

Original Research Article

Comparison of Gabapentin v/s Pregabalin for Preemptive Analgesia for Acute Postoperative Pain after Surgery under Spinal Anaesthesia**Rama Kant¹, Akil Husain^{2*}, Hemant Jingar³, Ganesh Gupta³, Mohammed Mishal⁴, Rajarajan.B⁴**¹*Assistant Professor, Department of Anaesthesia, Pacific Medical College & Hospital, Bhillo ka Bedla, Udaipur, Rajasthan, India*²*Associate Professor, Department of Anaesthesia, Jhalawar Medical College, Jhalawar, Rajasthan, India*³*Associate Professor, Department of Anaesthesia, Pacific Medical College & Hospital, Bhillo ka Bedla, Udaipur, Rajasthan, India*⁴*PG resident, Department of Anaesthesia, Jhalawar Medical College, Jhalawar, Rajasthan, India***Received: 12-12-2020 / Revised: 14-01-2021 / Accepted: 25-01-2021****Abstract**

Objectives: Preemptive analgesia involves the introduction of an analgesic regimen, before the onset of noxious stimuli, with the goal of preventing sensitization of the nervous system to subsequent stimuli that could amplify pain. This study was designed to compare the efficacy of Gabapentin and Pregabalin, with respect to increase in duration of analgesia and reduction in total post-operative requirements of analgesics, along with study of their side effects and complications. **Materials and methods:** This was a prospective randomized study, conducted on 62 ASA grade I or II patients, aged 20-50 years, having body weight 50-70 kg, scheduled for elective infra-umbilical surgeries under spinal anaesthesia. Total 62 patients were randomly allocated in two groups of 31 each- Group G received tablet Gabapentin 1200 mg while Group P received tablet Pregabalin 300 mg, 1 hour prior to spinal anaesthesia. Pain was assessed by Visual Analogue Scale in immediate postoperative period and every two hourly thereafter. Time since spinal anaesthesia to first dose of analgesic (diclofenac) and total doses of analgesics in first 24 hours was recorded. **Results:** In Group G rescue analgesic was needed after 10.00 ± 2.02 hours, while in Group P rescue analgesic was required after 14.48 ± 4.48 hours. In Group G subsequent rescue analgesic was required in only three cases while in Group P, subsequent rescue analgesic was required in only two cases. The incidence of somnolence and dizziness was less with Pregabalin than with Gabapentin. **Conclusion:** Single oral dose of Pregabalin (300 mg) given preoperatively provides better postoperative pain control and decreases postoperative rescue analgesic consumption compared to a single dose of Gabapentin (1200 mg) with fewer side effects.

Keywords: Gabapentin, analgesia, pain.

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Introduction

Postoperative pain is not purely nociceptive in nature, and may consist of inflammatory, neurogenic and visceral components. [1] Surgical stimulation leads to sensitization of the dorsal horn neurons, which are associated with augmentation of pain. [2] Prevention and treatment of postoperative pain continues to be a major challenge in postoperative care and plays an important role in the early mobilization and wellbeing of the surgical patient. Preemptive analgesia, an evolving clinical concept, involves the introduction of an analgesic regimen, before the onset of noxious stimuli, with the goal of preventing sensitization of the nervous system to subsequent stimuli that could amplify pain. Surgery offers the most promising setting for preemptive analgesia because the timing of noxious stimuli is known. Traditionally, the pathophysiology and treatment of postoperative pain and neuropathic pain have been considered as separate and distinct. Opioids, NSAIDs and local anaesthetics were the tools of those, dealing with acute pain; anticonvulsants and tricyclic antidepressants were for the chronic pain specialists. However, there is considerable overlap in their pathophysiology. Allodynia and hyperalgesia are cardinal signs and symptoms of

neuropathic pain, but they are also often present after trauma and surgery. Sensitization of neurons in the dorsal horns, a mechanism in neuropathic pain, has been demonstrated in acute pain models. [3] The persistence of this mechanism may be responsible for the increasingly recognized problem of chronic pain after surgery.

Objectives

The aim of present study was to evaluate the postoperative analgesic benefit of Gabapentin or Pregabalin, administered as premedication for surgery under spinal anaesthesia and to compare their postoperative efficacy with respect to increase in duration of analgesia, reduction in total postoperative requirements of analgesics and to study their side effects and complications, if any attributable to these drugs.

