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Original Research

Comparative Analysis of Gabapentin vs. Pregabalin for Preemptive Analgesia in Acute Postoperative Pain Following Surgery under Spinal Anesthesia

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ABSTRACT:

Background: Preemptive analgesia is a proactive approach that entails administering an analgesic regimen before exposure to noxious stimuli, aiming to hinder the sensitization of the nervous system and mitigate the amplification of pain from subsequent stimuli. This study was crafted to assess and compare the effectiveness of Gabapentin and Pregabalin. The focus was on examining their impact on prolonging analgesia duration, diminishing the overall need for post-operative analgesics, and scrutinizing potential side effects and complications. **Methods**: This prospective randomized study encompassed 124 patients classified as ASA grade I or II, aged between 20 and 50 years, with a body weight ranging from 50 to 70 kg. The participants were slated for elective infra-umbilical surgeries under spinal anesthesia. The cohort was randomly divided into two groups, each consisting of 62 individuals. Group G received a 1200 mg dose of Gabapentin, while Group P received a 300 mg dose of Pregabalin, administered one hour prior to spinal anesthesia.Pain levels were evaluated using the Visual Analogue Scale immediately in the postoperative period and subsequently every two hours. The time elapsed between spinal anesthesia and the initial analgesic dose (diclofenac) as well as the total analgesic doses administered within the first 24 hours were meticulously recorded for analysis. **Results**: Within Group G, participants necessitated rescue analgesia after an average of 12.00 ± 2.02 hours, while in Group P, this need arose later at 16.48 ± 4.48 hours. Additionally, in Group G, subsequent rescue analgesia was essential in only 6 cases, whereas in Group P, it was required in just 4 cases. Furthermore, the occurrence of somnolence and dizziness was less frequent with Pregabalin compared to Gabapentin. **Conclusion**: Administering a preoperative single oral dose of Pregabalin (300 mg) proves to be more effective in postoperative pain management and results in a reduction in the consumption of postoperative rescue analgesics when compared to a single dose of Gabapentin (1200 mg). Additionally, Pregabalin exhibits a favorable profile with fewer side effects in this context.

Keywords: Gabapentin, analgesia, pain.

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INTRODUCTION

Postoperative pain is a multifaceted experience that extends beyond simple nociception, involving a combination of inflammatory, neurogenic, and visceral components. When an individual undergoes surgery, the various stimuli associated with the procedure lead to sensitization of dorsal horn neurons in the spinal cord[1]. This sensitization amplifies the perception of pain, contributing to the complexity of postoperative pain.

Managing postoperative pain is crucial not only for immediate relief but also for facilitating early patient mobilization and overall well-being. This complex challenge has led to the development of preemptive analgesia as a strategic approach. Preemptive analgesia involves administering analgesic medications before the onset of noxious stimuli during surgery. The primary objective is to prevent the sensitization of the nervous system to subsequent stimuli, potentially reducing the overall intensity and duration of postoperative pain.Surgery, due to its predictable timing of noxious stimuli, provides an ideal setting for implementing preemptive analgesia[2,3]. By intervening before the initiation of surgery-related pain signals, healthcare professionals

aim to disrupt the cascade of events leading to heightened pain perception.

Traditionally, postoperative pain and neuropathic pain have been considered separate entities with distinct treatment approaches. In acute pain scenarios, opioids, non-steroidal anti-inflammatory drugs (NSAIDs), and local anesthetics have been the mainstay, while chronic pain specialists have turned to anticonvulsants and tricyclic antidepressants. However, an evolving understanding of pain pathophysiology reveals significant overlap between these two categories[4].Features typically associated with neuropathic pain, such as allodynia (pain from stimuli that are not normally painful) and hyperalgesia (increased sensitivity to painful stimuli), are not exclusive to chronic conditions. They are also observed after trauma and surgical procedures. Neuronal sensitization in the dorsal horns, a mechanism commonly found in neuropathic pain, has been demonstrated in acute pain models. This persistent mechanism might contribute to the increasingly recognized issue of chronic pain following surgery.In essence, the comprehensive comprehension of postoperative pain involves recognizing and addressing the diverse components contributing to the pain experience. Preemptive analgesia, by strategically intervening before the onset of surgical stimuli, represents a promising avenue for reshaping postoperative pain management[5]. This approach underscores the interconnected nature of acute and chronic pain states, providing insights into potential mechanisms that contribute to the development of persistent pain after surgery.

