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# Preoperative Use of Gabapentin or Pregabalin on Acute Postoperative Pain Following Laparoscopic Cholecystectomy

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## Abstract

**Introduction:** Pain is the earliest most common complain after elective laparoscopic cholecystectomy. Different modalities has been suggested to provide better relief from postoperative pain and to reduce opioid related side effects. Pregabalin or gabapentin on reducing postoperative pain following laparoscopic cholecystectomy has been suggested but comprehensive data regarding the optimal dosage are limited. We designed this study to compare the effectiveness of gabapentin or pregabalin for preemptive analgesia.

**Methodology:** Seventy two patients undergoing laparoscopic cholecystectomy under general anaesthesia were randomized to receive either gabapentin 600 mg [Group A (n=36) or pregabalin 150 mg [Group B (n=36)] 1 hour before surgery. Intraoperatively hemodynamics were monitored. The duration of analgesia, total doses of rescue analgesics, sedation score and post-operative complications were recorded at 0, 30mins, 1, 2, 6,12 and 24 hours.

**Results:** Patients in Group B had significantly longer duration of postoperative analgesia as compared to Group A (207.08±54.82min vs 245.97±56.15min p=0.004). Requirement of rescue analgesics for the first 24h was more in Group A (Tramadol 70.83±25mg vs 56.94 ±17.53mg p=0.008). Intra and postoperative haemodynamics, postoperative sedation scores and complications were comparable.

**Conclusion:** Pregabalin provides longer duration of postoperative analgesia as compared to gabapentin following laparoscopic cholecystectomy.

## Introduction

The response to pain differs among different individuals as well as in the same person at different times.[1] Inadequate relief of postoperative pain can contribute to significant morbidity, resulting in delay of recovery and return to daily activities.[2] Large percentage of patients reported to have experienced moderate to severe pain, particularly after laparoscopic cholecystectomy procedures.[3] After laparoscopic cholecystectomy three components of acute postoperative pain have been described : incisional pain, visceral deep pain and shoulder referred pain.[4]

Traditionally, opioids were the mainstay of management of pain in postoperative patients. However, opioid analgesics have various side effects like nausea, vomiting, constipation, urinary retention, drowsiness, respiratory depression in large doses, acute opioid tolerance, opioid induced hyperalgesia and delayed discharge.[5-8] There is increasing interest towards alternatives to systemic opioids for managing postoperative pain and an analgesic regimen with multimodal approach

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has been suggested to improve analgesia and to reduce opioid related side effects.[9]

Gabapentinoids cause reduction in central sensitization which decreases acute postoperative pain.[10] Pregabalin is a structural analog of gamma amino butyric acid (GABA).[11] Pregabalin has a role in treatment of acute postoperative pain by decreasing the excitability of dorsal horn neurons caused by tissue damage.[12] Pregabalin and gabapentin were originally developed as spasmolytic agents and adjuncts for the management of generalized or partial epileptic seizures resistant to conventional therapies.[13] Gabapentin has been found to be effective in treating a variety of chronic pain conditions, including post-herpetic neuralgia, diabetic neuropathy, complex regional pain syndrome, central pain, malignant pain, trigeminal neuralgia and headaches.[14] Gabapentin has been found to be useful for neuropathic pain[14] and postoperative pain after breast surgery,[15] spinal surgery,[16] and laparoscopic cholecystectomy.[17]

The aim of our study was to evaluate the duration of effective analgesia and compare the requirement of rescue analgesia in the first 24 hours postoperatively in patients undergoing laparoscopic cholecystectomy under general anaesthesia.

## Methodology

This was a Prospective Comparative Clinical Study conducted in the department of Anaesthesiology and Critical Care, BPKIHS. After ethical approval from the BPKIHS Institutional Review Committee (IRC/1094/017), 72 patients scheduled for laparoscopic cholecystectomy were included. The inclusion criteria for our study were; patients of either gender undergoing elective laparoscopic cholecystectomy under general anaesthesia in the age group (18-65 years) with ASA physical status I and II. The exclusion criteria were; not willing to participate in the study, allergy or any contraindication to study medication, patients with neurological and psychiatric disorders, coagulopathy. Drugs used for the study were, 600mg of gabapentin (2 capsules of 300mg) and 150 mg of pregabalin (2 capsules of 75 mg) and the patients were followed till 24 hours after the surgery.

An informed written consent was obtained for the procedure from all the patients who participated in the study. During the pre-anaesthetic checkup (PAC), the patients were familiarized and explained about the Numeric Rating Scale (NRS) score for pain assessment. Group allocation was done after arrival of the patient in the patient holding area of the operation theatre. Group A patients received 600mg gabapentin and Group B received 150mg pregabalin, approximately one hour prior to surgery. The study drug was given by the anaesthesiologist not involved in monitoring the outcome variables.

