Comparison of Nalbuphine and Tramadol As Post-Operative Analgesic In Laparoscopically Operated Patients

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**Introduction:** Post-operative pain is very common in laparoscopically operated cases specially in upper abdomen, lower abdomen, back or shoulder surgeries. By virtue of their efficacy, opioid analgesics have been used for the treatment of both acute and chronic pain. Aim: To compare intravenous nalbuphine and intravenous tramadol in relieving post-operative pain in patients undergoing upper abdominal laparoscopic surgery.

**Material and Methods:** Seventy patients scheduled for upper abdominal laparoscopic surgery under general anaesthesia were randomly divided into two groups. Thirty five patients in Group A patients received intravenous nalbuphine 0.2mg/kg whereas Group B patients received tramadol 1mg/kg. Post-operative follow up for pain by visual analogue scale was recorded initially for 10, 20, 30 minutes, 1 hour, 2 hours, 4 hours and 6 hours after giving intravenous nalbuphine or tramadol. Patients were observed for any side effects like nausea, vomiting, drowsiness etc. Primary outcome measures were visual analogue scale score whereas secondary outcome measures were untoward side effects. Comparison of quantitative and qualitative variables between groups was done using unpaired student’s “t” test and chi-square test respectively using statistical package for social sciences.

**Results:** The mean VAS score at 10 minutes, 20 minutes, 30 minutes, 2 hours, 4 hours and 6 hours was significantly higher (p = 0.001) in Group B compared to Group A. In Group A, 17.1% patients had sedation whereas in Group B 31.4% patients had nausea or vomiting.

**Conclusion:** Nalbuphine is more effective than tramadol as a post-operative analgesic for relief of post-operative pain.
INTRODUCTION:
Post-operative pain is one of the main concerns for the patient undergoing major surgery. It is a challenge to the treating surgeon and attending anesthesiologists as there are many adverse physiological and psychological effects associated with pain, which can hamper the normal recovery process. These patients are in considerable pain during transportation to wards and require adequate post-operative analgesia. Although pain has a teleological function in warning the patient about potential injury, it also exerts deleterious effects on respiratory, cardiovascular, neuroendocrine, gastrointestinal and other systems of the body. Hence, an effective pain relief after surgery is essential for optimal care of patient. Any method of post-operative analgesia must meet three basic criteria. It must be effective, safe and feasible.\(^1\)

Various techniques and drugs have been used for this purpose with variable success. Every technique and drugs have its own advantages and disadvantages. Post-operative pain is very common in laparoscopically operated cases specially in upper abdomen, lower abdomen, back or shoulders. Rapid insufflation of abdomen leads to shearing of blood vessels, traumatic traction on nerves and release of inflammatory mediators. Prolonged shoulder pain suggests excitation of phrenic nerve. These patients require adequate post-operative analgesia.\(^2\) By virtue of their efficacy, opioid analgesics have been used for the treatment of both acute and chronic pain. The present study compares intravenous nalbuphine and intravenous tramadol in relieving post-operative pain in patients undergoing upper abdominal laparoscopic surgery.

MATERIAL AND METHODS
This prospective, randomized double-blind controlled study was conducted between July 2015 and September 2016. After scientific advisory committee and institutional ethics committee approval, written informed consent was obtained from all patients included in the study. Patients aged 18 to 60 years of either sex scheduled for upper abdominal laparoscopic surgery under general anesthesia, and American Society of Anesthesiologist (ASA) grade I and II were included. Pregnant or lactating women, patients with severe hepatic or renal dysfunction, chronic respiratory ailments and patients who were not willing to give written informed consent were excluded from this study.

Out of 85 patients assessed for eligibility, after exclusion 70 patients were randomly divided into two equal groups of 35 each, using computer generated randomization code (Fig 1).

