Evaluating the efficacy of Methocarbamol and Nefopam in orthopedic surgical pain

By Ahmed Nasser Qasim Al-Nasrawi

WORD COUNT 2718
TIME SUBMITTED 19-APR-2024 01:15PM
PAPER ID 108378529

Word Count – Words: 2718

Evaluating the efficacy of Methocarbamol and Nefopam in orthopedic surgical pain

Ahmed Nasser Qasim Al-Nasrawi[1], Mustafa Wameedh Khalid Al-Ibrahim[2], Saif Ali Aljabran[3]

[1]Orthopedics department, Al-Sader Teaching Hospital- Basrah, Iraq

[2]Al-Sader Teaching Hospital- Basrah, Iraq

[3]Pharmacology Department, University of Basrah, College of Medicine, Basrah, Iraq

Ahmeds201258@yahoo.com

61001

Basrah, Iraq

ABSTRACT

Background. Pain after orthopedic surgeries represents a special concern in patients with fractures. The use of multimodal analgesia significantly reduced the opioid need and reduced the risk of their side effects. This study compared the effect of methocarbamol and nefopam in the reduction of post-operative pain for patients undergoing orthopedic surgeries.

Method. This prospective, double-blind, randomized controlled trial took place at Al-Sader Teaching Hospital in Basrah, Iraq, from early 2022 to the end of 2023. Participants were randomized into two groups, with pain intensity measured at 1-, 6-, and 12 hours post-operation using the Visual Analogue Scale (VAS). Side effects were also evaluated.

Results. The results showed remarkable similarities in mean age, gender distribution, and BMI, supported by robust p-values, affirming the effective matching of the two groups. Moving to pain management, we observed a significant advantage in favor of Methocarbamol. At all-time intervals (1 hour, 6 hours, and 12 hours post-operation), Methocarbamol consistently demonstrated lower mean Visual Analog Scale (VAS) scores compared to Nefopam. These differences were highly statistically significant, underscoring the superior pain relief efficacy of Methocarbamol. Exploring side effects, we found no statistically significant disparities in the occurrence of nausea and vomiting between the two groups. However, there was a noticeable trend towards higher tachycardia incidence in the Nefopam group, though it did not reach statistical significance.

Conclusion. In conclusion, this study demonstrated a superior efficacy of methocarbamol in reducing post-operative pain when compared to nefopam. Furthermore, it is important to note that both drugs exhibited a favorable safety profile, with no reports of serious adverse effects. There is no statistically significant difference in the occurrence of nausea and vomiting and tachycardia as side effects of both drugs.

.

Keywords: Methocarbamol, Nefopam, Orthopedic operations, Post-operative analgesia, Side effects

Introduction

Acute postoperative pain, which is frequently of medium-high degree, affects approximately 80% of patients who undergo surgery [1]. Less than half of surgical patients report receiving appropriate postoperative pain management, This percentage is a serious issue because it puts patients at an elevated risk of acquiring chronic pain related to the treatment and may result in unfavorable physiologic effects in the immediate postoperative term [2]. Adults with severe chronic postoperative pain account for 2 to 10% of cases [3].

The purpose of postoperative pain management is to ease the patient's return to normal activity and to lessen the harmful effects of acute postsurgical pain [4]. Opioid analgesic medication has always been the cornerstone of care for immediate postoperative pain. Nevertheless, the recent increase in morbidity and mortality linked to opioid abuse has increased the demand for more research into creating pain management plans that put a greater emphasis on employing a multimodal strategy [5]. Non-opioid analgesics with a range of modes of action offer the best pain treatment while lowering overall opioid intake and the adverse effects associated with opioid use. In numerous clinical studies, including orthopedic procedures, acetaminophen, gabapentin, lidocaine, ketamine, methocarbamol, dexmedetomidine, nefopam, and dexamethasone have shown opioid-sparing effects and the capacity to greatly reduce postoperative pain [6,7].

Nefopam is a centrally acting, non-opioid, non-steroidal anti-inflammatory analgesic medication. Its mechanism of action for relieving pain involves the inhibition of sodium and calcium channels at the synaptic area of the dorsal horn of the spinal cord, leading to actions against nociceptive and neuropathic pain [8]. It was supposed to reduce morphine intake and postoperative pain [9]. Nefopam also has a stronger analgesic effect in hip arthroplasty patients with considerable preoperative discomfort [10].

Methocarbamol is one of the centrally-acting striated skeletal muscle relaxants approved for the management of acute post-operative musculoskeletal pain, and has been licensed since 1957 [11]. Despite being widely used today, there is a lack of many high-quality studies comparing methocarbamol to a placebo or other treatments for pain from muscular origin, and there are no any meta-analyses either [12]. However, off-label use has been studied for a variety of painful conditions, which including acute and chronic non-specific low back pain, inflammatory arthritis, fibromyalgia, myofascial pain, rib fractures, and perioperative management of hip and knee replacements. currently, clinical use is typically restricted to the adjunctive treatment of acute pain of musculoskeletal origin [13-15].

