International Journal of Health Sciences and Research
Vol.10; Issue: 5; May 2020
Website: www.ijhsr.org
Original Research Article *ISSN: 2249-9571*

Effect of Oral Gabapentin vs. Pregabalin as Preemptive Analgesic for Postoperative Pain in Patients Undergoing Lumbar Spine Surgeries

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ABSTRACT

Background: Gabapentin is a novel drug used for the treatment of postoperative pain with antihyperalgesic properties and a unique mechanism of action, which differentiates it from other commonly used drugs. Recently, role of Gabapentinoids (Pregabalin and Gabapentin) in acute postoperative pain has been studied indicating its usefulness in preventing the acute nociceptive pain of surgery.
Aims and Objectives: To compare the efficacy of Gabapentin and Pregabalin with intravenous Paracetamol as preemptive analgesic.
Material and Methods: This prospective, randomized, double blind comparative study included one hundred and twenty patients who belonged to American Society of Anesthesiologists physical status class I to II, aged between 20-65 years who underwent lumbar spine surgery under general anaesthesia.
Results: Mean age of patients was 39.88±10.68 for placebo group followed by Gabapentin group 38.55±12.44 and Pregabalin group 37.30±11.26. Time to first analgesic showed lowest time for placebo group with as early as 76 minutes followed by Gabapentin group with 93 minutes. Pregabalin group subjects had the first analgesic request at the highest time with 136.5 minutes. The VAS score was significantly lower in the Pregabalin group at 0, 2, 3, 6, 9, 12 and 24 hrs after surgery. The VAS score was significantly lower in the Gabapentin group as compared to placebo at 0, 1, 3, 6, 12, 18 and 24 hrs after procedure. Headache was the most common among Gabapentin group, followed equally by placebo and Pregabalin groups. Nausea was equally reported by Gabapentin and placebo group. Dizziness was seen equally among placebo and Pregabalin group followed by Gabapentin group. Total rescue analgesic (Tramadol) dosage in the first 24 hrs after the surgery shows that Placebo group patients required more rescue analgesic i.e. 113.64±69.90 as compared to Pregabalin i.e. 110.50±57.67 and Gabapentin groups 110.00±53.17.
Conclusion: The **s**tudy concluded that Pregabalin along with IV Paracetamol has a better analgesic profile and delays the time for requirement of first dose of rescue analgesic compared to Gabapentin along with IV Paracetamol following lumbar spinal surgery.

Keywords: Gabapentin, Preemptive Analgesic, Postoperative pain, Lumbar spine

INTRODUCTION

Postoperative pain is a form of acute pain that starts with surgical trauma with an inflammatory reaction and irritation of an afferent neuronal barrage and ends with tissue healing. Postoperative pain is not only caused by tissue injury but also associated with inflammatory pain, neuropathic pain, and visceral pain. Peripheral sensitization and central sensitization both contribute to

pain. It is considered a multifactorial experience known to be influenced by culture, psychology, genetics, previous pain events, beliefs, mood, and ability to cope, as well as the type of procedure performed.[1] Moreover, patients often consider "postoperative pain" the most frightening aspect of undergoing surgical procedure.

Failure to administer appropriate analgesic treatment may result in worsening of pain and more frequent hospital readmissions, adding to the already high economic burden associated with pain therapy.[2]

Administration of analgesic medication, before the actual onset of painful stimulus, is more effective than that after the onset of painful stimulus.[3] The use of multimodal treatments has reduced the side effects and doses required for adequate analgesia. Multiple mechanisms suggest that a combination of different analgesics will reduce side effects and opioid dependence and will synergistically enhance analgesia. The goal of multimodal pain therapy is additive analgesia, with sub-additive or diminished toxicity, or, synergistic analgesia with only additive toxicity. Several approaches have been advocated based on different combinations of anti-inflammatory drugs, Gabapentinoids and regional anaesthesia (epidural, peripheral nerve blocks, paravertebral blocks and local Inj/infusion of local anaesthetics).

Paracetamol is often included with non-steroidal anti-inflammatory drugs in classifications of analgesics, even though it has differences in both action and side effect profile. In recent years, role of Gabapentinoids (Pregabalin and Gabapentin) in acute postoperative pain has been studied indicating its usefulness in preventing the acute nociceptive pain of surgery.[4]

There is now considerable interest in the potential use of Gabapentin and Pregabalin for postoperative pain relief. Gabapentin and Pregabalin have been used in treatment of neuropathic pain as well as postoperative pain with good results. Patients having lumbar spinal fusion or laminectomy surgeries often complain about severe postoperative pain and postoperative rehabilitation process can be affected negatively.[5] There is paucity of studies of both these drugs being used with a common and safe analgesic i.e., IV Paracetamol as preemptive analgesia. Hence, the present study was conducted to compare the efficacy of Gabapentin and Pregabalin with intravenous Paracetamol as preemptive analgesic, to assess the requirement of consumption of Tramadol as rescue analgesic, efficacy of Gabapentin and Pregabalin with respect to increase in duration of analgesia, adverse effects of the study drugs and to compare the sedation score of Gabapentin and Pregabalin postoperatively.

