International Journal of Research in Orthopaedics
Garg RN et al. Int J Res Orthop. 2024 Jan;10(1):96-105
http://www.ijoro.org

Original Research Article

DOI: https://dx.doi.org/10.18203/issn.2455-4510.IntJResOrthop20234046

A prospective and comparative study to evaluate the efficacy of oral pregabalin vs gabapentin combined with IV paracetamol as preemptive analgesic for post-operative pain in patients undergoing single level open lumbar spine decompression surgery in a tertiary health care center

Rohit N. Garg[1]*, Shweta Sonu Vaje[2], Hrishikesh Patil[1], Sanket Bajaj[1]

[1]Department of Orthopaedics, Bharatratna Doctor Babasaheb Ambedkar Municipal Hospital, Kandivali, Maharashtra, India
[2]Department of Anesthesia, Bharatratna Doctor Babasaheb Ambedkar Municipal Hospital, Kandivali, Maharashtra, India

Received: 20 October 2023
Accepted: 14 November 2023

***Correspondence:**
Dr. Rohit N. Garg,
E-mail: rohit.garg15@yahoo.com

ABSTRACT

Background: Post-operative pain in spine surgery, whether neuropathic or nociceptive, presents a significant challenge for both surgeons and patients. Previous research has demonstrated the effectiveness of pre-operative oral gabapentinoids in reducing postoperative pain, extending the time to first rescue analgesia, and diminishing overall analgesic requirements.
Methods: This study involved 120 patients undergoing lumbar discectomy for disc herniation. They were randomly assigned to receive pre-operative oral pregabalin, gabapentin, or a placebo, along with IV paracetamol as preemptive analgesia. The study assessed their efficacy through post-operative pain scores (VAS), and sedation scores (Ramsay sedation score) at various intervals, time to first rescue analgesia, and total analgesia consumption.
Results: No significant differences were found in demographic variables, surgical levels, or duration among the groups. The placebo group had the shortest time to first rescue analgesia, while the pregabalin group showed the longest, with a notable difference. Across most time frames, the pregabalin group reported the lowest mean postoperative VAS scores, whereas the placebo group had the highest. Initial variations in sedation scores converged in later time frames, with the placebo group consistently recording the lowest scores. Total rescue analgesia (tramadol) in the initial 24 hours was highest in the placebo group, followed by the gabapentin group, and lowest in the pregabalin group, with no significant variance.
Conclusions: This study affirms the superiority of pre-operative oral pregabalin with IV paracetamol. It effectively prolongs the time to first rescue analgesia and reduces overall analgesic consumption post-lumbar spine surgery, compared to pre-operative oral gabapentin with IV paracetamol.

Keywords: Gabapentin, Pregabalin, Ramsay sedation score, Tramadol, Visual analog scale

INTRODUCTION

Post-operative pain is one of the most challenging and debilitating obstacles for the operating surgeon.[1,2] Despite various advancements made in multimodal post-operative pain management, this issue has an overall negative effect on the post-operative clinical and functional outcomes of the patient, thus hampering overall satisfaction. It leads to a longer hospital stay, and longer rehabilitation protocols and thus burdens the health care expenditure and the

quality of life.[3-5] Postoperative pain is multifactorial and is influenced by culture, genetics, previous pain events, psychology, mood, ability to cope as well as the type of procedure performed.[6] Most commonly used drugs in this multimodal regime include a combination of nonsteroidalanti-inflammatorydrugs (NSAIDs), opioids, gabapentinoids (gabapentin and pregabalin), and regional anesthesia (local injection or infusion, epidural anesthesia, peripheral nerve blocks, and paravertebral blocks). These drugs when used in excess to suppress the pain have got their own set of side effects.[7,8] The main objective of this multimodal treatment is to have adequate additive and synergistic analgesia at reduced doses of individual drugs, so as to reduce the overall side effects as well as dependence of these drugs.

In the case of spine surgery, this postoperative pain may be either a nociceptive one or a neuropathic one. It is very important to distinguish between the two as the treatment modalities of both differ. Nociceptive pain occurs due to an inflammatory process secondary to the soft tissue injury that happens during the surgery and is well managed with non-steroidal anti-inflammatory drugs (NSAIDs) and opioids. Neuropathic pain is the result of any lesion or dysfunction of the nervous system which may be in the form of direct injury or compression of the neural structures intraoperatively. This neuropathic pain has its own set of cellular and molecular causative mechanisms. Any injury to the nerves leads to its demyelination which subsequently causes an increase in the concentration of sodium channels and inflammatory markers around the affected area which evokes spontaneous discharges from the cell bodies at the dorsal root ganglion (DRG) cell level; thus leading to pain stimuli.[9,10]

Spine surgeries are more commonly found to be associated with postoperative pain which can be either neuropathic or nociceptive one; which directly or indirectly hampers the rehabilitation and thus the favorable clinical and functional outcomes of the surgery.[11] Many studies have recently shown postoperative administration of gabapentinoids like pregabalin and gabapentin to be highly efficacious in decreasing this nociceptive as well as neuropathic pain and also prevents the conversion of acute neuropathic pain into chronic form.[12,13] However, very few studies have been attempted to look for the efficacy of these gabapentinoids in reducing postoperative pain in patients undergoing spine surgery; based on their preoperative administration.

