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THE ROLE OF GABAPENTINOIDS IN ORTHOPEDIC SURGERIES - IMPACT ON PAIN CONTROL, OPIOID CONSUMPTION, AND FUNCTIONAL OUTCOMES

Mikołaj Szewczykowski[1] ✉, ***Ewa Otręba[1]***, ***Michał Hebel[2]***, ***Julia Wendt[1]***, ***Szymon Stankowski[1]***, ***Tomasz Klinkosz[1]***, ***Szymon Korczyk[3]***, ***Dagmara Fredrich[4]***, ***Wiktor Fredrich[4]***

[1]*F. Ceynowa Specialist Hospital in Wejherowo, Poland*
[2]*Szpital Morski im. PCK, Gdynia, Poland*
[3]*St. Vincent de Paulo Hospital, Gdynia, Poland*
[4]*Medical University of Gdansk, Poland*

✉ ***m.szewczykowski98@gmail.com***

ABSTRACT

BACKGROUND

Postoperative pain after orthopedic surgery remains a major clinical problem and is commonly managed using multimodal analgesia. Gabapentinoids have been proposed as opioid sparing adjuncts, but their clinical effectiveness and impact on functional recovery remain uncertain.

AIM

To evaluate the effects of gabapentin and pregabalin on postoperative pain intensity, opioid consumption, and functional outcomes in patients undergoing orthopedic surgical procedures.

METHODS

A narrative literature review was performed based on prospective clinical trials published between 2015 and 2025. The literature search was conducted using the Google Scholar database. Twenty one prospective studies evaluating postoperative pain assessed by VAS or NRS scales, opioid consumption, and functional outcomes after orthopedic surgery were included.

RESULTS

The effects of gabapentinoids on postoperative pain reduction were variable across studies. Pregabalin demonstrated more consistent analgesic benefits compared with gabapentin, particularly in the early postoperative period. Several studies reported a reduction in opioid consumption associated with the use of gabapentinoids, although this effect

was not observed consistently. No improvement in long term functional outcomes was demonstrated in any of the included studies.

CONCLUSIONS

Current evidence suggests that gabapentinoids may provide modest and inconsistent benefits in postoperative pain control and opioid sparing after orthopedic surgery, with pregabalin showing more favorable results than gabapentin. Their use does not appear to influence long term functional recovery. The lack of standardized dosing protocols and limited data in pediatric populations highlight the need for further well designed clinical studies.

Keywords: gabapentin, pregabalin, orthopedics, postoperative pain, multimodal analgesia, opioids, postoperative care

INTRODUCTION

Orthopedic procedures such as trauma-related interventions or total joint arthroplasty are frequently associated with significant postoperative pain. [1] Effective pain control in the postoperative period is essential for enabling early mobilization, shortening hospital stay, and improving functional outcomes. [2] Despite advances in perioperative care, inadequate management of acute postoperative pain remains a common clinical challenge, contributing to delayed recovery and patient dissatisfaction. [3-4]

The scientific novelty of this study lies in the synthesis of prospective clinical data from 2015 to 2025, which will determine whether gabapentinoids successfully reduce postoperative pain and the need for opioid use after orthopedic surgeries. The significance of this review is rooted in addressing the persistent challenge of postoperative pain management in orthopedic surgeries.

Opioids have long been central to postoperative pain control, but their use is limited by well-known side effects such as nausea, vomiting, dizziness, sedation, constipation, urinary retention, and, in severe cases, respiratory depression. [5] There are reports stating that up to 80% of patients who received opioids suffer because of the side effects. [6] At the same time, increasing concern about opioid overuse and the potential for long-term dependence has encouraged a shift toward opioid-sparing approaches. Consequently, multimodal analgesia—combining agents that act through different mechanisms—has become a key element of enhanced recovery protocols in orthopedic surgery. [7-10]

Pregabalin and gabapentin, also known as gabapentinoids, both α2δ-ligands originally developed for the treatment of epilepsy and subsequently established as first-line agents for neuropathic pain, have gained attention as potential adjuvants in multimodal analgesia. [11-12] Their mechanism of action hypothetically involves binding to the α2δ-subunit of voltage-gated calcium channels in the central nervous system, reducing the release of excitatory neurotransmitters and attenuating central sensitization. [13] Because central sensitization plays a key role in the development of postoperative hyperalgesia, α2δ-ligands have been proposed as a means to reduce acute postoperative pain and opioid consumption. [14]