We used website [https://www.sealedenvelope.com/simple-randomiser/v1/lists](https://www.sealedenvelope.com/simple-randomiser/v1/lists) for creating a randomization list with block size four. Group A patients received intravenous nalbuphine 0.2mg/kg whereas Group B patients received tramadol 1mg/kg after surgery in the recovery room. Randomization code was provided to operation theatre nurse. An operation theatre nurse prepared syringes with nalbuphine or tramadol and put them into concealed envelopes according to the allocation orders. This was done under the supervision of senior anesthesiologist. Researcher and patients were blind as to group assignment. Pre-anesthesia check up was done one day prior to surgery. The patients were evaluated for any systemic diseases and laboratory investigations were recorded. Details of the procedure was explained to the patients. The patients were educated about the visual analogue scale (VAS) score. In operation theatre, adequate intra-venous (IV) access was confirmed. Standard monitors were attached. Noninvasive blood pressure, pulse-oximeter, electrocardiogram, end tidal CO\(_2\) (ET CO\(_2\)) were monitored after intubation. Before induction of anaesthesia, all patients were given IV glycopyrrolate 0.004 mg/kg, and IV ondansetron 75µg/kg. In all patients, anaesthesia was induced with IV fentanyl 2 µg / kg, IV propofol 2.0 mg / kg and IV succinylcholine 2mg/kg. Intubation was done with appropriate sized cuffed oral endo-tracheal tube (ETT). ETT placement was confirmed. Orogastric tube was placed for deflating stomach. This was removed at the end of surgery.

Anaesthesia was maintained with N\(_2\)O:O\(_2\) ratio of 70:30%, and sevoflurane 2.0 % with controlled ventilation. Injection atracurium 0.1mg/kg intravenously was repeated as required. Heart rate (HR), mean arterial blood pressure, ECG, SpO\(_2\), respiratory rate (RR), and end-tidal CO\(_2\) concentration was monitored every 5 minutes intra-operatively. After adequate spontaneous respiratory effort patient was reversed with injection neostigmine 50 µg /kg with injection glycopyrrolate 40 µg /kg. Patient was shifted to recovery for monitoring.

In recovery HR, systolic blood pressure, diastolic blood pressure, SpO\(_2\), RR were monitored. Post-operative follow up for pain by VAS score was recorded initially for 10, 20, 30 minutes, 1 hour, then for every 2 hours up to 6 hours after giving intravenous analgesics. Patients were observed for any side effects like nausea, vomiting etc. Patients who were calm, sleepy but can be easily aroused to verbal command were said to be sedated. Primary outcome measures were VAS score whereas secondary outcome measures were untoward side effects. On the basis of previously published studies\(^3\) a sample size of 35 patients in each group was calculated by a formula\(^4\) with 80 % power and 5 % probability of Type I error to reject null hypothesis.
Data collected were entered in the Excel 2007 and analysis of data was done using Statistical Package for Social Sciences (SPSS) version 20, IBM, USA. The comparison of quantitative variables between the groups such as mean age, mean weight, mean duration of surgery, mean heart rate, mean systolic blood pressure, mean diastolic blood pressure, mean SPO₂ and mean VAS score was done using unpaired student’s “t” test, whereas comparison of qualitative variables such as gender, ASA grade and complication rates was done by using chi-square test or Fisher’s exact test. The confidence limit for significance was fixed at 95% level with p-value < 0.05.

RESULTS

The present study was undertaken to compare the post-operative analgesic effects of intravenous nalbuphine and intravenous tramadol in patients undergoing upper abdominal laparoscopic surgery. Out of 85 patients assessed for eligibility, 10 were excluded because of renal dysfunction (2), chronic respiratory aliment (5), refused to participate (3). Seventy five patients were randomly allotted (Fig.1). Five patients were further excluded (3 patients from tramadol group and 2 patients from nalbuphine group) from analysis because these patients were converted to open surgery. In all data of 70 patients (35 patients in each group) were analyzed and compared.

### Table 1: Demographic profile

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Age in years (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 30</td>
<td>7(20.0)</td>
<td>10(28.6)</td>
<td>0.796</td>
</tr>
<tr>
<td>30&lt;40</td>
<td>13(37.1)</td>
<td>11(31.4)</td>
<td></td>
</tr>
<tr>
<td>40&lt;50</td>
<td>6(17.1)</td>
<td>7(20.0)</td>
<td></td>
</tr>
<tr>
<td>≥ 50</td>
<td>9(25.7)</td>
<td>7(20.0)</td>
<td></td>
</tr>
<tr>
<td>Mean age in years (SD)</td>
<td>39.4 (± 10.9)</td>
<td>38.7 (± 11.9)</td>
<td>0.594</td>
</tr>
<tr>
<td>Gender, no (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>17 (48.6)</td>
<td>18 (51.4)</td>
<td>0.811</td>
</tr>
<tr>
<td>Female</td>
<td>18 (51.4)</td>
<td>17 (48.6)</td>
<td></td>
</tr>
<tr>
<td>Mean weight in kg (SD)</td>
<td>62.09 (± 7.4)</td>
<td>64.23 (± 6.79)</td>
<td>0.212</td>
</tr>
<tr>
<td>ASA Grade (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>19(54.3)</td>
<td>19(54.3)</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>16(45.7)</td>
<td>16(45.7)</td>
<td></td>
</tr>
<tr>
<td>54 min 30 sec</td>
<td>55 min 40 sec</td>
<td>0.75</td>
<td></td>
</tr>
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</table>

