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The effect of preemptive analgesia with pregabalin on postoperative pain and opioid consumption in patients undergoing total hip arthroplasty: A randomized controlled trial

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Abstract
Background and Objective: Total hip arthroplasty (THA) is associated with significant postoperative pain, often requiring high doses of opioids, which carry risks of adverse effects. Preemptive analgesia with pregabalin, a gabapentinoid with antihyperalgesic properties, may reduce postoperative pain and opioid consumption. This study aimed to evaluate the efficacy of preemptive pregabalin in decreasing postoperative pain intensity and opioid requirements in patients undergoing THA.
Material and Methods: This prospective, double-blind, randomized controlled trial included 60 patients aged 40-75 years undergoing elective unilateral total hip arthroplasty under spinal anesthesia. This study was conducted at the department of anaesthesia, Dhanlakshmi Srinivasan Medical College and Hospital, Perambular, Tamil Nadu, India from June 2019 to May 2020. Patients were randomly assigned into two groups (n=30 each). Postoperative pain was assessed using the Visual Analog Scale (VAS) at rest and during movement at 2, 6, 12, and 24 hours. Total opioid consumption (intravenous morphine equivalents) over 24 hours, time to first analgesic request, and incidence of side effects (dizziness, sedation, nausea, vomiting) were recorded.
Results: VAS scores at rest and on movement were significantly lower in Group P at all time points ($p < 0.05$). The mean 24-hour opioid consumption was significantly reduced in the pregabalin group (18.4 ± 5.6 mg) compared to the control group (28.7 ± 6.2 mg, $p < 0.001$). Time to first analgesic request was longer in Group P (4.8 ± 1.3 hours) than in Group C (2.6 ± 1.0 hours, $p < 0.001$). The incidence of dizziness and mild sedation was higher in Group P, but not statistically significant. Nausea and vomiting were less frequent in the pregabalin group.
Conclusion: Preemptive administration of 150 mg pregabalin effectively reduces postoperative pain intensity and opioid consumption in patients undergoing total hip arthroplasty without a significant increase in adverse effects. Pregabalin may be considered a useful adjunct in multimodal analgesia for enhanced recovery after hip arthroplasty.

Keywords: Pregabalin, Preemptive analgesia, Total hip arthroplasty, Postoperative pain, Opioid consumption, Randomized controlled trial

Introduction
Total hip arthroplasty (THA) is one of the most frequently performed orthopedic procedures worldwide, primarily indicated for end-stage osteoarthritis, rheumatoid arthritis, or avascular necrosis of the femoral head. Although THA significantly improves function and quality of life, it is associated with moderate to severe postoperative pain, particularly during the first 24 to 48 hours after surgery. Effective pain control during this period is critical not only for patient comfort but also to facilitate early mobilization, reduce hospital stay, and prevent chronic post-surgical pain syndromes [1-3].
Opioids are commonly used for postoperative analgesia following THA. However, opioid-based analgesia is often associated with undesirable side effects such as sedation, nausea, vomiting, constipation, respiratory depression, and potential for tolerance or dependence. These complications can hinder recovery and negatively affect patient outcomes. As a result, there has been a growing emphasis on multimodal analgesia and preemptive pain management strategies to minimize opioid use while still ensuring effective pain relief [4-6].

Preemptive analgesia refers to the administration of analgesic agents before the onset of noxious stimuli (surgical incision) with the goal of preventing central and peripheral sensitization. This approach is thought to reduce the intensity of postoperative pain and decrease the need for opioids. Among the agents explored for preemptive analgesia, pregabalin, a structural analog of gamma-aminobutyric acid (GABA), has garnered considerable interest [7, 8].

Pregabalin binds to the α2δ subunit of voltage-gated calcium channels in the central nervous system, reducing excitatory neurotransmitter release and neuronal hyperexcitability. It has demonstrated analgesic, anxiolytic, and opioid-sparing effects in various surgical models, including spinal surgery, abdominal surgery, and joint replacement procedures. Several clinical trials and meta-analyses suggest that preoperative administration of pregabalin can reduce postoperative pain intensity and the total amount of opioids required, with an acceptable side effect profile [9, 10].

Despite these promising findings, results across studies have been variable due to differences in patient populations, types of surgeries, pregabalin doses, and outcome measures. Moreover, limited data are available specifically regarding the use of preemptive pregabalin in total hip arthroplasty under standardized conditions [11, 12].