MATERIALS AND METHODS

The present prospective, randomized, double blind comparative study was conducted in the Department of Anaesthesiology, and Critical Care, Command Hospital, Western Command, Chandimandir. After institutional review board approval, one hundred and twenty patients belonging to American Society of Anesthesiologists (ASA) physical status class I to II, between 20 - 65 years undergoing lumbar spine surgery (Microdiscectomy, Lumbar Spine Fusion Surgery, Spondylolisthesis) were included in the study. Patients were included in the study only after obtaining their informed consent and randomization was done according to simple randomization number table.

Patients with BMI >30 Kg/m^2 with coagulopathies, allergies to the study drugs, history of psychiatric disease, using psychotropic medication, history of alcohol/drug abuse, long term history of analgesic use, lactating or pregnant mothers, hepatic, renal, cardiac abnormality, chronic pulmonary disease, refusal/uncooperative patients were excluded from the study.

The patients were divided into three groups: **Group A**: Gabapentin plus Inj Paracetamol 1 gm IV - 40 patients who received 300 mg oral Gabapentin in the form of 2 capsules containing 150 mg of Gabapentin plus Inj Paracetamol 1 gm IV about 2 hrs prior to the induction of anaesthesia. **Group B**: Pregabalin plus Inj Paracetamol 1 gm IV - 40 patients who received 150 mg oral Pregabalin in the form of 2 capsules containing 75 mg Pregabalin plus Inj Paracetamol 1 gm IV about 2 hrs prior to the induction of anaesthesia. **Group C**: Placebo- 40 patients who received oral Vitamin B complex in the form of 2 capsules plus Inj Paracetamol 1 gm IV about 2 hrs prior to the induction of anaesthesia.

Before proceeding for the study, each patient was premedicated with Tab Alprazolam (0.25 mg) and Tab Ranitidine (150 mg) on the night before the surgery.

Preparation

On the morning of the surgery, patients were given one of the three oral drugs (Pregabalin, Gabapentin or Placebo) with sips of water and Inj Paracetamol IV depending on their position in the random number table about 2 hrs before surgery. Afterwards patients were shifted to the operation theatre. All the patients received similar preinduction drugs consisting of Inj glycopyrrolate (0.004 mg/kg), Inj ondansetron (4 mg) and Inj fentanyl (2 µg kg^{-1}) for intraoperative analgesia given intravenously approximately 3-5 min prior to endotracheal intubation. General anaesthesia was induced with Inj Propofol (1.5–2.5 mg kg^{-1}) after preoxygenation for 3 min, Inj vecuronium bromide (0.1 mg kg^{-1}) was used to facilitate endotracheal intubation.

Following endotracheal intubation patients were placed in prone position for spine surgery. Anaesthesia was maintained using an oxygen and nitrous oxide mixture in a ratio of 50:50, Inj vecuronium in aliquots of 1 mg each and sevoflurane upto 1 MAC. Inj Fentanyl was used in a bolus of 0.25 µg kg^{-1} for the management of pain intraoperatively. After the completion of surgery, the residual neuromuscular blockade was reversed using Inj Neostigmine (70 µg kg^{-1}) and Inj Glycopyrrolate (10 µg kg^{-1}). After extubation patients were shifted to the recovery room. On arrival to the recovery room, VAS and sedation score (Ramsay sedation score) was recorded and the time was designated as T_0. After stabilization of the patients, they were sent to the respective wards. In the wards, the pain and sedation scores of the patients were recorded at 1st hr, 2nd hr, 3rd hr, 6th hr, 9th hr, 12th hr, 18th hr, and 24th hr and the times were designated as T_1, T_2, T_3, T_6, T_9, T_{12}, T_{18}, and T_{24}, respectively**.**

Pain scores on Visual Analog scale (VAS) / Numeric Rating Scale. Pain was assessed postoperatively by visual analogue scale immediate postoperatively and at 1st hr, 2nd hr, 3rd hr, 6th hr,9th hr, 12th hr, 18th hr and 24th hr, and the times were designated as T_1, T_2, T_3, T_6, T_9, T_{12}, T_{18}, and T_{24}, respectively which was explained to the patient during preoperative visit. Blinding was done during follow up in ward. Any patient with VAS score of more than four was administered Inj Tramadol 50mg IV as a rescue analgesic. Sedation score (Ramsay sedation score) was assessed at the pre - designated time intervals.