The primary objectives of the study were focused on evaluating and comparing the postoperative analgesic benefits of administering either Gabapentin or Pregabalin as premedication for surgeries conducted under spinal anesthesia. The investigation aimed to shed light on the postoperative efficacy of these medications through a nuanced exploration of key parameters. Firstly, the study sought to quantify the duration of postoperative pain relief induced by Gabapentin and Pregabalin, providing valuable insights into the temporal effectiveness of these interventions. Secondly, the research aimed to assess the impact of these drugs on the overall requirements for additional analgesics in the postoperative period, emphasizing their potential to minimize the necessity for supplementary pain relief measures[6]. Finally, an integral aspect of the study involved a meticulous examination of potential side effects and complications associated with the administration of Gabapentin or Pregabalin. By systematically addressing these objectives, the study intended to contribute significant knowledge to the medical field, offering a comparative analysis that could inform and optimize postoperative pain management strategies, thereby enhancing patient outcomes and the overall quality of care in surgical contexts.

MATERIALS AND METHODS

This prospective, randomized, double-blinded study was conducted following the acquisition of institutional ethical clearance and informed consent from the subjects. The inclusion criteria encompassed patients classified as ASA grade I or II, of either gender, aged between 20 and 50 years, with a body weight ranging from 40 to 70 kg, and scheduled for elective infra-umbilical surgeries under spinal anesthesia[7]. Exclusion criteria comprised patients with uncontrolled or labile hypertension, allergies to the study drugs, pregnant or lactating women, individuals with psychiatric illnesses, hepatic or renal impairments, and those presenting any contraindications to spinal anesthesia.Determined by calculations derived from a previous study, a sample size of 62 patients in each group was deemed necessary to detect a clinically relevant difference in the duration of postoperative analgesia. With a study power of 80% at a 95% confidence interval (alpha = 0.05), a total of 124 patients were randomly assigned to two groups using an online randomizer. Group G (n = 62) received a preoperative dose of 1200 mg Gabapentin, while Group P (n = 62) received 300 mg Pregabalin, administered one hour before spinal anesthesia.Pre-anesthetic check-ups (PAC) were conducted a day before surgery, during which patients were familiarized with spinal anesthesia and postoperative pain relief procedures, including details about the Visual Analogue Scale (VAS) ranging from 0 to 10. Drug-containing bags, prepared by a pharmacologist not involved in the study, contained gelatin capsules of similar size and shape. In Group G, the bag contained 8 capsules of 300 mg Gabapentin each, while in Group P, it contained 8 capsules of 75 mg Pregabalin each. An anesthesiologist not participating in the study administered the medication to the patients one hour before spinal anesthesia, without instituting any other premedication.Upon arrival in the operating theater, routine monitoring (NIBP, pulse oximetry, and ECG) was initiated[8]. All patients were preloaded with 10 mL/kg lactated Ringer's solution before spinal anesthesia. Spinal anesthesia was induced with 3 mL of 0.5% bupivacaine (15 mg) at the L3 - L4 /L4 - L5 level. Intraoperative fluid administration was maintained, and any hypotension was addressed through fluid replacement and intravenous Mephentermine, overseen by another anesthetist.Pain assessment was a critical component of this study, conducted using the Visual Analogue Scale (VAS) in the immediate postoperative period and subsequently every 2 hours during the postoperative phase. The VAS scale ranged from 0 to 10, where 0 indicated no pain, and 10 denoted the most severe pain. The timing at which patients required rescue analgesics following surgery was carefully noted, providing insights into the duration of effective pain control.

