Journal of Advanced Medical and Dental Sciences Research

@Society of Scientific Research and Studies

Journal home page:www.jamdsr.com doi:10.21276/jamdsr Index Copernicus value [ICV] =82.06

(e) ISSN Online: 2321-9599; (p) ISSN Print: 2348-6805

Original Research

To compare the efficacy of Gabapentin and Pregabalin in providing preemptive analgesiafor acute postoperative pain after surgery under spinal anesthesia

[1]Sanjay Kumar, [2]Raghav Sharma

[1]Assistant Professor, Department of Pharmacology, Gouri Devi Institute of Medical Sciences & Hospital, Durgapur, West Bengal, India;
[2]Assistant Professor, Department of Anesthesiology, Gouri Devi Institute of Medical Sciences & Hospital, Durgapur, West Bengal, India

ABSTRACT:
Aim: To compare the efficacy of Gabapentin and Pregabalin in providing preemptive analgesia for acute postoperative pain after surgery under spinal anesthesia. **Materials and Methods:** 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. Total 100 patients were randomly allocated in two groups using an online randomizer- Group G (n = 50) received tablet Gabapentin 1200 mg while Group P (n = 50) received tablet Pregabalin 300 mg, 1 hour prior to spinal anaesthesia. **Results:** In Group G rescue analgesic was given after 9.89 ± 1.08 hours, while in Group P rescue analgesic was required after 15.02 ± 1.57 hours. There was a significant variation in thetime 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. In Group P, somnolence was seen in 7 out of 50 patients, while in Group G, it was seen in 12 out of 50 patients. Similarly, dizziness was observed in only 5 out of 50 patients in Group P and 10 out of 50 patients in Group G. **Conclusion:** 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.
Keywords: Gabapentin, Pregabalin, Postoperative pain,

Received: 11 August, 2018 Accepted: 14 September, 2018

Corresponding author: Raghav Sharma, Assistant Professor, Department of Anesthesiology, Gouri Devi Institute of Medical Sciences & Hospital, Durgapur, West Bengal, India

This article may be cited as: Kumar S, Sharma R. To compare the efficacy of Gabapentin and Pregabalin in providing preemptive analgesia for acute postoperative pain after surgery under spinal anesthesia. J Adv Med Dent Scie Res 2018;6(10):208-211.

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[3-8]. The persistence of this mechanism may be responsible for the increasingly recognized problem of chronic pain after surgery.

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-indication to spinal anaesthesia were excluded. Total 100 patients were randomly allocated in two groups using an online randomizer-Group G (n = 50) received tablet Gabapentin 1200 mg while Group P (n = 50) 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 (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 wasassessed 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 severityof 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 no catheterized 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 version 21.0 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 100 patients were enrolled in our study. Maximum number of participants belongedto the age group of 35 years and above. The male: female ratio was 1:1.5. 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 ± SD*)	P value
Group P	69.99 ± 5.64	0.14
Group G	63.32 ± 4.68	

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 9.89 ± 1.08 hours, while in Group P rescue analgesic was required after 15.02 ± 1.57 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 needof 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 ± SD)	P value
Group P	15.02 ± 1.57	0.0001
Group G	9.89 ± 1.08	

In Group P, somnolence was seen in 7 out of 50 patients, while in Group G, it was seen in 12 out of 50 patients. Similarly, dizziness was observed in only 5 out of 50 patients in Group P and 10 out of 50 patients in Group G. Thus, the incidence of somnolence (14%) and dizziness(10%) was less in Group P as compared to Group G (24% and 20%, 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	14%	10%
Group G	24%	20%

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 15.02 ± 1.57 hours in case of Pregabalin and 9.89 ± 1.08 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% and in the case of Gabapentin was 10%. 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.