The main objective of this prospective study was to evaluate and compare the efficacy of pre-operative administration of pregabalin and gabapentin combined with IVparacetamol as a preemptive analgesic; to assess the need for post-operative tramadol as a rescue analgesic; compare the efficacy of both these gabapentinoids with respect to duration of postoperative analgesia and adverse effects; and also to compare the post-operative sedation scores in all the patients undergoing single level open lumbar spine decompression surgery (no instrumentation) for prolapsed intervertebral lumbar disc (PIVD) by the same team of spine surgeons.

METHODS

The present study was a prospective, randomized double-blinded, and comparative one, conducted in the Department of Orthopaedics of Government Medical College, Nagpur from 2017 to 2020, with prior approval taken from the institutional ethical committee. The study population consisted of patients coming with low back ache due to prolapsed intervertebral disc (PIVD) at single lumbar level needing surgical decompression. There were a total of 120 patients who were diagnosed with PIVD based on clinical examination and radiological examination including standard spine X-rays and MRI. These patients were given a thorough trial of conservative management with medical treatment, physical therapy, and appropriate rest for a period of 12 weeks without success; before being selected for surgical intervention.

Inclusion criteria

Patients aged between 25-60 years of age, with radiculopathy symptoms without neuro deficits; with X-rays showing disc space reduction and MRI showing prolapsed intervertebral disc compressing the roots with minimal degenerative changes were included in the study.

Exclusion criteria

Patients with pathological spine diseases such as spondylolisthesis, spondylolysis, tumors (primary or secondary); inflammatory or infective conditions; having a previous history of spine interventions including surgery or injections (transforaminal, epidural, facetal) for pain relief; severe degenerative changes seen on MRI needing instrumentation or multilevel PIVD were excluded. Also, patients receiving any sort of pain modulation therapy like transcutaneous electrical nerve stimulation; with psychiatric disorders, alcohol/drug dependence, long-term history of any analgesia use, hepatic, renal, cardiac, or pulmonary abnormalities; or allergic to gabapentinoids were excluded from the study.

All the patients were operated with single-level open lumbar spine decompression surgery (no instrumentation) for prolapsed intervertebral lumbar disc (PIVD) by the same team of spine surgeons. They were randomly divided into 3 groups: Group A: Pregabalin plus Inj. Paracetamol group (n=40) - these patients were given Inj. Paracetamol 1gm plus 150 mg oral pregabalin in the form of 2 capsules of pregabalin 75mg every 2 hours before the induction of anesthesia; Group B: Gabapentin plus Inj. Paracetamol group (n=40) - these patients were given Inj. Paracetamol 1gm plus 300 mg oral gabapentin in the form of 2 capsules of gabapentin 150mg every 2 hours before the induction of anesthesia; and Group C: placebo group (n=40) - these patients were given Inj. Paracetamol 1gm plus vitamin

B12 complex 2 capsules 2 hours before the induction of anesthesia.

All the patients were operated on under general anesthesia with the same drugs given for induction, maintenance, muscle relaxation, and reversal by the same team of anesthetists. After extubation, patients were kept in the recovery room for 30 minutes. At this time the pain score (Visual Analog Scale-VAS score) and sedation score (Ramsay sedation score) were recorded and labeled as T_0. Patients were then shifted to respective wards and again the scores were recorded at the 1st, 3rd, 6th, 12th, 18th, and 24th hour and labeled as T_1, T_3, T_6, T_{12}, T_{18}, and T_{24} respectively. At any instance if the VAS score was found to be more than 6; inj. Tramadol was administered to the patient as a rescue analgesic. The time to 1st dose of analgesia administered after the surgery and the total dose of analgesia (tramadol) administered in 1st 24 hours was recorded.

Statistical analysis

All the data was collected in a Microsoft Excel spreadsheet. The nominal data (such as gender, smoker, hypertensive, diabetic, and surgical level) was expressed as a number. The continuous data (such as age, body mass index, VAS scores, Sedation scores, duration of surgery, time to first analgesic and the total dose rescue analgesia consumed in 1st 24 hours) was expressed as mean and standard deviation. Comparison for significance between the 3 groups was done using ANOVA test and comparison between any 2 groups was done by unpaired student's t-test. A p-value of <0.05 was considered statistically significant.

RESULTS

The study included a total of 120 patients, randomly divided into 3 groups: Group A-Pregabalin group, Group B - Gabapentin group, and Group C - Placebo group; with 40 patients in each group.The mean age of the total population was 46.92±10.89 years; which included a total of 47 male patients and 73 female patients. The mean age of the patients in Group A (13 male and 27 female patients) was 45.83±10.23 years, while those in Group B (16 male and 24 female patients) and Group C (18 male and 22 female patients) was 47.25±11.54 years and 47.68±10.91 years respectively. The difference in the means of the 3 groups was statistically insignificant.

The mean BMI of the entire population was 26.56±4.15 kg/m^2. The mean BMI of patients in Group A was 26.12±3.61 kg/m^2, while those in Group B and Group C were 27.14±4.02 kg/m^2 and 26.41±4.81 kg/m^2 respectively. The difference in the means of the 3 groups was statistically insignificant. The mean duration of surgery in Group A was 65.89±10.31 minutes; in Group B was 63.74±12.64 minutes; that in Group C was 66.27±11.84 minutes. The difference in the means of the 3 groups was statistically insignificant.

