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Original Research Article

Postoperative Analgesia with Nefopam or Tramadol in Adults Undergoing Laparoscopic Abdominal Surgeries: A Hospital Study

Neha Rusia Saxena[1], Deepesh Saxena[2], Rakesh Kumar Raju[3], Nitin Ojha[4*]

[1]Assistant Professor, Department of Anaesthesiology & Critical Care, Rajiv Gandhi Superspeciality Hospital, Tahirpur, New Delhi

[2]Associate Consultant, Neuroanesthesia & Neurocritical Care, Fortis Hospital, Noida

[3]Associate Professor, Department of Anaesthesiology, Narayan Medical College, Sasaram

[4*]Assistant Professor, Department of Anaesthesiology, Critical Care & Pain Medicine, Nalanda Medical College & Hospital, Patna, Bihar

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Corresponding author: Dr. Nitin Ojha

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Abstract:

Background and Aim: Nefopam and Tramadol have been employed as pharmacological agents for the management of postoperative pain in several therapeutic contexts. The objective of this study is to assess and contrast the analgesic effects following surgery in adult patients having laparoscopic abdominal procedures, specifically focusing on the intravenous administration of nefopam and tramadol.

Materials and Methods: A total of 126 adult patients, belonging to American Society of Anaesthesiologists physical Status I & II and aged between 20 and 60 years, were randomly assigned to two groups. These patients were scheduled to have either elective or emergency laparoscopic abdominal procedures under general anaesthesia. In the post-anaesthesia care unit, a total of 63 patients were assigned to Group N and 63 patients were assigned to Group T. Patients in Group N got an intravenous infusion of Nefopam at a dosage of 20 mg, while patients in Group T received an intravenous infusion of Tramadol at a dosage of 100 mg. Both infusions were administered in 100 ml of 0.9% saline solution over a period of 15 minutes. The administration of identical dosages occurred at intervals of 6 hours or when the Visual Analogue Scale (VAS) score reached or exceeded 4. The Visual Analogue Scale (VAS) ratings following the surgical procedure were documented at certain time intervals, including 30 minutes, 1.5 hours, 3 hours, 6 hours, 12 hours, 18 hours, and 24 hours. The hemodynamic variables were measured both before to and following the administration of the study medications. A significance level of $P < 0.05$ was deemed to indicate statistical significance.

Results: The pain score exhibited a statistically significant decrease in Group N compared to Group T. There was a statistically significant difference in the mean VAS scores among the two groups at 1.5 hours, 3 hours, 6 hours, 12 hours, 18 hours, and 24 hours after the surgery ($P < 0.05$). There wasn't any statistically significant disparity observed in the occurrence of adverse effects between the two groups.

Conclusion: The administration of intravenous Nefopam yielded superior analgesic efficacy compared to Tramadol in individuals having laparoscopic procedures while under the influence of general anaesthesia.

Keywords: Abdominal surgery; Analgesia; Laparoscopic surgery; Nefopam; Tramadol.

Introduction

The effective treatment of postoperative pain following laparoscopic surgery is crucial for achieving a favorable outcome in the patient's recovery process. While the degree of postoperative pain after laparoscopic surgery is often lower compared to open surgery, a considerable number of individuals nonetheless necessitate a substantial dosage of analgesic drugs, encompassing both opioids and non-opioids. In a retrospective research, the occurrence of persistent post-surgical pain following laparoscopic colorectal surgery was found to be 17%, which aligns with the rates described in existing literature following laparotomy procedures. [1] In this study, we aim to investigate the effects of a specific treatment on a particular population following laparoscopic cholecystectomy, a considerable proportion of patients, ranging from 50% to 70%, continue to have postoperative discomfort of moderate to severe intensity. [2] According to the second source, Insufficient management of postoperative pain has been found to potentially correlate with a range of systemic problems, limited mobility, thromboembolic incidents, delay in recovery,

extended hospitalization, and escalated total expenses. [3]