Materials and Methods

This was a prospective, randomized double blinded study, conducted in our hospital, after obtaining institutional ethical clearance and informed consent of the subjects. Inclusion criteria included patients of ASA grade I or II, of either sex, aged 20-50 years, having body weight 50-70 kg, scheduled for elective infra-umbilical surgeries under spinal anaesthesia. While those patients with uncontrolled or labile hypertension, allergic to the study drugs, pregnant and lactating women, patients with psychiatric illness, hepatic impairment, or renal impairment and patients having any contra-

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indication to spinal anaesthesia were excluded. As calculated from a previous study, to get a clinically relevant difference in the duration of postoperative analgesia, we needed 31 patients in each group, with a power of study 80% at 95% confidence interval ($\alpha = 0.05$). Total 62 patients were randomly allocated in two groups using an online randomizer- Group G ($n = 31$) received tablet Gabapentin 1200 mg while Group P ($n = 31$) received tablet Pregabalin 300 mg, 1 hour prior to spinal anaesthesia. A day before surgery, PAC (Pre-anaesthetic check up) was done. The patients were explained about the procedures of spinal anaesthesia and postoperative pain relief; along with details about VAS [8] (0-10). A pharmacologist of our institution, not involved in this study, prepared the drug containing bags, which had gelatin capsules of similar size and shape. In group G, the bag contained four capsules of Gabapentin (300 mg each); in group P, the bag contained four capsules of Pregabalin (75 mg each capsule). The medication was given to the patient by an anaesthesiologist not involved in the study, 1 hour before giving the spinal anaesthesia. No other premedication was instituted. On OT arrival, routine monitoring (NIBP, pulse oximetry and ECG) was started. All the patients were preloaded with 10 mL/kg lactated Ringer's solution, before spinal anaesthesia. Spinal anaesthesia was instituted with 3 mL of 0.5% bupivacaine (15 mg) at L3 - L4 / L4 - L5 level. Fluid administration was continued intraoperatively and hypotension, if any, was treated with fluid replacement and intravenous (IV) Mephentermine and this whole procedure was conducted by another anaesthetist. Pain was assessed by VAS scale in the immediate postoperative period and every 2 h thereafter postoperatively; where 0 = no pain and 10 = most severe pain. Time lapsed after the surgery when the patient needs rescue analgesic was noted. For sedation: Filos' numerical scale was used (Scale 1 = awake and nervous, Scale 2 = awake and relaxed, Scale 3 = sleepy

but easy to awake, Scale 4 = sleepy and hard to awake). Adverse events were also noted in the first 24 hours postoperatively, which included: dizziness/somnolence; diplopia; vomiting [the severity of PONV was graded on a 4-point ordinal scale; (0 = no nausea/vomiting; 1 = mild nausea; 2 = moderate nausea; 3 = severe nausea with vomiting)]; confusion (assessed by asking time, place, person); urinary retention in a noncatheterized patient; respiratory depression (defined as ventilatory frequency < 8 bpm and oxygen saturation $< 90\%$ without oxygen supplementation). In the ward, other anaesthesiologist (unaware of the premedication) was responsible for charting the pain score by VAS scale. Pain charting was done separately and anaesthetic chart was not attached with the case sheet, so the observer was unable to know the group of the patient. Patient with VAS score of more than 3 received diclofenac 1 mg/kg intramuscularly. Time since spinal anaesthesia to the first dose of analgesic and total dose of analgesic in the first 24 hours was recorded.

Statistical analysis-The computer software SPSS (Statistical Package for the Social Sciences Inc. released 2007, version 16.0. Chicago, Illinois, USA) was used for analysis of data. For all analyses, probability values (P value) < 0.05 were considered as statistically significant and p value < 0.01 were considered as statistically highly significant.

Results

A total of 62 patients were enrolled in our study. Maximum number of participants belonged to the age group of 40 years and above. The male: female ratio was 1:1.38. Both the groups were comparable in respect to demographic data, ASA physical status, the mean duration of surgery and the type of surgeries performed. The groups did not vary significantly with respect to the average time required for the surgical maneuver (as shown in Table 1).

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

Groups	Duration of surgery (minutes) (Mean \pm SD*)	P value
Group P (n-31)	70.10 \pm 25.48	0.3818
Group G (n-31)	64.76 \pm 22.13	

*SD- Standard Deviation.

In the 24 h of postoperative period, the mean VAS scores (at rest) of Group P were always significantly lower than those of Group G. In Group G, subsequent rescue analgesic was required in only three cases while in Group P, subsequent rescue analgesic was required in only two cases. In Group G rescue analgesic was given after 10.00 \pm 2.02 hours, while in Group P rescue analgesic was required after 14.48 \pm 4.48 hours. There was a significant variation in the time interval after surgery, when the VAS score was found to be 3 or more, signalling the need of rescue analgesic. In Group P, the time interval was significantly more compared to Group G (as shown in Table 2). Thus, Pregabalin showed significantly prolonged postoperative analgesia compared to Gabapentin.

