**ORIGINAL ARTICLE**

**Effect of Intravenous Nalbuphine on Haemodynamic Response to Laryngoscopy and Intubation**

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**ABSTRACT**

**BACKGROUND:** The aim of the study was to evaluate the effect of intravenous Nalbuphine in preventing rise in pulse rate, systolic blood pressure, diastolic blood pressure & mean arterial pressure i.e. haemodynamic response to laryngoscopy and intubation & to study complications if any. **MATERIALS & METHODS:** A prospective randomised placebo controlled study was conducted in 60 ASA I & II patients undergoing elective laparoscopic surgery. They were divided into two groups of 30 each. Group N received inj. Nalbuphine 0.2 mg/kg & Group NS received inj. Normal saline. Pulse rate, systolic blood pressure, diastolic blood pressure & mean arterial pressure were taken at regular intervals after intubation till 15 minutes and compared with baseline. **RESULTS:** Both the groups were demographically comparable. There was significant rise in pulse rate (34.17%) in Group NS at 1 minute after intubation with baseline as compared to Group N (18.75%). Mean arterial pressure showed rise of 10.98% in Group NS & 4.39% in Group N. Systolic blood pressure & diastolic blood pressure followed the same pattern as mean arterial pressure. Pulse rate , systolic blood pressure, diastolic blood pressure & mean arterial pressure then gradually decreased in both the groups but remained higher in Group NS at any point of time. **CONCLUSION:** Nalbuphine 0.2mg/kg prevented marked rise in pulse rate & mean arterial pressure associated with laryngoscopy and intubation.

**Keywords:** Nalbuphine, Endotracheal intubation, Haemodynamic response.

**INTRODUCTION**

Since its first demonstration in 1846, anaesthesia has undergone changes in leaps & bounds. Laryngoscopy followed by tracheal intubation is one of such important milestone in the history of anaesthesia. Haemodynamic changes have attained attraction since 1940 by Reid & Brace. Laryngoscopy & intubation serves as noxious stimuli leading to rise in serum catecholamine levels. Rise in sympathetic hormones during intubation is associated with complications in high risk patients which can increase morbidity & mortality. Many pharmacological interventions have been used in past to attenuate this response e.g. halothane, lignocaine, fentanyl, esmolol, propofol. Traditionally opioids belong to class “mu” agonist have been associated with side effects like respiratory depression, undesirable sedation, nausea, vomiting, dependence which were often troublesome. Nalbuphine a synthetic opioid derivative is a mixed kappa agonist mu antagonist essentially resembles Dynorphine B. It has cardiovascular stability, less respiratory depression, longer duration of analgesia & potential safety in overdosage i.e. ceiling effect in respiratory depression. Nalbuphine not only influence haemodynamic response but also provides haemodynamic stability. Nalbuphine could be promising in this setting.

**MATERIALS & METHODS**

After local research ethics committee approval & obtaining an informed consent, 60 patients were included in a randomized prospective placebo controlled comparative clinical study for elective laparoscopic surgery from January 2011 to January 2012 in S.S.G.H. Vadodara.

**Inclusion criteria:**
1. Adult patient of either gender between 15 to 50 years of age.
2. Patients undergoing elective laparoscopic surgery.
3. Patients of ASA status I & II.

**Exclusion criteria:**
1. Unwilling patient.
2. History of allergy to opioids or opioid abuse.
3. Patients on opioids, phenothiazines, tranquilizers, sedatives, hypnotics or any other CNS depressants.

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4. Patient with impaired respiration (bronchial asthma, COPD, uraemia)
6. Anticipated difficult intubations
7. Pregnant woman

**Explanation & consent:** All the selected patients were explained about the purpose, procedure & side effects of the study. After this a written & informed consent was taken. Tab, ranitidine 150 mg & Tab, diazepam 10 mg was given to all patients the night before the surgery.

