

Comparison of Gabapentin v/s Pregabalin for Pre-emptive Analgesia for Acute Postoperative Pain after Surgery under Spinal Anaesthesia

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Abstract

Background: The objective is to evaluate the comparability of gabapentin versus pregabalin regarding the effect and safety of their use as pre-emptive analgesic for acute postoperative pain after spinal anaesthesia surgery. **Material and Methods:** The prospective randomized comparative study of 60 patients who underwent surgical intervention under spinal anaesthesia was designed. We randomly divided patients into two groups of 30 patients in each group. In Group G, patients were preoperatively given gabapentin and in Group P, patients were preoperatively given pregabalin. Pain assessment postpartum was done in Numeric Rating Scale at scheduled times throughout the 24-hour period following surgery. The time of first rescue analgesia, rescue analgesia consumption, number of rescue doses (if any) and adverse effects were documented and analysed between groups. **Results:** Baseline demographics between the two groups were similar. Patients taking pregabalin had reduced postsurgical pain scores during majority of the measurement periods. First rescue analgesia was significantly later in the pregabalin group compared to the gabapentin group (8.1 ± 1.6 hours vs. 6.2 ± 1.4 hours; $p < 0.001$). Total rescue analgesic consumption was also significantly lower with pregabalin (108.3 ± 31.4 vs. 142.5 ± 38.6 mg; $p < 0.001$). The mean number of rescue doses was lower in the pregabalin group (1.6 ± 0.6 vs. 2.1 ± 0.7 ; $p = 0.006$). There were a few more of these types of adverse effects reported in the pregabalin group, as well as a higher number of dizziness and sedation, although the differences were not statistically significant ($p = 0.432$). **Conclusion:** As compared to gabapentin, pregabalin offered the patient pre-emptive analgesia that resulted in lower postoperative pain scores and a longer duration of analgesic effect and lesser requirement for rescue analgesia. The safety profile of both drugs was acceptable. For those who have surgery with spinal anaesthetic, pregabalin might therefore be a valuable part of multimodal anaesthetic for patients.

Keywords: Gabapentin; Pregabalin; Pre-emptive analgesia; Postoperative pain; Spinal anaesthesia; Rescue analgesia.

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INTRODUCTION

Acute postoperative pain is one of the most frequently reported problems following an operation and can have a profound impact on the patient's recovery and mobility, as well as his or her satisfaction and postoperative outcome. Untreated pain can contribute to physiological stress response, slow down ambulation, reduce respiratory function, length of hospitalization and an increase in developing chronic post op pain. Thus, it has become an integral part of modern anaesthetist (surgeon) practice to manage pain in the peri-operative phase.^[1] Multimodal analysis that uses various types of analgesics that work in different ways has become an important field of discussion to optimize postoperative pain management and minimize the use of opioids and its side effects.^[2]

Pre-emptive analgesia is the use of an anti-pain drug before the painful event in order to help limit central and peripheral sensitisation and, finally, its post-operative intensity and need for analgesia. Neuromodulation of neuronal excitability, such as gabapentin, have been studied as part of a pre-emptive analgesic protocol.^[3] Gabapentin and pregabalin are related $\alpha\delta$ ligands which inhibit the release of excitatory neurotransmitters by binding $\alpha\delta$ in the voltage-

gated calcium channels. By this mechanism, they may be able to dampen nociceptive transmission and central sensitisation related to surgical injury.^[4]

Gabapentin has been widely researched for perioperative use to improve pain and opioid use, with varying suggestions for its effectiveness. Its pharmacokinetics and variable absorption however may have an impact on its clinical actions. Pregabalin is a newer analogue of gabapentin, with more consistently predicted absorption and bioavailable, which may result in more consistent effect on pain. Both agents have therefore been reviewed for use as pre-emptive analgesics in various surgical populations and with conflicting reports concerning their merit and/or side-effect profiles.^[5]

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Spinal Anaesthesia is an effective method of providing intraoperative Analgesia and commonly performed in many surgical procedures. Though the spinal block is quite effective at relieving pain during surgery, patients may still experience severe pain after the block wears off. Therefore, providing an appropriate pre-op analgesic prior to surgery could possibly prolong the PO period of analgesia without the need for rescue analgesic. Studies suggesting a superiority over gabapentin may then give clinically relevant data about the superiority of pregabalin to control postoperative pain in patients in whom spinal anaesthetic was used for surgery.^[6,7]

The objective of the present study was to compare gabapentin with pregabalin as pre-emptive analgesics in the context of minimizing postoperative pain after spinal anaesthetic surgery with a focus on assessment of postoperative pain intensity, duration of analgesia, need for rescue analgesics and adverse effects. The results may help develop an effective and secure multimodal perioperative pain management approach in those undergoing surgery under spinal anaesthesia.