The goal of this study was to compare the effectiveness of methocarbamol and nefopam for treating of postoperative pain following orthopedic surgery.

Method

The study was conceived as a prospective, randomized, double-blind, controlled trial aimed at assessing the post-operative analgesic efficacy and safety of nefopam and methocarbamol injections in orthopedic surgical patients. The investigation was conducted at Al-Sader Teaching Hospital, a reputable medical facility situated in Basrah, southern Iraq. It spanned from early 2022 to the end of 2023, providing a substantial timeframe to accrue, evaluate, and interpret the necessary data.

The cohort comprised 110 adults aged 18-65 years who were undergoing elective open orthopedic surgeries including trauma and hip replacement surgeries. Exclusion criteria encompassed individuals with an allergy to methocarbamol or nefopam, a history of substance abuse, and severe hepatic or renal impairment. Participants were randomized using a computer-generated random number sequence into one of two treatment groups. Group A received a single dose of intramuscular nefopam 20 mg, and Group B received methocarbamol in a dosage of 1 gram IV as post-operative analgesics.

The primary outcome was the assessment of pain intensity at specified intervals post-operation. Secondary outcomes included, evaluation of side effects associated with the administered drugs.

Pain intensity was assessed at three post-operative intervals: 1, 6, and 12 hours using the Visual Analogue Scale (VAS). The evaluation of side effects was meticulously carried out, taking into account any adverse reactions or complications arising from the administration of nefopam and methocarbamol.

Data were collected using standardized data collection forms to capture demographic information, pain scores, adverse events, and other relevant data. Statistical analysis was

performed using descriptive statistics to summarize demographic and clinical characteristics. Independent t-tests or Mann-Whitney U tests were used for continuous variables, and Chi-square or Fisher's exact tests for categorical variables. The significance level was set at a p-value of <0.05 with a confidence interval (C.I) of 95%.

Results

The table compares two groups, Methocarbamol and Nefopam, with respect to age, gender distribution, and body mass index (BMI). The mean ages are similar (46.36 vs. 47.24 years), and gender distribution is comparable with a slightly higher male percentage in both groups (69.1% vs. 63.6% for Methocarbamol and Nefopam, respectively). The mean BMIs also show no significant difference (34.38 vs. 35.18). These findings, supported by p-values of 0.485, 0.545, and 0.411, respectively, suggest that the two groups are well-matched in terms of these variables.

Table 1. Demographical Data distribution among the studied groups

Variables	**Methocarbamol group (n= 55)**	**Nefopam group (n= 55)**	**P- value**
Age (Mean ±SD)	46.36±8.62	47.24±7.24	0.485
Gender			
Male	38 (69.1%)	35 (63.6%)	0.545
Female	17 (30.9%)	20 (36.4%)	
Body mass index (BMI), Mean ±SD	34.38± 5.68	35.18± 6.52	0.411

Standard deviation = SD, Body mass index =BMI, number = n

In this table, a comparison is made between two groups, based on Visual Analog Scale (VAS) at different time intervals. At 1 hour, the Methocarbamol group had a significantly lower mean VAS score (3.58) compared to the Nefopam group (5.31). This difference continued at 6 hours, with Methocarbamol (4.82) showing lower pain scores than Nefopam (5.53). After 12 hours, once again, Methocarbamol (3.07) had lower pain scores compared to Nefopam (4.71). All these differences were highly statistically significant with p-values <0.001, suggesting that Methocarbamol was more effective in managing pain compared to Nefopam at all time intervals.

Table 2. Visual analogue scale analysis among the studied groups

Visual Analog scale (VAS)	Methocarbamol group (n=55)	Nefopam group (n=55)	P- value
At 1 hour (Mean ±SD)	3.58 ±0.629	5.31±1.06	<0.001
After 6 hours (Mean ±SD)	4.82±1.27	5.53±0.92	<0.001
After 12 hours (Mean ±SD)	3.07±0.92	4.71±1.18	<0.001

In this table comparing side effects, there is no statistically significant difference in the occurrence of nausea and vomiting. Tachycardia shows a noticeable difference but does not reach statistical significance, suggesting a potential trend towards higher tachycardia incidence in the Nefopam group (21.81%) compared to the Methocarbamol group (9.09%).

