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ORIGINAL ARTICLE

Can gabapentinoids decrease perioperative opioid requirements in orthopaedic trauma patients? A single-centre retrospective analysis

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Abstract

Introduction Perioperative pain control in patients with orthopaedic trauma/extremity fractures has gained a lot of attraction from the scientific community in the last two decades. In addition to multimodal analgesia, the use of non-opioid drugs like gabapentinoids for pain relief is gradually finding its place in several orthopaedic subspecialties like spinal surgery, arthroplasty, and arthroscopic procedures. We envisage investigating the effectiveness of gabapentin in perioperative pain control in patients with extremity fractures undergoing surgical fixation.

Methodology This was a retrospective comparative study conducted between January 2020 and January 2022. Patients with isolated fractures of the extremity involving long bones who were treated at our trauma centre, during the study period were divided into two groups based on the analgesics they received. Patients who received gabapentin and paracetamol were placed in group GP and those who received only paracetamol were assigned group NGP. Gabapentin was given in a single dose of 300 mg 4 h before surgery. Postoperatively, they were given 300 mg 12 hourly for 2 days. All patients in our trauma centre are usually managed with parenteral paracetamol administration pre and postoperatively. VAS score was calculated postoperatively at 2, 6, 12, 24 and 48 h. Patients requiring additional analgesics for pain relief were administered intravenous tramadol or a buprenorphine patch was applied. Patients in both groups were compared in terms of pain control, the additional requirement of opioid analgesics, and any adverse event related to medications.

Results One hundred and nineteen patients were enrolled in the study. Out of 65 patients in the NGP group (non-gabapentin group), 74% of patients received additional opioid analgesics apart from paracetamol. Out of the 54 patients in the GP group (gabapentin group), only 41% required additional opioid analgesia for pain control. There was a significant difference in opioid consumption between the two groups ($p < 0.01$). VAS scores were not significantly different between the two groups at 2, 4, 6, 12, 24 and 48 h. Gender and fracture morphology did not affect opioid intake in the GP group. However, in the non-gabapentin group, there was a significant difference in opioid requirement in patients with intraarticular fractures ($p < 0.01$).

Conclusion Analgesic requirements vary from patient to patient depending on the injury's severity and surgery duration. However, there are no strict guidelines for pain relief in limb trauma surgeries which often leads to overuse and opioid-related complications or underuse and chronic pain. Gabapentinoids can supplement the analgesic effect of paracetamol in trauma patients during the perioperative period, decreasing the need for opioids.

Keywords Gabapentin · Opioid · Paracetamol · Trauma · VAS

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Introduction

Orthopaedic trauma results in significant pain to the patient and poor pain control can lead to long-term consequences including poor patient satisfaction or poor patient-reported outcome measures (PROM). Choosing appropriate analgesics both pre-and post-surgery is necessary to provide adequate pain control. Multimodal analgesia has been proven to be effective in literature [1], but the use of opioid drugs has associated side effects like overdose, falls and fractures, road traffic accidents, endocrinopathies, chronic constipation, and even death [2].

Gabapentin acts by binding to the α2δ1 subunit of voltage-gated calcium channels, causing a decrease in presynaptic calcium influx and release of excitatory neurotransmitters like glutamate. They avoid central sensitization by disrupting α2δ1 forward trafficking from the dorsal root ganglia, their endosomal recycling, and thrombospondin-mediated activities, and promote glutamate absorption by excitatory amino acid transporters [3]. This results in a protective effect over allodynia after chronic gabapentinoids usage. Few reports have already investigated the potential beneficial effect of gabapentinoids in perioperative analgesia [4].

The effects of gabapentin on postoperative analgesia have been studied in spinal surgery, arthroplasty, and arthroscopy. The effectiveness of gabapentin in orthopaedic trauma surgeries is yet to be explored. The primary aim of our study was to provide adequate postoperative analgesia and start early rehabilitation, as well as to minimize the nociceptive input and reduce the risk of transition to central sensitization and to assess the effectiveness of gabapentin in orthopaedic trauma surgeries. The current study was an attempt to ascertain the effect of gabapentin on the requirement of opioids in trauma patients.

Methodology

A retrospective observational study was conducted at our Level I Trauma Centre between January 2020 and January 2022 on patients who were operated on for isolated orthopaedic extremity fractures. Patients were divided into two groups based on the status of perioperative gabapentin use. Group GP are those patients who received gabapentin and paracetamol and Group NGP are those patients who received only paracetamol. The decision to administer gabapentin was at the discretion of the treating surgeon or at times on the choice of the patient, considering its potential effect on the decreased postoperative need for opioids.

Inclusion criteria consisted of skeletally mature patients with isolated fractures of the extremity involving long bones who were treated at our trauma centre during the study period. All patients satisfying the inclusion criteria were recruited and divided into two groups based on the analgesics they received. Skeletally immature patients, geriatric patients, those with isolated ligament injuries, spine fractures, patients with more than one system involvement, open fractures, patients allergic to gabapentin, and those who received peripheral nerve block or epidural analgesia for analgesia, were excluded from the study. Furthermore, patients who had chronic kidney disease and those suffering from chronic liver disease were also excluded from the study, as they could have adverse reactions to gabapentinoids due to delay in excretion of the same.