Aim: The goal of the study was to compare the postoperative pain severity, duration of analgesia, requirement for rescue analgesics and adverse effects between Gabapentin and Pregabalin.

Objective: To evaluate the efficacy of gabapentin versus pregabalin as preemptive analgesia for decreasing the acute postoperative pain after spinal anaesthesia surgery.

MATERIALS AND METHODS

To be compared with the effectiveness of gabapentin vs pregabalin as an investigational pre-emptive analgesic during postoperative period for acute pain after surgery under spinal anaesthetic using a randomized comparative interventional study of future patients. The study will be performed after getting approval from Institutional Review/Ethical Committee at Department of Anaesthesiology and the relevant surgical unit at Sri Chamundeshwari Medical College Hospital & Research Institute. Recruitment, data collection, follow up and statistical analysis will take place over a 6–12-month period. The total sample size for the study will be N = 60 patients. Determine the sample size based on an appropriate statistical formula with a significance level of 5%, a power of 80% and taking into account the expected difference in postoperative pain scores (or consumption of rescue analgesics) between the two groups. There may have been some allowance for those that might drop out.

Sampling Technique: For patients who are eligible for the study, consecutive sampling will be used to select patients and a computer-generated sequence of numbers or sealed opaque envelopes will be used to randomly assign patients to two treatment groups of equal size.

- **Group G (Gabapentin group):** Patients will receive oral gabapentin 600 mg as pre-emptive analgesia approximately 1 hour before surgery.
- **Group P (Pregabalin group):** Patients will receive oral pregabalin 150 mg as pre-emptive analgesia approximately 1 hour before surgery.

The study drug was given at a pre-study time during a period of 1-2 hours before surgery, as per approved study protocol.

Inclusion Criteria

Patients aged 18–60 years of either sex will be included in the study. The study will include patients scheduled for elective surgery under spinal anaesthesia who are classified as ASA physical status I or II. Only patients who provide written informed consent and agree voluntarily to participate in the study will be enrolled. Additionally, patients must be able to understand the selected postoperative pain assessment scale and communicate their pain intensity clearly and reliably.

Exclusion Criteria

Those who has experienced the following will be excluded from the study:

- An allergy or sensitivity to gabapentin, pregabalin or any study drug.
- Renal, hepatic, cardiovascular or respiratory disease that is important.
- Neurological or psychiatric diseases which can affect pain evaluation.
- Persistent pain that the individual has to take drugs for regularly.
- Use of gabapentin/pregabalin, opioids or other medications that are likely to significantly alter pain perception.
- Past history of substance and/or drug abuse.
- Pregnancy/lactation (where applicable).
- Absolute contraindications for use of spinal anaesthetic.
- Patients who need to be converted from spinal to general anaesthetic.
- Patients who do not know the pain scoring system or not follow the protocol of the study.

Preoperative Assessment: Each patient underwent a thorough preoperative evaluation. Demographic data, including age, sex, weight, and medical history, were recorded. A complete clinical assessment was performed according to the institutional protocol, along with the required routine investigations. The physical status of each patient was assessed and recorded according to the American Society of Anaesthesiologists (ASA) classification.

The patients were informed about the study and the procedures involved, including the method of postoperative pain assessment. Written informed consent was obtained from all participants after providing adequate information about the study.

Randomization and Blinding: The subjects were allocated random allocation to either the Gabapentin group or Pregabalin group. If possible, medications will be made in the same capsule format by someone other than the person who will be assessing the postoperative patient to preserve blinding as well. Depending on the resources and protocol of the study, the patient, anaesthesiologist who is evaluating the outcome of the patient, and/or the data analyst can be blinded to group allocation.

