A Comparative Study of Analgesic Potential of Nalbuphine Versus Fentanyl during General Anaesthesia

Hari Prasad K1, Ram Kumar P.A1, Rajagokilam R2, Vinithra Varadarajan3

ABSTRACT

Introduction: Intubation during general anaesthesia is associated with increase in heart rate and mean blood pressure which are deleterious for patients especially with hypertension and ischaemic heart disease. This study was conducted to compare analgesic potential and hemodynamic response of Nalbuphine and fentanyl during general anaesthesia.

Material and methods: A total of 40 adult inpatients scheduled for general anaesthesia for various surgeries with ASA I and II physical status were randomly assigned to two groups, Group A (Nalbuphine) and Group B (Fentanyl). Group A received 0.2mg/kg Nalbuphine and Group B received 2µg/kg fentanyl. Five minutes later general anaesthesia was administered. Respiratory rate, heart rate, ECG, oxyhemoglobin saturation and Non Invasive blood pressure were monitored at frequent interval during pre, intra and post operative period. Post operative pain score and hemodynamic intubation response were also recorded.

Result: Both groups had increased heart rate during intubation but that was statistically insignificant (P>0.05). Group A had significant rise in SBP and DBP during intubation compared to Group B. Maximum rise in SBP Group A and in Group B was 11.07% and 3.9% respectively. Time to 1st dose analgesic top up was significantly shorter in group B than in Group A.

Conclusion: Nalbuphine provides good hemodynamic and excellent post operative analgesia which is comparable to fentanyl but at a less frequent dosing thus decreasing the overall opioid requirement for general anaesthesia.

Keywords: Nalbuphine Versus Fentanyl

INTRODUCTION

Laryngoscopy and orotracheal intubation is associated with rise in concentrations of serum catecholamine levels like adrenaline, noradrenaline and dopamine. Rise in these hormones in high risk patients during laryngoscopy and endotracheal intubation is associated with frequent complications.6 Many pharmacological agents have been frequently used as adjuncts to decrease these effects.4,9 Potent analgesics with lesser side effects and longer duration of action are a must to decrease such stress responses and further complications while induction and intubation.3,5,6 Fentanyl was introduced in 1960’s when morphine and pethidine were used for analgesia during surgeries. Due to its short duration of action, minimal respiratory depression and cardiac stability fentanyl gained a good popularity. Since then fentanyl has become a gold standard in analgesia replacing morphine and pethidine.7

Nalbuphine is a opioid agonist-antagonist analgesic which is chemically related to opioid antagonist’s naloxone, naltrexone and opioid analgesic oxymorphone. Nalbuphine is a potent analgesic. It is an agonist at µ receptor and acts as antagonist at µ receptor. Nalbuphine has fewer side effects like tachycardia, hypertension, increased PAP when compared to butorphanol and pentazocine.10 Ultrashort acting beta-blocker (esmolol) and opioids (remifentanil) are used for blunting cardiovascular changes induced by tracheal intubation11. Nalbuphine is now commercially available in India. It can be obtained from pharmacy without an opioid license. It is widely used as an adjunct or as a sole analgesic during general anaesthesia.

Study aimed to study the effect of intra venous nalbuphine 0.2mg/kg and intravenous fentanyl 2µ/kg pre, intra and post operative periods during general anaesthesia and to compare the post operative side effects and complications with the post-operative pain score.

MATERIAL AND METHODS

After informed consent we studied 40 patients12 posted for surgery under general anaesthesia between the age group of 20 to 50. We conducted the study in a period of 6 months. Data was collected and analysed. Two groups of patients were made group A (Nalbuphine) and group B (fentanyl).

Group A – Inj. Nalbuphine 0.2mg/kg iv
Group B – Inj. Fentanyl 2µg/kg iv

ASA I and II patients were only included in the study.