Other demographic variables including co-morbidities such as diabetes and hypertension, smoking status, and surgical level operated upon are represented in Table 1. No statistical differences were observed between any of the demographic variables between the 3 groups like age, sex, BMI, co-morbidities like diabetes and hypertension, smoking status, surgical level, and duration of surgery (Table 1). This negates any confounding between the 3 groups with respect to demographic distribution, surgical level, and duration of surgery.

Table 1: Depicts the demographic distribution, surgical levels operated upon, duration of surgery and time to 1st rescue analgesia between the three groups.

Demographic data	Pregabalin group	Gabapentin group	Placebo group	P value
Cases	40	40	40	
Age (years)	45.83±10.23	47.25±11.54	47.68±10.91	>0.05
Sex (male/female)	13 males/27 females	16 males/24 females	18 males/22 females	>0.05
Body mass index (BMI) (kg/m^2)	26.12 ± 3.61	27.14 ± 4.02	26.41 ± 4.81	>0.05
Smoker (%)	14 (35)	15 (37)	16 (40)	>0.05
Diabetic (%)	23 (58)	24 (60)	25 (62)	>0.05
Hypertensive (%)	22 (55)	23 (58)	23 (58)	>0.05
Surgical level				
L3-4 (%)	8 (20)	7 (18)	7 (18)	>0.05
L4-5 (%)	17 (43)	17 (42)	16 (40)	
L5-S1 v	15 (37)	16 (40)	17 (42)	
Duration of surgery (minutes)	65.89±10.31	63.74±12.64	66.27±11.84	>0.05
Time to 1st analgesic dose (minutes)	107.29±23.41	96.54±18.71	89.56±14.26	<0.05

Table 2: Depicts the VAS scores of the three groups at different time frames.

Time	Pregabalin group (n=40)		Gabapentin group (n=40)		Placebo group (n=40)		
	Mean	SD	Mean	SD	Mean	SD	P value
T_0	2.98	1.74	3.84	2.12	4.81	2.21	<0.05
T_1	2.69	1.53	3.61	1.97	4.53	2.13	<0.05
T_3	3.61	1.62	4.03	2.11	4.46	1.91	>0.05
T_6	3.18	1.51	3.67	1.53	3.89	1.76	>0.05
T_{12}	2.91	1.26	3.49	1.35	3.57	1.49	<0.05
T_{18}	2.11	1.19	2.67	1.23	3.25	1.31	<0.05
T_{24}	1.81	0.67	2.26	1.13	3.07	1.17	<0.05

Table 3: Depicts the VAS scores of the pregabalin and gabapentin group at different time frames.

Time	Pregabalin group (n=40)		Gabapentin group (n=40)		
	Mean	SD	Mean	SD	P value
T0	2.98	1.74	3.84	2.12	<0.05
T1	2.69	1.53	3.61	1.97	<0.05
T3	3.61	1.62	4.03	2.11	>0.05
T6	3.18	1.51	3.67	1.53	>0.05
T12	2.91	1.26	3.49	1.35	<0.05
T18	2.11	1.19	2.67	1.23	<0.05
T24	1.81	0.67	2.26	1.13	<0.05

Table 4: Depicts the VAS scores of the pregabalin and placebo group at different time frames.

Time	Pregabalin group (n=40)		Placebo group (n=40)		
	Mean	SD	Mean	SD	P value
T0	2.98	1.74	4.81	2.21	<0.05
T1	2.69	1.53	4.53	2.13	<0.05
T3	3.61	1.62	4.46	1.91	<0.05
T6	3.18	1.51	3.89	1.76	>0.05
T12	2.91	1.26	3.57	1.49	<0.05
T18	2.11	1.19	3.25	1.31	<0.05
T24	1.81	0.67	3.07	1.17	<0.05

Time to 1st rescue analgesia in the current study showed the lowest time in the placebo group (Group C) with as early as 89.56±14.26 minutes; which was followed by Group B with 96.54 ± 18.71 minutes. The time to 1st rescue analgesia in Group A patients was as long as 107.29±23.41 minutes. There was a significant difference in the meantime to 1st rescue analgesia among the 3 groups. On pair-wise comparisons, pregabalin-gabapentin groups and pregabalin-placebo groups had a significant difference in the meantime to 1st rescue analgesia; while gabapentin-placebo groups had an insignificant difference in mean time to 1st rescue analgesia as depicted in Table 1.

Table 2 shows the comparison of the mean VAS scores at different time intervals of the 3 groups. There was a significant difference in the mean VAS scores of the 3 groups at all the time frames included in the study; except at T_6 and T_{12} time frames, where the difference in the mean VAS scores of the 3 groups was found to be insignificant. The mean VAS scores were lowest in the pregabalin group and were highest in the placebo group at all the time frames; with the gabapentin group showing intermediate scores at all the time frames.

Table 3 shows the comparison of the mean VAS scores at different time intervals between Group A (pregabalin) and Group B (gabapentin). There was a significant difference in the mean VAS scores of the 2 groups at all the time frames, with Group A having lower scores; except at T_3 and T_6 time frames, where the difference in the mean VAS scores of the 2 groups was found to be insignificant.

Table 4 shows the comparison of the mean VAS scores at different time intervals between Group A (pregabalin) and Group C (placebo). There was a significant difference in the mean VAS scores of the 2 groups at all the time frames, with Group A having lower scores; except at the T_6 time frame, where the difference in the mean VAS scores of the 2 groups was found to be insignificant.