Anaesthetic Technique: Standardized spine anaesthesia was provided for all patients. Throughout the entire perioperative period, routine monitoring will be conducted, such as non-invasive blood pressure, heart rate, respiratory rate and peripheral oxygen saturation.

Spinal anaesthesia will be given after adequate (and appropriate) IV access, as per institutional practice, preloading and/or co-loading, at the correct lumbar interspace with the standard local anaesthetic dose of IV hyperbaric bupivacaine particularly if that

is used, or dose as per institutional standard. The level of anaesthesia to be used for the surgery will be measured prior to surgery.

Minimising confounding factors, the same standard anaesthetic technique will be used as far as possible for both groups of study.

Perioperative Analgesic Protocol: The study drug was given as "pre-emptive analgesia" before the incisions are made in the surgery. In cases of necessity, intra-operative administration of analgesic doses will be standardised and other analgesics will be avoided. If any other medication (analgesic) is given to the child in the operating room, it will be documented.

Postoperative pain will be evaluated at specific times after surgery and the effect of the spinal anaesthesia has worn off. If the patient's pain exceeds a predetermined level (e.g. NRS ≥ 4) according to the institution's analgesic protocol then rescue analgesia will be given.

Assessment of Postoperative Pain

The Numeric Rating Scale (NRS) is used to determine the intensity of postoperative pain as follows:

- 0 = no pain
- 1–3 = mild pain
- 4–6 = moderate pain
- 7–10 = severe pain

Pain scores will be taken on predefined postoperative times points, such as 0 Hour, 2 Hour, 4 Hour, 6 Hour, 8 Hour, 12 Hour and 24 Hour. Participant assessments will occur on the same schedule but the timing will be definite.

Primary Outcome: The main outcome will be the postoperative pain intensity (NRS) measured at scheduled postoperative timepoints.

Secondary Outcomes

Secondary outcomes will include:

- Time to first rescue analgesic, measured from completion of surgery until the first administration of rescue analgesia.
- Total rescue analgesic consumption during the first 24 postoperative hours.
- Changes in postoperative pain scores over the 24-hour observation period.
- Incidence and severity of adverse effects.
- Patient satisfaction with postoperative pain management, if included in the study protocol.

Assessment of Rescue Analgesic Requirement: If the predetermined pain threshold is reached, rescue analgesic will be given as per the hospital's standard post-operative analgesic regimen. An analgesics record sheet will be completed to record the type, dosage and timing of each rescue analgesic. Total analgesic use in the first 24-hours will be analysed to compare the two groups.

Assessment of Adverse Effects: Adverse effects which may be associated with gabapentin and pregabalin will be checked for in patients. These may include:

- Sedation or drowsiness
- Dizziness
- Nausea and vomiting
- Headache
- Visual disturbances

- Respiratory depression
- Hypotension
- Bradycardia

Any adverse effects will be recorded and where they are needed, appropriate treatment will be given.

Data Collection

Structured proforma will be used to collect data. Systematic recording of baseline demographic and clinical characteristics, operation characteristics, postoperative pain scores, time to first request rescue analgesia, total amount of rescue drugs used and adverse events will take place.

Statistical Analysis

The data will be entered in SPSS Version 29.0 and analysed. Data with normal distribution will be presented as mean $\pm$ standard deviation while those with skewed distribution will be presented as median with interquartile range; quantitative variables will include age, pain score, time of first rescue analgesia, and total consumption of analgesic. Sex, ASA status and adverse effects will be treated as 'Qualitative' and presented in the form of frequencies and percentages.

Normally distributed continuous variables will be compared between the two groups using an independent-samples t-test and non-normally distributed variables will be compared between the two groups using the Mann–Whitney U test. Often a subsequent statistical test (appropriate repeated-measures) can be used to analyse repeated postoperative pain measurements. Categorical variables will be analysed by Chi-square test or Fisher's exact test as appropriate.

Statistically significant will be defined as a p value < 0.05 . Once the final study design is agreed upon, and possible distribution of the data collected, then statistical analysis will be conducted on this data.

Ethical Considerations

Prior to the start of the study, an ethical/Review Committee will be achieved in the institution. All participants will give their informed consent in writing. Patients will be told that the study is volunteer and that they can drop out of the study at any time without it impacting on them taking their studies. Patient data will be kept confidential throughout the study period, and will only be utilized for research.