**Group of patients:** Patients were randomly allocated into 2 groups of 30 patients each.

- **Group N (n=30):** Patients received inj. Nalbuphine 0.2 mg/kg IV 5 minutes before induction.
- **Group NS (n=30):** Patients received inj. Normal saline equal volume IV 5 minutes before induction.

**Anaesthetic procedure:**

- **Premedication:** Inj. glycopylorrate 0.2 mg & ing. Diclofenac sodium 75 mg IM was given 30 minutes before the induction to all patients.
- **Preinduction procedure:** After taking the baseline pulse rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), ECG, EtCO2 & SPO2, a wide bore IV line was secured & infusion of DNS was started.
- **Induction:** Five minutes after giving the study drug, patient preoxygenated with 100% oxygen and then was induced with inj.thiopentone sodium 4-7 mg/kg (2.5%) till loss of eyelid reflex followed by inj.succinylcholine 1.5 mg/kg & then endotracheal intubation performed within 60 seconds.
- **Observations:** Pulse rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, EtCO2 & SPO2 were observed at baseline(T1), 1(T2), 3(T3), 5(T4), 7(T5), 10(T6) & 15(T7) minute after intubation.
- **Maintenance:** Anaesthesia was maintained with 02:N20 (50:50), 1% isoflurane & inj.vacuronium bromide 0.1 mg/kg as loading dose then 0.025 mg/kg supplemented SOS as muscle relaxant in both the groups.
- **Reversal:** After completion of surgery reversal was achieved with inj.glycopylorrate 10 ug/kg & inj.neostigmine 50ug/kg. Patient then extubated after fulfilling extubation criteria.

**Statistical analysis:**

Using Med cal-C software and taking an alpha error of 0.01 and beta error of 0.01 for the parameter duration of effective analgesia, the minimum sample size required to conduct the study would be 22 per group. In order to compensate for the greater variability, 30 patients were included in each group.

The results of the study were tabulated & statistically compared.

Chi square test was used for qualitative data (ASA grade, motor grade).

For rest of the quantitative data, student t test was used(unpaired)

The **p-value** was considered significant as shown below:

1. **p > 0.05** not significant
2. **p < 0.05** significant
3. **p < 0.001** highly significant

**RESULTS**

The 2 groups are comparable to each other with respect to age, height, weight, ASA physical status & duration of surgery. There was no significant difference in baseline pulse rate & baseline SBP, DBP & MAP between group N & Group NS at T1.

**APulse rate:**

- **Group N :** Baseline pulse rate was 79.53±10.44 beats per minutes(T1). The maximum rise was 95±8.53 beats per minute i.e. 18.75% wise rise above the baseline level at 1 minute after intubation(T2). While in **Group NS:** baseline pulse rate was 78.9±11.96 beats per minute (T1), the maximum rise was 105.57±11.24 (p<0.001) beats per minute i.e. 34.17% wise rise above the baseline at 1 minute after intubation (T2).

**Table: 1 changes in the mean pulse rate (b.m.p.)**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group N</th>
<th>Intra-group P value</th>
<th>Group NS</th>
<th>Intra-group P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline T1</td>
<td>79.53±10.44</td>
<td>&gt;0.05</td>
<td>78.9±11.96</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>After Intubation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 min T2</td>
<td>95±8.53</td>
<td>&lt;0.001</td>
<td>105.57±11.24</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>3 min T3</td>
<td>94.4±10.96</td>
<td>&lt;0.001</td>
<td>105.57±8.62</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>5 min T4</td>
<td>93.66±6.70</td>
<td>&lt;0.001</td>
<td>98.8±6.62</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>7 min T5</td>
<td>83.66±6.13</td>
<td>&gt;0.05</td>
<td>104.63±6.83</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>10 min T6</td>
<td>82.83±8.79</td>
<td>&gt;0.05</td>
<td>95.4±8.56</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>15 min T7</td>
<td>81.33±9.99</td>
<td>&gt;0.05</td>
<td>97.2±8.51</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Acute effects of nalbuphine on haemodynamic response to laryngoscopy & intubation

Data are expressed as mean±standard deviation.