Table 5 shows the comparison of the mean VAS scores at different time intervals between Group B (gabapentin) and

Group C (placebo). There was a significant difference in the mean VAS scores of the 2 groups at all the time frames, with Group B having lower scores; except at T_3, T_6, and T_{12} time frames, where the difference in the mean VAS scores of the 2 groups was found to be insignificant.

Table 5: Depicts the VAS scores of the gabapentin and placebo group at different time frames.

Time	Gabapentin group (n=40)		Placebo group (n=40)		
	Mean	SD	Mean	SD	P value
T_0	3.84	2.12	4.81	2.21	<0.05
T_1	3.61	1.97	4.53	2.13	<0.05
T_3	4.03	2.11	4.46	1.91	>0.05
T_6	3.67	1.53	3.89	1.76	>0.05
T_{12}	3.49	1.35	3.57	1.49	>0.05
T_{18}	2.67	1.23	3.25	1.31	<0.05
T_{24}	2.26	1.13	3.07	1.17	<0.05

Table 6 shows the comparison of the mean sedation scores at different time intervals of the 3 groups. There was a significant difference in the mean sedation scores of the 3 groups at T_0, T_1, and T_3 time frames; while the difference in the mean sedation scores of the 3 groups at T_6, T_{12}, T_{18}, and T_{24} time frames was found to be insignificant. The mean sedation scores were lowest in the placebo group at all the time frames.

Table 7 shows the comparison of the mean sedation scores at different time intervals between Group A (pregabalin) and Group B (gabapentin). There was a significant difference in the mean sedation scores of the 2 groups at T_1 and T_6 time frames; while at other time frames, the difference in the mean sedation scores of the 2 groups was found to be insignificant. In the T_1 time frame, the pregabalin group had a significantly lower sedation score; while in the T_6 time frame, the gabapentin group had a significantly lower Sedation score.

Table 8 shows the comparison of the mean sedation scores at different time intervals between Group A (pregabalin) and Group C (placebo). There was an insignificant difference in the mean sedation scores of the 2 groups at all the time frames; except at T_0 time frame, where the difference in the mean sedation scores of the 2 groups was found to be significant, with placebo group having significantly lower sedation score.

Table 6: Depicts the sedation scores of the three groups at different time frames.

Time	Pregabalin group (n=40)		Gabapentin group (n=40)		Placebo group (n=40)		
	Mean	SD	Mean	SD	Mean	SD	P value
T_0	2.11	0.49	2.16	0.63	1.76	0.71	<0.05
T_1	2.02	0.31	2.29	0.67	1.82	0.69	<0.05
T_3	2.15	0.41	2.11	0.49	1.91	0.27	<0.05
T_6	2.19	0.56	1.98	0.31	2.12	0.35	>0.05
T_{12}	2	0	2	0	2	0	>0.05
T_{18}	2	0	2	0	2	0	>0.05
T_{24}	2	0	2	0	2	0	>0.05

Table 7: Depicts the sedation scores of the pregabalin and gabapentin group at different time frames.

Time	Pregabalin group (n=40)		Gabapentin group (n=40)		
	Mean	SD	Mean	SD	P value
T0	2.11	0.49	2.16	0.63	>0.05
T1	2.02	0.31	2.29	0.67	<0.05
T3	2.15	0.41	2.11	0.49	>0.05
T6	2.19	0.56	1.98	0.31	<0.05
T12	2	0	2	0	>0.05
T18	2	0	2	0	>0.05
T24	2	0	2	0	>0.05

Table 9 shows the comparison of the mean sedation scores at different time intervals between Group B (gabapentin) and Group C (placebo). There was an insignificant difference in the mean Sedation scores of the 2 groups at all the time frames; except at T_0, T_1, and T_3 time frames, where the difference in the mean sedation scores of the 2 groups was found to be significant, with placebo group having significantly lower sedation scores.

Table 8: Depicts the sedation scores of the pregabalin and placebo group at different time frames.

Time	Pregabalin group (n=40)		Placebo group (n=40)		
	Mean	SD	Mean	SD	P value
T0	2.11	0.49	1.76	0.71	<0.05
T1	2.02	0.31	1.82	0.69	>0.05
T3	2.15	0.41	1.91	0.27	>0.05
T6	2.19	0.56	2.12	0.35	>0.05
T12	2	0	2	0	>0.05
T18	2	0	2	0	>0.05
T24	2	0	2	0	>0.05

The total rescue analgesia dose (tramadol) given in the 1st 24 hours was found to be the highest in the placebo group with the mean being 143.5±53.45 grams; followed by the gabapentin group with the mean being 132.5±51.65 grams. The total analgesia dose in the pregabalin group was found to be the lowest with the mean being 128.5±42.25 grams. However, no significant difference was observed between

the means of the 3 groups; as well as group-wise comparison considering any two groups at a time.

Table 9: Depicts the sedation scores of the gabapentin and placebo group at different time frames.