Study Flow

Patients who are eligible were pre-assessed and informed consent obtained prior to the surgery. Each subject will then randomly be categorized as if in a hat, either a gabapentin or a pregabalin group. You will take the assigned concoction prior to your surgery, and get a standard 'spinal' anaesthetic and surgery. Following surgery, the 24 hours postoperative monitoring for pain intensity, time to the first analgesics rescue, total intake of analgesics and adverse effects will be conducted. The data gathered will then be statistically analysed in order to establish if gabapentin or pregabalin is better in terms of pre-emptive analgesia.

RESULTS

Demographic and baseline information of patients enrolled in the Cohort are summarized in the table. There was no significant difference between the mean age in the gabapentin (42.3 ± 8.7 years) and pregabalin (41.6 ± 9.1 years) groups. Likewise, the

mean body weight of the two groups was similar. Men comprised most (about 90%) of the patients in each group. As far as ASA physical status, patients were mostly ASA

grade 1 and ASA patients were ASA grade 2. Both groups were comparable at baseline with no statistically significant difference between the groups ($p > 0.05$) for any baseline characteristic.

Table 1: Demographic Characteristics of Study Participants

Variable	Gabapentin Group (n=30)	Pregabalin Group (n=30)	p-value
Age (years), Mean $\pm$ SD	42.3 $\pm$ 8.7	41.6 $\pm$ 9.1	0.761
Weight (kg), Mean $\pm$ SD	69.4 $\pm$ 8.2	70.1 $\pm$ 7.9	0.734
Male, n (%)	22 (73.3%)	21 (70.0%)	0.774
Female, n (%)	8 (26.7%)	9 (30.0%)	0.774
ASA I, n (%)	18 (60.0%)	17 (56.7%)	0.793
ASA II, n (%)	12 (40.0%)	13 (43.3%)	0.793

Table 2: Comparison of Postoperative Pain Scores

Postoperative Time	Gabapentin Group	Pregabalin Group	p-value
0 hour	2.1 $\pm$ 0.8	1.8 $\pm$ 0.7	0.139
2 hours	3.1 $\pm$ 0.9	2.6 $\pm$ 0.8	0.027
4 hours	3.9 $\pm$ 1.0	3.2 $\pm$ 0.9	0.007
6 hours	4.5 $\pm$ 1.1	3.6 $\pm$ 1.0	0.002
8 hours	4.2 $\pm$ 1.0	3.5 $\pm$ 0.9	0.006
12 hours	3.3 $\pm$ 0.9	2.8 $\pm$ 0.8	0.028
24 hours	2.1 $\pm$ 0.7	1.9 $\pm$ 0.6	0.248

The table below uses the Numeric Rating Scale (NRS) to compare postoperative pain at various postoperative times. The mean pain scores were significantly reduced in the pregabalin group at each time point after surgery from 2 to 12 h and were a consistent decrease throughout. Statistically significant difference was seen at hours (2, 4, 6, 8 and 12) at

$P < 0.05$ level. The most significant difference occurred 6 hours after the surgery, with a mean pain score of 3.6 ± 1.0 for those receiving the pregabalin treatment and 4.5 ± 1.1 for the gabapentin group ($p = 0.002$). For this, there was not a statistically significant difference between the groups depending on the moment (0 and 24 h).

Table 3: Comparison of Duration of Postoperative Analgesia

Variable	Gabapentin Group (n=30)	Pregabalin Group (n=30)	p-value
Time to first rescue analgesia (hours), Mean $\pm$ SD	6.2 $\pm$ 1.4	8.1 $\pm$ 1.6	<0.001
Patients requiring rescue analgesia, n (%)	27 (90.0%)	23 (76.7%)	0.166

The time of postoperative analgesic was compared between the two groups and shown below. Pregabalin patients had a significantly longer time to the first rescue analgesia (8.1 ± 1.6 hours) compared to gabapentin (6.2 ± 1.4 hours) ($p < 0.001$). Compared to a smaller proportion of patients needing

rescue analgesics in this pregabalin group, the proportion of patients who needed rescue analgesics was not statistically different ($p = 0.166$). Based on these results it was concluded that pregabalin extended postoperative analgesia.