For the evaluation of sedation, Filos' numerical scale was employed, categorizing patients into different

levels: Scale 1 denoted being awake and nervous, Scale 2 represented being awake and relaxed, Scale 3 indicated being sleepy but easily awakened, and Scale 4 signified being sleepy and challenging to rouse[9].Adverse events within the initial 24 hours postoperatively were meticulously documented. These events included dizziness and somnolence, diplopia (double vision), vomiting graded on a 4-point ordinal scale (0 = no nausea/vomiting; 1 = mild nausea; 2 = moderate nausea; 3 = severe nausea with vomiting), confusion assessed through questions about time, place, and person, urinary retention in noncatheterized patients, and respiratory depression defined as a ventilatory frequency less than 8 breaths per minute and oxygen saturation below 90% without oxygen supplementation.

Charting of pain scores using the VAS scale in the ward was carried out by another anesthesiologist who was unaware of the premedication status of the patients. This separation ensured that the observer remained blinded to the patient's group assignment. In cases where the VAS score exceeded 3, diclofenac was administered intramuscularly at a dose of 1 mg/kg. The time elapsed from spinal anesthesia to the first dose of analgesic and the total dose of analgesic administered within the initial 24 hours were meticulously recorded, providing a comprehensive understanding of the postoperative pain management outcomes.

RESULTS

Our study encompassed a total of 124 participants, with the majority falling into the age group of 40 years and above. Among the enrolled patients, the male-to-female ratio was 1:1.38, indicating a slight predominance of female participants. Notably, both study groups demonstrated comparability across various parameters, including demographic characteristics, ASA physical status, mean duration of surgery, and the types of surgeries performed. This equivalence in baseline characteristics between the groups ensures a balanced and unbiased comparison. Furthermore, no significant differences were observed between the groups concerning the average time required for the surgical maneuver. This homogeneity in key variables enhances the validity of the study, allowing for a more accurate assessment of the effects of premedication with Gabapentin and Pregabalin on postoperative outcomes.

Table 1: Comparison of duration of surgery in both the groups

Groups	Duration of surgery (minutes) (Mean ± SD*)	P value
Group P (n-62)	70.10 ± 25.48	0.3818
Group G (n-62)	64.76 ± 22.13	

Over the 24-hour postoperative period, the mean Visual Analogue Scale (VAS) scores at rest in Group P consistently demonstrated statistically significant lower levels compared to Group G. This indicates that patients who received Pregabalin experienced lower perceived pain intensity during the specified timeframe[10]. Notably, in Group G, only 6 cases required subsequent rescue analgesics, while in Group P, this need arose in only 4 cases. The time at which rescue analgesics were administered differed significantly between the two groups, with Group G requiring it after an average of 12.00 ± 2.02 hours, whereas Group P showed a longer duration with rescue analgesics needed after 16.48 ± 4.48 hours.The study revealed a substantial variation in the time interval after surgery when the VAS score reached 3 or more, indicating the necessity for rescue analgesia. In Group P, this interval was significantly longer compared to Group G, highlighting the superior efficacy of Pregabalin in providing prolonged postoperative analgesia when compared to Gabapentin. This observation underscores the potential clinical benefits of choosing Pregabalin as a premedication option for enhanced postoperative pain management.

