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Original Research Article

The Effects of Nefopam Hydrochloride and Tramadol Hydrochloride on Postoperative Pain in Patients Undergoing Long Bone Fracture Fixations: A Randomised Triple Blinded Study

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Abstract:

Background: Postoperative pain arising out of orthopedic surgeries has detrimental effects on the patients. Nefopam hydrochloride a benzoxazocine derivative, nonopioid, nonsteroidal, and centrally-acting analgesic drug has been proven to be potent analgesic in the treatment of postoperative pain. Tramadol hydrochloride a synthetic, centrally-acting analgesic agent, has been shown to control moderate to severe postoperative pain.

Aims: To evaluate the analgesic efficacy and side effects of nefopam hydrochloride and tramadol hydrochloride on postoperative pain in patients undergoing long bone fracture fixations

Material & Methods: This prospective randomized controlled study triple blinded study was conducted in the Orthopaedic department of our tertiary care Hospital from September 2022 till August 2023. 140 patients(18-60 years) admitted for close reduction and internal fixation with the nailing of a single long bone fracture in the lower limb & with American Society of Anaesthesiologists(ASA) class I and II were recruited in the study. The surgeries were done under spinal anesthesia & the study drugs were administered intravenously starting one hour post-operatively for 24 hrs. Group N - received Tramadol hydrochloride; Group T - received Nefopam hydrochloride Patients were asked to rate their pain experienced on a Visual Analogue Scale & Verbal Rating Scale. The frequency of administration of rescue analgesia, and side effects including gastrointestinal disturbances, headache, constipation, and itching were recorded.

Results: The mean patient age in Group N was 38.56±13.24 yrs & in Group T, it was 37.41±16.25 yrs. Femur fracture was observed in 28 & 32 patients of Group N & T resp. Tibia fracture was observed in 42 & 38 patients of group T & N . Group T had statistically significantly lower VAS scores than Group N at all periods ($p<0.05$). At 24 hrs, the difference between VRS scores was statistically significantly lower in Group T (1.42 ± 0.23) than in Group N (2.02±1.1). Nausea was observed in 2.2% and 2.4 % of patients of group N and group T, respectively. Vomiting was present in only 2.2% of patients in group N and absent in group T. Rescue analgesic Diclofenac sodium 75 mg was administered in 5.7% of group-T and in 17.7% of group-B which was statistically significant ($p<0.05$).

Conclusion: Tramadol Hydrochloride was more effective in controlling postoperative pain with fewer side effects as compared to Nefopam Hydrochloride.

Keywords: Tramadol Hydrochloride, Nefopam Hydrochloride, Long Bone Fracture, Postoperative Pain.

Introduction

Orthopedic surgeries produce a much greater intensity of pain compared to any other treatment procedure due to the highly sensitive bone periosteum. There is inevitable moderate to severe pain after orthopedic surgeries, which persists especially in the first 3 days postoperatively. [1] Poorly managed postoperative pain results in delayed functional recovery, patient dissatisfaction & discomfort, metabolic complications & increased chances of readmission. Thus providing effective pain relief is of utmost importance & critical. Effective post-operative pain relief results in psychological benefits, early mobilization, quicker return to daily work, and improves patient comfort & satisfaction. [2]

Studying the pain mechanisms, noted the observations that sensitization of both the Central nervous system (CNS) and Peripheral nervous system (PNS) due to acute pain leads to the development of chronic pain. [3] Surgeons should attempt to reduce the post-operative pain as

minimally as possible & while taking into account the side effects of analgesics like hypoventilation due to respiratory depression, coagulation anomalies, drug dependence or tolerance, and gastrointestinal disturbances. [4]

Different analgesics control postoperative pain by different mechanisms. The common analgesics administered are opioids and/or nonsteroidal anti-inflammatory drugs (NSAIDs). Both of these classes of drugs have significant undesired side effects, also inhibiting bone healing and functional recovery. [3]

Nefopam is a nonopioid centrally acting drug that acts by inhibiting the reuptake of norepinephrine and serotonin. [5] It produces a morphine-sparing effect, thus minimizing the side effects There is no effect on platelet aggregation and CNS depression. [6] Minor side effects like nausea, vomiting, sweating, and sedation have been observed in 15% to 30% of the patients. [7]

Tramadol is a synthetic analgesic that acts centrally via opioid receptors & causes inhibition of the reuptake of norepinephrine and 5-hydroxytryptamine (serotonin). There is lesser respiratory depression than other opioids with a higher incidence of nausea and vomiting. [8]

Thus, the present randomized controlled clinical study aimed to evaluate the analgesic efficacy and side effects of nefopam hydrochloride and tramadol hydrochloride on postoperative pain in patients undergoing long bone fracture fixations.