Gabapentin was given in a single dose of 300 mg 4 h before surgery. Postoperatively gabapentin was administered at 300 mg 12 hourly for 2 days. Paracetamol was given via the parenteral route pre and postoperatively, every 8 h. VAS score was calculated postoperatively at 2,4,6,12,24 and 48 h. Patients requiring additional analgesia were given intravenous tramadol and buprenorphine patch and their frequency was documented. Stronger opioids like morphine and fentanyl were reserved for patients who did not achieve adequate analgesia with weaker opioids like tramadol and buprenorphine, and those patients were not included in the study. We further noticed that there was no set timeframe for the postoperative opioid demand; it varied greatly from patient to patient. As opposed to VAS, which was calculated in all patients at regular, defined intervals.

The primary outcome measures were the requirement of additional analgesics and the calculation of the VAS score in the postoperative period for 48 h. The secondary outcome measure was to assess the effectiveness of gabapentin for adequate analgesia. Adverse events related to all the medications administered in both groups were documented. SPSS version 26 was used to analyse the statistical data. Patient demographic details and VAS scores between the two groups were deduced using the Independent T test. We performed a chi-square test to find the difference in opioid consumption between the 2 groups. A p value of < 0.01 was considered to be significant.

Results

A total of 297 patients with isolated extremity fractures presented to our trauma centre during the study period. One hundred and nineteen patients were enrolled in the study. Out of the remaining 178 patients, 42 patients had open fractures, 39 were in the paediatric age group, 30 were geriatric fractures, 12 had incomplete VAS documentation, 32 patients had additional requirement of stronger opioids like morphine or fentanyl, and 23 were managed

nonoperatively. Sixty-five patients belonged to the NGP group, who received Paracetamol and opioids in the perioperative period. Whereas the GP group consisted of 54 individuals who underwent surgery at the same time frame for comparable reasons. The mean age of patients that received gabapentin (group GP) was 38.14 ± 15 years, and the mean age of patients that did not receive gabapentin (group NGP) was 43.57 ± 14.37 years. There was no significant difference in age between the 2 groups ($p = 0.656$). The male to female ratio was 44:21 and 32:22 in groups NGP and GP respectively and the difference in gender distribution was not significant ($p = 0.704$). The mean surgical duration in group NGP was 115.89 ± 31.34 min and in group GP was 124.31 ± 32.06 and we found no significant difference in the duration of surgery between the two groups ($p = 0.387$).

Out of 65 patients in group NGP 74% of patients received additional analgesics (opioids or Buprenorphine patch) for postoperative pain relief. In group GP, out of 54 patients, only 22 (41%) patients had inadequate analgesia with gabapentin. 32 (59%) patients had adequate pain control with only gabapentin and paracetamol, and they did not require any additional opioids for adequate pain relief. The difference between the 2 groups, in terms of opioid requirement, was measured using the chi-square test $x^2 = 13.346$ and there was a statistically significant difference ($p = 0.000$). There was no statistically significant difference in VAS scores at 2, 4, 6, 12, 24 and 48 h between the 2 groups but the VAS scores were comparatively better in group GP (Table 1).

The two groups were further divided based on fracture morphology (Table 2). No significant difference was noted in opioid intake in group GP based on fracture morphology (intra and extra-articular fractures) ($p = 0.269$). However, in group NGP, statistical significance was observed in opioid intake, where patients with intraarticular fractures required additional opioids to achieve pain relief ($p < 0.01$).

Table 1 Comparison of VAS scores between the group NGP and group GP at varied intervals for initial 48 h

	Vasgroup	N	Mean	Std. deviation	*p* value
Vas2	Group NGP	65	8.0154	.81953	0.282
	Group GP	54	7.9444	.73758	
Vas4	Group NGP	65	7.6769	.84977	0.412
	Group GP	54	7.3519	.73092	
Vas6	Group NGP	65	6.8154	.72656	0.196
	Group GP	54	6.5370	.71935	
Vas12	Group NGP	65	6.1077	.75256	0.080
	Group GP	54	5.7963	.59494	
Vas24	Group NGP	65	5.2769	.80054	0.994
	Group GP	54	5.0741	.63992	
Vas48	Group NGP	65	4.9692	1.13150	0.828
	Group GP	54	5.1111	1.11027	

Table 2 Morphological distribution of patients based on the fracture pattern and involved extemity to group GP and Group NGP

S. no.	Site	Morphology		GP	NGP
1	IA	UL	24	11	13
		LL	24	10	14
2	EA	UL	40	17	23
		LL	31	16	15

IA Intraarticular; *EA*, Extra articular; *UL*, Upper limb; *LL*, Lower limb; *GP*, Gabapentin group; *NGP*, Non Gabapentin group

Discussion

Multimodal analgesia or patient-controlled analgesia is the treatment of choice and was found to be superior to an individual group of medications, which is preferred for trauma individuals during the perioperative period [1, 5]. However, the availability of expert personnel to administer block is not always available in all centres. This leads to more use of parenteral medications for pain control and more opioid usage. The purpose of the study was to find an alternative option to provide adequate postoperative pain relief as well as avoid central sensitization.

