Comparative Study of Efficacy of Preoperative Nalbuphine Hydrochloride and Pentazocine Lactate on Hemodynamic Response to Tracheal Intubation and Postoperative Analgesia

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Abstract

Background: For General anaesthesia perioperative administration of opioids are choice of drugs to attenuate intubation response and to provide good intraoperative and postoperative analgesia. Mixed agonist-antagonist opioids produces powerful analgesia without undesirable side effects. Aim: Aim of present study to compare efficacy of Nalbuphine and Pentazocine on hemodynamic response to tracheal intubation and postoperative analgesia. Settings: Present study carried out in operation theater. Design: This is prospective randomized double blind controlled trial. Material and Methods: Patients of ASA physical status I and II, age 20-60 years undergoing abdominal surgical procedure of 1-2 hour duration were randomly divided into two groups of 30 patients each (Group N) receiving nalbuphine 0.3 mg.kg⁻¹ and (Group P) receiving pentazocine 0.6 mg.kg⁻¹ intravenously before induction. Baseline vital parameters were noted and then noted till 15 minutes after intubation to see hemodynamic response. Time of rescue analgesia required was noted postoperatively. Statistical Analysis: Chi-square test, paired and unpaired t-test were used for statistical analysis. Results: There is rise in heart rate, blood pressure after intubation in both groups but rise was more with Pentazocine as compared to Nalbuphine (\( P < 0.05 \)). Postoperatively within 30 minutes 60% of patient from Pentazocine group require rescue analgesia compare to only 16.60% of patient of Nalbuphine group (\( P = 0.05 \)) which is highly significant. Conclusion: Nalbuphine is potent mixed opioid analgesic which can be used for attenuation of pressor response of tracheal intubation and for perioperative analgesia with minimal side effects.

Keywords: Intubation response, nalbuphine, pentazocine, postoperative analgesia

Introduction

Anesthesia is a reversible condition of comfort and quiescence for a patient within physiological limits that render the patient unaware or unresponsive for painful stimuli.

Laryngoscopy, tracheal intubations, surgical stimulus, pain rises the levels of catecholamines leads to sympathetic overactivity in the form of increased heart rate, blood pressure, intracranial pressure leading to myocardial ischemia, arrhythmia, and intracranial hemorrhage which increases mortality and morbidity in high-risk patients.[1]

Opioids are important drugs in the management of attenuation of pressure response. Use of opioids before induction of general anesthesia makes intraoperative course smooth, decreases intraoperative requirement of anesthetic agents and minimizes postoperative pain.[2] Opioids produce analgesia by binding to receptors such as \( \mu \), \( \delta \), and \( k \) receptors. They are classified as a pure agonist, partial agonist, and mixed agonist-antagonist. Mixed agonist-antagonist opioids such as butorphanol, nalbuphine, dezocine, pentazocine act as an agonist or partial agonist at \( \mu \) receptor and strong or weak antagonist at \( \mu \) receptor producing powerful analgesia without undesirable side effects such as nausea, vomiting, pruritis, dependence, and respiratory depression in humans when administered as sole opioid agents.[3]

Nalbuphine is mixed opioid agonist-antagonist structurally related to naloxone (opioid antagonist) and to oxymorphone
Sadafule and Karhade: Nalbuphine and pentazocine for intubation response

Nalbuphine is distinguished from other agonist-antagonist analgesics in having greater antagonist activity at µ receptors and fewer behavioral effects at analgesic doses than pentazocine, butorphanol or buprenorphine. At equianalgesic doses nalbuphine is qualitatively similar to nalorphine in regard to its large ratio of antagonist to analgesic activity. Unlike nalorphine or pentazocine, nalbuphine produces few overt behavioral or autonomic effects in animals at doses over 300 times its analgesic range. These findings show that nalbuphine produced few psychotomimetic effects even at an elevated dose level. Nalbuphine has few effects on cardiovascular hemodynamics in patients without cardiac disease or in stable ischemic disease. In patients of acute myocardial ischemia, nalbuphine has an advantage over morphine, pentazocine, and butorphanol of not producing hypotension. Nalbuphine has the same potency as morphine as an analgesic with same onset, peak, and duration of action. Its onset of action occurs within 2–3 min after intravenous administration, and the plasma half-life of nalbuphine is 5 h hence can be used for surgical procedures ranging from 3 to 5 h. Nalbuphine has ceiling effect on respiratory depression and analgesia when used in dose above 20 mg. This increases the safety of nalbuphine for perioperative analgesia.