ADVERSE EFFECTS AND PERIOPERATIVE SAFETY OF GABAPENTIN AND PREGABALIN

Gabapentin and pregabalin, when used perioperatively, are generally well tolerated but are associated with several common adverse effects, primarily related to central nervous system depression. The most frequently reported side effects include dizziness, somnolence, sedation, and impaired coordination, which may affect early mobilization and postoperative recovery. Additional effects such as visual disturbances, peripheral edema, blurred vision, dry mouth, and nausea have also been described. [15-16] Furthermore, broad meta-analyses have confirmed that gabapentinoids may reduce nausea but not eliminate other risks of CNS adverse effects. [17] Moreover, a large randomized clinical trial assessing the effect of perioperative gabapentin on postoperative outcomes found no statistically significant difference in the overall number of adverse events or in the rate of medication discontinuation due to sedation or dizziness between the gabapentin and placebo groups. This suggests that, within this mixed surgical cohort, gabapentin did not significantly increase the risk of these particular adverse events compared with placebo. [18] In a randomized controlled trial involving patients undergoing arthroscopic surgery, no meaningful differences were observed between the gabapentin and pregabalin groups with regard to dizziness or sedation at either the 6-hour or 24-hour postoperative assessments. Nausea and vomiting, however, occurred less frequently in patients receiving gabapentin during the early postoperative period, with a significant difference noted at 6 hours. This early advantage was not sustained at 24 hours, when the incidence of nausea and vomiting was low and comparable between groups. [19]

HEMODYNAMIC CONSIDERATIONS

Available clinical data suggest that perioperative administration of gabapentinoids does not produce significant changes in intraoperative hemodynamic parameters such as heart rate, blood pressure, or mean arterial pressure in

otherwise stable patients. [20] In a randomized study examining the use of gabapentin versus pregabalin as premedication in lower limb orthopedic surgery under combined spinal–epidural anesthesia, both agents were reported to provide effective analgesia without altering hemodynamic stability, with sedation being the more notable side effect. [21] Similarly, broader clinical observations indicate that patients receiving gabapentinoids in the perioperative context do not experience notable negative cardiovascular effects, and measures such as blood pressure and heart rate generally remain within expected ranges during and after surgery. [22] Overall, available evidence suggests that standard perioperative doses of gabapentin and pregabalin do not lead to clinically significant hemodynamic instability (e.g., marked hypotension, bradycardia, or arrhythmias) in the absence of other risk factors. While some studies have explored modulation of pressor responses (e.g., to laryngoscopy), they generally show attenuation rather than detrimental effects on blood pressure and heart rate. Therefore, hemodynamic changes directly attributable to gabapentinoids remain uncommon in perioperative practice. [23]

AIM

To evaluate the impact of gabapentinoids gabapentin and pregabalin on postoperative pain intensity assessed by VAS and NRS scales, opioid analgesic consumption, and functional outcomes in patients undergoing orthopedic surgical procedures, based on the analysis of prospective clinical studies.

Research objectives

1. To analyze data from prospective clinical studies on the effects of gabapentin and pregabalin on the severity of postoperative pain after orthopedic surgeries.
2. To assess the opioid sparing effect of gabapentinoids in the early postoperative period.
3. To compare the effectiveness of gabapentin and pregabalin in pain control and reduction of opioid consumption.
4. To analyze the impact of gabapentinoid use on functional outcomes following orthopedic interventions.
5. To summarize data on the safety and tolerability of gabapentinoids in the perioperative period of orthopedic surgery.

METHODS

This study is a narrative literature review without quantitative synthesis. The choice of a narrative review design was determined by the substantial heterogeneity of study designs, surgical procedures, dosing regimens, and outcome measures across the available prospective clinical trials, which precluded formal quantitative analysis.

The literature search was conducted using the Google Scholar database only. This approach was selected to identify a broad range of prospective clinical studies across different orthopedic subspecialties. Publications published between 2015 and 2025 were considered. The search terms used were pregabalin, gabapentin, orthopaedics. The date of the last literature search was 15.12.2025.

The screening process involved an initial review of titles and abstracts, followed by full text evaluation of potentially eligible publications to determine final inclusion.

Inclusion criteria were defined as follows: prospective clinical trials; orthopedic surgical interventions on upper or lower limbs; adult and pediatric populations; outcomes including postoperative pain intensity assessed by VAS or NRS scales, consumption of opioid and nonopioid analgesics, and functional outcomes after surgery.

Exclusion criteria were defined as follows: review articles, systematic reviews, and meta-analyses; case reports and small case series; experimental and preclinical studies; studies not involving surgical interventions; studies focusing on non orthopedic procedures when orthopedic outcomes were not reported separately; and publications not available as full text.