Opioids are commonly employed for the purpose of postoperative pain management following laparoscopic surgery, owing to their well-established effectiveness. Nevertheless, opioids have been found to be linked with a range of undesirable consequences, such as gastrointestinal problems, pruritus, respiratory depression, prolonged hospitalization, and delayed discharge. [4] Non-steroidal anti-inflammatory medicines (NSAIDs) have been found to offer effective pain relief, but with potential adverse effects on the gastrointestinal system, platelet aggregation, and wound healing. [5] Tramadol is classified as an atypical opioid that exhibits a lower degree of respiratory depression compared to morphine. It was shown that the pain scores were consistently lower with the administration of this treatment compared to Ketorolac. Additionally, there was no significant difference seen in the occurrence of postoperative nausea and vomiting (PONV) following laparoscopic sterilization. [6]

Nefopam is a centrally acting analgesic that falls under the category of non-opioid, non-steroidal compounds. It has been documented to exhibit notable efficacy in reducing postoperative pain ratings and diminishing the need for opioids in the context of laparoscopic cholecystectomy. [2] According to the second source, Nefopam or tramadol were administered to a distinct subgroup of participants who had undergone diverse abdominal surgical procedures. Nevertheless, there is a paucity of research examining the experiences of individuals undergoing abdominal laparoscopic procedures.

Aims and Objectives:

The purpose of this research is to compare the analgesic efficacy of intravenous nefopam to that of tramadol in the postoperative period following laparoscopic abdominal surgery in adult patients.

Materials and Methods:

The present investigation was done at a centre for tertiary care using a prospective, randomised, double-blind design. The necessary clearance was obtained from the institutional ethics committee. Each patient provided written informed consent after receiving a comprehensive description of the research design. The patient was provided with an explanation of the Visual Analogue Scale (VAS) ranging from 0 to 10 during the preanesthetic check-up (PAC).

The study had a total of 126 participants, encompassing individuals of both genders aged between 20 and 60 years. These participants were selected from ASA physical status Grade I and II categories. Additionally, the participants had a weight range of 50 to 75 kg. All participants were scheduled to have either elective or emergency laparoscopic abdominal procedures under the administration of general anaesthesia (GA). The study excluded individuals who had a prior history of using analgesics, sedatives, or antidepressants within 24 hours before to the surgical procedure. Additionally, those with opioid dependency, alcohol or drug misuse, motion sickness or postoperative nausea and vomiting (PONV), convulsions, psychiatric disorder, and known hypersensitivity to the medications being investigated were also removed from the study. Exclusion criteria encompassed pregnant women, breastfeeding moms, and anyone who declined participation in the study.

Using computer-generated random numbers, patients were randomly allocated into one of the two predefined Groups, A or B, with 63 patients in each. In PACU, all patients received the first dose of study drugs according to their group allocation, 30 min after completion of surgery. The principal investigator prepared the study drugs, and the co-investigators were blinded to the study drugs being administered to the patients. Both the patient and the co-investigators were blinded to group allocation. Participants received IV infusion (in 100 ml 0.9% saline) of 20 mg Nefopam hydrochloride in Group N and 100 mg Tramadol hydrochloride in Group T, respectively, over 15 min. The dose was repeated every 6^{th} hour or if the VAS score was ≥ 4. The maximum dose of Nefopam and Tramadol was set at 120 mg/day and 400 mg/day, respectively.

Upon entering the operating room, the patient's fasting status, permission, and pre-anesthetic check (PAC) were verified, and standard monitors were used. Intravenous (IV) access was established, and the administration of Ringer's lactate solution was initiated. Following a period of preoxygenation lasting 3 minutes with 100% oxygen, general anaesthesia (GA) was initiated with the administration of intravenous fentanyl at dosage of 2 mcg/kg, Propofol at dosage of 2 mg/kg, and atracurium.

After the process of induction and sufficient paralysis, the trachea was successfully intubated using a properly sized cuffed endotracheal tube. General anaesthesia (GA) was sustained using a mixture of oxygen and air at a ratio of 50:50. The minimum alveolar concentration (MAC) of sevoflurane was titrated to achieve the desired level of anaesthesia. Atracurium was administered as the maintenance dosage for muscle relaxation, and positive pressure ventilation was employed. In the context of laparoscopic surgery, the intraabdominal pressure was consistently controlled within the range of 10-14 mm Hg. In all patients, intravenous Ondansetron at a dosage of 4 mg was delivered 45 minutes prior to the conclusion of the surgical

procedure. Intraoperatively, all patients were administered intravenous paracetamol at a dosage of 1 gm, along with an extra fentanyl dosage of 1 mcg/kg/hr.