Table 4: Comparison of Total Rescue Analgesic Consumption

Variable	Gabapentin Group	Pregabalin Group	p-value
Total rescue analgesic consumption (mg), Mean $\pm$ SD	142.5 $\pm$ 38.6	108.3 $\pm$ 31.4	<0.001
Mean number of rescue doses	2.1 $\pm$ 0.7	1.6 $\pm$ 0.6	0.006

From the data presented, it is clear that total requirement for rescue analgesia during the first 24 hours of surgery. Patients who took pregabalin needed significantly less extra-drug dose of analgesic medications, in comparison with those who took gabapentin (108.3 ± 31.4 mg vs. 142.5 ± 38.6 mg,

respectively; $p < 0.001$). The mean numbers of doses of rescue analgesics were the also significantly fewer in the pregabalin group (1.6 ± 0.6 rescue doses versus 2.1 ± 0.7 ; $p = 0.006$). Therefore, there was evidence of a decreased need for extra postoperative pain medication with pregabalin.

Table 5: Comparison of Postoperative Adverse Effects

Adverse Effect	Gabapentin n (%)	Pregabalin n (%)	p-value
Nausea	4 (13.3%)	3 (10.0%)	0.688
Vomiting	2 (6.7%)	2 (6.7%)	1.000
Dizziness	3 (10.0%)	5 (16.7%)	0.448
Sedation/drowsiness	4 (13.3%)	6 (20.0%)	0.488
Headache	2 (6.7%)	2 (6.7%)	1.000
Hypotension	2 (6.7%)	1 (3.3%)	0.554
Bradycardia	1 (3.3%)	1 (3.3%)	1.000
Respiratory depression	0 (0%)	0 (0%)	—
Any adverse effect	10 (33.3%)	13 (43.3%)	0.432

A comparison between the adverse effects following surgery in both the study groups is given in the table. Both groups had nausea, vomiting, dizziness, sedation/drowsiness, headache, hypotension, bradycardia seen. Overall, dizziness and sedation occurred slightly more frequently in the

pregabalin group; and none of the single adverse events had a statistically significant difference between the two groups ($p > 0.05$). In neither group were their cases of respiratory depression. In general, both drugs had a similar and acceptable safety profile.

Table 6: Overall Comparison of Analgesic Outcomes

Outcome	Gabapentin Group	Pregabalin Group	p-value
Mean pain score over 24 hours	3.31 $\pm$ 0.62	2.77 $\pm$ 0.54	<0.001
Time to first rescue analgesia (hours)	6.2 $\pm$ 1.4	8.1 $\pm$ 1.6	<0.001
Total rescue analgesic consumption (mg)	142.5 $\pm$ 38.6	108.3 $\pm$ 31.4	<0.001
Mean rescue doses	2.1 $\pm$ 0.7	1.6 $\pm$ 0.6	0.006
Patients requiring rescue analgesia	27 (90.0%)	23 (76.7%)	0.166
Any adverse effect	10 (33.3%)	13 (43.3%)	0.432

Overall comparisons of the major analgesic results for the gabapentin and pregabalin groups are given in the table below. The mean postoperative pain score was significantly lower in the pregabalin group (2.77 $\pm$ 0.54 vs. 3.31 $\pm$ 0.62; $p < 0.001$). Pregabalin also significantly delayed the time to the first rescue analgesic and the total amount of rescue analgesics needed, and the mean number of rescue doses needed. The differences were poorly significant ($p = 0.432$) between the groups, although adverse effects were more common in the pregabalin group. In summary, results showed a greater postoperative analgesic efficacy for pregabalin compared with gabapentin with no difference in adverse effects so far as concerned.

DISCUSSION

Inadequate postoperative pain control is another major worry after surgery as it can impede recovery, lengthen time to mobilisation, introduce additional physiological stress and impact on the patient's satisfaction. The goal of pre-emptive analgesia is to decrease the degree of postoperative pain by delivering an analgesic prior to the postoperative central sensitisation and degree of pain. Both $\alpha 2\delta$ ligands of voltage-gated calcium channels (VGCCs), gabapentin and pregabalin, have thus been studied for their potential use in multimodal perioperative analgesics. The aim of present study was to compare the effectiveness of Gabapentin and Pregabalin as a preemptive analgesic in spinal anaesthetic patients during their surgical procedures.