Time	Gabapentin group (n=40)		Placebo group (n=40)		
	Mean	SD	Mean	SD	P value
T0	2.16	0.63	1.76	0.71	<0.05
T1	2.29	0.67	1.82	0.69	<0.05
T3	2.11	0.49	1.91	0.27	<0.05
T6	1.98	0.31	2.12	0.35	>0.05
T12	2	0	2	0	>0.05
T18	2	0	2	0	>0.05
T24	2	0	2	0	>0.05

Dizziness was seen most among the Group A patients, followed equally by Group B and C patients. However, headache and nausea were seen most among the Group B patients, followed by Group A patients, and least seen among the Group C patients. However, these findings were statistically insignificant.

DISCUSSION

Post-operative pain is one of the most challenging and debilitating obstacles for the operating surgeon. Despite various advancements made in multimodal post-operative pain management, this issue has an overall negative effect on the post-operative clinical and functional outcomes of the patient, thus hampering overall satisfaction. Most commonly used drugs in this multimodal regime include a combination of nonsteroidalanti-inflammatory drugs (NSAIDs), opioids, gabapentinoids (gabapentin and pregabalin), and regional anesthesia (local injection or infusion, epidural anesthesia, peripheral nerve blocks, and paravertebral blocks). The main objective of this multimodal treatment is to have adequate additive and synergistic analgesia at reduced doses of individual drugs, so as to reduce the overall side effects as well as dependence of these drugs. Of this multimodal regime, Paracetamol is a very important analgesic agent, which when given intravenously (IV); has its rapid onset of action due to its earlier and greater penetration into cerebrospinal fluid; and its ability to achieve high C_{max} and earlier V_{max} levels in plasma as compared to oral and rectal routes. Various studies have been conducted using IV paracetamol perioperatively, to look for its efficacy as preemptive (preoperatively) and preventive (postoperatively) analgesia. A study conducted by Hasan et al concluded intravenous paracetamolis equally effective in controlling post-operative pain in patients undergoing elective cesarean section; when used as preemptive (preoperatively) vs preventive (immediate postoperatively) analgesic.[14] A study conducted by Vincet et al concluded significant beneficial effects of intravenous paracetamol as a preemptive analgesic in patients undergoing lower abdominal surgeries. In this study, the postoperative VAS scores were found to be significantly lower in patients who were given preemptive IV paracetamol as compared to those who were not given.[15]

In the case of spine surgery, this post-operative pain may be either a nociceptive one or a neuropathic one. Nociceptive pain occurs due to an inflammatory process secondary to the soft tissue injury that happens during the surgery and is well managed with non-steroidal anti-inflammatory drugs (NSAIDs) and opioids. Neuropathic pain is the result of any lesion or dysfunction of the nervous system which may be in the form of direct injury or compression of the neural structures intraoperatively; leading to its demyelination which subsequently causes an increase in the concentration of sodium channels and inflammatory markers around the affected area which evokes spontaneous discharges from the cell bodies at dorsal root ganglion (DRG) cell level; thus increasing the CNS sensitivity and leading to pain stimuli. Gabapentinoids like gabapentin and pregabalin are amino butyric acid analogs containing analgesic properties and also are anti-nociceptive. These analogs when given before any trauma which can be either surgical or inflammatory one; either bind directly to the gamma-amino-butyric acid receptors(GABA-A and B) or increase the level of GABA; thus reducing the CNS sensitivity as well as pain transmission across the nerves.[16]

In our study, we included oral pregabalin or gabapentin along with IV paracetamol as a preemptive analgesic for patients undergoing open lumbar disc herniation surgery.

Pregabalin has been designed to have more potent pharmacological properties than gabapentin and also have been used to increase the overall biological activity of gabapentin.[17-20] It has more extensive and rapid absorption, high bioavailability, high mean elimination half-life, low T_{max} (time to maximal plasma concentration), and high dose proportional C_{max} (maximal plasma concentration). Many studies have shown a dose of 150 mg oral pregabalin for effective preemptive analgesia, and thus dose of 150mg oral pregabalin along with IV paracetamol was chosen as preemptive analgesic in one of the group in our study.[21-22]

Various studies have shown 300mg of oral gabapentin to be effective in reducing postoperative pain and opioid consumption in patients undergoing laparoscopic cholecystectomy and lower limb orthopedic surgeries. However, in study conducted by Pandey et al; dose of oral Gabapentin used in patients undergoing lumbar discectomy was 600mg.[23] In a study conducted by Montazeri et al, oral gabapentin in a dose of 300mg was used as a preemptive analgesic 2 hours before the lower limb orthopedic surgery; and was found to decrease the postoperative VAS scores as well as the opioids requirement.[24] Thus in our study, we decided to choose a dose of 300 mg oral gabapentin along with IV paracetamol as a preemptive analgesic in one of the groups.

In this study out of a total of 120 patients, there were 47 males (40%) and 73 females (60%); with the mean age of the study population being 46.92±10.89 years. The mean duration of surgery in the pregabalin group was 65.89±10.31 minutes; the gabapentin group was 63.74±12.64 minutes; while that in the Placebo group was 66.27±11.84 minutes. The difference in the means of the 3 groups was statistically insignificant. These results are in accordance with the study conducted by Ghai et al; which was done to compare the effectiveness of pregabalin and gabapentin on postoperative pain in patients undergoing abdominal hysterectomy. In their study, it was found that the mean duration of surgery was highest in the control group followed by the pregabalin group, and least in the gabapentin group; but was statistically insignificant.[25]