During the surgical procedure, many physiological parameters were measured, including heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), respiratory rate (RR), oxygen saturation (SpO2), end-tidal carbon dioxide, and temperature. Upon completion of the surgical procedure, patients underwent extubation subsequent to the reversal of any remaining neuromuscular blockade, and were thereafter transferred to the post anaesthesia care unit (PACU). Upon arrival at the Post-Anesthesia Care Unit (PACU), the patients exhibited a state of comfort, absence of pain, complete responsiveness, and orientation to vocal commands. The participants were instructed to indicate the level of discomfort they experienced using a visual analogue scale (VAS) ranging from 0 to 100 mm. Breakthrough pain was defined as pain scores that reached or exceeded a value of 5, even after the administration of the study medication. The administration of intravenous Diclofenac sodium (1.5 mg/kg) was employed for analgesic purposes, with the option to repeat the dosage as needed. The postoperative VAS scores were measured at certain time intervals including 30 minutes, 1.5 hours, 3 hours, 6 hours, 12 hours, 18 hours, and 24 hours. The measurements of heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and respiratory rate (RR) were documented both before to and during the administration of the experimental medications. During the 24-hour postoperative period, the patients were monitored for potential adverse effects, including nausea & vomiting, headache, dizziness, itching, and sweating.

Sample size calculation:

The sample size was determined using an online calculation tool available at https:// clincalc.com/stats/samplesize.aspx. The researcher had hypothesized that there would be a 20% disparity or a two-point variation (on an 11-point scale) in the VAS score among the two groups. Given a significance level (alpha error) of 0.05 and a statistical power of 95%, it was necessary to include a minimum number of 63 patients in each group for the investigation. Due to the possibility of participant attrition, a total of 130 individuals were included in the present investigation.

Statistical analysis:

The data collected in its original form were inputted into a Microsoft Excel Spreadsheet and afterwards subjected to analysis using the well-recognized statistical programmer, SPSS® statistical package version 21.0 (SPSS Inc., Chicago, IL, USA). The mean ± standard deviation is used to display continuous data, whereas absolute numbers and percentages are used to describe categorical variables. The statistical analysis involved the utilization of the Student's t-test to compare the normally distributed continuous variables across the different groups. The Chi-squared test or Fisher's exact test, if applicable, were utilized to compare nominal categorical data among the groups. A significance level of $P < 0.05$ was deemed to indicate statistical significance.

Results

A total of 126 individuals were recruited for the trial, with 63 patients assigned to Group N and 63 patients assigned to Group T. No patients were excluded from the study. Both groups had similar demographic characteristics. The majority of patients in both groups fell within the age range of 31-40 years, as determined by the mean age. [Table 1]

Table 1: Demographic data

Variables	Group N (N=63)	Group T (N=63)	P- Value
Age (years)	39.18±9.09	39.58±9.05	0.798
Gender (M:F)	16:52	11:47	0.277
Weight (kg)	60.21±10.81	54.71±12.71	0.077
ASA (I:II)	51:12	48:15	0.737

Table 2 presents the pre- and post-administration vital signs of the patients who received the research medicines. The systolic blood pressure (SBP) and diastolic blood pressure (DBP) exhibited a significant decrease in group N ($P<0.001$) subsequent to intravenous administration of Nefopam.

Table 2: Hemodynamic parameters before and after administration of study drugs

Parameters		Group N	Group T	P- Value
HR (bpm)	Before Induction	77.84±6.88	76.85±6.22	0.402
	After Induction	76.85±6.43	78.18±5.75	0.217
SBP (mmHg)	Before Induction	124.49±9.38	125.72±9.83	0.472
	After Induction	122.44±7.48	128.06±8.09	<0.001
DBP (mmHg)	Before Induction	70.61±6.58	72.49±5.27	0.083
	After Induction	70.17±4.77	75.12±4.82	<0.001
RR (per minute)	Before Induction	15.98±1.37	16.31±1.37	0.172
	After Induction	14.66±1.47	14.22±1.28	0.072

