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The Efficacy of Gabapentin for Postoperative Pain Management Following Total Hip Arthroplasty: A Systematic Review

Abstract

Background: Postoperative pain following total hip arthroplasty (THA) impacts patients' rehabilitation and quality of life. Although gabapentin has been widely used for pain control, its effectiveness in hip arthroplasty is not well established. The aim of our systematic review is to evaluate the effect of gabapentin on postoperative pain after THA.

Methods: A systematic search was conducted in three databases: MEDLINE, PsycINFO, and Embase, through OVID, using the keywords gabapentin, pain, and hip arthroplasty, with no restrictions on language or publication date. To evaluate the quality of the articles, the Cochrane Collaboration tool was used.

Results: Five studies, including 728 patients, were included in our systematic review. Gabapentin 600 mg was used in three and 1200 mg in two studies. The results of these studies showed that gabapentin had no significant effect on pain or morphine consumption after THA. Besides, gabapentin use was associated with side effects such as rash, nausea, headache, vomiting, and pruritus.

Conclusion: Gabapentin does not decrease pain or morphine consumption after THA. However, future studies with a larger sample size and longer follow-up period are required.

Keywords: Total hip arthroplasty, Gabapentin, Postoperative pain, Systematic review

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Introduction

Total hip arthroplasty (THA) is one of the most commonly performed orthopaedic procedures to treat advanced osteoarthritis, rheumatoid arthritis, and osteonecrosis of the hip joint [(1)]. It is estimated that 280,000 THA procedures are being carried out annually, the rate of which is increasing with aging [(2)]. THA improves pain and range of motion, patient's function, and quality of life [(3)]. Postoperative pain is a common complication and a major adverse outcome of this procedure [(4)]. Studies have indicated that 30% of patients undergoing THA suffer from postoperative pain and use analgesic agents [(5)]. Moreover, many patients suffer from moderate to severe pain after surgery that can lead to a delay in the recovery process, which in turn is associated with complications such as pulmonary embolism and deep vein thrombosis [(6)]. Hence, pain management after surgery is essential since it is associated with improved patients' outcomes and function [(7)]. Multiple pain control methods are being used in patients undergoing THA, such as local anesthesia, blocking of the femoral nerve, and epidural anesthesia. However, the optimal strategy is still under investigation [(8)]. Gabapentin is a structural analog of γ-aminobutyric acid commonly used as an anticonvulsant to treat partial seizures and neuropathic pain [(9)]. It is also used to treat anxiety disorders, posttraumatic stress disorder, addiction, and bipolar disorder [(10)]. Additionally, studies have indicated that gabapentin is an effective method for postoperative pain management after head and neck surgeries, chest wall surgeries, cardiac surgeries, and varicocelectomy [(11)]. Gabapentin mechanisms of action are not fully known; however, several mechanisms may contribute to its analgesic effects [(12)]. Gabapentin selectively binds to the α2δ

Subunit of N-type calcium channels, which likely accounts for its analgesic effect [12].
Several studies have evaluated the efficacy of gabapentin for pain management after THA. However, the use of gabapentin for postoperative pain relief is controversial. A systematic review is needed to evaluate the efficacy of gabapentin in THA, as current studies do not allow a definitive conclusion. Furthermore, there is insufficient evidence to explain how gabapentin affects pain after hip arthroplasty. This study aims to evaluate the effect of gabapentin on pain after THA and on morphine consumption as a secondary outcome.