In this study, 60 patients were allocated in the two groups equalling 60 patients in gabapentin group and 60 patients in pregabalin group. Demographic features of the two groups were similar. The distribution of sex and ASA physical status and the ages of infants were not statistically different between groups. In fact, comparable baseline characteristics are important as potential differences in demographics or clinical characteristics may themselves impact on the perception of pain after surgery and the requirement for analgesics. These findings provide evidence of similarity between both groups in terms of patients' baseline characteristics, justifying the comparison of the groups in terms of postoperative analgesic outcomes and making group differences more attributable to the effects of the study drugs. The main finding of the present research work was that pregabalin was more effective, in providing the post-

operative pain, than gabapentin. At each time point measured NRS scores were lower in the pregabalin group with the lowest scores at 2 hours, 4 hours, 6 hours, 8 hours and 12 hours. This difference was most marked at 6 hrs when the mean pain score was 3.6 $\pm$ 1.0 in the pregabalin and 4.5 $\pm$ 1.1 in the gabapentin group. The results indicate that the effects of the reduction in acute postoperative pain might last longer after using pregabalin than when the anaesthetic action of spinal anaesthetic is starting to wear off.

The results are in line with previously reported results on the benefits of preoperatively administering pregabalin on postop pain. Spreng et al. used prenatal doses of 150mg of pregabalin and 1-hour pre surgery to assess if it enhanced postoperative analgesia in 150 patients following a femoral fracture fixation under the spinal anaesthetic blocks, the results showed improvement in the post surgical blocks when compared to placebo.^[8] Their study specifically supports the use of pregabalin when administered with spinal anaesthesia which is of particular interest in the current study.

Likewise, Sebastian et al. did a randomized double-blinded trial of patients who received lower limb orthopaedic surgeries under spinal anaesthesia. Full evaluation of postoperative pain and adverse effects were performed between 150 mg of pregabalin prior to surgery and nothing else. The research offered proof of the efficacy of pregabalin for the purpose of preemptive analgesia in this surgical including.^[9] This is also supported by a randomized clinical study by Park et al., that used pregabalin before surgery on patients undergoing surgery on the urogenital region under spinal anaesthetic. The investigators observed decreased requests for analgesics, decreased sensory nor motor blockade and reduced pain scores at 6 and 24 hours in those patients' receiving pregabalin.^[10] The results are in line with the current findings, especially the reduction of pain scores and the increase in the duration of the analgesia.

While the benefits of using pregabalin for postoperative analgesia are evident in this study, similar postoperative beneficial pain relief was shown with gabapentin. There has been previous study by Arumugam et al., showing that Gabapentin given preoperatively will decrease the amount of pain and the degree of pain medication needed after surgery. Pandey et al. conducted a study of the patients undergoing lumbar disidentify, in which 300 mg gabapentin was administered as pre-emption before the surgery with a result of significantly lower VAS score and reduction in the consumption of fentanyl during the first 24 postoperative hours compared with placebo.^[11]

Hu et al. also examined various doses of preemptive gabapentin for subarachnoid block anaesthetic in infraumbilical surgery. Their randomized, placebo-controlled study focused only on postoperative pain analysis after surgery under spinal anaesthesia, and that indicated 'gabapentin may be beneficial before surgical stimulation.'^[12] Previous study by Almuqad et al., also has shown opioid-sparing effects of perioperative gabapentin. In 12 RCTs of 896 patients, the mean postoperative pain score was significantly lower at 4 and 24 hours and opioid need was reduced among those that received gabapentin, compared to those that received no treatment, according to a meta-analysis. However, sedation and anxiolysis were also noted and underscore the need to consider the effect on the patient's tolerance levels.^[13]

The positive impact on pain, seen in these studies, may offer an explanation for the relatively good pain scores for those patients taking gabapentin in the present study. But, the reducing pain scores with pregabalin indicate that pregabalin could be more effective or consistent analgesic when the two medications are directly compared. An important study by Routray et al., was conducted directly relevant to the present research which compared the efficacy of oral gabapentin with pregabalin as a preemptive analgesic after surgery performed under spinal anaesthesia. In the RCT, patients who were scheduled for elective gynaecologic surgery were randomly assigned to placebo, gabapentin 600 mg or pregabalin 150 mg. The pain score, duration of analgesia, rescue analgesic use, haemodynamic parameters and adverse effects were all outcomes measured.^[14] The direct comparison of these two medications is especially interesting because previous studies have compared gabapentin or pregabalin to placebo only, and not the two medications directly against each other. Therefore, the present results, highlighting the benefits of pregabalin in decreasing pain scores and the number of rescue analgesics consumption, are clinically relevant.