The mean visual analogue scale (VAS) score exhibited no significant difference between Group N & Group T at the 30-minute interval following the administration of the research medications. The statistical analysis revealed a significant difference ($P < 0.05$) in the mean Visual Analogue Scale (VAS) scores between Group N and Group T at 1.5 hours, 3 hours, 6 hours, 12 hours, 18 hours, and 24 hours. There was no need for rescue analgesic medicine among any of the patients in the two groups. [Figure 1]

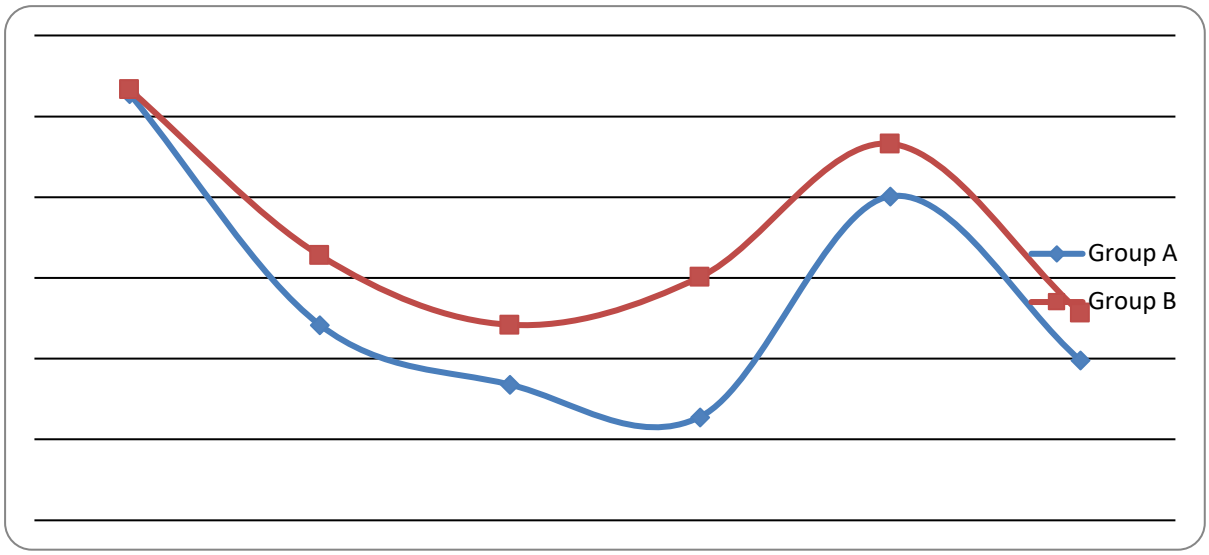

Figure 1: Mean pain scores (Visual Analog Score Scale) at different time intervals

Table 3 presents a comprehensive overview of the different adverse effects associated with the administration of study medicines in both experimental groups. The observed difference did not reach statistical significance, as indicated by a p-value greater than 0.05. The occurrence of nausea and vomiting was observed as the predominant adverse event in both groups.

Table 3: Associated Side-effects

Side-effects	Group N (N=63)	Group T (N=63)	P- Value
Nil	33 (52.4)	28 (44.4)	0.558
Nausea & Vomiting	06 (9.5)	10 (15.9)	0.409
Headache	02 (3.2)	05 (7.9)	0.361
Dizziness	05 (7.9)	03 (4.8)	0.568
Dry mouth	05 (7.9)	04 (6.3)	0.787
Pruritus	05 (7.9)	04 (6.3)	0.787
Hypertension	01 (1.6)	0	0.428
Tachycardia	03 (4.8)	02 (3.2)	0.720
Sweating	03 (4.8)	04 (6.3)	0.761

Discussion

The current randomized controlled research demonstrated that intravenous administration of Nefopam resulted in a reduced Visual Analogue Scale (VAS) score and superior analgesic effects compared to intravenous tramadol in individuals having laparoscopic abdominal procedures.