Table 2: Comparison of time elapsed after surgery when VAS score > 3

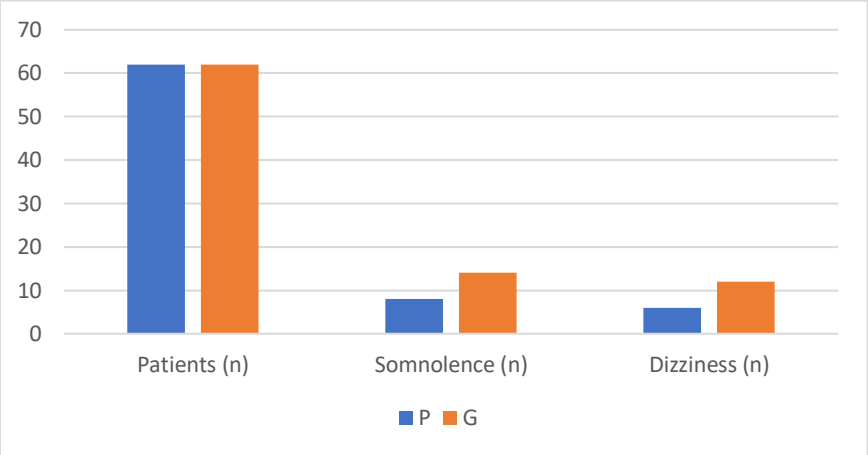
Groups	Hours after surgery when VAS > 3 (Mean ± SD)	P value
Group P (n-62)	16.48 ± 4.08	0.0001
Group G (n-62)	12.00 ± 2.22	

In Group P, somnolence was noted in 8 out of 62 patients, while in Group G, a higher occurrence was observed with 14 out of 62 patients experiencing somnolence. Similarly, the incidence of dizziness was lower in Group P, with 6 out of 62 patients affected, compared to Group G, where 12 out of 62 patients reported experiencing dizziness. Consequently, the overall incidence of somnolence (12.90%) and dizziness (9.68%) was notably lower in Group P in comparison to Group G (22.59% and 19.35%, respectively. Notably, there were no reported incidences of nausea and vomiting in either of the study groups. These findings suggest a favorable safety profile for Pregabalin, indicating a lower likelihood of somnolence and dizziness compared to Gabapentin in the context of premedication for surgeries under spinal anesthesia.

Table 3: Comparison of adverse events seen in both the groups

Group	Patients (n)	Somnolence (n)	Dizziness (n)
P	62	8	6
G	62	14	12

Table 3: Comparison of adverse events seen in both the groups



DISCUSSION

Numerous studies have consistently highlighted the efficacy of both Gabapentin and Pregabalin in perioperative contexts, showcasing their potential to reduce postoperative pain, decrease analgesic requirements, minimize side effects, extend the duration of analgesia, and enhance overall patient satisfaction. The management of pain and its associated complications during the postoperative period remains a formidable challenge in clinical practice[11-13].Preemptive analgesia, a strategic approach involving the administration of analgesics before the onset of noxious stimuli, emerges as a crucial tool in mitigating postoperative pain. By preventing the establishment of altered sensory processing that amplifies pain, preemptive analgesia has proven effective in reducing the impact of noxious stimuli on the central nervous system. This proactive approach has been demonstrated to protect the central nervous system from the deleterious effects of surgical trauma, ultimately leading to a reduction in allodynia and mitigating the likelihood of increased postoperative pain.Incorporating pre-incisional analgesia has been particularly notable for its effectiveness in controlling postoperative pain. This approach not only addresses the immediate perioperative period but also plays a pivotal role in safeguarding the central nervous system against the detrimental effects of noxious stimuli. The outcome is a reduction in allodynia and a decreased propensity for heightened postoperative pain, contributing to improved pain management strategies and enhanced patient comfort.In summary, the utilization of Gabapentin and Pregabalin, particularly in preemptive and pre-incisional analgesia, stands out as a valuable approach in perioperative care[14]. These interventions not only contribute to alleviating postoperative pain but also demonstrate a potential to enhance the overall patient experience by minimizing side effects and optimizing pain control during the critical postoperative period.Gabapentin and Pregabalin, both widely recognized for their antiallodynic and anti-hyperalgesic properties in the treatment of neuropathic pain, have emerged as promising options for managing acute postoperative pain. A recent comprehensive review, encompassing data from 22 randomized controlled trials (RCTs), revealed an intriguing finding—namely, the reduction in 24-hour opioid consumption induced by Gabapentin was not significantly contingent on the dosage administered. This intriguing insight prompted the selection of a single highest safe dose for both Gabapentin (1200 mg) and Pregabalin (300 mg) in the present study, aligning with the dosages frequently employed in various research investigations.