### Table 2: Comparison of VAS between Group A and Group B postoperatively.

<table>
<thead>
<tr>
<th>Time</th>
<th>VAS(cm)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group A</td>
<td>Group B</td>
</tr>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Baseline</td>
<td>6.54</td>
<td>0.7</td>
</tr>
<tr>
<td>10 minutes</td>
<td>4.86</td>
<td>0.69</td>
</tr>
<tr>
<td>20 minutes</td>
<td>2.77</td>
<td>0.65</td>
</tr>
<tr>
<td>30 minutes</td>
<td>0.8</td>
<td>0.63</td>
</tr>
<tr>
<td>60 minutes</td>
<td>0.26</td>
<td>0.44</td>
</tr>
<tr>
<td>120 minutes</td>
<td>0.06</td>
<td>0.24</td>
</tr>
<tr>
<td>240 minutes</td>
<td>0.06</td>
<td>0.24</td>
</tr>
<tr>
<td>360 minutes</td>
<td>1.54</td>
<td>0.98</td>
</tr>
</tbody>
</table>

### Table 3: Comparison of heart rate between Group A and Group B postoperatively.

<table>
<thead>
<tr>
<th>Time</th>
<th>VAS(cm)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group A</td>
<td>Group B</td>
</tr>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>10 minutes</td>
<td>82.54</td>
<td>3.55</td>
</tr>
<tr>
<td>20 minutes</td>
<td>81.14</td>
<td>3.33</td>
</tr>
<tr>
<td>30 minutes</td>
<td>80.77</td>
<td>3.39</td>
</tr>
<tr>
<td>60 minutes</td>
<td>81.37</td>
<td>3.25</td>
</tr>
<tr>
<td>240 minutes</td>
<td>81.37</td>
<td>3.53</td>
</tr>
<tr>
<td>360 minutes</td>
<td>79.66</td>
<td>3.38</td>
</tr>
</tbody>
</table>

### Table 4: Comparison of diastolic blood pressure between Group A and Group B postoperatively.

<table>
<thead>
<tr>
<th>Time</th>
<th>VAS(cm)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group A</td>
<td>Group B</td>
</tr>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>10 minutes</td>
<td>80.3</td>
<td>3.76</td>
</tr>
<tr>
<td>20 minutes</td>
<td>79.4</td>
<td>2.94</td>
</tr>
<tr>
<td>30 minutes</td>
<td>79.8</td>
<td>2.35</td>
</tr>
<tr>
<td>60 minutes</td>
<td>80.1</td>
<td>3.46</td>
</tr>
<tr>
<td>240 minutes</td>
<td>78.3</td>
<td>3.12</td>
</tr>
<tr>
<td>360 minutes</td>
<td>78.7</td>
<td>3.32</td>
</tr>
</tbody>
</table>

### Table 5: Comparison of incidence of side effects between Group A and Group B postoperatively.

<table>
<thead>
<tr>
<th>Time</th>
<th>VAS(cm)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group A</td>
<td>Group B</td>
</tr>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>No.</td>
<td>%</td>
<td>No. %</td>
</tr>
<tr>
<td>Nil</td>
<td>25</td>
<td>71.4</td>
</tr>
<tr>
<td>Nausea</td>
<td>3</td>
<td>8.6</td>
</tr>
<tr>
<td>Vomiting</td>
<td>1</td>
<td>2.9</td>
</tr>
<tr>
<td>Sedation</td>
<td>6</td>
<td>17.1</td>
</tr>
<tr>
<td>Total</td>
<td>35</td>
<td>100</td>
</tr>
</tbody>
</table>
**Fig 1: CONSORT Diagram**