Material & Methods

This prospective randomized controlled study triple blinded study was conducted in the Orthopaedic department of our tertiary care Hospital from September 2022 till August 2023. Patients (n=140) in the age range of 18-60 years admitted for close reduction and internal fixation with the nailing of a single long bone fracture in the lower limb & with American Society of Anaesthesiologists(ASA) class I and II were recruited in the study. Patients were excluded if suffering from cardiac disease, renal or hepatic insufficiency, glaucoma, psychiatric disturbance & epidural analgesia during/after surgery. Approval was taken from the institutional ethical board and written informed consent was taken from the patients before the start of surgery.

A detailed patient history, medical history, and mode of injury were recorded. Pre-operative investigations like complete blood count, Coagulation profile (Bleeding time/Clotting time), Blood grouping, kidney function test, liver function test, chest x-ray, and electrocardiogram (ECG) were carried out. The surgeries were done under spinal anesthesia & the study drugs were administered intravenously starting one hour post-operatively for 24 hrs.

The patients were randomized into two groups through the computerized allotment method. The principal investigator prepared the study drugs The patients and study coinvestigators were blinded to the study drugs & outcome evaluation.

Group N - received Tramadol hydrochloride (100 mg in 100ml normal saline IV infusion over a 15 min period, every 6th hour)

Group T - received Nefopam hydrochloride (20 mg in 100 ml normal saline IV infusion over a 15 min period, every 6th hour)

Patients were asked to rate their pain experienced on a Visual Analogue Scale (VAS) (where 0=no pain and 10= worst pain), Verbal Rating Scale (VRS) score (none, mild, moderate, and severe) at 15 minutes, 30 minutes, 1 hour, 4 hours, 6 hours, 12 hours and 24 hours after 1st dose of drug administration.

If the patient complained of severe pain with a VAS score of more than 8, rescue analgesia as diclofenac sodium 75 mg iv was administered. The frequency of administration of rescue analgesia, and side effects including gastrointestinal disturbances, headache, constipation, and itching were recorded.

Statistical Analysis: The collected data were tabulated & put in Excel sheets & analyzed using statistical software version Ind 22. A comparison of data between the groups was done using student paired t-test. The results were expressed as mean ± standard deviation (SD). For all statistical analyses, $p < 0.05$ was considered statistically significant.

Results

This prospective study recruited 140 patients, 85 males and 55 females. There was no significant difference between the two groups with respect to age and gender. The mean patient age in Group N was 38.56±13.24 yrs & in Group T, it was 37.41±16.25 yrs. Femur fracture was observed in 28 patients of Group N, and 32 patients of Group T. Tibia fracture was observed in 42 patients of Group A and 38 patients of Group B. Group T had statistically significantly lower VAS scores than Group N at all time periods ($p<0.05$). The reduction in VAS scores was also greater in Group T than in Group N . (Fig 1) VRS score was lower in Group T at all time intervals with no statistically significant difference. At 24 hrs, the difference between VRS scores was statistically significantly lower in Group T (1.42 ± 0.23) than in Group N (2.02±1.1).

Nausea was observed in 2.2% and 2.4 % of patients of group N and group T, respectively. Vomiting was present in only 2.2% of patients in group N

and absent in group T. No statistically significant difference between side effects was observed between the groups($p>0.05$). Rescue analgesic Diclofenac sodium 75 mg was administered in 5.7% of group-T and in 17.7% of group-B which was statistically significant ($p<0.05$).