Data extracted from the included studies comprised type of surgical procedure, patient population, dosing regimen of gabapentinoids, timing and duration of administration, pain assessment scales used, opioid and nonopioid analgesic consumption, reported adverse effects, and functional outcome measures.

Only English language publications were included. No formal assessment of study quality or risk of bias was performed, in accordance with the narrative design of the review, and methodological limitations of individual studies were considered descriptively during interpretation of the results.

RESULTS

CHARACTERISTICS OF INCLUDED STUDIES

Across the included studies, six investigated gabapentin, ten investigated pregabalin, and five directly compared gabapentin and pregabalin. Considerable heterogeneity was observed with respect to dosing regimens and duration of treatment. For gabapentin, single doses ranged from 75 mg to 1300 mg, with total daily doses up to 1800 mg administered in three divided doses in adult populations. In the pediatric study, gabapentin was administered as a single dose of 10 mg per kilogram of body weight. For pregabalin, single doses ranged from 50 mg to 300 mg, with 150 mg being the most frequently used dose. In twelve studies, gabapentinoids were administered only preoperatively, whereas in the remaining studies, treatment was continued postoperatively, with the longest reported duration being 17 days. The most common ways to evaluate a patient's pain after the surgery are the commonly used Numerical Rating Scale (NRS) and Visual Analogue Scale (VAS)—ranging from 0 (no pain) to 10 (the worst pain imaginable). [24]

POSTOPERATIVE PAIN AND OPIOID CONSUMPTION – GABAPENTIN

Only one of six studies included in this section showed a significant reduction of pain after a single dose of gabapentin given preoperatively, while the other five studies showed no such effect. Regarding opioid requirements, gabapentin was associated with reduced opioid consumption in two studies, a higher opioid discontinuation rate in one study, and no statistically significant effect in two studies.

In Hamal et al. (2015), the VAS scores at rest were significantly lower 2 and 24 hours after lower limb surgeries in the gabapentin group compared to the control group (1.23 vs 2.12 and 2.19 vs 2.77, respectively), with no difference at 4 and 6 hours. [25] In Mardani-Kivi et al. (2016), patients who took gabapentin before the arthroscopic Bankart surgery had lower, nevertheless statistically insignificant, VAS scores (4.9 vs 5.4 at 6 h and 4.7 vs 5.3 at 24 h, $P > 0.05$). [19] In both studies (Haml et al. and Mardani-Kivi et al.) reduction of opioid consumption was shown in the pregabalin groups. [19,25] The Hah et al. (2017) study, with 2 years of observation, showed no statistically significant difference in the time to pain cessation between gabapentin and placebo groups. However, the rate of opioid cessation was higher in the gabapentin group. The list of surgeries in this publication was more heterogeneous; however, most of the patients underwent either total knee replacement or total hip replacement. [18] Paul et al. (2015) showed no difference in pain at rest, with passive movement and weight bearing after total hip arthroplasty (THA) during the period of the study (3 days). Additionally, no effect on opioid demand was described. [26] In the Lunn et al. (2015) study, the use of gabapentin (900-1300 mg) did not impact both the pain intensity and opioid demand during the first 6 days after total knee arthroplasty (TKA). [27] A follow-up study with the time of observation prolonged to 3 years confirmed no difference in pain between gabapentin and placebo. [28]

Table 1. The impact of gabapentin on opioid consumption after orthopedic surgeries. HR - hazard ratio, THA - total hip arthroplasty, TKA - total knee arthroplasty.

Study	Operation	Gabapentin	Opioid consumption
Mardani-Kivi et al. (2016) [19]	Arthroscopic Bankart surgery	600 mg - single dose before the operation	first 24 hours ↓
Hamal et al. (2015) [25]	Lower limb surgeries	600 mg - single dose before the operation	first 24 hours ↓
Paul et al. (2015) [26]	THA	600 mg before the operation, additional 200 mg after the operation, and 3x 200 mg in two postoperative days	no effect
Lunn et al. (2015) [27]	TKA	900 or 1300 mg before and after the operation for 6 days	no effect
Hah et al. (2017) [18]	Mainly total hip and knee replacement	1200 mg before the operation, 3 days of 3x 600 mg after the operation	Higher rate of opioid cessation compared to placebo

POSTOPERATIVE PAIN AND OPIOID CONSUMPTION – PREGABALIN

Ten studies examined the impact of pregabalin on postoperative pain in orthopedic operations. Seven studies showed a reduction in pain levels after the use of pregabalin; however, in two of them, the effect was weaker compared to

other drugs (paracetamol, dexmedetomidine). In the other three studies no such effect was confirmed. Five studies showed reduction of opioid consumption thanks to the use of pregabalin; in contrast, three studies showed no effect in this regard (Table 2).