Statistical Analysis

At the end of the study, the data was collected and analysed statistically by using Analysis of variance (ANOVA) for quantitative and Chi-square test for qualitative data. Comparison between the three groups was done by ANOVA test. Comparison between any two groups was done by Student's t-test & comparison between three groups was done by post-hoc analysis. A P-value of <0.05 was considered statistically significant.

RESULTS

In the present study, maximum subjects were presented in age range of 31-35 years followed by 36-40 years and 41-45 years. Age range of 51-55 years had 7.5% of

study subjects whereas 56-60 years comprised only 2.5% of study population. Subjects more than 60 years were 5.8% of the study population. Mean age of patients was 39.88±10.68 for placebo group followed by Gabapentin group 38.55±12.44 and Pregabalin group 37.30±11.26. There was insignificant difference between the mean age of subjects among three study groups (p=0.606). There was insignificant difference in the mean weight of three study groups (p=0.785). The mean duration of surgery in Pregabalin group was the highest at 121.75 minutes followed by placebo group 116.25 minutes and Gabapentin group (116 minutes) which was statistically insignificant (p=0.614). Time to first analgesic in the present study showed that lowest time for placebo group with as early as 76 minutes which was followed by Gabapentin group with 93 minutes of first analgesic request. Pregabalin group subjects had the first analgesic request at the highest time with 136.5 minutes (Fig. 1). There was significant difference in the mean time of first analgesic request among three study groups. On pair-wise comparisons, Pregabalin-placebo and Pregabalin-Gabapentin groups had significant difference. Table 1 and Fig. 2 shows the comparison of different variables among male and female subjects.