Exclusion criteria

• Patient refusal
• ASA III or above
• Emergency surgeries and poly trauma
• All obstetric and Pediatric surgeries
• Known allergy to the trial drugs
• Patient on any medication that will potentiate or change the action of the trial drugs
• Surgeries longer than 1 hour
• Patients with airway difficulties

A careful pre-anesthetic evaluation was done noting the medical history, a thorough systemic examination was carried out to rule out any systemic disorders. Investigations were done as needed. All patients were kept nil orally for more than 6 hours before surgery. All patients received premedication (glycopyrrolate 0.2mg, ranitidine 50mg, and ondansetron 4mg intravenous)

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Table-1: Changes in mean systolic blood pressure between Group A and Group B

<table>
<thead>
<tr>
<th>Time</th>
<th>Group A (mm of hg) Mean ± SD</th>
<th>% of change from base line</th>
<th>Group B (mm of hg) Mean ± SD</th>
<th>% of change from base line</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base line</td>
<td>123.13</td>
<td></td>
<td>125.58</td>
<td></td>
</tr>
<tr>
<td>3 minutes after drug</td>
<td>115.45</td>
<td>6.6</td>
<td>116.52</td>
<td>7.77</td>
</tr>
<tr>
<td>During intubation</td>
<td>138.46</td>
<td>11.07</td>
<td>130.76</td>
<td>3.96</td>
</tr>
<tr>
<td>1 min after intubation</td>
<td>130.64</td>
<td>5.74</td>
<td>125.43</td>
<td>0.1</td>
</tr>
<tr>
<td>3 mins after intubation</td>
<td>128.29</td>
<td>4.02</td>
<td>120.35</td>
<td>4.3</td>
</tr>
<tr>
<td>5 mins after intubation</td>
<td>128.45</td>
<td>4.14</td>
<td>120.16</td>
<td>4.5</td>
</tr>
<tr>
<td>10 mins after intubation</td>
<td>125.93</td>
<td>2.22</td>
<td>119.25</td>
<td>5.3</td>
</tr>
<tr>
<td>15 mins after intubation</td>
<td>124.42</td>
<td>1.03</td>
<td>118.34</td>
<td>6.1</td>
</tr>
<tr>
<td>20 mins after intubation</td>
<td>124.10</td>
<td>0.78</td>
<td>115.69</td>
<td>8.5</td>
</tr>
<tr>
<td>30 mins after intubation</td>
<td>122.68</td>
<td>0.3</td>
<td>115.48</td>
<td>8.7</td>
</tr>
<tr>
<td>40 mins after intubation</td>
<td>119.35</td>
<td>3.1</td>
<td>110.93</td>
<td>13.2</td>
</tr>
</tbody>
</table>

Table-2: Post operative vas based 1st top up dose of analgesic requirement

<table>
<thead>
<tr>
<th>Group</th>
<th>Time to 1st Topup analgesia after intial dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A</td>
<td>140.60 Minutes</td>
</tr>
<tr>
<td>Group B</td>
<td>65.36 Minutes</td>
</tr>
</tbody>
</table>

Figure-1: Heart rate between Group A and Group B before shifting into the operation theatre. Base line vitals (pulse, BP, SpO2, ECG) were recorded before induction.

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RESULTS

Both groups were compared in respect with the age, sex, weight, ASA status. Increase in SBP (systolic blood pressure) and DBP (diastolic blood pressure) during intubation was statistically analyzed for periodic intervals during pre and post intubation. SBP and DBP during intubation was more in Group A when compared with Group B even after 15 minutes. Maximum rise in SBP in group A was 11.07% but in Group B was 3.96% (table-1). After intubation SBP started decreasing and 15 minutes after intubation it was lower than base line value in Group B. Baseline heart rate between two groups compared. Both groups had comparable similar rise in heart rate (Figure-1). Post operatively HR, SBP and DBP were similar in both groups. Time to 1st dose analgesic top up was significantly shorter in group B (65.36 minutes) compared to Group A (140.63 minutes) (table-2). Invariably, all Group B patients required analgesic immediately in the post op period when compared with Group A. Group A showed overall decrease in muscle relaxant requirement and maintenance dose also. Post operatively Group A need less frequent analgesic top ups. Group A patient were more awake and had less nausea compared to Group B (Figure-2).