In both Sahni et al. (2019) and Adharsh et al. (2024), a single dose of pregabalin given before lower extremity surgery provided better pain control and lower painkiller intake in the first 24 hours after the surgery. [22,29] Although a similar study conducted by Damirchi et al. (2019) showed that the analgesic effect and reduction of opioid consumption obtained with the use of pregabalin is weaker compared to the effect of paracetamol. [30] The addition of pregabalin to celecoxib before TKA resulted in lower NRS up to 48 hours after surgery and lower fentanyl demand. [31] In another study regarding TKA, both pregabalin and duloxetine showed a reduction in pain levels up to 48 hours after the operation, with the advantage of pregabalin at 6 and 12 hours. [32] In the Lee et al. (2018) study, the pregabalin group had lower pain levels and analgesic use than the placebo group in the first 24 hours after TKA/ THA, although higher than the dexmedetomidine group. Furthermore, the addition of pregabalin to dexmedetomidine showed no further reduction of pain. [33] In Clarke et al. (2015) study, patients who received pregabalin before and after THA had similar pain scores at rest and during movement in the first 4 postoperative days (during hospitalization) compared to the placebo group. However, in the next 7 days after the discharge, the pain scores were lower in the research group. The research group also had lower morphine demand during and after the hospitalization. [34]

Three studies showed no impact of pregabalin on pain level or opioid consumption in TKA and operative treatment of rotatory ankle fracture. [35-37]

Table 2. The impact of pregabalin on opioid, paracetamol, and nonsteroidal anti-inflammatory drugs (NSAIDs) consumption after orthopedic surgeries. THA - total hip arthroplasty, TKA - total knee arthroplasty.

Study	Operation	Pregabalin	Analgetics consumption
Adharsh et al. (2024) [22]	Lower extremity surgery	Single dose of 150 mg before the operation	First 24 hours tramadol ↓
Damirchi et al. (2019) [30]	Lower extremity surgery	Single dose of 150 mg before the operation	Opioids ↓, weaker effect than paracetamol
Lee et al. (2015) [31]	TKA	Single dose of 150 mg before the operation	First 12 hours fentanyl ↓
Lee et al. (2018) [33]	TKA, THA	Single dose of 150 mg before the operation	First 24 hours PCA ↓, weaker effect than dexmedetomidine
Clarke et al. (2015) [34]	THA	150 mg before the operation, 150 mg 2x per day for 7 days	First 24 hours (during hospitalization) and one week after the discharge morphine ↓
Choi et al. (2024) [35]	Surgical treatment of the rotatory ankle fracture	75 mg before the operation, 75 mg 14 days	no effect since the operation up to 6 months
Yik et al. (2019) [36]	TKA	75 mg before the operation, 75 mg 2x per day for 5 days	no effect in the first 72 hours post-op
YaDeau et al. (2015) [37]	TKA	100 mg/ 200 mg/ 300 mg before the operation and after for 14 days	no effect during first 14 days post-op

PREGABALIN AND GABAPENTIN COMPARISON

During the research four studies were found comparing the efficiency of pregabalin and gabapentin. Three of them showed better pain control in the pregabalin group in 12- and 24-hour periods after the operations of the upper and lower extremities. [21,38-39] On the contrary, Kheirabadi et al. (2020) showed no statistical significance in pain control after the lower extremity operations at the 2-, 6-, 12-, 18-, and 24-hour time points between pregabalin, gabapentin, and celecoxib. Only at the 1-hour time point pregabalin showed advantage compared to gabapentin and celecoxib. [40]

Three studies compared opioid consumption between pregabalin and gabapentin. Lower opioid consumption (pethidine, tramadol, and fentanyl epidural top-ups) was established in pregabalin groups in all three studies. [21,39-40]

PEDIATRIC POPULATION

Only one study in this review examined the effect of gabapentin in the pediatric population. Reduction in pain was observed at 4 and 8 hours after the operation with no reduction of opioid consumption. Postoperative agitation was reduced by the use of pregabalin. [41]

FUNCTIONAL OUTCOMES

All studies (five in total), showed that the use of pregabalin resulted in similar functional outcomes compared to placebo, despite the type of operation. Different tools were used to achieve this conclusion, including evaluation of range of motion of the knee, Knee Society Score, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), or 36-Item Short Form Survey (SF-36). The period of time after which these tests were conducted ranged from 1 day up to 6 months after the operation. [31-32,34-36].