In the current study, post-operative pain evaluation was done based on VAS scores. It was found that the pregabalin group had the lowest scores at all the time frames as compared to the gabapentin and placebo (highest VAS scores) groups; with significant differences observed at all time frames except at T_3 and T_6 time frames. Also on group-wise comparison, the pregabalin group had significantly lower scores when compared to the gabapentin group and the placebo group individually. This is in accordance with a study conducted by Mishra et al, which concluded statistically significant lower post-operative VAS scores and lower opioid consumption in patients undergoing laparoscopic cholecystectomy surgery; given pre-operative oral pregabalin as compared to oral gabapentin as a preemptive analgesic.[26] Similar results were seen in a study conducted by Eidy et al, where pre-operative oral pregabalin was found to significantly decrease post-operative pain as compared to pre-operative oral gabapentin.[27] Rajshree et al, conducted a study comparing 150mg oral pregabalin to 900mg oral Gabapentin as a preemptive analgesic in patients undergoing laparoscopic cholecystectomy; and concluded that the pregabalin group had significantly lower post-operative VAS scores, prolonged time to 1st rescue analgesia and less opioid consumption as compared to gabapentin group. They also concluded that the analgesic profile in both the pregabalin and gabapentin groups was significantly better as compared to the placebo group; which is similar to the findings of our current study.[21] Routray et al, conducted a study on patients undergoing spine surgery and concluded significantly better analgesic profile and low opioid consumption; in the patients given pre-operative oral pregabalin as compared to oral gabapentin as a preemptive analgesic; which is similar to the findings of our current study.[28]

In contrast to this, a study conducted by Kochhar et al, concluded that a preoperative single dose of oral pregabalin (150mg) or gabapentin (300mg); was equally efficacious in providing adequate post-operative analgesia in patients undergoing laparoscopic cholecystectomy.[29] However, the Saraswat et al, study concluded that a single pre-operative dose of oral pregabalin (300mg) or gabapentin (1200mg) in patients undergoing surgery under spinal anesthesia; provided prolonged post-spinal analgesia, with the pregabalin group showing better analgesic effects than gabapentin group.[30] Similarly in a study on patients undergoing surgery under spinal anesthesia, conducted by Trivedi et al, it was concluded that pre-operative oral pregabalin (150mg) had significantly better and long-lasting postoperative analgesia, prolonged time to 1st rescue analgesia and opioid-sparing effects than preoperative oral Gabapentin (600mg) as a preemptive analgesic.[31] These are in accordance with the findings of our study. In study done by Akhavnakbari et al, on patients undergoing lower limb orthopedic surgery; it was found that pre-operative oral pregabalin (150mg) was significantly effective in decreasing the post-operative VAS scores and total analgesia consumption as compared to the placebo group; which was similar to the findings of our study.[32] In a study done by Turan et al, on patients undergoing spinal surgeries; it was found that pre-operative oral gabapentin was significantly effective in decreasing the early post-operative (less than 4 hours) VAS scores and total analgesia consumption as compared to the placebo group; which was similar to our study's finding.[33]

Yilmaz et al, in their study, found pregabalin and gabapentin to be equally effective in controlling neuropathic pain in patients suffering from spinal cord injury. However, they also concluded that there was a statistically significant difference in the mean time to 1st rescue analgesia in the three study groups; with the placebo group having the least time while the pregabalin group had the highest time to 1st rescue analgesia.[34] This finding was similar to our study. Similarly, the study conducted on patients undergoing open cholecystectomy by Maqsood et al; it was found that pre-operative oral pregabalin as a preemptive analgesic had significantly prolonged time to post-operative 1st rescue analgesia requirement as compared to preoperative oral gabapentin.[35] In a study conducted by Agarwal et al, it was found that a single pre-operative dose of oral pregabalin as a preemptive analgesic had significantly lower post-operative VAS scores and lower requirement of post-operative opioids, in patients undergoing laparoscopic cholecystectomy.[36]

In our study, we found lower post-operative sedation scores in the placebo group as compared to the other two groups. Also, we found that the pregabalin group had the lowest post-operative analgesic consumption, followed by the gabapentin group; and the highest consumption was by the placebo group; though the difference was statistically insignificant. Routray et al, in their study on patients undergoing lumbar spine surgery with pregabalin or gabapentin as a preemptive analgesic, found the highest post-operative sedation scores in the pregabalin group, followed by the gabapentin group, and the least sedation was encountered in the placebo group. It was also found that the total post-operative analgesic requirement was significantly lower in the pregabalin and gabapentin groups as compared to the placebo group; thus indicating opioid sparring effects of both pregabalin and gabapentin.

This was similar to the findings of our study.[28] Similarly Bekawi MS and colleagues, in their study on patients undergoing laparoscopic cholecystectomy, found both pregabalin and gabapentin when used as preemptive analgesics individually, to have significant post-operative opioid sparring effectsas compared to the control group.[22]

Dizziness, headache, and nausea were the major side effects encountered in our study. Dizziness was seen most commonly in the patients receiving pregabalin, followed equally by patients receiving gabapentin and placebo. However, headache and nausea were seen most commonly amongst the patients receiving gabapentin, followed by the pregabalin group, and least seen amongst the patients in the placebo group. However, these findings were statistically insignificant. In a study by Routray et al, the major side effects that were encountered were dizziness, nausea and vomiting.[28] However, in their study dizziness and nausea was most commonly seen in patient receiving gabapentin as compared to the pregabalin group. However, these findings were insignificant. In a study by Trivedi et al, the major side effects that were encountered were dizziness, nausea, and rigors; which were more commonly seen in the gabapentin group.[31]