Methods

A systematic search was conducted in three databases, MEDLINE, PsycINFO, and Embase, through OVID from inception until January 2023. This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline [13]. Relevant studies were identified using the following keywords: gabapentin, THA, total hip arthroplasty, and total hip replacement. The references of eligible articles and Google Scholar were also reviewed to find relevant articles. The inclusion criteria were studies in English and Farsi using gabapentin, on patients who underwent THA, and assessing pain as the primary outcome. Systematic reviews, meta-analyses, studies using the same dataset, animal studies, conference abstracts and guidelines, articles containing duplicate content, or articles with contents outside the objectives of this study were excluded from our review. Initially, the search was conducted by two researchers to identify studies related to the purpose of our review. All articles from each database were entered into Covidence. After removing duplicate articles, the titles and abstracts of all articles were evaluated for the final review of the full texts to include articles that met our inclusion criteria. Disagreements between reviewers were resolved by the decision of a third independent reviewer. Two reviewers independently reviewed full texts of eligible studies and extracted the following data from each article: the first author, publication date, country, study design, intervention, participants, results, protocol, primary outcome, and adverse events. The risk of bias (RoB) in randomized trials was assessed using the Cochrane Collaboration tool (Figure 1). The RoB was assessed by the following five domains: bias arising from the randomization method, bias emerging from deviations from intended interventions, bias arising from missing outcome data, bias in outcome assessment, and bias in the selection of the reported result [14].

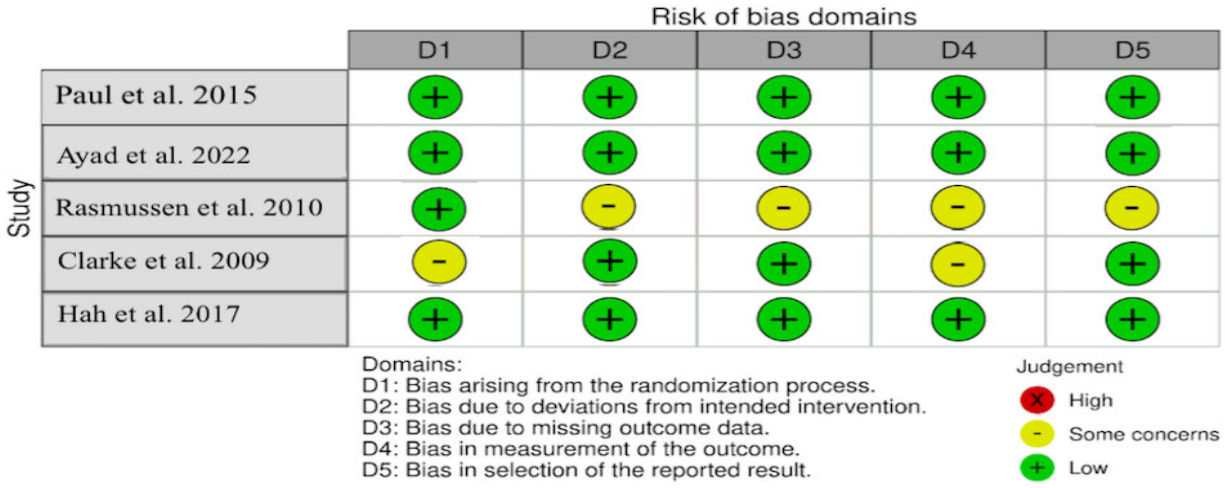

Figure 1: Risk of bias assessment and study quality in randomized trials

Results

From a total of 30 records obtained through the literature search, the title/abstract of the remaining records was screened after removing duplicate articles. Twenty articles were excluded based on the title/abstract. The full texts of the remaining papers (n = 10) were reviewed in detail based on our inclusion criteria. Five out of 10 records were excluded from our review. Finally, five articles involving 728 patients met the inclusion criteria and were included in this systematic review (Table 1).

