

A prospective comparative evaluation of gabapentin vs pregabalin for the acute post-operative pain management in lower limb surgeries under spinal anaesthesia

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Abstract

Background: Pre-emptive analgesia is a multimodal approach where drug is used before surgery and has potential to be more effective than a similar analgesic treatment initiated after surgery. Pregabalin and Gabapentin are GABA analogue used as pre-emptive analgesic. Its analgesic action is mediated through $\alpha\delta$ subunit of voltage-gated calcium channels on dorsal horn neurons. **Material and Method:** 96 patients satisfying selection criteria were enrolled for this study and divided into three groups: Group P, Group G and Group C, each having 32 patients. All patients were explained about visual analogue score. **Result:** There is a significant difference between three groups regarding time of first rescue analgesia and tramadol consumption. The mean time for rescue analgesia was longer in the pregabalin group than the gabapentin group (482.7 ± 113.5 min vs 343.35 ± 70.74 min). The mean amount of dose of tramadol requirement was also less in the pregabalin and gabapentin group (164.32 ± 39.41 vs 178.32 ± 48.21 vs 272.82 ± 83.01) in comparison to control. **Conclusion:** The VAS score was significantly higher in control than the pregabalin and gabapentin groups. Both pregabalin (group P) and gabapentin (group G) are comparable to each other regarding VAS score at different time intervals in the post-operative period. Ramsay sedation score was significantly higher in the pregabalin and gabapentin groups up to 4 hours post-operatively but after that there was no significant difference between the two groups. Both pregabalin (group P) and gabapentin (group G) are comparable to each other regarding Ramsay sedation score at different time intervals in the post-operative period.

Keyword: Gabapentin, pregabalin, post-operative pain.

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INTRODUCTION

Acute post-operative pain is defined as pain that is present in surgical patients after the procedure. ¹It occurs due to inflammatory response of surgical trauma and afferent neuronal outflow leads to several unpleasant sensory, emotional and mental experiences due to it. Aim of post-operative pain relief is to provide subjective comfort and to blunt nociceptive autonomic, endocrine-metabolic and physiological responses so that patient will be made mobile early and recovery will be fast and duration of stay in hospital will reduce.^{2,3} Effective pain management should start before surgery. For effective post-operative pain management multimodal analgesia is recommended.^{4,5} In multimodal analgesia simultaneously

multiple analgesic that work synergistically are used to achieve clinically required analgesia with minimal adverse effect. Pre-emptive analgesia is multimodal approach where drug is used before surgery and has potential to be more effective than a similar analgesic treatment initiated after surgery.^{6,7} There are various drugs which are used for pre-emptive analgesia which include, non-steroidal anti-inflammatory drug, NMDA receptor antagonist, opioids, local anaesthetic agent and GABA analogues. Pregabalin and Gabapentin are GABA analogue used is used as pre-emptive analgesic. Its analgesic action is mediated through $\alpha 2\delta$ subunit of voltage gated calcium channels on dorsal horn neurons. Pregabalin has six times more affinity to $\alpha 2\delta$ subunit of voltage gated calcium channels than gabapentin, so it is six times more potent and it has less side effects than gabapentin.^{9,10} After literature survey we have found that there is little literature available regarding comparison of pregabalin and gabapentin as pre-emptive analgesia. Mishra R, Tripathi M, Chandola HC *et al.* from New Delhi has concluded that pregabalin group had lower VAS score, prolonged timing of first rescue analgesic, and less opioids consumption than the gabapentin group. Both gabapentinoids had better postoperative analgesic profile than placebo.¹¹ Dauri M, Faria S, Gatti A, Celidonio L, Carpenedo R, Sabato AF *et al.* from Rome Italy has concluded that Gabapentin and pregabalin reduce pain and opioid consumption after surgery in confront with placebo.¹² Based on above finding present study has been designed to compare the pre-emptive analgesic efficacy of oral gabapentin versus oral pregabalin in lower limb surgeries under spinal anaesthesia and incidence of adverse effect in our clinical establishment.