The administration of nefopam resulted in a notable decrease in systolic blood pressure (SBP) and diastolic blood pressure (DBP) subsequent to the infusion. The adverse effects profiles of both medications exhibited similarity. Nefopam has been employed for the management of nociceptive pain, as well as for both the prevention and treatment of postoperative shivering and hiccups. [7] According to a study, Nefopam 20 mg was shown to have similar potency as morphine 6-12 mg and meperidine 50 mg in surgical contexts. Additionally, it was seen to have a morphine-sparing effect ranging from 30% to 50%.In the present investigation, the average visual analogue scale (VAS) score, indicating significant pain when exceeding 5, was reduced to a score below 3, indicating mild or acceptable pain, within a time frame of 30 minutes following the administration of the medication in both experimental groups. Nevertheless, nefopam demonstrated superior effectiveness compared to tramadol ($p<0.05$) over the majority of the observed follow-up periods. At the 18-24 hour mark, both cohorts exhibited Visual Analogue Scale (VAS) ratings indicating the presence of discomfort at a level considered mild and manageable.

Our findings are consistent with the research undertaken by Ali Najeh Al-Awwady. [9] According to the author, it was discovered that the utilization of intraoperative paracetamol-Nefopam combinations yielded more efficacy in alleviating immediate pain following surgery for elective laparoscopic cholecystectomy when compared to the administration of paracetamol alone or the paracetamol-tramadol combination, all while avoiding any adverse effects. [9] The researchers McLintock et al. conducted a study in which they discovered notable analgesic and morphine sparing effects resulting from the administration of a 20 mg dose of nefopam in the context of postoperative pain. [8] According to Oh et al. (year), it was shown that equipotent dosages of nefopam or fentanyl patient-controlled analgesia resulted in similar levels of analgesia in patients undergoing laparoscopic gynecological surgery. [10]

The delivery of the initial dosage of nefopam resulted in a decrease in heart rate. Nevertheless, the observed reduction did not exhibit statistical significance when compared to the group administered with tramadol. Nefopam exhibited a statistically significant reduction in both systolic blood pressure (SBP) and diastolic blood pressure (DBP) compared to individuals in Group T. Both nefopam and tramadol were shown to reduce the respiratory rate (RR), however the observed difference between the groups was not statistically significant. The potential reduction in vital signs may be attributed to the analgesic effects of the research medications or the anticipated impact of opioids on the cardiovascular and respiratory systems. Abeloos et al. [11] observed slight alterations in blood pressure, heart rate, and respiratory rate after to intravenous injection of nefopam.

Several adverse effects were noticed in groups, including nausea-vomiting, headache, dizziness, dry mouth, itching, tachycardia, and sweating. A single participant within Group N had symptoms of hypertension. In a study conducted by Pandit et al. [12], a comparison was made between nefopam and Pentazocine. The findings revealed that the nefopam group exhibited a lower incidence of side effects (16%) compared to the Pentazocine group (40%) ($P< 0.05$) No notable adverse effects were observed in patients who received the Paracetamol-Nefopam combination, as reported by Ali Najeh Al-Awwady. [9]

In recent times, there has been a growing trend towards the use of opioid-free anaesthesia, a practice that relies on the implementation of multimodal analgesic therapy. It has been shown that there is a correlation between decreased postoperative opioid intake and a reduction in unfavourable effects caused by opioid usage, while also promoting improved recovery and restoration of bowel function. The efficacy of Nefopam 20 mg in enhancing opioid analgesia and decreasing opioid use by roughly 40% has been demonstrated.[13] This substance is classified as a non-opioid analgesic due to its ability to hinder the absorption of monoamines in the central nervous system. Additionally, it indirectly affects the N-methyl-D-aspartate (NMDA) receptor. Consequently, the reduction of c-Fos expression in the dorsal horn of the spinal cord leads to the alleviation of allodynia and hyperalgesia induced by opioids.[14] In the present investigation, it was shown that intravenous (IV) nefopam had superior efficacy in providing postoperative pain management compared to IV tramadol.

Limitations of the study:

There are some limitations associated with our investigation. Instead than focusing on a specific surgical procedure, we incorporated a comprehensive range of laparoscopic abdominal operations. The VAS score was not compared based on gender distribution. There may exist variations in pain thresholds between male and female patients. Additional research is necessary to determine the most effective dose schedule, compare its efficacy to different opioids and non-opioid analgesics, and assess the practicality of administering it to patients classified as ASA III and IV.

Conclusion

The use of intravenous nefopam yielded superior analgesic effects in adult individuals having elective or emergency laparoscopic abdominal operations, as compared to the use of Tramadol. Therefore, it is our contention that Nefopam exhibits more efficacy as an analgesic in comparison to Tramadol. The adverse event profiles of both medications shown similarity.

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