Exploring the landscape of preemptive analgesia, prior studies utilizing Pregabalin in this context have employed a single dose ranging from 100-150 mg. Noteworthy examples include investigations by Paech et al. in minor gynecological surgery involving the uterus, Jokela et al[15]. in day-case gynecological laparoscopic surgery, and Agarwal et al. in laparoscopic cholecystectomy. However, a departure from these lower doses was deemed necessary in the present study. The rationale behind opting for a single preemptive dose of 300 mg of Pregabalin was grounded in the consideration that lower doses might prove subtherapeutic. This decision was particularly salient given the nature of the surgical procedures undertaken in the present study, which involved more intricate and potentially more painful interventions such as laminectomy, discectomy, and instrumentation[16]. The deliberate selection of a higher dose sought to ensure a robust preemptive analgesic effect, attuned to the specific demands and potential intensity of pain associated with the procedures

involved in this study.
The study revealed that the duration after surgery, when rescue analgesic was required, was statistically and significantly lower in the case of Gabapentin compared to Pregabalin—12.00 ± 2.02 hours for Gabapentin versus 16.48 ± 4.08 hours for Pregabalin. Additionally, the subsequent dose required in the Pregabalin group was 6.45%, while in the Gabapentin group, it was 9.68%. This outcome contrasts with the findings of other studies. For instance, a study by Paech et al. in 2007, involving women undergoing minor gynecological surgery, found no significant difference between oral Pregabalin and placebo groups in terms of postoperative pain, recovery room Fentanyl requirement, or the quality of recovery at 24 hours postoperatively[17]. Similarly, Agarwal et al. reported reduced postoperative pain and Fentanyl consumption with Pregabalin in laparoscopic cholecystectomy, and Sahu et al. observed significantly lower mean VAS scores and rescue analgesic consumption in Pregabalin-treated patients in infra-umbilical surgeries under spinal anesthesia.
Notably, somnolence and dizziness, common side effects associated with both Gabapentin and Pregabalin, exhibited a lower incidence in the Pregabalin group compared to the Gabapentin group, consistent with earlier studies. Although somnolence and dizziness are generally well-tolerated and may even confer anti-anxiety effects, the study highlights a potentially more favorable side effect profile for Pregabalin.
Nevertheless, the study has acknowledged limitations. The use of a single dose of Gabapentin and Pregabalin poses a challenge in drawing conclusions about the optimal dose and treatment duration, considering their relatively short half-life[18]. The study's findings, favoring Pregabalin's efficacy over Gabapentin, suggest the need for further investigations to comprehensively understand the long-term benefits of perioperative Gabapentin and Pregabalin. Additionally, the absence of a control/placebo group in this study is noteworthy, as both drugs have demonstrated efficacy in enhancing postoperative analgesia and reducing analgesic requirements in previous research. This limitation emphasizes the need for future studies incorporating control groups to validate and contextualize theobserved outcomes.

CONCLUSION

In conclusion, our study demonstrates that the preemptive use of a single oral dose of Pregabalin (300 mg) yields superior and prolonged postoperative pain control compared to a preemptive single oral dose of Gabapentin (1200 mg). The findings suggest that Pregabalin's efficacy extends to a more prolonged duration of analgesia and reduced postoperative rescue analgesic requirements. Both Gabapentin and Pregabalin emerge as effective tools in the anaesthesiologist's arsenal for perioperative pain management. While they can be utilized as standalone analgesics, our results emphasize their potential role as part of a multimodal analgesic strategy. Further research is warranted to explore the long-term benefits and optimal dosing regimens of Gabapentin and Pregabalin in perioperative pain management comprehensively.

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