Pentazocine is partial agonist-antagonist which is a benzomorphan derivative and has opioid agonistic (κ-receptors) as well as a weak antagonist (µ-receptor). Ceiling effects for analgesia and respiratory depression are observed when used in doses above 50–100 mg.

Nalbuphine is noncontrolled, nonabusive opioid analgesic. As both these drugs are easily available in this study, we are comparing the analgesic potency of nalbuphine with pentazocine at our institute as they are compared to other opioids. Similarly, ours is the teaching institute, the aim of this study is to make the residents aware of the clinical and pharmacological profile, and hence, we are evaluating the efficacy of these two drugs in attenuating hemodynamic response during tracheal intubation and postoperative pain.

**Materials and Methods**

This is prospective, randomized double-blind controlled study carried out in our institute over a period of 6 months after obtaining local ethical committees permission. Randomization of the patients carried out by computer generated random number table. The observer was blinded to the preparation and administration of the study drug.

**Inclusion criteria**

Patients American Society of Anesthesiologists physical Status I and II, age 20–60 years, either of sex, weight 40–80 kg, undergoing abdominal surgical procedures, expected surgical duration 1–3 h were included in this study.

**Exclusion criteria**

Patients unwilling to participate in the study, having systemic diseases such as severe hypertension, ischemic heart disease hepatic or renal disorder, anticipated hemodynamic instability, patients on tricyclic inhibitors, pregnant and lactating females, patients on chronic opioid therapy, and addiction to any drug or alcohol are excluded from the study.

After preoperative clinical examination, investigations such as complete blood count, urine analysis, liver function tests, renal function test, bleeding time, and clotting time were carried out. Informed written consent was obtained. All selected patients were made familiar with visual analog scale (VAS) for grading of postoperative pain intensity. Patients were randomly divided into two groups of 30 each.

Group P: Patients received pentazocine lactate 0.6 mg/kg intravenously before induction.

Group N: Patients received nalbuphine hydrochloride 0.3 mg/kg intravenously before induction.

After confirming the adequate starvation period, patients were taken inside the operating room, all routine monitors including noninvasive blood pressure, pulse-oximeter, ECG attached to the patient. Wide-bore intracath 18 G was secured in all patients. All patients were premedicated with intravenous glycopyrrolate 0.004 mg/kg, ondansetron 0.008 mg/kg and then according to the randomization patients were given either pentazocine 0.6 mg/kg or nalbuphine 0.3 mg/kg slowly over 30 s. Five minutes after administration of the drugs heart rate, blood pressure, and saturation were noted. Patients were preoxygenated for 5 min, anesthesia was induced with injection propofol 2 mg/kg in titrated doses. Neuromuscular blockade was achieved with injection vecuronium 0.1 mg/kg and all patients were manually ventilated with O₂: N₂O (40:60) for 3 min.

Vital parameters were noted and tracheal intubation was done under direct laryngoscopy by the experienced anesthesiologist. Systolic and diastolic blood pressure, SPO₂, and heart rate were noted just before intubation, at the time of intubation, then at every 1 min till first 5 min and thereafter at 10 min and at 15 min of the intubation.

Anesthesia was maintained with isoflurane, vecuronium within O₂ and N₂O and intermittent injection propofol so that blood pressure and heart rate should remain within 20% of baseline value.

No other analgesia was given throughout the procedure. At the end of surgery isoflurane tapered gradually and after completion of the procedure and resuming the spontaneous respiration anesthesia was reversed with neostigmine 0.05 mg/kg and glycopyrrolate 0.008 mg/kg. All patients were extubated after resuming good muscle tone and respiration, vital parameters were noted and shifted to the postoperative care unit.