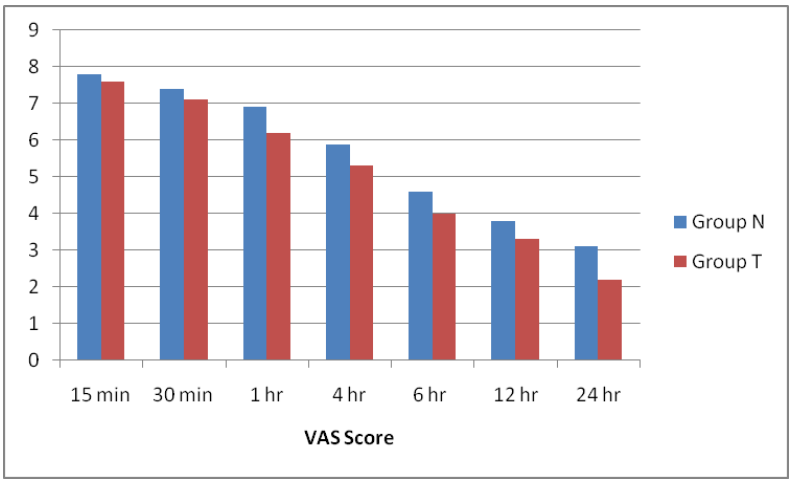

Figure 1: VAS Scores at various time intervals

Discussion

Postoperative pain remains a significant distressing factor for patients and prevents a challenge for anesthetists & orthopedic surgeons. It is a complex physiological reaction to tissue injury that manifests from autonomic & behavioral responses. Postoperative pain leads to a rise in perioperative complications, thus postoperative pain should be managed well. [10]

Various analgesics are used to control the postoperative pain. Insufficient control of acute pain results in the development of chronic postsurgical pain. This hampers the psychosocial well-being of the patient with frequent hospitalization, interference in the daily activities & overall health of the individual. [11] This study compared the effects of Nefopam hydrochloride and Tramadol hydrochloride on the control of postoperative pain following long bone fracture fixations.

In the present study the mean age group was Group-N was 38.56±13.24 yrs & in Group-T, it was 37.41±16.25 yrs.No statistically significant difference was observed between the groups concerning age & gender. Similarly, Dholariya RD et al 2022 study concluded no difference concerning age and gender between the two groups. [12] Paudel R et al 2017, noted baseline characteristics to be a par between the groups with the majority being males. [13]

In the present study, VAS pain scores observed statistically significant differences at all time intervals with Group T showing lower scores. Thus, Tramadol hydrochloride exhibited a better analgesic efficacy than Nefopam hydrochloride. Similarly, Dholariya RD et al 2022 study concluded better postoperative pain control by Tramadol than Nefopam at all time intervals except at 15 min. [12] Study conducted by Swarnkar et al 2022 concluded iv nefopam provided better postoperative pain relief than Tramadol in patients undergoing laparoscopic surgeries under general anesthesia. [14] Koh et al. (2019) recorded no significant difference in VAS score between the Nefopam and Control group. [15]

In the present study, the VRS score was lower in Group T at all time intervals with no statistically significant difference. At 24 hrs, the difference between VRS scores was statistically significantly lower in Group T than in Group N. Accordingly, Du Manoir et al 2003 concluded no

The difference in VRS scores between the Nefopam group and placebo group after orthopedic surgery.[16] Dholariya RD et al 2022 concluded VRS scores to be significant ($p=0.002$) between the groups only at 24 hours. The score was lower in the tramadol group than in nefopam. [12]

In the present study, nausea & vomiting were present in both the groups which was statistically insignificant. Dholariya RD et al 2022 presented similar incidences of side effects in both groups. [12] Du Manoir et al 2003 study comparing the analgesic efficacy of nefopam after orthopedic surgery observed side effects of nausea, retention of urine, vomiting and drowsiness & sweating. [16] Kumar et al 2017 noted significant adverse events of nausea & vomiting. [17] To control gastrointestinal adverse events ondansetron was the drug of choice, without affecting the analgesic efficacy. [18,19]

In the present study, the rescue analgesic Diclofenac sodium 75 mg was administered in

5.7% of Group-T and in 17.7% of Group-N which was statistically significant ($p<0.05$). Similar findings were observed by Dholariya et al 2022. [12] Solanki RN et al 2015 observed the administration of iv Diclofenac sodium in patients after orthopedic surgery, to be higher in the tramadol group than the nalbuphine group when administered eight hourly. [20]

Conclusion

Thus the present study concludes that both tramadol and nefopam have potent analgesic efficacy. Tramadol hydrochloride shows better analgesic effects, fewer side effects & reduced usage of rescue analgesics as compared to Nefopam hydrochloride in controlling postoperative pain following long bone fracture fixations.