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

Groups	Hours after surgery when VAS > 3 (Mean \pm SD)	P value
Group P (n-31)	14.48 \pm 4.08	0.0001
Group G (n-31)	10.00 \pm 2.22	

In Group P, somnolence was seen in 4 out of 31 patients, while in Group G, it was seen in 7 out of 31 patients. Similarly, dizziness was observed in only 3 out of 31 patients in Group P and 6 out of 31 patients in Group G. Thus, the incidence of somnolence (12.90%) and dizziness (9.68%) was less in Group P as compared to Group G (22.59% and 19.35%, respectively) (as shown in Table 3). There was no incidence of nausea and vomiting in both the groups.

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

Groups	Somnolence	Dizziness
Group P (n-31)	12.90%	9.68%
Group G (n-31)	22.59%	19.35%

Discussion

Several studies have reported the usefulness of Gabapentin and Pregabalin in perioperative settings, resulting in reduced postoperative pain, postoperative analgesic requirement, side effects, prolongation of analgesia and higher patient satisfaction. [9, 10] Management of pain and its complications in the postoperative period still is a major challenge. Preemptive analgesia prevents establishment of the altered sensory processing that amplifies postoperative pain. Pre-incisional analgesia has been shown to be

more effective in the control of postoperative pain by protecting the central nervous system from deleterious effects of noxious stimuli and resulting allodynia, and increased pain. [11] Gabapentin and Pregabalin have antiallodynic and anti-hyperalgesic properties useful for treating neuropathic pain and may also be beneficial in acute postoperative pain. [12, 13] In a recent review of 22 RCTs, analysis suggested that the Gabapentin induced reduction in the 24 hour opioid consumption was not significantly dependent on the Gabapentin dose. Hence, single highest safe dose of Gabapentin (1200 mg) and Pregabalin (300 mg) was selected for this study,

which is same as used in most of the studies. In some of the studies conducted with Pregabalin as preemptive analgesic, like minor gynaecological surgery involving the uterus by Paech et al. [16], day-case gynaecological laparoscopic surgery by Jokela et al. [14] and laparoscopic cholecystectomy by Agarwal et al. [17], a single dose of 100-150 mg was used. The pain scores in the placebo group of the earlier studies mentioned were substantially low, however the present study used a single preemptive 300 mg dose of Pregabalin, as lower dose would have been sub therapeutic because more painful procedures like laminectomy, discectomy, and instrumentation were involved in the present study. The duration after surgery, when rescue analgesic was required was 14.48 ± 4.08 hours in case of Pregabalin and 10.00 ± 2.02 hours in case of Gabapentin, which was statistically and significantly lower in the case of Gabapentin. Subsequent dose required in the case of Pregabalin was 6.45% and in the case of Gabapentin was 9.68%. Paech et al. [16] in 2007 conducted the study in 90 women having minor gynaecological surgery involving the uterus. Patients received either oral Pregabalin 100 mg or placebo approximately 1 hour before surgery. There was no significant difference between the groups regarding pain experienced in the recovery room or thereafter or for recovery room Fentanyl requirement (42% group Pregabalin versus 27% group placebo, P value = 0.12) or the quality of recovery at 24 hours postoperatively. Agarwal et al. [17] evaluated the efficacy of a single preoperative dose of 150 mg Pregabalin, when given 1 hour before surgery, for attenuating postoperative pain and Fentanyl consumption after laparoscopic cholecystectomy compared to the placebo. Results revealed that postoperative pain and postoperative patient-controlled Fentanyl consumption were reduced in the Pregabalin group compared with the placebo group ($P < 0.05$). Sahu et al. [18] used Pregabalin in infra-umbilical surgeries under spinal anaesthesia and found that patients in the Pregabalin group had significantly lower mean VAS postoperatively and lower rescue analgesic consumption than the placebo group ($P < 0.05$), which were nearly similar to our results. Somnolence and dizziness are the two most common side effects associated with Gabapentin and Pregabalin, however, lower incidence seen in Pregabalin group than Gabapentin group, and this was similar to earlier studies. This is usually not disabling and anti anxiety effect has been found to be beneficial in some studies. [15] The limitation of the current study design is that single dose of Gabapentin and Pregabalin has been used. The half-life of these drugs is 5-7 hours and conclusions about the optimal dose and duration of the treatment cannot be made. Although Pregabalin has been more effective than Gabapentin in the present study, further studies are needed to determine the long-term benefits of perioperative Gabapentin and Pregabalin comprehensively. Secondly, control/placebo group has not been added to the study, as both drugs have already proved to increase post operative analgesia and reduce analgesic requirement in most of the studies.

Conclusion

Thus, we concluded that preemptive use of single oral dose of Pregabalin (300 mg) provides better and prolonged postoperative pain control and therefore, decreases postoperative rescue analgesic administration as compared to preemptive single oral dose of Gabapentin (1200 mg). Gabapentin and Pregabalin both can be an effective tool in the armamentarium of anaesthesiologist in treatment of perioperative pain. They can be used as part of multimodal therapy if not as sole analgesic.

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