In the postoperative room, vital parameters were noted in the form of pulse rate, blood pressure, oxygen saturation, and pain on the pain scale. Rescue analgesia provided in the form of injection tramadol 100 mg.
Statistical analysis
The data obtained was expressed as a mean and standard deviation. The difference in demographic data between two groups was sought with Chi-square test. The hemodynamic variables were analyzed using paired t-test within the group and unpaired t-test for group comparisons. Visual analog score and duration of the requirement of rescue analgesia after extubation was compared using unpaired t-test. The value of \( P < 0.05 \) was considered as statistically significant.

RESULTS
These two groups were comparable with respect to age, weight, and gender ratio.

Both groups are comparable with respect to the type of surgeries undertaken and duration of surgeries.

As shown in Table 1, mean baseline heart rates in both groups measured before premedication were similar; however, there was a significant increase of heart rate after intubation in both groups. However, this was significant after giving pentazocine and remained significantly high for further 15 min. In nalbuphine group heart rate was significantly raised from the baseline but as compared to pentazocine this increase was less marked and after 15 min it touches the baseline.

Table 2 shows systolic blood pressure changes after intubation. Systolic blood pressure after giving pentazocine is higher as compared to nalbuphine. After intubation both the groups showed a rise in blood pressure but on comparing both groups, rise was less prominent in group of patients received nalbuphine. After 10 minutes of intubation blood pressure remained persistently high in pentazocine and on other hand, in nalbuphine group, blood pressure returned to baseline after 10 minutes of intubation.

As shown in Table 3, diastolic blood pressure raised in both group of patients after intubation but more rise seen with pentazocine and this rise seen for a longer time as compared to nalbuphine.

After extubation, VAS score noted for both groups. Table 4 shows 60% of patients of pentazocine group and 16.66% of patients of nalbuphine group had received rescue of analgesia within 30 min of extubation. Further in next 30 min that is within the 1st h of extubation, 100% means all patients of pentazocine group required rescue analgesia, but only 70% of patients of nalbuphine required rescue analgesia. From Table 5, it is seen as pentazocine group patients require rescue analgesia early as compared to nalbuphine group of patients.

DISCUSSION
Laryngoscopy and intubation are commonly associated with cardiovascular changes like tachycardia or bradycardia, rise in systolic or diastolic blood pressure and variety of arrhythmias. These effects are deleterious in susceptible individuals leading to perioperative myocardial ischemia, acute heart failure, or cardiovascular accidents.[11]

Pentazocine and nalbuphine have many similarities in producing analgesia by action on \( \kappa \) receptor, but pentazocine is weaker \( \mu \) receptor antagonist, or partial agonist as compared to nalbuphine which is strong \( \mu \) receptor antagonist, due to this nalbuphine can reverse \( \mu \) receptor associated side effects such as respiratory depression, vomiting, and pruritis in contrast to pentazocine.[12] In this study, we have not assessed sedation and other side effects.

The present study compared nalbuphine hydrochloride 0.3 mg/kg and pentazocine lactate 0.6 mg/kg administration.

### Table 1: Heart rate during and after induction

| Time          | Mean±SD, (Paired t-Value) | Unpaired P |
|---------------|---------------------------|------------|
|               | Group P (n=30)            | Group N (n=30) |         |
| Baseline      | 74.03±7.504               | 74.8±7.194  | 0.841    |
| After premedication | 73.33±6.890 (0.482)     | 75.03±6.856 (0.070) | 0.856    |
| After analgesia | 80.27±7.08 (0.000)        | 76.20±5.641 (0.048) | 0.017    |
| After induction | 76.60±7.968 (0.103)       | 73.87±5.303 (0.291) | 0.101    |

### Table 2: Systolic blood pressure during induction

| Time          | Mean±SD, (Paired t-Value) | Unpaired P |
|---------------|---------------------------|------------|
|               | Group P (n=30)            | Group N (n=30) |         |
| Baseline      | 114.93±9.962              | 115.67±7.466 | 0.801    |
| After premedication | 115.17±9.556 (0.783)     | 116.87±7.300 (0.08) | 0.710    |
| After analgesia | 122.30±9.250 (0.000)     | 118.80±6.678 (0.003) | 0.008    |
| After induction | 116.679±7.32 (0.223)     | 111.80±6.678 (0.003) | 0.020    |
| After intubation | 141.93±9.620 (0.000)    | 136.83±4.800 (0.000) | 0.000    |