MATERIAL AND METHOD

Place of study: Department of anaesthesia Konaseema institute of medical science and research Amalapuram'

Period of study: From April 2018 to January 2021

Study design: This study was conducted as a prospective comparative clinical study.

Ethics: Before start of this study an approval from institutional ethics committee was taken. A written informed consent was obtained from all patients before enrolling them for study.

Selection of patients: Patients posted for elective patients admitted in the department of orthopaedics for lower limb surgery under spinal anaesthesia included for this study as per following inclusion and exclusion criteria.

Inclusion criteria:

1. Age 18 to 60 years

2. American Society of Anaesthesiologists (ASA) Classes I and II

Exclusion criteria: Diabetes mellitus, spinal deformities, bleeding or clotting disorders, Cardiopulmonary, renal and hepatic abnormality, peripheral neuropathy, hypersensitivity to drug and CNS disorder, chronic alcoholic

Sample size calculation: Based on true mean difference between treatment and control group and Expected population standard deviation, SD from previous study, type 1 error 0.5 and power of study 0.8 sample sizes was calculated to be 32 in each group. So 96 patients satisfying selection criteria were enrolled for this study and divided in to three groups Group P, Group G and Group C each having 32 patients. All patients were explained about visual analogue score.

Group P: 32 patients of this group were received 150 mg pregabalin in the form of two capsules each having 75 mg strength one hour before surgery

Group G: 32 patients of this group were received 900 mg gabapentin in the form of three capsules each having 300 mg strength one hour before surgery

Group C: 32 patients of this group were received two vitamin B complex capsules one hour before surgery

Inside the operation theatre intravenous line was secured with 18G cannula. Monitor was attached and baseline parameters like heart rate (HR), systolic blood pressure (SBP), systolic blood pressure (SBP), respiratory rate, SpO₂, and electrocardiography (ECG) tracing was recorded. All patients included in this study have received same pre medication and same spinal anaesthesia protocol was followed. At the end of surgery and on arrival to recovery room heart rate (HR), systolic blood pressure (SBP), systolic blood pressure (SBP), respiratory rate, visual analogue score for pain and sedation score (Ramsay sedation score) were recorded. The time was considered as T₀. After that visual analogue score for pain and sedation score (Ramsay sedation score) were recorded continuously 1,2,3,4,6,9,12 and 24 hours post operatively When visual analogue score was more than 4 injection tramadol 2mg/kg was given intramuscularly and time for first requirement of analgesic(T₁) and total dose of analgesic required in first 24 hour was recorded.

Statistical analysis:

Data were recorded in excel sheet and statistical Analysis was done with software SPSS-14 version. Qualitative data were calculated as percentage and proportions and were analyzed by Chi-square test. Quantitative data were expressed as mean \pm SD and these data were analyzed by unpaired student t test.

RESULT

As per selection criteria 96 patients were included in this study and divided in to three study groups.

Table 1; Demographic profile of three groups under study

Variable	Group P	group G	Group C	P value
Age	41.21±12.02	42.56±10.71	46.15±6.83	.1426
sex				
M	22	24	21	.7
F	10	8	11	
BMI(kg/m ²)	23.4±1.51	22.27±1.90	23.05±1.89	.2423
Duration of surgery(minutes)	105.85±25.79	110.6±17.94	113.75±18.37	.51
ASA				
I	21	18	20	.64
II	11	14	10	

As per table 1, regarding demographic profile of subjects three groups are comparable to each other with respect with respect to age (41.21±12.02 vs 42.56±10.71 vs 46.15±6.83) and sex. The P value was more than .05. There was no statistical significant difference between three groups regarding body mass index (kg/m²) (23.4±1.51 vs 22.27±1.90 vs 23.05±1.89) and duration of surgery (minutes) (105.85±25.79 vs 110.6±17.94 vs 113.75±18.37). (P>0.05) ASA status of patients in all three groups is also comparable to each other.