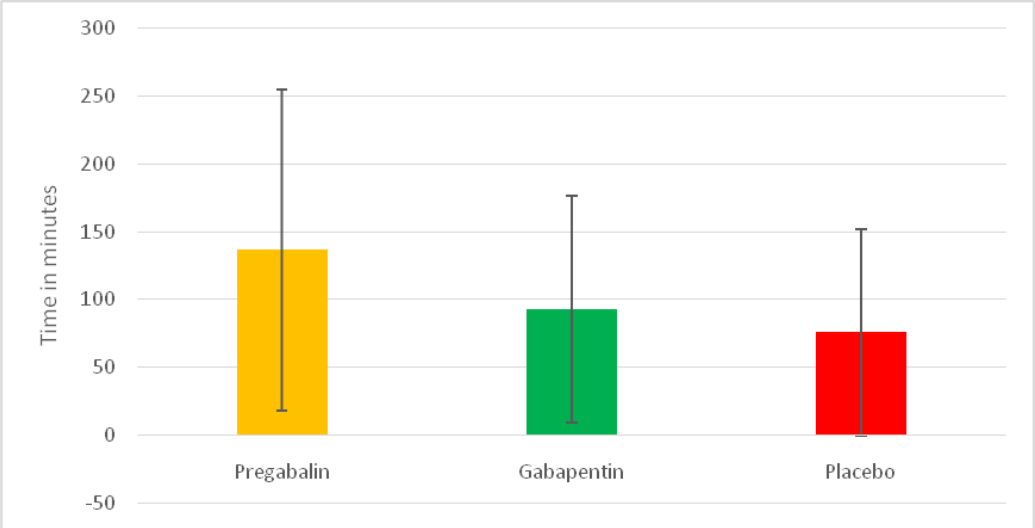

Figure 1: Error bar showing time to first analgesic among study groups

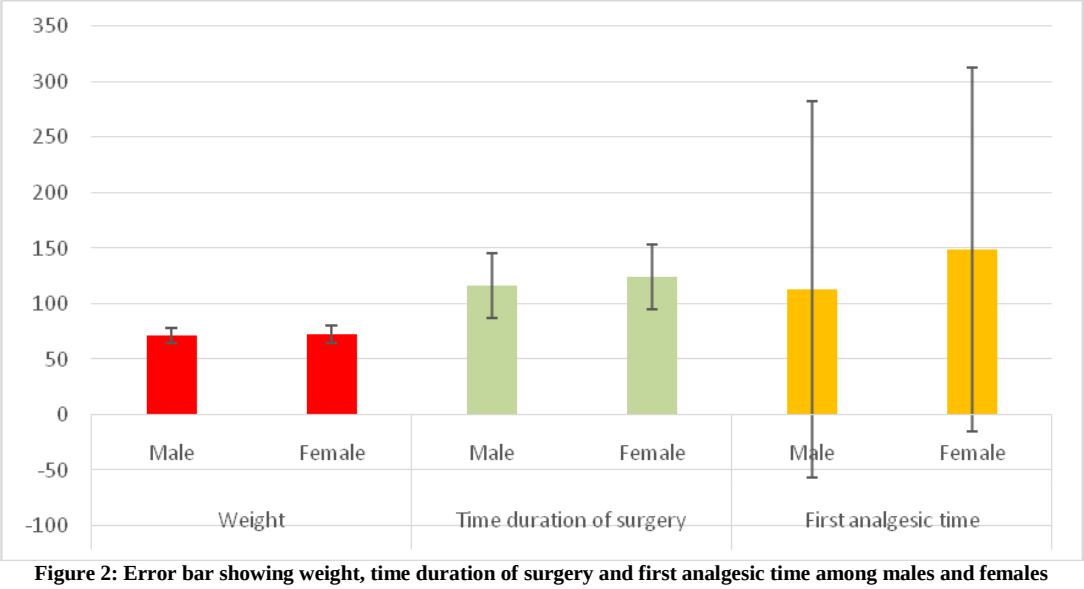

Figure 2: Error bar showing weight, time duration of surgery and first analgesic time among males and females

Table 1: Weight, Time duration of surgery and Time to first analgesic among male and female

	Sex	Mean	Std. Deviation	P-value
Weight	Male	71.23	6.47	0.526
	Female	72.22	7.70	
Time duration of surgery	Male	116.60	29.22	0.283
	Female	123.91	29.19	
Time to first analgesic	Male	112.98	169.60	0.363
	Female	148.69	163.68	

Table 2 shows the VAS score comparison among three study groups. There was significant difference in the VAS score of three groups viz. Gabapentin, Pregabalin and placebo. The VAS score was significantly lower in the Pregabalin group at various time periods i.e. at 0, 1, 2, 3, 9, 12, 18 and 24 hrs. The VAS score of placebo group was highest as compared to other groups. Only at 6th hr after surgery, there was no significant difference between the three study groups.

Table 2: Comparison of VAS Score among three groups

Time	Gabapentin (n=40)		Placebo (n=40)		Pregabalin (n=40)		
	Mean	SD	Mean	SD	Mean	SD	P-value
T0	3.72	2.10	4.26	2.34	2.97	1.77	0.035
T1	3.66	1.03	3.95	1.47	3.51	1.50	0.036
T2	4.13	1.03	4.20	1.11	3.59	1.07	0.033
T3	3.66	0.84	4.36	1.55	3.41	1.40	0.006
T6	4.20	0.90	3.95	1.21	3.62	1.21	0.095
T9	3.84	0.87	4.06	0.68	3.44	0.75	0.003
T12	3.49	0.84	4.00	0.84	3.05	0.76	<0.001
T18	3.03	1.35	3.66	0.94	2.65	0.72	<0.001
T24	3.38	1.23	2.40	1.19	2.72	1.26	0.003

Table 3 shows the comparison between Pregabalin and Gabapentin study groups. The VAS score was significantly lower in the Pregabalin group at 0, 2, 3, 6, 9, 12 and 24 hrs after surgery. At other time periods, the VAS score was comparable between the both groups.

Table 3: Comparison of VAS Score between Pregabalin and Gabapentin

Time	Pregabalin (n=40)		Gabapentin (n=40)		
	Mean	**SD**	**Mean**	**SD**	**P-value**
T0	2.97	1.77	3.72	2.10	**0.001**
T1	3.51	1.50	3.66	1.03	0.063
T2	3.59	1.07	4.13	1.03	**0.030**
T3	3.41	1.40	3.66	0.84	**0.036**
T6	3.62	1.21	4.20	0.90	**0.025**
T9	3.44	0.75	3.84	0.87	**0.034**
T12	3.05	0.76	3.49	0.84	**0.020**
T18	2.65	0.72	3.03	1.35	0.135
T24	2.72	1.26	3.38	1.23	**0.024**

Table 4 shows the comparison of VAS score between the Pregabalin and placebo group at various time periods. The VAS score was significantly lower in the Pregabalin group at the baseline and 1, 2, 3, 6, 9, 12 and 18 hrs after surgery. At 24 hrs after procedure the VAS score was comparable between the two groups.