Effect of gabapentin on postoperative pain

Paul et al. (2015) conducted a randomized clinical trial (RCT) in which patients in the intervention group received 600 and 200 mg of gabapentin before and after surgery, respectively. Patients received gabapentin 200 mg three times a day until 2 days after surgery. Prior to the surgery, all patients received 30 mg of ketorolac and 1000 mg of intravenous acetaminophen. After the surgery, patients received morphine along with ketorolac 15 mg and acetaminophen 1000 mg every 6 hours. The primary outcome of this study was the mean morphine consumption 72 h post-surgery. The average morphine consumption was 55.8 mg in the gabapentin group compared to 60.7 mg in the control group, which had no significant difference. Besides, there were no significant differences in secondary outcomes, including pain and range of motion, between the two groups [15]. Moreover, the analgesic effects of low-dose gabapentin, dexamethasone, and ketamine in combination with paracetamol and ketorolac were compared with paracetamol and ketorolac alone after THA in a study by Rasmussen et al. (2010). In this study, 42 patients were randomly divided into two groups: treatment group (gabapentin 1200 mg + dexamethasone 8 mg + ketamine + paracetamol 1 g + ketorolac 15 mg) or control group (placebo + paracetamol 1 g + ketorolac 15 mg). Morphine consumption, pain at rest and during movement was evaluated in this study. The results showed no significant difference in morphine consumption between the two groups [16]. Ayad et al. (2022) conducted an RCT and randomized patients to a placebo or gabapentin 600 mg twice daily from the day before surgery and for 3 days afterward. The primary outcome of this study was pain and morphine consumption 72 h after the surgery. A total of 60 patients were included in gabapentin (n=28) and placebo (n = 32) groups. The results of this study demonstrated no significant differences in pain scores and morphine consumption between the two groups [17].

Clarke et al. (2009) conducted an RCT in 126 patients who underwent THA. Patients were randomly divided into three groups (G1: placebo/placebo, G2: gabapentin/placebo, and G3: placebo/gabapentin). Patients received gabapentin 600 mg (G2) or a placebo (G1 and G3) 2 h before the surgery. In the post-anesthesia care unit, patients received gabapentin 600 mg (G3) or placebo (G1 and G2). In the ward, patients received 1000 mg of acetaminophen daily. The effect of gabapentin on pain and morphine consumption was investigated in this study. The average morphine consumption 48 h and the pain score 12, 24, 36, and 48 h after surgery did not significantly differ among the groups. Six months after the surgery, the number of patients who reported chronic pain (G1 = 10, G2 = 12, and G3 = 9) did not significantly differ between the groups [18]. In another study, Hah et al. (2018) investigated the effect of gabapentin on postoperative pain. Patients were randomly assigned to placebo (n = 202) and gabapentin (n = 208) groups. The baseline characteristics of the groups were similar. The results of this study indicated that gabapentin did not significantly affect pain after the surgery. However, participants who received gabapentin had a 24% increase rate in morphine discontinuation after surgery [19].

Table 1. Characteristics of included studies.

Author, Year	Country	Study Design	Intervention	Participants	Results	Primary Outcome	Adverse Events
Paul et al. 2015	Canada	Randomized clinical trial	Single dose gabapentin 600 mg before surgery, then gabapentin 200 mg 3 times a day for 2 weeks	Control group = 48 Gabapentin group = 54	No significant difference in pain and morphine consumption between the two groups.	Morphine consumption 72 hours after surgery	Nausea/vomitin, pruritus
Rasmussen et al. 2010	Denmark	Randomized clinical trial	Gabapentin 1200 mg + Dexamethasone 8 mg + Ketamine + Paracetamol 1 g + Ketorolac 15 mg or placebo + Paracetamol 1 g + Ketorolac 15 mg	Control group = 21 Gabapentin group = 21	No significant difference in the consumption of morphine between the groups. Overall pain scores improved in the combination group compared to the control group both at rest and during movement.	Morphine consumption	Nausea/vomiting
Ayad et al. 2022	USA	Randomized clinical trial	Gabapentin 600 mg daily from 1 day before surgery to 3 days after surgery	Control group = 32 Gabapentin group = 28	No significant difference in pain and morphine consumption between the two groups.	Pain	_
Clarke et al. 2009	Canada	Randomized clinical trial	Gabapentin 600 mg before and after surgery	G1= 38 G2=38 G3=38	No significant difference in pain and morphine consumption between the two groups.	Morphine consumption	Nausea
Hah et al. 2017	USA	Randomized clinical trial	Gabapentin 1200 mg before surgery and 600 mg 3 times a day After surgery	Control group = 202 Gabapentin group = 208	No significant difference in pain between the two groups. The morphine consumption in the gabapentin group was lower than the control.	Pain	Nausea Headache Rush

Discussion

In this study, we systematically identified, reviewed, and evaluated the articles that evaluated the efficacy and safety of gabapentin on pain after THA. The results of our study show that gabapentin does not significantly affect pain after THA.