Table 2: Comparison of VAS score of pregabalin (group P), gabapentin (group G) and control (Group C)

Variable	Group P	group G	Group C	P value
0	1.78±.69	1.81±.46	2.09±.57	.07
1	1.87±.64	1.96±.75	2.84±.36	.00001
2	1.96±.67	2.0±.55	3.59±.94	.00001
3	2.06±.71	2±.76	4.34±1.10	.00001
4	2.42±.88	2.86±.75	5.04±.94	.00001
6	2.87±.64	2.96±.78	5.64±1.10	.00001
9	2.89±.78	2.88±.86	5.33±.98	.00001
12	2.84±.84	2.76±.72	5.31±1.12	.00001
24	3.01±.89	3.12±.88	5.68±.98	.00001

Visual analogue score for pain were recorded continuously 0 hour, 1 hour, 2 hours, 3 hours, 4 hours, 6 hours, 9 hours, 12 hours and 24 hours post operatively. The VAS score of pregabalin group at 0 hour, 1 hour, 2 hours, 3 hours, 4 hours, 6 hours, 9 hours, 12 hours and 24 hours post operatively was 1.78±.69, 1.87±.64, 1.96±.67, 2.06±.71, 2.42±.88, 2.87±.64, 2.89±.78, 2.84±.84 and 3.01±.89, for gabapentin group it was 1.81±.46, 1.96±.75, 2.0±.55, 2±.76, 2.86±.75, 2.96±.78, 2.88±.86, 2.76±.72 and 3.12±.88 and for control group the VAS score at above mentioned time interval was 2.09±.57, 2.84±.36, 3.59±.94, 4.34±1.10, 5.04±.94, 5.64±1.10, 5.33±.98, 5.31±1.12 and 5.68±.98 respectively. This VAS score was significantly higher in control then pregabalin and gabapentin group.

Table 3: Comparison of VAS score of pregabalin (group P) and gabapentin (group G)

Time	Group P	group G	P value
0	1.78±.69	1.81±.46	.85
1	1.87±.64	1.96±.75	.70
2	1.96±.67	2.0±.55	.84
3	2.06±.71	2±.76	.75
4	2.42±.88	2.86±.75	.68
6	2.87±.64	2.96±.78	.65
9	2.89±.78	2.88±.86	.45
12	2.84±.84	2.76±.72	.52
24	3.01±.89	3.12±.88	.44

Both pregabalin (group P) and gabapentin (group G) are comparable to each other regarding VAS score at different time interval in post operative period.

Table 4: Comparison of sedation score (Ramsay sedation score) of pregabalin (group P), gabapentin (group G) and control (Group C)

Time	Group P	group G	Group C	P value
0	2.52±.67	2.68±.71	1.98±.78	0.0024
1	2.46±.44	2.54±.74	1.80±.44	.0001
2	2.46±.44	2.44±.86	1.71±.36	.0001
3	2.01±.26	2.12±.48	1.65±.67	.0001
4	1.89±.54	1.96±.44	1.56±.39	.012
6	1.76±.24	1.86±.62	1.7±.49	.074
9	1.65±.65	1.60±.24	1.59±.51	.12
12	1.66±.44	1.69±.34	1.54±.47	.18
24	1.51±.32	1.53±.12	1.56±.21	.11

Ramsay sedation score were recorded continuously 0 hour, 1 hour, 2 hours, 3 hours, 4 hours, 6 hours, 9 hours, 12 hours and 24 hours post operatively. The Ramsay sedation score of pregabalin group at 0 hour, 1 hour, 2 hours, 3 hours, 4 hours, 6 hours, 9 hours, 12 hours and 24 hours post operatively was 2.52±.67, 2.46±.44, 2.46±.44, 2.01±.26, 1.89±.54, 1.76±.24, 1.65±.65, 1.66±.44 and 1.51±.32, for gabapentin group it was 2.68±.71, 2.54±.74, 2.44±.86, 2.12±.48, 1.96±.44, 1.86±.62, 1.60±.24, 1.69±.34 and 1.53±.12 and in control group Ramsay sedation score at various time interval was 1.98±.78, 1.80±.44, 1.71±.36, 1.65±.67, 1.56±.39, 1.7±.49, 1.59±.51, 1.54±.47 and 1.56±.21. Ramsay sedation score was significantly higher in pregabalin and gabapentin group up 4 hour post operatively but after that there was no significant difference between two groups.