Therefore, the present study was designed to evaluate the effect of a single preoperative dose of pregabalin (150 mg) on postoperative pain scores and opioid consumption in patients undergoing elective THA. The study also aimed to assess the time to first analgesic request and the incidence of common adverse effects such as dizziness, sedation, and nausea. We hypothesized that preemptive pregabalin would lead to lower postoperative pain scores, reduced opioid requirement, and delayed need for rescue analgesia compared to placebo, without a significant increase in side effects.

Materials and Methods

This was a prospective, randomized, double-blind, placebo-controlled clinical trial conducted at the department of anaesthesia, Dhanlakshmi Srinivasan Medical College and Hospital, Perambular, Tamil Nadu, India from June 2019 to May 2020. A total of 60 adult patients scheduled for elective unilateral total hip arthroplasty (THA) under spinal anesthesia were enrolled in the study. Participants were randomly allocated into two equal groups using a computer-generated randomization sequence. Both the patients and the medical personnel involved in intraoperative and postoperative care were blinded to group allocation. All patients received standardized spinal anesthesia with 0.5% hyperbaric bupivacaine. No intraoperative opioids or sedatives were used. Postoperative pain was managed using intravenous morphine via patient-controlled analgesia (PCA). Pain intensity was assessed using the Visual Analog Scale (VAS) at rest and on movement at 2, 6, 12, and 24 hours postoperatively.

Inclusion Criteria

- Patients aged 40-75 years.
- ASA physical status I or II.
- Scheduled for elective unilateral total hip arthroplasty under spinal anesthesia.
- Ability to understand and use the VAS scale and PCA device.
- Provided written informed consent.

Exclusion Criteria

- Known hypersensitivity or contraindication to pregabalin.
- Chronic opioid use or long-term use of anticonvulsants, antidepressants, or sedatives.
- History of chronic pain disorders or neuropathic pain.
- Renal impairment (creatinine clearance < 60 mL/min)
- Hepatic dysfunction or severe cardiovascular/respiratory disease.
- Cognitive impairment, psychiatric illness, or inability to follow study instructions.
- Pregnant or lactating women.
- Participation in another clinical trial within the last 30 days.

Results

A total of 60 patients were enrolled and completed the study. All baseline characteristics were comparable between the two groups, ensuring homogeneity.

Table 1: Demographic and Surgical Characteristics

Parameter	Group P (n=30)	Group C (n=30)	p-value
Age (years)	62.4 ± 6.7	61.8 ± 7.1	0.72
Gender (M/F)	18/12	17/13	0.79
Weight (kg)	69.5 ± 8.2	70.1 ± 9.0	0.68
ASA I/II (n)	14/16	15/15	0.81
Duration of surgery (min)	94.2 ± 15.6	96.1 ± 14.8	0.63

No statistically significant differences were observed in age, sex distribution, weight, ASA status, or surgical duration between the two groups ($p > 0.05$), confirming comparability at baseline.

Table 2: Visual Analog Scale (VAS) Scores at Rest and on Movement

Time (hrs)	VAS at Rest (Mean ± SD)		VAS on Movement (Mean ± SD)	
	Group P	Group C	Group P	Group C
2	2.4 ± 0.6	3.5 ± 0.8	3.8 ± 0.7	5.1 ± 1.1
6	2.1 ± 0.5	3.4 ± 0.9	3.5 ± 0.8	5.0 ± 1.0
12	2.0 ± 0.6	3.1 ± 0.8	3.2 ± 0.9	4.8 ± 1.2
24	1.8 ± 0.7	2.9 ± 0.7	2.9 ± 0.8	4.5 ± 1.0

VAS scores at rest and during movement were significantly lower in the pregabalin group (Group P) at all time intervals ($p < 0.01$), demonstrating superior analgesic efficacy compared to placebo.

Table 3: Total Opioid Consumption in 24 Hours

Parameter	Group P (n=30)	Group C (n=30)	p-value
Total morphine (mg)	18.4 ± 5.6	28.7 ± 6.2	<0.001
Patients requiring >30 mg morphine	4 (13.3%)	15 (50%)	0.002

Group P showed significantly lower total opioid consumption over 24 hours than Group C ($p < 0.001$). Fewer patients in the pregabalin group required high-dose morphine (>30 mg), supporting its opioid-sparing effect.

Table 4: Time to First Analgesic Request

Parameter	Group P (n=30)	Group C (n=30)	p-value
Time to first request (hrs)	4.8 ± 1.3	2.6 ± 1.0	<0.001

The time to first analgesic request was significantly prolonged

in the pregabalin group compared to the control group ($p < 0.001$), indicating an extended duration of pain relief from preemptive pregabalin administration.