Table 4: Comparison of VAS Score between Pregabalin and Placebo

Time	Pregabalin (n=40)		Placebo (n=40)		
	Mean	**SD**	**Mean**	**SD**	**P-value**
T0	2.97	1.77	4.26	2.34	**0.010**
T1	3.51	1.50	3.95	1.47	**0.020**
T2	3.59	1.07	4.20	1.11	**0.021**
T3	3.41	1.40	4.36	1.55	**0.006**
T6	3.62	1.21	3.95	1.21	**0.024**
T9	3.44	0.75	4.06	0.68	**<0.001**
T12	3.05	0.76	4.00	0.84	**<0.001**
T18	2.65	0.72	3.66	0.94	**<0.001**
T24	2.72	1.26	2.40	1.19	0.269

Table 5 shows the comparison of VAS score between Gabapentin and placebo groups. The VAS score was significantly lower in the Gabapentin group as compared to placebo at 0, 1, 3, 6, 12, 18 and 24 hrs after procedure. At other time periods i.e. 2ndand 9th hrs after procedure the VAS score was similar in the placebo and Gabapentin group.

Table 5: Comparison of VAS Score between Gabapentin and Placebo

Time	Gabapentin (n=40)		Placebo (n=40)		
	Mean	**SD**	**Mean**	**SD**	**P-value**
T0	3.72	2.10	4.26	2.34	**0.030**
T1	3.66	1.03	3.95	1.47	**0.033**
T2	4.13	1.03	4.20	1.11	0.077
T3	3.66	0.84	4.36	1.55	**0.020**
T6	4.20	0.90	3.95	1.21	**0.032**
T9	3.84	0.87	4.06	0.68	0.239
T12	3.49	0.84	4.00	0.84	**0.011**
T18	3.03	1.35	3.66	0.94	**0.023**
T24	3.38	1.23	2.40	1.19	**0.001**

Table 6 shows the sedation score (on Ramsay sedation scale) comparison among three study groups. There was significant difference in the sedation score of three groups viz. Gabapentin, Pregabalin and placebo at 0 hr, 1sthr, 2ndhr and 3rdhr with

Gabapentin group having highest sedation score on Ramsay sedation scale followed by Pregabalin group. Placebo group had the lowest sedation score.

Table 6: Comparison of Sedation Score among three groups

Time	Gabapentin (n=40)		Placebo (n=40)		Pregabalin (n=40)		
	Mean	SD	Mean	SD	Mean	SD	P-value
SS0	2.13	0.61	1.80	0.69	2.08	0.42	**0.030**
SS1	2.23	0.66	1.80	0.65	2.03	0.36	**0.005**
SS2	2.05	0.39	1.85	0.43	2.10	0.30	**0.009**
SS3	2.13	0.46	1.98	0.16	2.13	0.46	**0.014**
SS6	2.08	0.35	2.10	0.38	2.15	0.53	0.072
SS9	2.03	0.16	2.05	0.32	2.00	0.00	0.55
SS12	2.00	0.00	2.00	0.00	2.00	0.00	1.00
SS18	2.00	0.00	2.00	0.00	2.00	0.00	1.00
SS24	2.00	0.00	2.00	0.00	2.00	0.00	1.00

Table 7 shows the sedation score (on Ramsay sedation scale) comparison among Gabapentin and Pregabalin groups. There was significant difference in the sedation score of the two groups at 3rd and 6th hrs with Gabapentin group having lower sedation score.

Table 7: Comparison of Sedation Score between Gabapentin and Pregabalin

Time	Gabapentin (n=40)		Pregabalin (n=40)		
	Mean	SD	Mean	SD	P-value
SS0	2.13	0.61	2.08	0.42	0.669
SS1	2.23	0.66	2.03	0.36	0.096
SS2	2.05	0.39	2.10	0.30	0.052
SS3	2.13	0.46	2.13	0.46	**0.001**
SS6	2.08	0.35	2.15	0.53	**0.025**
SS9	2.03	0.16	2.00	0.00	0.495
SS12	2.00	0.00	2.00	0.00	1.00
SS18	2.00	0.00	2.00	0.00	1.00
SS24	2.00	0.00	2.00	0.00	1.00

Table 8 shows the sedation score (on Ramsay sedation scale) comparison among Placebo and Pregabalin groups. There was significant difference in the sedation score of the two groups at 0 hr and 2nd hr with Placebo group having lower sedation score.

