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Comparison of Pregabalin and Gabapentin as Pre-emptive Analgesics in Patients Undergoing Abdominal Surgeries

Hafiz Ahmed Hassam Bhalli, Shmyla Hamid*, Muhammad Rashid Iqbal, Sheharyar Baig, Tanveer Ahmed Khan, Mehr-un-Nisa Ayub**

Combined Military Hospital/National University of Medical Sciences (NUMS) Rawalpindi Pakistan, *Rawalpindi Medical University, Rawalpindi Pakistan, **Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore Pakistan

ABSTRACT

Objective: To compare the analgesic effects of Pregabalin and Gabapentin during elective abdominal surgeries.
Study Design: Quasi-experimental study.
Place and Duration of Study: Combined Military Hospital, Rawalpindi Pakistan, from Feb to Aug 2021.
Methodology: Patients with ASA physical status I, II, and III were enrolled in the study. The total number of patients was 152, divided into Group-A, which received 300mg of oral Gabapentin. In contrast, Group-B received 75 mg of oral Pregabalin an hour before induction of general anaesthesia. In addition, the analgesic requirement in the postoperative period, pain visual analogue scores and side effects were recorded.
Results: Out of 152 patients recruited in the study 68(44%) were males whereas 84(56%) were females with a mean age of 42.86±7.07 years. Based on ASA classification, 33(22%) patients were from ASA-I, 91(60%) patients were from ASA-II, and 27(18%) patients were from ASA-III. Pregabalin was a potent analgesic with a significant influence on the visual analogue score, increased duration to the first analgesic administration and a decreased consumption of opioids post-operatively compared with Gabapentin revealing significant results (p-value <0.001). However, no statistically significant association was derived regarding adverse effects between the two groups.
Conclusion: Pregabalin significantly reduces post-operative visual analogue scores, increased duration to first analgesic dose requirement and Opioid consumption post-operatively when compared with Gabapentin with no significant difference in adverse effect profile.

Keywords: Abdominal Surgery, Analgesia, Gabapentin, Pregabalin.

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INTRODUCTION

Providing appropriate and adequate postoperative analgesia is a crucial concern of an anaesthetist. Opioids were considered the cornerstone of pain management ranging from moderate to severe pain.[1,2] However opioids exhibit an unfavourable adverse effect profile leading to undesirable postoperative patient outcomes, reduction in patient satisfaction, and failure to achieve early recovery protocols.[3,4] Recently, to explore more favourable analgesic agents that will reduce undesirable effects and promote early recovery in postoperative periods, Gabapentinoids have attracted the interest of anesthesiologists.[5,6]

Antiallodynic, anti-hyperalgesic and central sensi--tisation reduction with slight influence on normal nociception is the postulated mechanisms of analgesia.[7,8] Gabapentin is an anticonvulsant that influences neurotransmitters to modulate seizures. Although Pregabalin shares oddity with Gabapentin, it is a structural analogue of gamma-aminobutyric acid with relatively enhanced pharmacokinetic and established analgesic profile in neuropathic pain with notable opioid-sparing actions postoperatively.[9,10]

The rationale of this study is to determine postoperative advantages of oral Gabapentin or Pregabalin in terms of enhancement of duration of analgesia, reduction in postoperative visual analogue scores, opioid-sparing impact, and adverse effect profile with the study drugs in patients undergoing elective laparoscopic cholecystectomy under general anaesthesia.

METHODOLOGY

The quasi-experimental study was carried out at Combined Military Hospital, Rawalpindi, after approval of the Ethical review board (ERB Number 203/02/2021) over six months from February to August 2021. The sample size for the study was calculated by the WHO calculator taking the prevalence of postoperative pain after abdominal surgery was 11% reported by Gan *et al*.[11] Using non-probability consecutive sampling 152 participants were distributed randomly in two uniform groups Gabapentin (Group-A) and Pregabalin (Group–B).

Correspondence: Dr Hafiz Ahmed Hassam Bhalli, Department of Anesthesia, Combined Military Hospital, Rawalpindi, Pakistan.
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Inclusion Criteria: Patients aged 35 - 55 years with ASA-I, II or III undergoing elective cholecystectomy with laparoscopic guidance, which provided informed written consent, were included in the study.