Table 5: Incidence of Adverse Effects

Adverse Effect	Group P (n=30)	Group C (n=30)	p-value
Dizziness	6 (20%)	2 (6.7%)	0.12
Sedation	4 (13.3%)	2 (6.7%)	0.38
Nausea	3 (10%)	8 (26.7%)	0.09
Vomiting	1 (3.3%)	5 (16.7%)	0.09
Respiratory depression	0 (0%)	1 (3.3%)	0.31

Although dizziness and mild sedation were more frequent in Group P, the differences were not statistically significant. Interestingly, nausea and vomiting occurred more frequently in the control group, possibly due to higher opioid use.

Discussion

This randomized controlled trial investigated the efficacy of preemptive pregabalin (150 mg) in managing postoperative pain and reducing opioid consumption following total hip arthroplasty (THA). The results demonstrated that a single preoperative dose of pregabalin significantly reduced postoperative pain scores, lowered opioid requirements, and prolonged the time to first analgesic request, without a significant increase in adverse effects [13, 14].

The observed reduction in VAS pain scores in the pregabalin group aligns with findings from earlier studies. Clarke *et al*. (2009) and Mathiesen *et al*. (2007) reported that preoperative pregabalin administration effectively attenuated postoperative pain and enhanced the analgesic profile in patients undergoing orthopedic and abdominal surgeries. Our study further supports these findings in the context of THA, where pain is often intense and difficult to manage in the early postoperative period [15-17].

The opioid-sparing effect observed in our study is consistent with previous literature. Tiippana *et al*. (2007) conducted a meta-analysis that concluded pregabalin significantly reduces opioid consumption across various surgical models. This reduction is particularly important in the context of enhanced recovery after surgery (ERAS) protocols, where minimizing opioid use is a key goal to reduce complications and facilitate early mobilization.

Pregabalin's mechanism of action—binding to the α2δ subunit of voltage-gated calcium channels—helps reduce central sensitization and hyperalgesia, contributing to its effectiveness as a preemptive analgesic (Kaka *et al*., 2019). Our finding that the time to first rescue analgesia was significantly prolonged in the pregabalin group supports the hypothesis that pregabalin modifies central nociceptive processing when administered before surgical insult [17-19].

Although adverse effects such as dizziness and sedation were slightly more common in the pregabalin group, these differences were not statistically significant and were clinically manageable. These side effects are well-documented in previous trials (Ziegeler *et al*., 2008; Jokela *et al*., 2008), especially with higher doses (>300 mg), suggesting that the 150 mg dose used in our study provides a balance between efficacy and tolerability [18, 19].

Interestingly, the control group experienced a higher incidence of nausea and vomiting, likely related to greater morphine consumption. Similar findings were reported by Buvanendran *et al*. (2010), who noted a correlation between reduced opioid use and decreased incidence of opioid-induced nausea and vomiting when pregabalin was used as an adjunct.

Several studies have also explored the role of pregabalin in joint replacement surgeries. For example, Kim *et al*. (2011) observed reduced pain and improved patient satisfaction following total knee arthroplasty with pregabalin use, while Lunn *et al*. (2015) demonstrated enhanced pain control when pregabalin was combined with multimodal analgesia in hip surgery [19-21].

Despite the promising results, our study has limitations. The sample size was modest, and long-term outcomes such as chronic pain development and functional recovery were not assessed. Additionally, the use of a single fixed dose of pregabalin precludes dose-response analysis. Future studies with larger cohorts and varying dosing regimens are warranted to optimize pregabalin use in THA. In conclusion, our findings contribute to the growing body of evidence supporting the use of preemptive pregabalin as an effective component of multimodal analgesia for total hip arthroplasty, offering better pain control and a reduction in opioid-related adverse effects.

Conclusion

Preemptive administration of 150 mg pregabalin significantly reduced postoperative pain intensity and opioid consumption in patients undergoing total hip arthroplasty. It also delayed the time to first analgesic request and improved overall analgesic effectiveness without a statistically significant increase in adverse effects. These findings support the use of pregabalin as a safe and effective component of multimodal analgesia protocols in orthopedic surgery, particularly in total hip arthroplasty. Further large-scale studies are warranted to optimize dosing strategies and evaluate long-term outcomes, including chronic pain prevention.

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Conflict of interest

None.

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