Table 8: Comparison of Sedation Score between Placebo and Pregabalin

Time	Placebo (n=40)		Pregabalin (n=40)		
	Mean	SD	Mean	SD	P-value
SS0	1.80	0.69	2.08	0.42	**0.033**
SS1	1.80	0.65	2.03	0.36	0.058
SS2	1.85	0.43	2.10	0.30	**0.003**
SS3	1.98	0.16	2.13	0.46	0.056
SS6	2.10	0.38	2.15	0.53	0.063
SS9	2.05	0.32	2.00	0.00	0.32
SS12	2.00	0.00	2.00	0.00	1.00
SS18	2.00	0.00	2.00	0.00	1.00
SS24	2.00	0.00	2.00	0.00	1.00

Table 9 shows the sedation score (on Ramsay sedation scale) comparison among Gabapentin and Placebo groups. There was significant difference in the sedation score of the two groups at 0 hr, 1sthr and 2ndhr with Placebo group having lower sedation score.

Table 9: Comparison of Sedation Score between Gabapentin and Placebo

Time	Gabapentin (n=40)		Placebo (n=40)		
	Mean	SD	Mean	SD	P-value
SS0	2.13	0.61	1.80	0.69	**0.028**
SS1	2.23	0.66	1.80	0.65	**0.005**
SS2	2.05	0.39	1.85	0.43	**0.031**
SS3	2.13	0.46	1.98	0.16	0.056
SS6	2.08	0.35	2.10	0.38	0.076
SS9	2.03	0.16	2.05	0.32	0.656
SS12	2.00	0.00	2.00	0.00	1.00
SS18	2.00	0.00	2.00	0.00	1.00
SS24	2.00	0.00	2.00	0.00	1.00

Headache was seen the most among Gabapentin group, followed equally by placebo and Pregabalin groups. Nausea was equally reported by Gabapentin and placebo group. Dizziness was seen equally among placebo and Pregabalin group followed by Gabapentin group.

Total rescue analgesic (Tramadol) dosage in the first 24 hrs after the surgery shows that Placebo group patients required more rescue analgesic i.e. 113.64±69.90 as compared to Pregabalin i.e. 110.50±57.67 and Gabapentin groups 110.00±53.17, but the difference was not statistically significant.

DISCUSSION

Patients having lumbar spinal fusion or laminectomy surgeries often complain about severe postoperative pain due to which the rehabilitation process can be affected negatively. The analgesic benefits of controlling postoperative pain are generally maximized when a multimodal strategy to facilitate the patient's convalescence is implemented. Principles of a multimodal strategy include control of postoperative pain to allow early mobilization, early enteral nutrition, education, and attenuation of the perioperative stress response through the use of regional anaesthetic techniques and a combination of analgesic agents (i.e., multimodal analgesia). Paracetamol is an important component of multimodal analgesic approach. Compared with other routes of administration, intravenous delivery of Paracetamol achieves higher Cmax and earlier Tmax than oral and rectal Paracetamol.

IV Paracetamol may be the preferred route of administration for treating acute pain in the perioperative setting over other Paracetamol dosage forms (oral and rectal) because of its more rapid onset, reduced intrapatient variability in plasma levels, and earlier and greater cerebrospinal fluid penetration. Hassan HI studied perioperative analgesic effects of IV Paracetamol in 60 patients undergoing elective caesarean section as preemptive analgesia (preoperative) and preventive analgesia (at the end of surgery) and found both preventive and preemptive Paracetamol were effective in pain relief during anesthetic management of elective CS.[6] Vincent et al studied IV Paracetamol as pre-emptive analgesic in patients undergoing lower abdominal surgeries under general anaesthesia and concluded IV Paracetamol is beneficial as a pre-emptive analgesic in patients who undergo lower abdominal surgeries as the VAS score was significantly lower in the IV Paracetamol group as compared to the control group.[7]

In the current study, IV Paracetamol was used in a dose of 1 gm along with the study drug in all the three groups as a form of multimodal analgesia. The reason for this was that this preparation of Paracetamol is easily available and has lesser side effects. Neuropathic and inflammatory pain experimental models have shown that amino butyric acid analogues such as Gabapentin and Pregabalin contain analgesic components and are anti-nociceptive. It is postulated that CNS sensitivity may lead to post-operative pain growth. Administering amino butyric acid analogues before surgery, before inflammatory trauma, or surgical stimulation may reduce the degree of sensitivity of the CNS.[8]

This study has demonstrated the effect Oral Gabapentin or Pregabalin along with IV Paracetamol as preemptive analgesic for postoperative pain in patients undergoing lumbar spine surgeries. Although the study done by Pandey et al identified 600 mg as the optimal dose of Gabapentin for lumbar discectomy[9], various other studies have shown Gabapentin 300 mg to be effective in reducing postoperative pain and opioid consumption following laparoscopic cholecystectomy and lower limb orthopaedic surgery. Montazeri et al demonstrated the analgesic effect of preemptive use of 300 mg oral Gabapentin after orthopaedic surgery on the lower extremities. A decrease in total morphine consumption along with a significant decrease in VAS pain scores was found in patients who received Gabapentin two hours before surgery.[10] Gabapentin in a dose of 300 mg has been used in this study as a preemptive analgesic.

