th>
<th>Group-D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>122.00±8.45</td>
<td>122.80±8.77</td>
<td>120.14±4.04</td>
<td>120.45±6.45</td>
</tr>
<tr>
<td>After premedication</td>
<td>120.66±4.56</td>
<td>120.16±10.25</td>
<td>118.66±8.45</td>
<td>121.10±4.65</td>
</tr>
<tr>
<td>After study drug</td>
<td>124.04±4.65</td>
<td>119.50±14.5</td>
<td>120.64±4.78</td>
<td>121.10±12.18</td>
</tr>
<tr>
<td>At laryngoscopy &amp; intubation</td>
<td>120.27±16.21</td>
<td>129.30±15.06</td>
<td>138.80±16.90</td>
<td>146.33±15.91</td>
</tr>
<tr>
<td>1min</td>
<td>114.60±4.25</td>
<td>120.40±13.10</td>
<td>125.77±19.01</td>
<td>131.73±14.87</td>
</tr>
<tr>
<td>3min</td>
<td>107.47±14.55</td>
<td>114.70±9.91</td>
<td>115.17±15.19</td>
<td>123.17±11.41</td>
</tr>
<tr>
<td>5min</td>
<td>100.80±10.63</td>
<td>110.20±8.84</td>
<td>111.17±10.94</td>
<td>119.50±10.22</td>
</tr>
</tbody>
</table>

Table 4
Showing The Mean Diastolic Pressure Changes In All 4 Group Showing As The Given Diastolic Pressure Changes (mmHg)

<table>
<thead>
<tr>
<th>Group</th>
<th>Group-A</th>
<th>Group-B</th>
<th>Group-C</th>
<th>Group-D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>83.13±7.66</td>
<td>82.20±6.43</td>
<td>80.40±6.64</td>
<td>78.83±6.79</td>
</tr>
<tr>
<td>After premedication</td>
<td>81.45±4.35</td>
<td>79.43±10.43</td>
<td>78.77±6.77</td>
<td>81.43±20.26</td>
</tr>
<tr>
<td>After study drug</td>
<td>80.75±5.29</td>
<td>79.10±10.73</td>
<td>74.10±6.40</td>
<td>80.33±9.69</td>
</tr>
<tr>
<td>After induction</td>
<td>72.73±9.34</td>
<td>77.17±4.79</td>
<td>77.00±10.62</td>
<td>76.50±8.89</td>
</tr>
<tr>
<td>At Laryngoscopy &amp; intubation</td>
<td>84.73±13.83</td>
<td>92.00±9.66</td>
<td>100.27±15.50</td>
<td>95.90±11.57</td>
</tr>
<tr>
<td>1min</td>
<td>76.57±10.44</td>
<td>84.40±2.05</td>
<td>74.80±11.99</td>
<td>80.71±4.59</td>
</tr>
<tr>
<td>3min</td>
<td>69.53±10.13</td>
<td>76.4±5.05</td>
<td>76.80±10.99</td>
<td>79.40±4.94</td>
</tr>
<tr>
<td>5min</td>
<td>65.45±8.458</td>
<td>77.07±1.12</td>
<td>74.03±12.45</td>
<td>74.30±4.5</td>
</tr>
</tbody>
</table>

Discussion

In our current study we compare, the intravenous Clonidine (2mcg/kg), lidocaine (1.5mg/kg), Esmolol (1mg/kg) and placebo was done in attenuating circulatory responses to endotracheal intubation.
**Changes in heart rate**

The mean baseline heart rate of all group didn’t showing any statically significant as because there p value was 0.5 at the same time induction was no significant difference in mean heart rate among the four groups there P value was 0.07. after the endotracheal intubation completed there was a little rise in heart rate showing in all 4 group. the lowest raise value show in group A while compare our study with Vucevic et al six in which study the observed that efficacy of Esmolol and Carabineetal³ which observed the efficacy of Clonidine. In our study we observed that the lidocaine attenuation rise in heart rate is inefficiency while comparing our study with Singh et al.¹⁰ Van der beghetal.¹¹ the heart rate in group A stayed significantly lower than all other groups even at 5 minutes after intubation (p value = 0.001). The heart rate in group A stayed significantly lower than all other groups even at 5 minutes after intubation (p value = 0.001), but in group B it stayed significantly lower than group L and group P till 3 minutes after intubation. After this there was no significant difference among group B C and D which can be explained by the short duration of action of Esmolol. Thus it is inferred that though Clonidine and Esmolol are equally.

**Changes In Systolic Blood Pressure**

Bases line systolic pressure don’t show any baseline difference due to its p value (p = 0.137) in all 4 group. Even after the induction there was no difference in systolic blood pressure of all the groups (p = 0.650). After the intubation there was showing some sudden increase in it all 4 group. But in case of A and B group showing there was sudden increase in Systolic pressure and in group C and D differed in attenuation of pressor response to intubation from group A and Group B statistical significance (p value 0.01). Group C had at least rise in systolic blood pressure which when compared with group E was statistically significant (p-value 0.007). But There was no difference between group C and group D (p value 0.231) Even after 5 minutes, group A differed from all other groups showing a sustained attenuation of pressor response. At 3 minutes and 5 minutes, but there were no statistically significant differences in systolic blood pressure among groups B, C and D (p value 0.120). Probably due to shorter duration of action group B could not show much difference from group C and group D at 3 minutes and 5 minutes interval. Attenuation of pressor responses by group E in our study matches with studies conducted by Zulandaro MP et al.¹² in 2001 which show Clonidine was more effective than Esmolol in attenuating press corresponded to endotracheal intubation.

**Changes in Diastolic and mean arterial pressure**

There was no significant changes show in base line diastolic blood pressure among the four groups (p = 0.87) and also in baseline an arterial pressure (p = 0.073). During induction of anesthesia, the groups did not show any significant difference in diastolic blood pressure or any change in mean arterial pressure. After intubation, there was a sudden increase showing in diastolic and mean arterial pressures in all the of 4 group. Group A and group differed from groups C and D with statistical significance in rise in diastolic blood pressure (p value 0.001) as well as in rise in mean arterial pressure (p value 0.001). Group A had least rise
in diastolic blood pressure and mean arterial pressure which when compared with group B were statistically significant (p value being 0.006 and 0.009 respectively). There was no difference between group C and group D both in the diastolic blood pressure (p value 0.462) and mean arterial pressure (p= 0.312). Even after 5 minutes, group C differed from all other groups showing a sustained attenuation of pressor response. At 3 minutes and 5 minutes, there were no statistically significant difference in both diastolic blood pressure and mean arterial pressure among groups B, C and D (p value 0.223 and 0.412 respectively). Again probably due to shorter duration of action, group B did not show much difference from group C and group D at 3 minutes and 5 minutes interval. Attenuation of press or response by group B in our study mismatch with the difference between group C and group E matches with study conducted by Zulandaro MP et al 12 in 2001 which proved Clonidine was more effective than Esmolol in attenuating press or response to endotracheal intubation.

**Conclusion**

From our current study we found that the hemodynamic changes associated with endotracheal intubation can be safely and effectively obtunded by using intravenous Clonidine prior to induction of anaesthesia. In our study we found that the Clonidine is found to be effective in blunting hemodynamic responses to laryngoscopy and in intubation, as followed by Esmolol. Lignocaine and placebo were ineffective in attenuating these responses to laryngoscopy and endotracheal intubation. Much more study required for better outcome

**References**

11. Vanden Berg A. A., Savva D., Honjol N. M. Attenuation of the haemodynamic responses to noxious stimuli in patients undergoing cataract surgery. A comparison of magnesium sulphate, esmolol, and