REFERENCES

1. Kochhar A, Chouhan K, Panjiar P, Vajifdar H. Gabapentinoids as a part of multi-modal drug regime for pain relief following laparoscopic cholecystectomy: A randomized study. Anesth Essays Res 2017; 11: 676-80.
2. Turan A, Kaya G, Karamanlioglu B, Pamukcu Z, Apfel CC. Effect of oral gabapentin on postoperative epidural analgesia. Br J Anaesth2006;96:242-6.
3. Eidy M, Fazel MR, Abdolrahimzadeh H, Moravveji AR, Kochaki E, Mohammadzadeh M. Effects of pregabalin and gabapentin on postoperative pain and opioid consumption after laparoscopic cholecystectomy. Korean J Anesthesiol 2017; 70:434-8.
4. Liu B, Liu R, Wang L. A meta-analysis of the preoperative use of gabapentinoids for the treatment of acute postoperative pain following spinal surgery. *Medicine (Baltimore)* 2017;96:e8031.
5. Lou ZD, Calcutt NA, Higuera ES, et al. Injury type-specific calcium channel alpha2delta-1 subunit up-regulation in rat neuropathic pain models correlates with antiallodynic effects of gabapentin. J Pharmcol Exp Ther 2002; 303: 1199–205.
6. Mishra R, Tripathi M, Chandola HC. Comparative clinical study of gabapentin and pregabalin for postoperative analgesia in laparoscopic cholecystectomy. *Anesth Essays Res.* 2016;10:201–6.
7. Pande AC, Crockatt JG, Feltner DE, et al. Pregabalin in generalized anxiety disorder: a placebo-controlled trial. Am J Psychiatry 2003;160:533-540.
8. Saraswat V, Arora V. Preemptive gabapentin vs Pregabalin for acute postoperative pain after surgery under spinal anaesthesia. Indian J Anaesth.2008;52:829.
9. Al-Mujadi H, A-Refai A R, Katzarov M G, Dehrab N A, Batra Y K and Al-Qattan A R. Preemptive gabapentin reduces postoperative pain and opioid demand following thyroid surgery. Canadian Journal of Anesthesia 2006:53:268-273.
10. Turan A, Kaya G, Karamanlioglu B, Pamukcu Z and Apfel C C. Effect of oral gabapentin on postoperative epidural analgesia. British Journal of Anaesthesia 2006;96:242– 6.
11. Van Elstraete AC, Tirault M, Lebrun T, Sandefo I, Bernard JC, Polin B, et al. The median effective dose of preemptive gabapentin on postoperative morphine consumption after posterior lumbar spinal fusion. AnesthAnalg.2008;106:305-8.
12. Rusy LM, Hainsworth KR, Nelson TJ, Czarnecki ML, Tassone JC, Thometz JG, et al. Gabapentin use in pediatric spinal fusion patients: A randomized, double-blind, controlled trial. Anesth Analg. 2010;110:1393-8.
13. Rosenstock J, Tuchman M, LaMoreaux L, Sharma U. Pregabalin for the treatment of painful diabetic peripheral neuropathy: A double-blind, placebo-controlled trial. Pain 2004;110:628- 38.
14. Jokela R, Ahonen J, Tallgren M, Haanpää M, Korttila K. A randomized controlled trial of perioperative administration of Pregabalin for pain after laparoscopic hysterectomy. PAIN. 2008;134:106-12.
15. Ménigaux C, Adam F, Guignard B, Sessler D I, Chauvin M. Preoperative gabapentin decreases anxiety and improves early functional recovery from knee surgery. Anesth Analg.2005;100:1394-1399.
16. Paech MJ, Goy R, Chua S, Scott K, Christmas T, Doherty DA. A randomized, placebo- controlled trial of preoperative oral Pregabalin for postoperative pain relief after minor gynecological surgery. Anesth Analg. 2007;105:1449-53.
17. Agarwal A, Gautam S, Gupta D, Agarwal S, Singh PK Singh U. Evaluation of a single preoperative dose of Pregabalin for attenuation of postoperative pain after laparoscopic chole- cystectomy. Br J Anaesth 2008; 101:700-4.
18. Sahu S. Sachan S, Verma A, Pandey HD. Chitra. Evaluation of Pregabalin for attenuation of postoperative pain in below umbilical surgeries under spinal anaesthesia. J Anaesth Clin Pharmacol 2010;26:167-71