In contrast to Gabapentin, Pregabalin has a more favourable pharmacokinetic profile, including dose-independent absorption. It has extensive and rapid absorption which is proportional to dose. Time to maximal plasma concentration is 1 hr. High bioavailability, a mean elimination half-life ($t_{1/2}$) of 6.3 hr, and dose-proportional maximal plasma concentrations and total exposures predict a

dose–response relationship in clinical practice and allow an effective starting dose of 150 mg/day in clinical practice without need for titration. This study limited the dose of Pregabalin to 150mg which is supported by many other studies.[11,12]

In this study, out of total 120 study subjects, 80.8% were males. About 67.5 % subjects were below 40 years of age (mean age 38.58±11.44 yrs.). Subjects in the Pregabalin group had the highest duration of surgery (121 min) followed by placebo group and Gabapentin group (116 min) but it was not significant. In the study conducted by Ghai et al to compare Pregabalin with Gabapentin for postoperative pain in abdominal hysterectomy, the mean duration of surgery was highest in control group closely followed by Pregabalin and Gabapentin groups and it was statistically insignificant.[13]

In the current study, the pain severity was determined based on VAS score. The VAS score was found to be significantly lower in the Pregabalin group as compared to Gabapentin and placebo group (Highest VAS Score), at the pre-determined time durations. Mishra et al in their study to evaluate postoperative analgesic benefit in patients administered with oral Gabapentin or Pregabalin as premedication for laparoscopic cholecystectomy found Pregabalin group had lower VAS score and less opioid consumption than the Gabapentin group.[14] Eidy et al also found Pregabalin superior to Gabapentin for reducing postoperative pain as the pain score was significantly less in Pregabalin group.[15] Routray et al also concluded that Pregabalin has a better analgesic profile and delays the time for requirement of first dose of rescue analgesic compared to Gabapentin following spinal surgery[16] which is similar to the current study. Rajshree et al studied 150 mg Pregabalin and 900mg Gabapentin as pre-emptive analgesic in laparoscopic cholecystectomy. They found lower visual analogue scale (VAS) score, prolonged time of first rescue analgesic, and less opioid consumption in Pregabalin group compared to Gabapentin group. However, both Gabapentin and Pregabalin group had better analgesic profile than placebo group which was also similar to the findings of the current study.[11]

Trivedi et al also showed that in infraumblical surgery, Gabapentin (600mg) and Pregabalin (150mg), when given preoperatively, prolong the analgesic effects of spinal analgesia, decrease rescue analgesic requirements study groups. The analgesic effect is longer lasting following Pregabalin as compared to Gabapentin.[17] Saraswat *et al* in their study compared pre-emptive Gabapentin (1200mg) and Pregabalin (300 mg) for acute postoperative pain after surgery under spinal anaesthesia. The authors reported that Gabapentin and Pregabalin both provided prolonged postspinal analgesia, but Pregabalin was more potent than Gabapentin.[18]

However, Kochhar et al concluded that a single preoperative dose of Pregabalin (150mg) or Gabapentin (300mg) were equally efficacious in providing pain relief following laparoscopic cholecystectomy as a part of multimodal regime without any side effects.[19]

In contrast, Yilmaz *et al* found no statistically significant difference between Gabapentin and Pregabalin in the treatment of neuropathic pain associated with spinal cord injury.[20] When compared the mean time of first analgesic administered to subjects among three study groups, the lowest time was for placebo group, followed by Gabapentin group. Pregabalin group subjects had the first analgesic request at the highest time with 136.5 minutes which was statistically significant on post hoc analysis. This is similar to the study conducted by Maqsood et al to compare the mean time duration of patient's first analgesic request after open cholecystectomy which concluded that preoperative use of Pregabalin provides significantly prolonged postoperative analgesia compared to Gabapentin after open cholecystectomy.[21]