DISCUSSION

The aim of this review was to assess the clinical usefulness of gabapentinoids in perioperative pain management in orthopedic surgeries – focusing on upper and lower limb surgeries. Analysis of 21 prospective studies revealed heterogeneous and inconsistent results.

Gabapentinoids might have opioid-sparing effect in early postoperative care. This effect was noticed across five studies (out of eight) for pregabalin [22,30-34], three studies (out of five) for gabapentin [18-19,25], and in all three comparative studies between the two drugs, which demonstrated the greater effect for pregabalin. [21,39-40]. Further studies are needed to establish the impact of gabapentinoids on the opioid consumption. Although several studies reported statistically significant reductions in pain intensity (measured using VAS or NRS scores), this effect was not unequivocally confirmed in all studies and the time of observation was often limited to early postoperative care. Gabapentin reduced pain in only one out of six studies [25], pregabalin in seven out of ten studies [22,29,31-34]. Furthermore, comparative studies showed more favourable results for pregabalin (three studies out of four). [21,38-39]

A critical question in presented studies is whether one gabapentinoid offers superior clinical benefit over the other. Our review highlights that both drugs share similar mechanisms of action, however pregabalin seems to be more effective than gabapentin in both pain reduction and reduction of opioid consumption. [21,38-40]

A noteworthy finding of this review is the lack of concordance between improvements in early pain management and long-term functional outcomes. Specifically, despite modest analgesic benefits in the immediate postoperative period, the use of gabapentinoids did not result in superior functional recovery in any of presented studies (five studies). [31-33,35-36] This finding implies that gabapentinoids do not modify any determinants of long-term orthopedic recovery.

Gabapentinoids use requires careful consideration. Although their application may reduce opioid-related adverse effects, gabapentinoids themselves are associated with side effects such as dizziness and somnolence. In orthopedic patients these effects may interfere with early mobilization, which is a key component of postoperative recovery and thromboprophylaxis. This particularly applies to older adults undergoing hip or knee arthroplasty. Furthermore, increased fall risk in this population must be balanced against the analgesic benefits offered by these agents. [18,20]

LIMITATIONS AND FUTURE RESEARCH DIRECTIONS

The principal limitation behind this review is the fundamental heterogeneity in dosing presented substances. Reported doses varied, ranging from 75 mg to 1300 mg for gabapentin and from 75 mg up to 300 mg before surgery for pregabalin. This fact complicates direct comparisons and hinders the establishment of an optimal dosing strategy. Taking into consideration possible adverse effects and limited effectiveness of pregabalin and gabapentin, more comparative studies need to be done to establish potential benefits and risk of using these drugs as co-analgetics. Additionally, the near absence of pediatric data (only one study included pediatric patients) represents an important

gap in the current literature. Accordingly, future investigations should focus on establishing standardized protocols, with clear guidance on timing and dosage, while also addressing long-term outcomes and populations that remain insufficiently studied, particularly pediatric and elderly patients.

CONCLUSIONS

The effectiveness of gabapentinoids in reducing postoperative pain after orthopedic surgeries varies across studies. Pregabalin is associated with more consistently favorable analgesic outcomes compared with gabapentin.

Several studies demonstrated a reduction in opioid consumption with the use of pregabalin and gabapentin. However, this opioid sparing effect was not observed consistently across all included trials.

The use of gabapentinoids does not appear to improve long term functional outcomes following orthopedic surgery.

There is currently no standardized dosing protocol for gabapentinoids in orthopedic practice. Considerable variability exists, particularly with respect to gabapentin dosing, indicating the need for the development of standardized therapeutic protocols and clinical guidelines.

Evidence regarding the use of gabapentinoids in pediatric orthopedic surgery remains limited, identifying an important gap in the literature and a priority area for future clinical research.

AUTHORS' CONTRIBUTIONS

Conceptualization: Mikołaj Szewczykowski; Szymon Korczyk; Michał Hebel

Literature search and data analysis: Dagmara Fredrich; Wiktor Fredrich; Julia Wendt.

Writing – original draft preparation: Mikołaj Szewczykowski; Szymon Korczyk; Michał Hebel

Writing – review and editing: Mikołaj Szewczykowski; Szymon Korczyk; Michał Hebel; Tomasz Klinkosz.; Ewa Otręba; Szymon Stankowski

Data presentation in the form of the tables: Julia Wendt

All authors approved the final version of the manuscript

USE OF AI

We acknowledge the use of ChatGPT based on the GPT-5.1 (https://chatgpt.com/). Artificial intelligence (AI) was utilized during the preparation of this manuscript for language-related assistance, specifically to identify and correct grammatical, stylistic, and spelling errors in the text.

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