At the operation theatre, non invasive blood pressure (NIBP) cuff, electrocardiography (ECG) leads and pulse oximetry (SpO2) probe were attached to the patient and the baseline ECG, NIBP, respiratory rate (RR), heart rate (HR) and SpO2 were monitored. After IV access, preoxygenation was done for three minutes using 100% oxygen. General anaesthesia was induced with fentanyl 1.5µg/kg IV, and propofol 1.5-2.5mg/kg IV till the patient slept. Vecuronium bromide 0.1 mg/kg IV was given and tracheal intubation facilitated. Anaesthesia was maintained with a mixture of oxygen with air and Isoflurane to maintain end tidal carbon dioxide (ETCO2) between 35 to 45 mm Hg. The surgery was performed using standard four port technique for laparoscopic cholecystectomy in all patients. Ketorolac 30 mg IV and ondansetron 4 mg IV was given intraoperatively. In both groups, paracetamol 15 mg/kg IV, not exceeding 1 gm was infused intraoperatively. At the end of the surgery, 20 ml of 0.25% plain bupivacaine was instilled in gall bladder fossa. Then 10 ml of 0.25% plain bupivacaine was infiltrated at the port sites. Isoflurane was discontinued after the last skin suture.

Awake extubation was done after reversing with neostigmine 0.05 mg/kg IV and glycopyrrolate 0.01 mg/kg IV after which patients were transferred to the PACU. All the patients received IV Paracetamol at the dose of 15mg/kg (not exceeding 1 gm) every 6 hourly in the postoperative period.

In the post anaesthesia care unit (PACU), then at 0, 30 minutes,1,2,6,12 and 24 hours respectively, pain and sedation were assessed. Pain intensity was measured by using a Numeric Rating Scale score at rest and on movement, 0 being no pain and 10 being the worst pain imaginable. Postoperative sedation was assessed by the Modified Ramsay's sedation scale (MRSS).

Adverse effects attributable to study drugs in the postoperative period were noted such as headache, bradycardia (HR <50 bpm), nausea, vomiting, dizziness, somnolence, respiratory depression.

### Management of pain

Injection tramadol 50 mg was given slowly IV every time the patient asked for analgesia or when the NRS score was more than 3. The time of administration of rescue analgesic was noted and the total amount of analgesic drug consumed during the study period was noted.

Data was entered in Microsoft Excel 2016 and converted into Statistical package for social sciences (SPSS 11.5) for statistical analysis. For descriptive statistics, percentage, proportion, mean, median, standard deviation, Interquartile range as appropriate was calculated along with graphical and tabular representation of data. For inferential statistics, Chi square test and Independent t-test was applied to find out the significant differences between the groups with selected clinical variables and socio-demographic characters at 95% Confidence Interval and probability of significance (P) <0.05.

## Results

This study showed no statistical significance in the demographic and operative variables like age, gender and body weight between the two groups.

**Table 1:** Summary of demographic characterstics

| Variables | Group A(n=36) | Group B(n=36) | p value |
|---|---|---|---|
| Gender(M/F) | 11/25 | 14/22 | |
| Age(years) | 40.78±13.74 | 40.39±13.73 | 0.905 |
| Weight(kg) | 63.86±6.26 | 62.56±10.10 | 0.512 |

Similarly, our study showed no statistical significance in preoperative vital parameters and intraoperative haemodynamic parameters among the two groups.

**Table 2:** Duration of effective analgesia and requirement of rescue analgesics in first 24 hours

| Observation | Group A(n=36) | Group B(n=36) | p value |
|---|---|---|---|
| Duration of effective analgesia | 207.08±54.82 min | 245.97±56.15 min | 0.004* |
| Requirement of rescue analgesia (Tramadol) | 70.83±25 mg | 56.94 ±17.53 mg | 0.008* |

* p value statistically significant

As with other parameters, level of sedation was also assessed at 0min, 30 min,1, 2, 6, 12 and 24 hours during the postoperative period using the Modified Ramsay Sedation Scale (MRSS). The MRSS among the two groups at various points in time was found to be statistically insignificant (p>0.05).

**Table 3:** Comparison of MRSS between two groups at various time

| Time | Group A (n=36) | | Group B (n=36) | | p value |
|---|---|---|---|---|---|
| | Mean ±SD | Median | Mean ±SD | Median | |
| 0 min | 1±0 | 1 | 1±0 | 1 | 1.000 |
| 30 min | 1±0 | 1 | 1±0 | 1 | 1.000 |
| 1 h | 1.92±0.28 | 2 | 2±0 | 2 | 0.079 |
| 2 h | 2±0 | 2 | 2±0 | 2 | 1.000 |
| 6 h | 2±0 | 2 | 2±0 | 2 | 1.000 |
| 12 h | 2±0 | 2 | 2±0 | 2 | 1.000 |
| 24 h | 2±0 | 2 | 2±0 | 2 | 1.000 |

The common adverse effects observed during the study were dizziness, somnolence and headache. These adverse effects were observed in both the study groups. However, these comparisons were statistically insignificant.