Table 3. Side effects analysis among the studied groups

Side effect	Methocarbamol group (n=55)	Nefopam group (n=55)	P- value
Nausea	1 (1.8%)	2 (3.6%)	0.628
Vomiting	0 (0.0%)	1 (1.8%)	0.315
Tachycardia	5 (9.09%)	12 (21.81%)	0.065

Discussion

As this study represents the inaugural investigation into the analgesic properties of methocarbamol and nefopam in mitigating post-operative pain, it contributes novel and substantial insights to the existing medical literature, which has hitherto advocated the utilization of multimodal analgesic approaches in the management of postoperative pain associated with fractures.

In recent years, there has been a discernible upsurge in the utilization of multimodal pain management strategies aimed at enhancing pain control and mitigating opioid exposure. Methocarbamol, classified as a skeletal muscle relaxant, exerts its effects by inhibiting acetylcholinesterase activity at the neuromuscular junction, thereby inducing muscle relaxation without a direct impact on striated muscle [16]. Notably, a retrospective investigation conducted by Aljuhani et al. failed to provide substantive evidence supporting the use of methocarbamol in the context of traumatic injury, as it did not demonstrate a significant reduction in pain intensity during hospitalization, opioid consumption, or duration of hospital stay [17]. Conversely, the current study yielded noteworthy findings, revealing a substantial discrepancy in pain alleviation between the methocarbamol and nefopam groups, particularly evident one hour post-administration. This observation aligns with the outcomes of a study conducted by Lindsay et al., which explored the efficacy of methocarbamol in managing pain among patients with traumatic rib fractures and reported a marked reduction in pain scores [18].

Nefopam administration both before the skin incision and upon the completion of surgery failed to exert a discernible influence on the total morphine consumption or the intensity of postoperative pain, as indicated by a study encompassing patients undergoing open spine procedures [19]. In a similar vein, an investigation involving patients subjected to minimally invasive spine surgery unveiled that the incorporation of a 24-hour nefopam infusion did not

yield any incremental analgesic benefits or lead to improved functional outcomes post-surgery [20].

Several plausible explanations can be advanced to rationalize why nefopam demonstrated a comparatively weaker analgesic effect than methocarbamol in our study. First, the mode of nefopam administration via intramuscular injection may be less efficacious than intravenous delivery over a 30-minute interval [21]. Second, it is plausible that muscular spasms around the fractured bone or the surgical site significantly contributed to overall pain perception and limited range of motion, corroborating our findings [22]. This is particularly relevant given that a substantial proportion of the patients in our study presented with femur, tibia, or spinal fractures, all of which are heavily encased by musculature, potentially intensifying the sensation of pain.

The safety profiles of both methocarbamol and nefopam were meticulously assessed in our study, and reassuringly, no severe adverse effects were observed with either medication. Nonetheless, it is noteworthy that tachycardia was more frequently documented among patients receiving nefopam compared to those administered methocarbamol. This aligns with prior research where approximately 50% of patients receiving nefopam experienced tachycardia in the immediate postoperative period [23]. It is imperative to acknowledge that various infrequent and non-serious adverse effects have been reported in association with methocarbamol use in previous studies, including drowsiness, skin rash, weakness, and hyperhidrosis [24]. Importantly, these side effects typically abate shortly after the cessation of treatment.

Several limitations were identified in the course of this study. Firstly, all participants received nefopam exclusively via intramuscular injection. Additionally, certain parameters, such as range of motion and length of hospital stay, were not included as endpoints in this study, warranting further investigation to comprehensively assess the overall impact of nefopam and methocarbamol in the context of orthopedic surgical care. These limitations underscore the need

for future research endevors to provide a more comprehensive understanding of the outcomes associated with these analgesic agents in orthopedic surgery.

Conclusions

In conclusion, this study demonstrated a superior efficacy of methocarbamol in reducing post-operative pain when compared to nefopam. Furthermore, it is important to note that both drugs exhibited a favorable safety profile, with no reports of serious adverse effects. There is no statistically significant difference in the occurrence of nausea and vomiting and tachycardia as side effects of both drugs

Conflict of Interest: The authors declare no conflicts of interest related to this research.

Acknowledgment: The authors would like to express their sincere appreciation to the staff and patients of Al-Sader Teaching Hospital in Basrah, Iraq, for their valuable contributions and cooperation during this study.