Additionally, gabapentin was safe and without serious adverse events. However, the following adverse events were reported in the reviewed studies: rash, nausea, headache, vomiting, and pruritus, which were resolved after medication discontinuation. Previous studies have also indicated that gabapentin use is safe without serious adverse events [20,21]. The results of included studies did not

evidence the use of gabapentin for the control of pain after THA. The results of our study are similar to meta-analysis studies and other review articles on the effect of gabapentin on pain after hip and knee arthroplasty [22, 23].

In a study by Erkilich et al. (2018), gabapentin was associated with a decrease in interleukin 6 (IL-6) levels 24 h after surgery, but the visual analogue scale (VAS) pain score 24 h post-surgery was not significantly different between gabapentin and placebo groups [24]. The results of this study are in-line with our results. However, the results of our systematic review contrast with several previous systematic studies evaluating the use of gabapentin for postoperative pain in different surgeries, such as cesarean section, breast cancer surgery, and spine surgery [25,26,27]. The reason for these contradictions may be due to different mechanisms and responses to pain at different surgical sites.

Several studies have investigated the effect of gabapentin on pain management after orthopedic surgeries. Mardani Kivi et al. (2013) evaluated the effect of gabapentin on pain after arthroscopic anterior cruciate ligament reconstruction. Patients were randomly divided into treatment (gabapentin 600 mg) or control groups. The primary and secondary outcomes of this study were pain and morphine consumption, respectively. The results of this study showed significantly lower pain scores and morphine consumption in the gabapentin group than in the control group [28]. Entezari et al. (2019) investigated the effect of gabapentin on pain after total knee arthroscopy. In this RCT, 114 patients, who underwent anterior cruciate ligament and posterior cruciate ligament knee arthroscopy, were randomly assigned to receive dextromethorphan or gabapentin alone or in combination. Pain intensity was measured using the Numerical Rating Scale (NRS) [29, 30]. The results of this study indicated significantly lower pain scores and analgesic agents use in patients who received a combination of dextromethorphan and gabapentin [29]. The results of these studies are inconsistent with that of Adam et al. (2006), who investigated the effect of gabapentin on pain after shoulder arthroscopy. Sixty patients were randomly assigned to receive oral gabapentin 800 mg or placebo 2 h before surgery. Pain scores, analgesic medications requirement, and adverse events were evaluated 48 h after surgery. The results of this study showed no significant differences in pain scores and analgesic medication requirements between the gabapentin and placebo groups. The adverse event rates were comparable in both groups, except for headache, which was lower in the gabapentin group [31].

Pain control after surgery is associated with early mobility, which is an important and fundamental factor for preventing post-surgery complications, including deep vein thrombosis, pulmonary embolism, infection, and reducing the length of hospitalization [32]. Future studies should aim to evaluate the effect of gabapentin on these factors as they are highly associated with functional improvement.

Our study has limitations that may affect the interpretation of the results. First, all included studies had small sample sizes and short postoperative follow-ups. Since this topic is still a relatively new research topic, there are a few published articles. Finally, a meta-analysis was not possible due to insufficient data in the included studies.

Conclusion

This study indicated that the current evidence does not support the routine administration of gabapentin for postoperative pain management after THA. However, future high-quality, controlled clinical trials with large sample sizes are still required to elucidate this issue. Future studies should also compare the effect of gabapentin with other oral medications, such as non-steroidal anti-inflammatory drugs (NSAIDs), and determine the long-term safety and appropriate dosage of gabapentin.

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