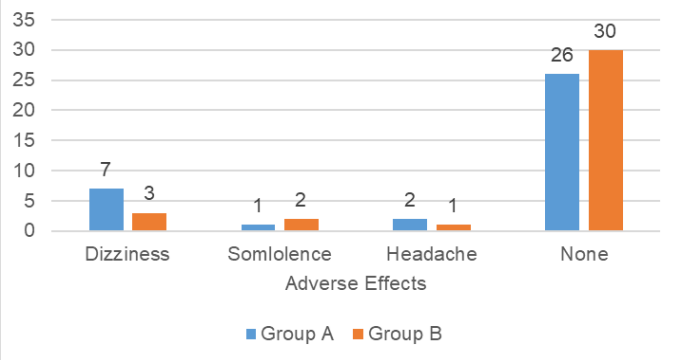


**Fig 1:** Adverse effects observed in the two groups of patients

## Discussion

The present study aimed to compare the duration of effective analgesia along with other parameters (hemodynamic changes, complications, sedation and requirement of rescue analgesia) of orally administered low yet effective dose of gabapentin and pregabalin following laparoscopic cholecystectomy under general anaesthesia. Till date various studies have been undertaken to determine as well as to compare the effectiveness of pregabalin and gabapentin in the control of post-operative pain, either as preemptive analgesics, preventive analgesics or even during the post- operative period. Various studies support the conclusion that perioperative use of gabapentinoids reduce early postoperative pain and opioid use. Evidences support gabapentin in reducing early postoperative pain and there is also sufficient evidence for clinicians to choose pregabalin as an alternative.[18] Studies have demonstrated that patients receiving 600, 900 and 1200 mg of gabapentin had lower visual analog scale score than those receiving 300mg or placebo. Studies have also found that 150 mg not 75 mg of pregabalin was superior in reducing postoperative opioid consumption and pain scores.[18] The lowest effective oral doses of 600 mg of gabapentin and 150 mg of pregabalin were thus used in our study.

The present study has demonstrated statistically significant prolonged duration of effective analgesia in patients with 150 mg oral pregabalin (245.97 ± 56.15 min) in comparison to 600 mg gabapentin (207.08 ± 54.82 min) when administered approximately one hour before surgery. Maqsood et al,[19] in their study, concluded that preoperative use of pregabalin provides significantly prolonged postoperative analgesia compared to gabapentin after open cholecystectomy. Mishra et al,[10] in their study found that pregabalin group had lower pain score and prolonged timing of first rescue analgesic which was comparable to our study. Akin to the findings of our study Ghai A[20] and colleagues found that patients in gabapentin group required analgesic earlier and more than patients in pregabalin group. Pandey et al,[17] in their study on the role of gabapentin as postoperative analgesic in laparoscopic cholecystectomy demonstrated that the

total fentanyl consumption postoperatively was significantly less in gabapentin group than in the tramadol group and placebo group. The requirement of higher dose of analgesia in gabapentin than pregabalin group was shown by Mishra et al,[10] which is similar to our study. Our findings were also supported by Bafna et al[21] and Saraswat et al[22], who observed that preemptive pregabalin or gabapentin significantly reduced the post-operative analgesia requirement after regional spinal anaesthesia.

The hemodynamic parameters were stable throughout the period of study {intra operative and post operative} . Similar to our study, Routray et al[23] also concluded that there was no significant difference in the hemodynamic parameters both intraoperatively and postoperatively among the gabapentinoid groups. Mishra et al,[10] observed that no significant statistical difference in between the groups in their study which is similar to ours. In our study, the complications were categorized as headache, dizziness and somnolence. Somnolence was evaluated using Modified Ramsey Sedation Scale (MRSS) where a scale of ≥2 was considered to be sedated. The sedation score, occurrence of headache and dizziness between the two groups of our study were all comparable. Contrary to our findings of the sedation scores, Mishra et al,[10] found that postoperative sedation was significantly more in the pregabalin group till 3 hours postoperatively compared to the gabapentin and placebo groups. Study conducted by Routray et al[23] favoured our study in that the complications such as dizziness, sedation, nausea, vomiting, headache, and respiratory depression did not show any statistical significance. Similar observations of no significance in the postoperative complications including at least the sedation score, headache and dizziness between the two groups were made by Ghai et al[20] and Saraswat et al.[22]

Similarly, study with different doses of both gabapentin and pregabalin needs to be done to arrive at an appropriate analgesic dose. We have not included a control group in our study, thus we could not observe the analgesic effects of pregabalin and gabapentin alone.

## Conclusion

A single preoperative dose of oral pregabalin 150 mg is more effective as preemptive analgesia in comparison to gabapentin 600mg for the management of postoperative pain following laparoscopic cholecystectomy with minimal side effects.

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**Conflict of Interest:** None

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