References

1. Kelley BP, Shauver MJ, Chung KC: Management of acute postoperative pain in hand surgery: a systematic review. The. Journal of hand surgery. 2015, 40:1610-9. 10.52338/JOP.2024.1005
2. Lovich-Sapola J, Smith CE, Brandt CP: Postoperative pain control. Surg Clin North Am. 2015, 95:301-18. 10.1016/j.suc.2014.10.002
3. Rawal N: Current issues in postoperative pain management. Eur J Anaesthesiol. 2016, 33:160-71. 10.1097/EJA.0000000000000366
4. Horn R, Kramer J: Postoperative pain control. 2019.
5. Bartels K, Mayes LM, Dingmann C, et al.: Opioid Use and Storage Patterns by Patients after Hospital Discharge following Surgery. PloS one. 2016, 11:0147972. 10.1371/journal.pone.0147972. eCollection 2016
6. Lamperti M, Tufegdzic B, Avitsian R: Management of complex spine surgery. Current Opinion in Anaesthesiology. 2017, 30:551-6. 10.1097/ACO.0000000000000494
7. Patanwala AE, Aljuhani O, Kopp BJ, Erstad BL: Methocarbamol use is associated with decreased hospital length of stay in trauma patients with closed rib fractures. The. American Journal of Surgery. 2017, 214:738-42. 10.1016/j.amjsurg.2017.01.003
8. Kim KH, Abdi S: Rediscovery of nefopam for the treatment of neuropathic pain. The. Korean journal of pain. 2014, 27:103-11. 10.3344/kjp.2014.27.2.103
9. Girard P, Chauvin M, Verleye M: Nefopam analgesia and its role in multimodal analgesia: a review of preclinical and clinical studies. Clinical and Experimental Pharmacology and Physiology. 2016, 43:3-12. 10.1111/1440-1681.12506
10. Du Manoir B, Aubrun F, Langlois M, et al.: Randomized prospective study of the analgesic effect of nefopam after orthopaedic surgery. British journal of anaesthesia. 2003, 91:836-41. 10.1093/bja/aeg264
11. Methocarbamol. LiverTox: Clinical and Research Information on Drug-Induced Liver Injury. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; 2012.
12. See S, Ginzburg R: Choosing a skeletal muscle relaxant. Am Fam Physician. 2008, 78:365-70.
13. Richards BL, Whittle SL, van der Heijde DM, Buchbinder R: The efficacy and safety of muscle relaxants in inflammatory arthritis: a Cochrane systematic review. J Rheumatol Suppl. 2012, 90:34-9. 10.3899/jrheum.120340
14. Beebe FA, Barkin RL, Barkin S: A clinical and pharmacologic review of skeletal muscle relaxants for musculoskeletal conditions. Am J Ther. 2005, 12:151-71. 10.1097/01.mjt.0000134786.50087.d8

15. Looke TD, Kluth CT: Effect of preoperative intravenous methocarbamol and intravenous acetaminophen on opioid use after primary total hip and knee replacement. Orthopedics. 2013, 36:25-32. 10.3928/01477447-20130122-54
16. de Gray LE, Seth B: Drugs used to treat joint and muscle disease. Anaesthesia & Intensive Care Medicine. 2021, 22:70-6. 10.1016/j.mpaic.2014.12.001
17. Aljuhani O, Kopp BJ, Patanwala AE: Effect of methocarbamol on acute pain after traumatic injury. Am J Ther. 2017, 24:202-6. 10.1097/MJT.0000000000000364
18. Deloney LP, Smith Condeni M, Carter C, et al.: Efficacy of methocarbamol for acute pain management in young adults with traumatic rib fractures. Annals of Pharmacotherapy. 2021556, 705-10. 10.1177/1060028020964796
19. Eiamcharoenwit J, Chotisukarat H, Tainil K, Attanath N, Akavipat P: Analgesic efficacy of intravenous nefopam after spine surgery: a randomized, double-blind, placebo-controlled trial. F1000Research. 2020, 9:516. 10.12688/f1000research.22909.2
20. Chalermkitpanit P, Limthongkul W, Yingsakmongkol W, et al.: Analgesic effect of intravenous nefopam for postoperative pain in minimally invasive spine surgery: a randomized prospective study. Asian Spine Journal. 2022, 16:651. 10.31616/asj.2021.0337
21. Remérand F, Le Tendre C, Rosset P, et al.: Nefopam after total hip arthroplasty: role in multimodal analgesia. Orthopaedics & Traumatology: Surgery & Research. 2013, 99:169-74. 10.1016/j.otsr.2012.08.007
22. Järvinen TAH, Järvinen TLN, Kääriäinen M, et al.: Muscle injuries: optimising recovery. Best practice & research Clinical rheumatology. 2007, 21:317-31. 10.1016/j.berh.2006.12.004
23. Park HJ, Park JU, Yoo W, Moon YE: Analgesic effects of nefopam in patients undergoing bimaxillary osteotomy: A double-blind, randomized, placebo-controlled study. Journal of Cranio-Maxillofacial Surgery. 2016, 44:210-4. 10.1016/j.jcms.2015.11.012
24. Jung H, Chae HK: The safety and efficacy of methocarbamol as a muscle relaxant with analgesic action: analysis of current data. 2019. 10.20535/ibb.2019.3.4.183336