There have been various studies where these gabapentinoids have been used as preemptive analgesics; with major studies concluding beneficial effects of these gabapentinoids in decreasing the post-operative pain, prolonging the time to 1st rescue analgesia, and having opioid sparring effects as compared to the placebo; which was similarly seen in our study as well. Also, these studies showed the beneficial effects of pregabalin over gabapentin as a preemptive analgesic with respect to decreasing the post-operative pain, prolonging the time to 1st rescue analgesia, having opioid sparring effects, and having lesser side effects; which was similarly observed in the current study as well. However, pregabalin was seen to have more post-operative sedation when compared to gabapentin and placebo.

However, our study had few limitations. Firstly, the sample size was small. Secondly, we did not consider other factors that would influence post-operative pain and outcomes like psychological and social status and stress. Third, we chose the fixed doses of pregabalin and gabapentin in all the patients of their respective groups, without taking into consideration their physiological adaptation to these gabapentinoids in the event of surgical stress. And lastly, we did not take into consideration the effects of these gabapentinoids on long-term complications of spine surgeries like chronic pain syndrome, which usually develops weeks and months after the surgery.

However, there few strengths in our study as well. We made use of 1 gm IV paracetamol along with these gabapentinoids as a part of a multimodal preemptive analgesia model, to have better post-operative results; which very few previous studies have taken consideration into. Secondly, the study was double-blinded where the resident doctor administrating the drugs pre-operatively and examining and recording the data of the patients post-operatively were different and were blinded from their pre-operative analgesia status.

CONCLUSION

Our study concluded the beneficial effects of pre-operative oral gabapentinoids as a preemptive analgesic in decreasing post-operative pain, prolonging the time to 1st rescue analgesia, and having opioid sparring effects as compared to the placebo. Of the two gabapentinoids studied, pregabalin was found to have more beneficial effects as compared to gabapentin as a preemptive analgesic with respect to decreasing the post-operative pain, prolonging the time to 1st rescue analgesia, having opioid sparring effects, and having lesser side effects. However, pregabalin was seen to have more post-operative sedation when compared to gabapentin and placebo. Therefore, this study recommends the use of pre-operative IV paracetamol with oral pregabalin over oral gabapentin as a preemptive analgesicas a multimodal analgesic regime. However, further studies with larger sample sizes are needed to look for the beneficial effects of these gabapentinoids as a multimodal preemptive analgesic and also to determine their doses subjected to the patient's physiological demands and look into their effects on the long-term complications of spine surgery.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Lellan K. Postoperative pain: strategy for improving patient experiences. J Adv Nurs. 2004;46(2):179-85.
2. Chung JW, Lui JC. Postoperative pain management: study of patients' level of pain and satisfaction with health care providers' responsiveness to their reports of pain. Nurs Health Sci. 2003;5(1):13-21.
3. Barrington JW, Halaszynski TM, Sinatra RS, Expert Working Group On Anesthesia And Orthopaedics Critical Issues In Hip And Knee Replacement Arthroplasty FT. Perioperative pain management in hip and knee replacement surgery. Am J Orthop. 2014;43(4):1-16.
4. Pearce CJ, Hamilton PD. Current concepts review: regional anesthesia for foot and ankle surgery. Foot Ankle Int. 2010;31(8):732-9.
5. Sinatra R. Causes and consequences inadequate management of acute pain. Pain 7. Med 2010;11(12):1859-71.
6. Lovich-Sapola J, Smith CE, Brandt CP. Wadhera R. Postoperative pain control. SurgClin North Am. 2015;95(2):301-18.