### Table: 2 changes in the mean pulse rate (b.p.m.)

<table>
<thead>
<tr>
<th>Time</th>
<th>Group n</th>
<th>% wise rise</th>
<th>Group ns</th>
<th>% wise rise</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1 (baseline)</td>
<td>79.3±10.4</td>
<td>18.7±5.6</td>
<td>5.3±1.9</td>
<td>34.17</td>
</tr>
<tr>
<td>T2 (after intubation at 1 min)</td>
<td>95.8±5.3</td>
<td>18.7±5.6</td>
<td>5.3±1.9</td>
<td>34.17</td>
</tr>
<tr>
<td>T3 (after intubation at 3 min)</td>
<td>94.2±10.9</td>
<td>17.5</td>
<td>5.3±1.9</td>
<td>34.17</td>
</tr>
<tr>
<td>T4 (after intubation at 5 min)</td>
<td>93.6±6.7</td>
<td>16.2±5.6</td>
<td>5.3±1.9</td>
<td>22.5</td>
</tr>
<tr>
<td>T5 (after intubation at 7 min)</td>
<td>83.6±6.13</td>
<td>5.0</td>
<td>5.3±1.9</td>
<td>31.25</td>
</tr>
<tr>
<td>T6 (after intubation at 10 min)</td>
<td>82.8±8.79</td>
<td>3.75</td>
<td>5.3±1.9</td>
<td>18.75</td>
</tr>
<tr>
<td>T7 (after intubation at 15 min)</td>
<td>81.5±9.99</td>
<td>2.5</td>
<td>5.3±1.9</td>
<td>21.25</td>
</tr>
</tbody>
</table>

Data are expressed as mean±standard deviation.

### Table: 3 changes in mean arterial pressure (mm of hg)

<table>
<thead>
<tr>
<th>Parameters (Before Drug )</th>
<th>Group N</th>
<th>Intra-group P value</th>
<th>Group NS</th>
<th>Intra-group Pvalue</th>
<th>Inter-group Pvalue</th>
</tr>
</thead>
<tbody>
<tr>
<td>After Intubation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>T1</td>
<td>90.76±6.85</td>
<td>&gt;0.05[NS]</td>
<td>90.76±5.36</td>
<td>&gt;0.05[NS]</td>
</tr>
<tr>
<td>1 min T2</td>
<td>95.2±6.37</td>
<td>&lt;0.001</td>
<td>101.7±4.8</td>
<td>&lt;0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>3 min T3</td>
<td>92.2±6.74</td>
<td>&lt;0.05</td>
<td>98.9±4.75</td>
<td>&lt;0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>5 min T4</td>
<td>91.6±7.91</td>
<td>&lt;0.05</td>
<td>98.0±5.4</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>7 min T5</td>
<td>91.9±8.04</td>
<td>&lt;0.05</td>
<td>100.6±4.37</td>
<td>&lt;0.05</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>10 min T6</td>
<td>91.6±8.79</td>
<td>&lt;0.05</td>
<td>96.5±5.51</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>15 min T7</td>
<td>90.6±7.9</td>
<td>&lt;0.05</td>
<td>96.9±5.62</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Data are expressed as mean±standard deviation.