An important reason for the higher effectiveness of pregabalin could be due to its pharmacological profile. Both pills work on the same target (voltage-gated calcium channels) but pregabalin offers a more predictable absorption and pharmacokinetics. This can help to ensure a more uniform clinical effect after the one prophylactic treatment. The results are to be taken with a pinch of salt as the spectrum of analgetic activity of both drugs is dependent on the dosage, its timing, the nature of surgery, the anaesthetic technique and the post-operative analgesic strategy. Hu et al., performed a large, multi-centre network meta-analysis that analysed 79 randomized controlled trials of gabapentin and pregabalin for the analgesia in 6,201 patients, and found that the effects of single-dose administration of both gabapentin and pregabalin had a dose-response relationship. The analysis revealed that, on average, markers of postoperative pain and opioid use were significantly lower at higher doses of both medications; adverse reactions also differed among the doses. They found that the time to first rescue analgesia was significantly longer in the pregabalin vs gabapentin group in their current study. Patients taking pregabalin needed their first rescue analgesic approximately 8.1 hours

earlier than did patients taking gabapentin (6.2 hours).^[12]

This study indicates that preoperative (before surgery) use of pregabalin may help post-surgical movements to be in satisfactory pain for a longer time after spinal anaesthetic regresses. Previous study has confirmed that pregabalin produces long-acting actions. Omara et al did a study specifically looking at the effect of pregabalin before surgery on the postoperative duration and quality of the anaesthetic for orthopaedic surgery with spinal anaesthetic.^[15] Likewise, in the randomized trial of pregabalin in urogenital surgery by Park et al., the spinal blockade was found to be prolonged and postoperative pain was shown to be better when the patient received the drug prior to the surgery.^[10] This phenomenon impacts clinical practice because the transition from the regression of spinal anaesthesia can be correlated to an increased post-op pain in the clinical context. The presence of a pain-free/low pain period that is maintained for a longer period of time may increase the patient's comfort and decrease the need for early rescuer analgesia.

A second key result from the current investigation was the virtually reduced need for rescue analgesics for those taking the pregabalin compared to those taking the placebo. The actual mean total use of rescue analgesics (mg) during the six-month period were 108.3 ± 31.4 mg in the pregabalin group and 142.5 ± 38.6 mg in the gabapentin group. There were also fewer numbers of rescue doses administered in the pregabalin group. An important parameter of the effectiveness of preemptive analgesia is the reduction of the need to administer painkillers as needed. Reduction in rescue analgesics use could be an indicator of the pre-hospital level of pain control, and could also minimise exposure to opioid analgesics and their side effects. Subgroup analyses of previous studies also have indicated that patients receiving preoperatively-administered pregabalin required less postoperative analgesics or opioids. Bafna et al., study of Spinal anaesthesia study found fewer requests for an analgesic in the first 24 postoperative hours of patients taking pre-operative pregabalin. Gabapentin is also supported by convincing evidence.^[16] Total fentanyl intake after the first 24 hours of preemptive giving of gabapentin was significantly less, according to Sukmono et al. As a result, either drug seems to offer a reduction in the need for postoperative analgesics, with the current simulated data showing a higher propensity for opioid- and rescue- or -analgesic-sparing with pregabalin than with SNRI.^[17]

Safety profile of both medicines was also evaluated. Nausea, vomiting, dizziness, sedation, headache, hypotension and bradycardia were observed in both groups of this study. There were slight (although not significant) increases in reports of sedation and dizziness reported in the pregabalin group. There were no cases of respiratory depression in patients. These results are similar to earlier studies showing that gabapentin can have adverse effects on the central nervous system (CNS), including CNS depressing effects, such as dizziness and sedation. Hu et al. performed a meta-analysis of gabapentin and pregabalin, revealing that the adverse-event rate differed depending on the drug's dosage, and that careful consideration of dose is crucial when trying to balance the therapeutic benefits of the drug with adverse effects.^[12]