During early postoperative hours, the Ramsay sedation score was found to be low in placebo group, as compared to Gabapentin and Pregabalin groups. Pregabalin group had more sedation score than other two groups as the patients were calm and more tranquil during early post-operative hrs. This was similar in the study conducted by Routray et al[16] who compared Pregabalin with Gabapentin as preemptive analgesic in lumbar spine surgery. They also compared the sedation score between the groups in the first 12 hrs postoperatively. Pregabalin group had more sedation score than other two groups for the first 6 hrs. Similarly, Gabapentin had higher sedation score than placebo group which is similar to this study. The postoperative rescue analgesic requirement was low in Gabapentin and Pregabalin groups as compared to placebo indicating the opioid sparing effect of both Pregabalin and Gabapentin. This was similar to the study conducted by Bekawi MS and colleagues which demonstrated safety and efficacy of 1200 mg Gabapentin and 150 mg Pregabalin for relieving pain after laparoscopic cholecystectomy. In their study, Pregabalin and Gabapentin groups had significantly lower 24-hr requirement of pethidine as compared to control group.[12]

Agarwal et al evaluated a single preoperative dose of Pregabalin for attenuation of postoperative pain and postoperative PCA fentanyl consumption in patients undergoing laparoscopic cholecystectomy and found it to be effective in reducing postoperative PCA fentanyl consumption indicating the opioid sparing effect of Pregabalin which is similar to this study.[22]

Headache, Nausea and dizziness were the main adverse effects reported in all groups in this study. Headache was experienced mainly in those receiving Gabapentin, but also equally by those who received placebo and Pregabalin. Nausea was equally reported by Gabapentin and placebo group. Dizziness was seen equally among placebo and Pregabalin group followed by Gabapentin group. Routray et al also found dizziness, nausea and vomiting as the major side effects in their study.[16] However, the authors reported a higher incidence of dizziness and nausea in those patients who received Gabapentin as compared to Pregabalin group but it was not statistically significant. In the study conducted by Trivedi et al to compare Pregabalin and Gabapentin as preemptive analgesic in abdominal hysterectomy surgeries[17], the incidence of side effects was significantly higher amongst Gabapentin group as compared to Pregabalin group, however they were minor and easily controllable. Nausea, dizziness and rigors were the main side effects predominating in the Gabapentin group. This was similar to this study except dizziness which was more in Pregabalin group in this study.

Similar to this study, Akhavanakbari et al observed that pre-operative Pregabalin (150 mg) was effective as compared to placebo, in reducing post-operative pain along with post-operative pethidine consumption in subjects undergoing lower limb orthopedic surgery.[23]

The VAS score was significantly lower in the Gabapentin group as compared to placebo at 0, 1, 3, 6, 12, 18 and 24 hrs after procedure. At other time periods the VAS score were similar in the placebo and Gabapentin group. Turan et al investigated the effects of Gabapentin on acute postoperative pain and morphine consumption in spinal surgeries and concluded that pain scores at early postoperative hrs (1st, 2nd, and 4th hr) were significantly lower in the Gabapentin group when compared with the placebo group[24], similar to this study. Also the total morphine consumption was significantly lower in the Gabapentin group indicating the opioid sparing effect of Gabapentin. These findings were similar to the current study.

CONCLUSION

Although both Pregabalin and Gabapentin have a proven role in postoperative analgesia and both of these

can be used as pre-emptive analgesic in lumbar spine surgeries, none of the studies using Gabapentinoids as preemptive analgesics have used IV Paracetamol as a form of multimodal analgesia. This study has used IV Paracetamol along with Oral Pregabalin or Gabapentin as Preemptive analgesia 2 hrs before surgery. This study found Pregabalin along with IV Paracetamol has a better analgesic profile and delays the time for requirement of first dose of rescue analgesic compared to Gabapentin along with IV Paracetamol following lumbar spinal surgery. Therefore, this study recommends the preferential use of IV Paracetamol along with Pregabalin over Gabapentin as multimodal analgesia. Although in this study Pregabalin has been found to be more effective than Gabapentin, to determine the long-term benefits of perioperative Gabapentin and Pregabalin comprehensively, further studies are needed. Larger studies are needed to determine the minimum dose of rescue analgesia. Larger cohorts are also needed to determine the effect of Gabapentinoids on the long-term complications and incidence of chronic pain syndromes after spinal surgery, which develop within weeks and months after the surgery. Hence, further studies, investigating the benefits and outcome with different doses of Pregabalin and Gabapentin as part of multimodal analgesia should be conducted.

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How to cite this article: Sharma A, Datta R, Sharma VB. Effect of oral gabapentin vs. pregabalin as preemptive analgesic for postoperative pain in patients undergoing lumbar spine surgeries. Int J Health Sci Res. 2020; 10(5):181-191.

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