References

1. Nurhussen Riskey Arefayne, Shimelis Seid Tegegne, Amare Hailekiros Gebregzi, Salh Yalew Mustofa, Incidence and associated factors of post-operative pain after emergency Orthopedic surgery: A multi-centered prospective observational cohort study, International Journal of Surgery Open, Volume 27,2020, Pages 103-113, ISSN 2405-8572.
2. Mohammadi MT, Tavakoli F. Multi-Modal Preemptive Analgesia with Pregabalin, Acetaminophen, Naproxen, and Dextromethorphan in Radical Neck Dissection Surgery: A Randomized Clinical Trial. Anesth Pain Med. 201 6;6(4):e33526.
3. Pountos I, Georgouli T, Calori GM, Giannoudis PV. Do nonsteroidal anti-inflammatory drugs affect bone healing? A critical analysis. Sci World J. 2012; 2012:606404.
4. MA, Kim DW, Kim JY, Ki HS. Effects of nefopam with fentanyl in intravenous patient-controlled analgesia after arthroscopic orthopedic surgery: A prospective double-blind randomized trial. Turk J Med Sci. 2018;48(1):1 42–9.
5. Remérand F, LeTendre C, Rosset P, Peru P, Favard L, Pourrat X, et al.Nefopam after total hip arthroplasty: role in multimodal analgesia.Orthop Traumatol Surg Res. 2013;99(2): 169–74.
6. Kim KH, Abdi S. Rediscovery of nefopam for the treatment of neuropathic pain. Korean J Pain. 2014 Apr;27(2):103-11.
7. Durrieu G, Olivier P, Bagheri H, Montastruc JL; French Network of Pharmacovigilance Centers. Overview of adverse reactions to nefopam: an analysis of the French Pharmacovigilance database. Fundam Clin Pharmacol. 2007 Oct;21(5):555-8.
8. Pathan H, Williams J. Basic opioid pharmacology: an update. Br J Pain. 2012 Feb; 6(1):11-6.
9. Chou R, Gordon DB, De Leon-Casasola O, Rosenberg JM, Bickler S, Brennan T, et al. Management of Postoperative Pain: a clinical practice guideline from the American pain society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' committee on regional anesthesia, executive committee, and administrative council. J Pain. 2016;17(2):131 –57.
10. Thapa P, Euasobhon P. Chronic postsurgical pain: current evidence for prevention and management. Korean J Pain 2018; 31:155-73.
11. Ishida Y, Okada T, Kobayashi T, Funatsu K, Uchino H. Pain Management of Acute and Chronic Postoperative Pain. Cureus. 2022 Apr 9;14(4):e23999.
12. Dholariya R D, Marviya J, Aggarwal S, Beri S, The effects of nefopam hydrochloride and tramadol hydrochloride on postoperative pain in patients undergoing long bone fracture fixations: A randomised triple blinded study. Indian J Orthop Surg 2022;8(3):190-19.
13. Paudel R, Deka A, Gupta HK, Nepal HP. Comparative evaluation of analgesic efficacy of tramadol and diclofenac-sodium in postoperative orthopedic patients. Int J Basic Clin Pharmacol. 2017;6(3):643–7.
14. Swarnkar, Yogesh Kumar; Gupta, Rajiv1; Arora, Anand Mohan; Mistry, Tuhin2,. Comparison of Intravenous Nefopam and Tramadol for Postoperative Analgesia in Adult Patients Scheduled for Laparoscopic Abdominal Surgeries under General Anesthesia: A Prospective, Randomized, Double-Blind Study. The Indian Anaesthetists Forum 23(1):p 25-30, Jan–Jun 2022. | DOI: 10.4103/ TheIAForum. TheI A Forum_156_21
15. Koh HJ, Joo J, Kim YS, Lee YJ, Yoo W, Lee MS. Analgesic effect of low dose nefopam hydrochloride after arthroscopic rotator cuff repair: a randomized controlled trial. J Clin Med. 2019;8(4):553.
16. Manoir BD, Aubrun F, Langlois M, Guern MEL, Alquier C, Chauvin M, et al. Randomized prospective study of the analgesic effect of nefopam after orthopaedic surgery. Br J Anaesth. 2003;91(6):836–41.
17. Kumar J, Sinha PK, Prasad BK, Simbha A. Comparative study of nalbuphine and tramadol for postoperative pain relief in patients of short surgical procedures under TIVA. Int J Contemp Med Res. 2017;4(4):977–99.
18. Lu KZ, Shen H, Chen Y, Li MG, Tian GP, Chen J. Ondansetron does not attenuate the analgesic efficacy of nefopam. Int J Med Sci. 201 3;10(12):1790.

19. Kiran KS, Vyas V, Patil S. Comparative efficacy and safety of intravenous tramadol and nalbuphine for pain relief in postoperative patients. Indian Journal of Pain. 2018;32(2):96–96

20. Solanki RN, Gosai ND, Joshi GM, Patel BM, Modi HV, Jain R. A comparative study of intravenous nalbuphine HCl and tramadol HCl for post-operative pain relief following orthopaedic surgeries. Asian Pac J Health Sci. 2015;2(1):155–60.