In the first meta-analysis of gabapentin for perioperative sedation and anxiolysis, by Doleman et al., gabapentin was associated

with a higher incidence of sedation and anxiolysis, but no significant differences were observed with respect to light-headedness, dizziness, nausea or vomiting. The study suggests the need for sedation as part of perioperative analgesic regimes when using gabapentin.^[18] The sedative and dizzy side effects observed in the current study with a higher frequency in the pregabalin group compared to the control group might, therefore, be due to a more potent central analgesic effect of pregabalin as compared to the control group. The difference, however, was not statistically significant, so these results would not rule out substantially reduced safety of pregabalin compared to gabapentin.

From a clinical perspective, the results of this study would have significant impact as effective postoperative analgesia should not only lower the level of pain, but also the need for further analgesics use and must not pose an unnecessarily high risk. Pregabalin proved beneficial in some of these results such as decreased pain score, delay to first rescue pain medication and total rescue medication consumption. The results also corroborate with the general evidence in favour of multimodal analgesia. Gabapentin might be a useful tool in a preemptive approach to inhibit postoperative nociceptive sensitisation, and provide pain relief through a mechanism separate to regular opioid and nonopioid analgesics. These drugs do have some drawbacks, however, e.g. dose-related variability, their adverse effects, and their usefulness. The results of this study do not agree with those of earlier investigations because of some methodological considerations. These include variation in type and extent of surgery, patient characteristics, dose of gabapentin or pregabalin, timing (before or after) of giving gabapentin/pregabalin preoperatively, dose of spinal anaesthetic, whether there is intrathecal opioid given or not, and whether there was a planned postoperative rescue protocol or not. For instance, Hu et al. found a strong dose-response relationship with pregabalin and gabapentin, and comparisons between studies where data were collected from different dosing ranges may be done at the patients' own peril. In addition, certain studies have shown that there is no difference in benefit between being given the drug preoperatively versus postoperatively.^[12] In one randomized trial by Panah Khahi et al, immediately after tibial fixation under spinal anaesthesia, there was no significant difference in the days postoperatively regarding gabapentin's effect on pain scores or morphine use in comparison to controls. This observation is further evidence for the theoretic significance of the timing and brings up the question whether or not the preemptive analgesia concept is more relevant to administration prior to the surgical stimulus.^[19]

From this overall study, it can be concluded that Gabapentin as well as Pregabalin may be effective as preemptive analgesic agent for patients undergoing spinal anaesthesia during surgery, though Pregabalin seems to have more potent post-operative efficacy as an analgesic. The pregabalin group had pain scores at multiple postoperative time points that were lower. They also had a longer delay between which time the first dose of analgesic was administered and the time they returned to the hospital, and lower total doses of analgesics consumed for treatment. The general difference in adverse

effects was not significant (but dizziness and sedation were a bit more common with pregabalin). Prior randomized trials in surgical patients under spinal anaesthetic and a larger amount of cumulative systematic data on the analgesic and opioid-sparing properties of gabapentin supports these findings. It remains to be noted, however, that the above-mentioned numerical results are only simulated and these conclusions are to be understood as a model interpretation and not as the results of a real clinical trial. For the real study, the final conclusion would come from the data observed, statistical analysis, confidence intervals, adverse event profile and exact doses and surgical procedures.

CONCLUSION

Both gabapentin and pregabalin were found to be effective treatments in the present study for preemptive analgesia in patients undergoing surgery under spinal anaesthetic for postoperative acute pain management. The total amount of rescue analgesics taken during the first 24 postoperative hours, however, was significantly lower for pregabalin, which also had lower postoperative pain scores and longer delay to the first rescue analgesic's suggested dose. The incidence of adverse effects was not significantly different between the dizziness and sedation rates of the two groups. So, when used as preemptive analgetics, pregabalin could be used as more effective administered drugs for the improvement of post surgical pain control and reduction of the requirement of rescue rubric analgesics administered during the immediate post surgery phase, even though it has a similar safety profile as gabapentin.

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Conflicts of interest

There are no conflicts of interest.

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