- Assessed for eligibility n = 85
- Randomized n = 75
- Excluded n = 10
  - Chronic respiratory element-5
  - Renal dysfunction-2
  - Refused to participate n = 3

**Fig. 2: Comparison of respiratory rate, systolic blood pressure, and SPO₂ between Group A and Group B postoperatively.**

**Inter-Group Comparison of Respiratory Rate**

<table>
<thead>
<tr>
<th>Time</th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-Min</td>
<td>6.5</td>
<td>6.8</td>
</tr>
<tr>
<td>20-Min</td>
<td>6.7</td>
<td>6.9</td>
</tr>
<tr>
<td>30-Min</td>
<td>6.9</td>
<td>7.1</td>
</tr>
<tr>
<td>60-Min</td>
<td>7.2</td>
<td>7.3</td>
</tr>
<tr>
<td>240-Min</td>
<td>7.0</td>
<td>7.1</td>
</tr>
<tr>
<td>360-Min</td>
<td>6.8</td>
<td>6.9</td>
</tr>
</tbody>
</table>
Both groups were comparable with respect to mean age, sex distribution, mean weight, ASA physical status and duration of surgery [Table 1]. As depicted in table 2, the baseline and 60 minute mean VAS score did not differ significantly between two intervention groups whereas the mean VAS score at 10 minutes, 20 minutes, 30 minutes, 120 minutes, 240 minutes and 360 minutes was significantly higher in Group B compared to Group A. Mean HR at 10 minutes and 20 minutes was significantly higher in Group B compared to Group A whereas mean baseline and 30 minutes, 60 minutes, 240 minutes and 360 minutes HR did not differ significantly between two groups [Table 3]. As shown in table 4, mean diastolic blood pressure at 30 minutes, 60 minutes and 360 minutes did not differ significantly between two whereas mean diastolic blood pressure at 10 minutes, 20 minutes and 240 minutes was significantly higher in Group B compared to Group A. As depicted in table 5, in Group A, the majority of patients had sedation (6 patients) and in Group B majority of patients had nausea. As shown in Figure 2, mean systolic blood pressure, mean respiratory rate and mean SPO2 did not differ significantly between two groups.

**DISCUSSION**

In the present study, the mean VAS score at 10 minutes, 20 minutes, 30 minutes, 120 minutes, 240 minutes and 360 minutes was significantly higher in Group B compared to Group A. The post-operative analgesic effect of nalbuphine and tramadol compared by Alon E. et al [5] concluded that there was no significant differences between two groups. Shaila S Kamath et al [3] conducted a double blind prospective randomized study comparing analgesic effect of intravenous nalbuphine and tramadol in patients with post-operative pain. They observed that percentage of pain relief was highly significant (p<0.001) with mean VAS score 0.72±0.64 in nalbuphine group as compared to tramadol with mean VAS score of 1.72±0.75 30 minutes post-operatively. In present study similar results were seen with VAS score of 0.80±0.63 and 2.14±0.88 in group A (nalbuphine) and group B (tramadol) respectively at 30 minutes.

In 2015, R N Solanki et al [6] reported that nausea & vomiting were significantly higher in tramadol group i.e. 62% compared to 7.5% in nalbuphine group. Shaila S Kamath et al [3] reported nausea and or vomiting in 10/40(25.0%) patients. In present study similar observations were seen. Nausea and or vomiting were higher in tramadol group.
11/35 (31.4%) than nalbuphine group 4/35 (11.5%). Shaila S Kamath et al [3] reported that in nalbuphine group 5/40 (12.5%) patients developed drowsiness which is comparable to the present study. In present study, in Group A (nalbuphine) 6/35 (17.1%) patients had sedation and Group B (tramadol) no patient experienced sedation. Thus, nalbuphine showed sedation as a side effect which is beneficial in post-operative patients as they remain calm. Limitations of the present research were that the duration of study was only 6 hours and all the side effects of the drugs were not compared. Further studies with larger sample size and longer post-operative follow up are required to firmly establish efficacy and safety of the both drugs.

CONCLUSION
Nalbuphine was more effective than tramadol as a post-operative analgesic for relief of post-operative pain. Incidence of post-operative nausea and vomiting was significantly more in tramadol group whereas incidence of sedation was more with nalbuphine group.

REFERENCES

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