DISCUSSION

Laryngoscopy and intubation are two most consistent manoeuvres that lead to significant increase in blood pressure and heart rate. Various drugs like β blockers, vasodilators, opioids, sedatives have been tried to obtund the pressure response to intubation. Narcotics can be used as sole or supplementary agent for induction of anaesthesia. Narcotics such as Nalbuphine are inexpensive and easily available. The safety of nalbuphine has been established from decades and has a comparable analgesic potential to morphine this has been demonstrated in the study done by Joseph Yanulevich in 1983.13,14 Kendrick15 has compared Naloxone with nalbuphine infusion for prophylaxis of epidural morphine-induced pruritus and has revealed that Nalbuphine, when used as intravenous infusion can reduce morphine induced pruritus.

According to Baxter et al14 Pruritus, nausea, vomiting and urinary retention, are common with all opioids, but the most serious complication is respiratory depression. Nalbuphine has a plateau effect over respiratory depression and it has

STATISTICAL ANALYSIS

All patients were observed post operatively for side effects and complications. Pain score (visual analogue score) was noted at regular intervals (15 minutes) for the next 6 hours. Unpaired “t” test was used for data analysis. A p-value of < 0.05 was considered significant. SPSS 11.0 software was used for statistical analysis.
the potential to reverse the respiratory depression caused by morphine. Thus nalbuphine has a higher safety profile when compared with morphine and other opioids. Mark W. Guniona in his study ratiocales the Use of the mixed agonist—antagonist nalbuphine in opioid based analgesia. Thus nalbuphine is potent and cost effective alternative for the routine use for peri-operative analgesia. Zeng, Z. et al concluded that nalbuphine has comparable analgesic profile to morphine and has lesser side effects especially regarding pruritus and respiratory depression.

Muhammad Ahsan has compared nalbuphine with placebo and noticed that the placebo group had elevated haemodynamic responses when compared with nalbuphine group in his study. This is similar to our study where there is increase in HR and SBP with nalbuphine after induction.

Khan had compared nalbuphine with fentanyl and showed no significant increase in MAP after endotracheal intubation but documented 25% rise in HR after intubation was in the nalbuphine group when compared with fentanyl group in his study. The same study showed comparable incidence of nausea and vomiting in both the groups but duration of analgesia was shorter in fentanyl when compared to nalbuphine (37 minutes’ vs 62 minutes). In contrast, our study showed no significant increase in HR and SBP after intubation with both nalbuphine and fentanyl group. The top up requirement is longer in nalbuphine compared to fentanyl group which is similar to that study.

Weiss et al studied fentanyl and nalbuphine for coronary Artery Bypass Surgery. In their study during and after intubation all patients were given nalbuphine and only one patient was given fentanyl, required nitroglycerin to control MAP. They also found higher level of epinephrine, norepinephrine, vasopressin and cortisol in nalbuphine group compared to baseline value, whereas in fentanyl group.

N Sharma had also compared effects of nalbuphine versus fentanyl on haemodynamic response and showed no significant increase in both SBP, DBP and HR which is similar to our study. In that study there were no complication like arrhythmias, bradycardia, nausea, vomiting, respiratory depression or pruritus in both groups unlike our study which showed sedation, pruritus, shivering in fentanyl group.

Mikita J. Chaudhari had compared Efficacy of nalbuphine in preventing haemodynamic response to laryngoscopy and intubation in comparison to clonidine. The results obtained with nalbuphine (duration of action, onset and haemodynamic responses) in this study is similar to that of the nalbuphine group.

Due to certain limitations we have not been able compare this drug in emergencies and long surgeries. We need more studies to compare the action of the drug in acute and sever pain. We have observed that in sever pain VAS score >8 in the post operative period of major surgeries with nalbuphine performed poorly and needed adjuncts like NSAID’s or benzodiazepines to make the patients calm. At times, anxious patients post -operatively needed mild sedation in nalbuphine group.

CONCLUSION

We conclude that Nalbuphine provides good hemodynamic and excellent post operative analgesia which is comparable to fentanyl but at a less frequent dosing thus decreasing the overall opioid requirement for general anesthesia. Nalbuphine has lesser side effects and provides adequate analgesia in most of the surgeries when given at above recommended dose. Its has lesser respiratory depression than most of the opioids and due to its availability in India without a opioid license, makes it an ideal analgesic for small hospitals and out of hospital care.

REFERENCES