Exclusion Criteria: Patients subjected to emergency surgery, those mentally incapacitated, and past pertinent history (e.g. allergy to the study drug contents, coagulation disorders, thrombosis and chronic kidney disease) were not included in the study.

In the preoperative period, patients were kept nil per oral and documentation was done per the institute protocol. Pre- anaesthesia assessment performed as per guidelines (standard laboratory test, chest x-ray and echocardiography) before scheduling surgery and Re-evaluated on the day of surgery by a senior consultant anaesthetist. Group-A was administered 300mg oral Gabapentin, whereas Group-B received oral 75 mg Pregabalin orally an hour before induction of general anaesthesia.

Patients were shifted to the operation theatre on an operative day, and non-invasive blood pressure monitoring, oxygen probe, electrocardiography electrodes and temperature probe were attached.

An intravenous line was placed in the upper limb using an aseptic technique. Medications were administered before the procedure; Nalbuphine 0.1mg/kg, Paracetamol 15mg/kg, Dexamethasone 0.08mg/kg and Metoclopramide 0.1mg/kg intravenously as stat doses. Preoxygenation was done for 3 minutes with a 100% inspired oxygen concentration. Then, induction was performed with intravenous Propofol at a dose of 2mg/kg as an induction agent and 0.5mg/kg of intravenous injection Atracurium as a muscle relaxant. Laryngoscopy was done, followed by intubation after 03 mins by a consultant anaesthetist. After surgery, muscle relaxant antagonism was achieved by injecting Neopyrolate containing 2.5mg of Neostigmine and 0.5mg of Glycopyrrolate. After complete recovery of spontaneous respiratory effort, patients were extubated and shifted to the post-anaesthesia care unit, where vital signs and oxygen saturation were recorded and ultimately shifted to the ward on achievement of satisfactory recovery scores.

Post-operatively visual analogue score (VAS) was recorded at the 1st, third, sixth, 12th, and 24th hour. If at any point patient presented with VAS of ≥4, 50mg of intravenous Tramadol hydrochloride was administered as a rescue agent, and the total amount consumed in 24 hours was also recorded. Complications such as nausea, vomiting and others were also recorded. In addition, Intravenous Ondansetron was given as an antiemetic agent in the postoperative period.

Statistical package for the social sciences (SPSS) version 23.0 was used to analyse the data. Quantitative variables were expressed as mean±SD and qualitative variables were expressed as frequency and percentages. The categorical groups were compared using the Chi-square test, while mean values were compared using the Independent samples t-test. The *p*-value of ≤0.05 was considered significant.

RESULTS

Out of 152 total patients, 68(44%) were males whereas 84(56%) were females with the mean age of 42.86±7.07(Range: 35–55 years). Out of the participants, 33(22%), 91(60%), and 27(18%) patients were from the ASA Grade I, II, and III, respectively. The duration of surgery in Group-A and Group-B was 75.80±13.10 and 75.33±9.69 minutes respectively. The postoperative visual analogue score between the two groups are enumerated in Table–I.

Table-I: Postoperative Visual Analogue Score (n=152)

	Group–A (n=76) Mean±SD	Group–B (n=76) Mean±SD	*p*–value
1st Hour	2.98±0.82	1.9 ± 0.82	<0.001
3rd Hour	4.09±0.89	2.22±0.98	<0.001
6th Hour	3.98±1.41	2.97±1.00	<0.001
12th Hour	4.82±1.58	2.40±1.30	0.07
24th Hour	4.95±1.63	2.32±1.32	0.08

Opioid consumption and first analgesic dose administration are enumerated in Table–II, showing that Pregabalin has a significant reduction of post-operative visual analogue scores, increased duration to first analgesic dose demand and Opioid consumption post-operatively when compared with Gabapentin. Adverse Effects experienced by the patients are shown in Table–III, showing no significant difference.