### Table: 4 changes in mean arterial pressure (mm of hg)

<table>
<thead>
<tr>
<th>Time</th>
<th>Group N</th>
<th>% Wise Rise</th>
<th>Group Ns</th>
<th>% Wise Rise</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1 (baseline)</td>
<td>90.76±6.85</td>
<td>4.39</td>
<td>101.7±4.8</td>
<td>10.98</td>
</tr>
<tr>
<td>T2 (after intubation at 1 min)</td>
<td>95.2±6.37</td>
<td>2.19</td>
<td>98.9±4.75</td>
<td>8.79</td>
</tr>
<tr>
<td>T3 (after intubation at 3 min)</td>
<td>92.2±6.74</td>
<td>1.90</td>
<td>98.0±5.4</td>
<td>7.69</td>
</tr>
<tr>
<td>T4 (after intubation at 5 min)</td>
<td>91.6±7.91</td>
<td>2.19</td>
<td>100.6±4.37</td>
<td>10.98</td>
</tr>
<tr>
<td>T5 (after intubation at 7 min)</td>
<td>91.9±8.04</td>
<td>2.19</td>
<td>96.5±5.51</td>
<td>6.59</td>
</tr>
<tr>
<td>T6 (after intubation at 10 min)</td>
<td>91.6±6.79</td>
<td>2.19</td>
<td>96.9±5.62</td>
<td>6.59</td>
</tr>
<tr>
<td>T7 (after intubation at 15 min)</td>
<td>90.6±7.9</td>
<td>Nil</td>
<td>96.9±5.62</td>
<td>6.59</td>
</tr>
</tbody>
</table>

Data are expressed as mean±standard deviation.

MAP then gradually decreased in both the groups but it remained higher in group NS at any point of time (table 3,4).

### C] SBP, DBP followed the same pattern as MAP.

### D] There were no statistically significant changes in SP02, EtCO2 in both the groups.

### E] In group NS 2 patients had hypertension. No other complications noted in any other groups.

### DISCUSSION

Various drugs like opioids, vasodilators, sedative, alpha blockers have been tried to attenuate the haemodynamic response to laryngoscopy & intubation but each has its own limitations. 6,7 An ideal drug should have rapid onset of action, safe, cost effective, administrable, relatively short duration of action.

Pure opioid agonists like morphine & pethidine carry the risk of dose related respiratory & cardiovascular depression, nausea & vomiting. Nalbuphine is a kappa agonist with cardiovascular stability, lesser potential for respiratory depression, onset of action between 2 -3 minutes, duration of action of action of 3 to 6 hours with minimal side effects in dose of 0.2 mg/kg. F.n.minal (2003), Muhamad-ahsan-ul-haq (2005) & Priti chawda (2010) studied nalbuphine 0.2 mg/kg with placebo. They noticed Nalbuphine when given 3 to 5 minutes before induction prevented haemodynamic response to laryngoscopy and endotracheal intubation while significant rise in heart rate & MAP were noted after intubation from baseline in placebo group. Considering all these facts we decided to carry out our study of effect of inj.Nalbuphine 0.2 mg/kg on haemodynamic response to laryngoscopy & intubation.

In group N patients received nalbuphine 0.2 mg/kg while normal saline was given in group NS as placebo (total volume being 5 ml)5 minutes before induction. Nalbuphine attenuated the rise of mean pulse rate SBP, DBP& MAP following laryngoscopy & intubation. This could be explained by it resemblance to Dynorphine B i.e. it decreases release of nor epinephrine, decreased cardiac adrenergic stimulation & sensitivity of heart to

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Data are expressed as mean±standard deviation.
Pulse rate then gradually decreased in both the groups but it remained higher in group NS at any point of time.(table1, 2)

### B] Mean arterial pressure

**Group N**: Baseline MAP was 90.76±6.85 mm of hg(T1), the maximum rise was 95.2±6.37 mm of hg i.e. 4.39% wise rise above the baseline level at 1 minute after intubation(T2).

While in **Group NS**: Baseline MAP was 90.76±5.36 mm oh hg(T1), the maximum rise was 101.7±4.8 mm of hg(p<0.001) i.e. 10.98% wise rise above the baseline level at 1 minute after intubation(T2) (table 3,4)
epinephrine. Chestnut & F.N.Minal studied the effect of nalbuphine on haemodynamic response & noticed excellent control over haemodynamic response but noticed nausea & vomiting at end of surgery. We did not notice nausea & vomiting or any other complications in our patients.

CONCLUSION
In conclusion, Nalbuphine when given IV in the dose of 0.2 mg/kg 5 minutes before induction of anaesthesia prevents marked rise in pulse rate, SBP, DBP& MAP following laryngoscopy & intubation without any serious side effects.

Source of support: Nil

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Conflicts of interest-Non declared

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