7. Vallejo R, Casasola O, Benyamin R. Opioid therapy and immunosuppression: a review. Am J Ther. 2004;11(5):354-65.
8. Dolin SJ, Cashman JN. Tolerability of acute postoperative pain management: nausea, vomiting, sedation, pruritus, and urinary retention. Evidence from published data. Br J Anaesth. 2005;95(5):584-91.
9. Rowbotham M, Harden N, Stacey B, Bernstein P, Magnus-Miller L. Gabapentin for the treatment of post herpetic neuralgia: a randomized controlled trial. JAMA. 1998;280(21):1837-42.
10. Devor M, Wall PD. Cross-excitation in dorsal root ganglia of nerve-injured and intact rats. J Neurophysiol. 1990;64(6):1733-46.
11. Bernard JM,Surbled M, Lagarde D, Trennec A. Analgesia after surgery of thespine in adults and adolescents. Cah Anesthesiol. 1995;43(6):557-64.
12. Gajraj NM. Pregabalin: its pharmacology and use in pain management. Anesth Analg. 2007;105(6):1805-15.
13. Menachem EB. Pregabalin pharmacology and its relevance to clinical practice. Epilepsy. 2004;45:13-8.
14. Hassan HI. Perioperative analgesic effects of intravenous paracetamol: Preemptive versus preventive analgesia in elective cesarean section. Anesth Essays Res. 2014;8(3):339-44.
15. Vincent D, Vishma K. Study of paracetamol infusion as pre-emptive analgesia in lower abdominal surgeries. IOSR J Dental Med Sci. 2017;16:92-6.
16. Werner MU, Perkins FM, Holte K, Pedersen JL, Kehlet H. Effects of gabapentin in acute inflammatory pain in humans. Reg Anesth Pain Med. 2001;26(4):322-8.
17. Yorimitsu E, Chiba K, Toyama Y, Hirabayashi K. Long-term outcomes of standard discectomy for lumbar disc herniation: a follow-up study of more than 10 years. Spine. 2001;26(6):652-7.
18. Caraceni A, Zecca E, Bonezzi C, Arcuri E, Tur RY, Maltoni M, et al. Gabapentin for neuropathic cancer pain: a randomized controlled trial from the Gabapentin Cancer Pain Study Group. J Clin Oncol. 2004;22(14):2909-17.
19. Jacquy J, Lossignol D, Sternon J. Pregabalin (Lyrica) and neuropathic pain syndromes. RevMed Brux. 2006;27(5):445-50.
20. Jokela R, Ahonen J, Tallgren M, Haanpaa M, Korttila K. Premedication with pregabalin 75 or 150mgwith ibuprofen to control pain after day-case gynaecological laparoscopic surgery. Br J Anaesth. 2008;100(6):834-40.
21. Mishra R, Tripathi M, Chandola HC. Comparative clinical study of gabapentin pregabalin for postoperative analgesia in laparoscopic cholecystectomy. Anesth Essays Res. 2016;10(2):201-6.
22. Bekawi MS, El Wakeel LM, Al Taher WM, Mageed WM. Clinical study evaluating pregabalin efficacy and tolerability for pain management in patients undergoing laparoscopic cholecystectomy. Clin J Pain. 2014;30(11):944-52.
23. Pandey CK, Navkar DV, Giri PJ, Raza M, Behari S, Singh RB, et al. Evaluation of the optimal preemptive dose of gabapentin for postoperative pain relief after lumbar Although in this study Pregabalin has been diskectomy: a randomized, double-blind, placebo-controlled study. J Neurosurg Anesthesiol. 2005;17(2):65-8.
24. Montazeri K, Kashefi P, Honarmand A. Preemptive gabapentin significantly reduces postoperative pain and morphine demand following lower extremity orthopaedic surgery. Sing Med J. 2007;48(8):748-51.
25. Ghai A, Gupta M, Hooda S, Singla D, Wadhera R. A randomized controlled trial to compare pregabalin with gabapentin for postoperative pain in abdominal hysterectomy. Saudi J Anaesth. 2011;5(3):252-7.
26. Mishra R, Tripathi M, Chandola H. Comparative clinical study of gabapentin Gabapentinand pregabalin for postoperative analgesia in laparoscopic cholecystectomy. Anesth Essays Res. 2016;10(2):201-9.
27. Eidy M, Fazel MR, Abdolrahimzadeh H, Moravveji AR, Kochaki E, Mohammadzadeh M. Effects of pregabalinand gabapentin on postoperative pain and opioid consumption after laparoscopic cholecystectomy. Korean J Anesthesiol. 2017;70(4):434-8.
28. Routray SS, Pani N, Mishra D, Nayak S. Comparison of pregabalin with gabapentin as preemptive analgesic in lumbar spine surgery. J Anaesthesiol Clin Pharmacol. 2018;34(2):232-6.
29. 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(3):676-80.
30. SaraswatV, Arora V. Preemptive gabapentin vspregabalin for acute postoperative pain after surgery under spinal anaesthesia. Ind J Anaes. 2008;52(6):829-35.
31. Trivedi PA, Mehta M, Trivedi J. Preemptive gabapentin versus pregabalin for post-operative analgesia after abdominal hysterectomy under spinal anaesthesia. Int J Res Med. 2015;4(1):53-8.
32. Akhavanakbari G, Entezariasl M, Isazadehfar K, Mirzarahimi T. The effects of oral pregabalin on post-operative pain of lower limb orthopedic surgery: a double-blind, placebo-controlled trial. Pers Clin Res. 2013;4(3):165-70.
33. Turan A, Karamanlioglu B, Memis D, Hamamcioglu MK, Tükenmez B, Pamukçu Z, et al. Analgesic effects of gabapentin after spinal surgery. Anesthes 2004;100(4):935-8.
34. Yilmaz B, Yasar E, Koroglu OO, Goktepe AS, Tan AK. Gabapentin vs Pregabalin for the treatment of neuropathic pain in patients with spinal cord injury: a crossover study. Turk J Phys Med Rehab. 2014;61(1):1-5.

35. Maqsood S, Khan RA, Arshad A. A comparison of preemptive gabapentin with pregabalin for relief of postoperative pain in patients undergoing cholecystectomy. Pak Armed Forces Med J. 2017;67(5):843-6.
36. Agarwal A, Gautam S, Gupta D, Agarwal S, Singh PK, Singh U. Evaluation of single preoperative dose of pregabalin for attenuation of postoperative pain after laparoscopic cholecystectomy. Br J Anaesth. 2008;101(5):700-4.

Cite this article as: Garg RN, Vaje SS, Patil H, Bajaj S. A prospective and comparative study to evaluate the efficacy of oral pregabalin vs gabapentin combined with IV paracetamol as preemptive analgesic for post-operative pain in patients undergoing single level open lumbar spine decompression surgery in a tertiary health care center. Int J Res Orthop 2024;10:96-105.