### Table 3: Diastolic blood pressure during induction

| Time          | Mean±SD, (Paired t-Value) | Unpaired P |
|---------------|---------------------------|------------|
|               | Group P (n=30)            | Group N (n=30) |         |
| Baseline      | 76.60±7.968               | 77.60±8.835 | 0.101    |
| After premedication | 76.20±5.641 (0.048)     | 77.60±8.835 (0.101) | 0.050    |
| After analgesia | 76.60±7.968 (0.103)      | 75.87±5.303 (0.291) | 0.101    |
| After induction | 76.60±7.968 (0.103)      | 75.87±5.303 (0.291) | 0.101    |
| After intubation | 76.60±7.968 (0.103)     | 75.87±5.303 (0.291) | 0.101    |

\( P<0.05 \) is significant. SD=Standard deviation.
intravenously which was considered equipotent doses by other studies, like the study of Minai and Khan et al.[15] Nalbuphine 0.2 mg/kg is more effective to reduce hemodynamic response to intubation than morphine 0.1 mg.

Pandèle et al.[16] also found significantly higher systolic blood pressure with pentazocine as compared to nalbuphine same as to our studies. On the other hand, Graham et al.[13] in their study found no significant changes in heart rate or blood pressure at induction and skin incision while using these two drugs.

As compared to morphine stable hemodynamics were noted with nalbuphine by Fahmy in 1980. Alderman et al.[17] compared the hemodynamic response to iv morphine and pentazocine on IHD patients and found that cardiac work is decreased by morphine and increased by pentazocine.

All above results confirm that nalbuphine is likely to maintain stable hemodynamic than pentazocine as seen in the present study.

Some difference in duration of analgesia produced by two drugs was noted in the present study. Patients following pentazocine required pain relief earlier, and postoperative analgesia remained for a significantly longer time with nalbuphine compared to pentazocine.

From these studies, it appears that nalbuphine is able to provide effectively and longer duration of analgesia as compared to pentazocine, similarly can be used to attenuate pressure response of laryngoscopy and intubation. In this study, we have not monitored the sedation score and long-term side effects of these two drugs. In this study, injection propofol was given intermittently to maintain heart rate and blood pressure within 20% of baseline value which interfere with postoperative sedation score, and hence, we have not commented about the sedative property of these two drugs.

**Table 3: Diastolic blood pressure during induction**

| Time               | Mean±SD, (Paired P value) | Unpaired P   |
|--------------------|---------------------------|--------------|
|                    | Group P (n=30)            | Group N (n=30) |   |
| Base line          | 75.70±8.832 (0.00)       | 73±7.58     | 0.234 |
| After premedication| 76.03±6.941 (0.786)      | 73.17±7.373 (0.362) | 0.158 |
| After analgesia     | 77.00±7.569 (0.270)      | 75.13±4.447 (0.071) | 0.119 |
| After induction     | 77.00±8.800 (0.481)      | 71.70±4.949 (0.402) | 0.099 |
| After intubation    | 92.7±10.14 (0.000)       | 87.13±5.374 (0.000) | 0.010 |

P<0.05 is significant. SD=Standard deviation

**Table 4: Time-wise distribution of the first dose of postoperative analgesia**

| Postoperative time | Group P | Group N                  |
|--------------------|---------|--------------------------|
| <30 min            | 18 (60) | 1 (16.66)                |
| <60 min            | 30 (100)| 21 (70)                  |
| <90 min            | -       | 30 (100)                 |

**Table 5: Duration of analgesia**

| Period from extubation to first rescue analgesia | Mean±SD     | P     |
|-------------------------------------------------|-------------|-------|
| Group P                                         | 36.50±19.571| 62.00±20.026 | 0.000 |
| Group N                                         |             |       |

P<0.05 is significant. SD=Standard deviation

**Conclusion**

Nalbuphine can be used to attenuate pressure response of laryngoscopy and tracheal intubation. Similarly can be used as sole anesthetic agent that gives intraoperative and perioperative analgesia without side effects.

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Nil.

**Conflicts of interest**

There are no conflicts of interest.

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