Opioids are the most commonly used medications with proven efficacy for moderate to severe pain in trauma individuals during the perioperative period. However, their usage is limited due to the side effect profile such as nausea, vomiting sedation, dizziness, altered sleep pattern, constipation, and increased postoperative fatigue [2, 6]. Opioid-free analgesics are the first line of drugs for trauma individuals to reduce their side effects. Gabapentinoids were used in our study to reduce the need for analgesic (read 'opioid' to be more precise) in the perioperative period.

Gabapentin, the alpha 2 delta receptor modulator, has been reported to provide adequate analgesia in the perioperative period by reducing the VAS scores significantly at 48 h in arthroscopic and major orthopaedic spine surgeries [7, 8]. It has an additional anxiolytic property which is helpful to control pain and anxiety during the preoperative period in trauma individuals. In our series also, we found that a significant proportion of patients (59% or 32 patients) in the gabapentin GP group had adequate pain control during the perioperative period without the need for additional opioid medications. According to Hamner et al., gabapentin reduced the incidence of nightmares, increased the length of sleep, and improved the quality of sleep, offering a potentially effective treatment for PTSD [9].

The most commonly reported side effects of gabapentin are mainly central nervous system-related issues such as somnolence, dizziness, headache, ataxia, and fatigue. Other side effects such as respiratory depression, myopathy, suicidal behaviour, and visual defects were noticed in a

limited number of studies [10–12]. Due to the short duration of gabapentin administration within a safe dosage, and the relatively simple injury profile of our patients, no serious adverse events were noted in our study. However, considering its propensity to get excreted mainly in urine in an unchanged form, the authors recommend being cautious of using this drug in patients with impaired renal function [13].

Paracetamol is the most commonly used parenteral analgesic agent in trauma individuals for pain management in the perioperative period following orthopaedic surgery. However, the need for additional analgesics like opioids during the perioperative period for 48 h after orthopaedic surgery has been reported to be up to 60% [14, 15]. Compared to the previous studies, 74% or 47 of our patients in the NGP group needed additional analgesics in the form of tramadol or buprenorphine during the perioperative period for adequate analgesia.

Uncontrolled postoperative pain is a significant factor in the development of chronic pain that affects the rehabilitation process of the patients and hence affects the functional outcome [16]. Clark et al. in their study on wounded soldiers noted the difficulty in carrying out rehabilitation due to inadequate control of pain [17]. Gabapentin is an effective analgesic agent for chronic neuropathic as well as traumatic pain and helps in better rehabilitation of the patient during the perioperative period [18, 19]].

Fracture surgeries are one of the most commonly performed orthopaedic procedures, and the use of opioids for perioperative pain control is unbridled in this part of the world, as expertise for peripheral nerve block is not always available. In a setup without a reliable step-down facility, the possible long-term negative effects are frequently disregarded. The proposed option can potentially lessen undesired side effects and central sensitization while also suggesting a less expensive approach to reducing opioid use during the perioperative phase. Based on our findings, for postoperative analgesia, we advocate the use of non-opioid medications like gabapentin. To further validate the findings, the authors are planning to conduct an RCT.

One of the limitations of the study is that it is a retrospective study, involving a narrow cohort of patients with isolated fractures. The patients were observed for analgesia in the perioperative period only and hence, long-term adverse effects and their analgesic effect during the rehabilitation period could not be assessed in our study population. While conducting the analysis, the fracture anatomy and the patient's nutritional status were not taken into consideration, which may have skewed the results. Also, we could not perform a regression analysis of our relatively narrow set of data to find out potentially important parameters that can indirectly affect opioid-seeking behaviour as well as pain control in the perioperative period. Given that the study was retrospective, there might have been selection bias. Since VAS scores were computed at regular intervals rather than at the time that opioids were administered, a correlation between the two could not be done. The degree of training and experience the operating surgeons at different stages of their careers may have had an impact on the study's conclusion.

Conclusion

Adequate perioperative pain control is of paramount importance in patients with orthopaedic injuries as it facilitates early rehabilitation and better functional outcome. Alpha 2 delta receptor modulators like Gabapentin can supplement the analgesic effect of paracetamol in postoperative patients of orthopaedic trauma victims. This can potentially reduce the need for opioids and their associated adverse effects on patient outcomes. Though retrospective, our study suggests that Gabapentin can be used safely as an analgesic agent for perioperative analgesia in this patient population. However, the interaction and effectivity of gabapentin in patients with polytrauma or multiple fractures may need further exploration. Moreover, the authors do believe that further research on a larger patient population with a robust methodology can further validate our findings.

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Declarations

Conflict of interest The authors declare that there is no conflict of interest.

Informed consent No ethical clearance or informed consent was obtained as it was a retrospective study.

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