Table–II: Opioid Consumption and First Analgesic Dose Administration (n=152)

	Group–A (n=76) Mean±SD	Group–B (n=76) Mean±SD	*p*–value
Time of first analgesic dose administration(min)	161.40±3.92	301.73±21.62	<0.001
Total Tramadol consumption postoperatively in 24 Hours(mg)	134.67±21.62	69.51±18.02	<0.001

Table–III: Adverse Effects Experienced (n=152)

	Group–A (n=76)	Group–B (n=76)
Sedation	30(39.47%)	35(46.05%)
Nausea and Vomiting	12(15.78%)	10(13.15%)
Vertigo	7(9.21%)	10(13.15%)

DISCUSSION

The study elucidated postoperative advantages of Pregabalin in terms of enhancement of duration of analgesia, reduction in postoperative visual analogue scores, and opioid-sparing impact when compared with Gabapentin. However, adverse effect profile of the study drugs was similar in patients undergoing elective laparoscopic cholecystectomy under general anaesthesia. Gamma-aminobutyric acid analogues such as Gabapentin and Pregabalin are recognised as analgesics due to their antinociceptive and anti hyperalgesic properties, as approved by various studies.[12,13]

Mishra *et al*. conducted a study to quantify the analgesic properties of Gabapentin and Pregabalin in laparoscopic cholecystectomy by comparing three groups of a placebo, Gabapentin, and Pregabalin. They recorded a significant superiority of Pregabalin over Gabapentin in terms of postoperative VAS scores (*p*-value <0.001) and Opioid consumption (*p*-value <0.001).[14] Asgari *et al*. performed a randomised, double-blinded controlled clinical trial to observe the preemptive analgesic effect of Pregabalin administered in different doses in patients undergoing laparoscopic hysterectomy. They enrolled 96 women in the study and subjected them to four groups who received oral Pregabalin doses of 75mg, 150mg, and 300mg, whereas the Fourth Group was given a placebo. All doses provided a significant reduction in postoperative VAS (*p*-value <0.001) with no variability of adverse effects (*p*-value <0.98). However, there was a significant difference in the sedation score between the three groups (<0.001); hence, using higher doses does not provide any advantage.[15]

Bartholdy *et al*. analysed the influence of Gabapentin on analgesic morphine requirement and pain after laparoscopic sterilisation (Filshie clips used). Results revealed that 32(84%) and 37(97%) patients in the drug and Placebo Group did consume Morphine as a rescue analgesic (*p*-value 0.049), respectively. This contradicted the study results regarding the provision of analgesia by Gabapentin as a preemptive adjuvant.[16] Kochhar *et al*. used Gabapentinoids as multimodal analgesia for postoperative pain relief after laparoscopic cholecystectomy. Fifty patients in each group were administered pregabalin 150mg or gabapentin 300mg two hours before elective laparoscopic cholecystectomy. According to their study results in duration for the requirement of the first rescue, the agent was 5.4±1.1 hours in the Pregabalin-Group and 4.6±1.6 hours Gabapentin-Group (*p*-value 0.015), findings inconsistent with this study results where the statistically significant association was found between Pregabalin and Gabapentin-Group (*p*-value 0.001).[17]

Exploration of multimodal intraoperative and postoperative analgesia is a desired achievement in anesthesiology with the aim of adequate pain management and reduction of adverse effects of opioids.[18,19] Non-steroidal Anti Inflammatory agents, Cyclooxygenase II inhibitors and Gabapentinoids are drugs set one's sight on.[20,21] Hence, this study results provide a safe option of preemptive analgesia with minimal adverse effects in patients undergoing elective laparoscopic cholecystectomy.

CONCLUSION

Pregabalin significantly reduces postoperative visual analogue scores, increases duration to first analgesic dose demand, and Opioid consumption post-operatively compared with gabapentin with no significant difference in adverse effects profile.

Conflict of Interest: None.

Author's Contributions

Following authors have made substantial contributions to the manuscript as under:

HAHB & SH: Conception, study design, drafting the manuscript, approval of the final version to be published.

MRI & SB: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

TAK & MNA: Critical review, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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