Table 5: Comparison of sedation score (Ramsay sedation score) of pregabalin (group P) and gabapentin (group G)

Time	Group P	group G	P value
0	2.52±.67	2.68±.71	.324
1	2.46±.44	2.54±.74	.74
2	2.38±.56	2.44±.86	.57
3	2.01±.26	2.12±.48	.09
4	1.89±.54	1.96±.44	.58
6	1.76±.24	1.86±.62	.07
9	1.65±.65	1.60±.24	.14
12	1.66±.44	1.69±.34	.26
24	1.51±.32	1.53±.12	.55

Both pregabalin (group P) and gabapentin (group G) are comparable to each other regarding Ramsay sedation score at different time interval in post operative period.

Table 6: Time of first rescue analgesia and tramadol consumption of pregabalin (group P), gabapentin (group G) and control (Group C)

Variable	Group P	group G	Group C	P value
Time of first rescue analgesia	482.7±113.5	343.35±70.74	142.55±26.51	.0001
tramadol consumption	164.32±39.41	178.32±48.21	272.82±83.01	.0001

There is significant difference between three groups regarding time of first rescue analgesia and tramadol consumption. The mean time for rescue analgesia was longer in pregabalin group then gabapentin group (482.7±113.5 min vs 343.35±70.74 min). The mean amount of dose of tramadol requirement was also less in pregabalin and gabapentin group(164.32±39.41 vs 178.32±48.21 vs 272.82±83.01) in comparison control.

Table 7: Adverse drug reaction

Adverse reaction	Group P	group G	Group C
Nausea and vomiting	2(6.25%)	1(3.125%)	5(15.62%)
Headache	0	1(3.125%)	1(3.125%)
Somnolence	5(15.62%)	6(18.75%)	2(6.25%)
Dizziness	4(12.5%)	5(15.62%)	3(9.375%)

Somnolence and dizziness was common in pregabalin and gabapentin group but frequency of nausea and vomiting was more in control.

DISCUSSION

The effective postoperative pain management in essential for early mobilisation and reduce the duration of stay in

hospital. The goal of post operative pain management is to reduce or eliminate the pain with minimum adverse effect. For this multi modal approach is used and pre-emptive use

of various pharmacological agents is recommended.¹⁶ Gabapentinoids (gabapentin and pregabalin) were used as antiepileptics but it has analgesic, anticonvulsant, and anxiolytic effects as well. Pregabalin and Gabapentin are GABA analogue used is used as pre-emptive analgesic.¹⁷ Its analgesic action is mediated through $\alpha 2\delta$ subunit of voltage gated calcium channels on dorsal horn neurons. Present study has been conducted based on this. In this study we have divided patients in to three groups Group P (pregabalin), Group G (gabapentin) and Group C (control) each having 32 patients. The dose of pregabalin was 150 mg, gabapentin was 900 mg and group c has been given vitamin b complex capsule. All groups are comparable to each other with respect to demographic profile. This finding is supported by the work of V Saraswat¹, Vishal Arora *et al.* and Khalid G Abd El-Maksoud *et al.*^{13,14} The VAS score was significantly higher in control then pregabalin and gabapentin group. Both pregabalin (group P) and gabapentin (group G) are comparable to each other regarding VAS score at different time interval in post operative period. Eidy M, Fazel MR, Abdolrahimzadeh H *et al.* has concluded that a single dose of gabapentin or pregabalin decreased postoperative pain and nausea, as well as vomiting and opioid consumption after laparoscopic cholecystectomy. Moreover, the findings revealed that pregabalin was superior to gabapentin for reducing postoperative pain¹⁸. First part of this conclusion is supporting our finding but second part of conclusion in not corroborated with our study. Ramsay sedation score was significantly higher in pregabalin and gabapentin group up 4 hour post operatively but after that there was no significant difference between two groups. Both pregabalin (group P) and gabapentin (group G) are comparable to each other regarding Ramsay sedation score at different time interval in post operative period. This finding is supported by the work of Mishra R, Tripathi M, Chandola HC *et al.* and Tashi Chotton, Nongthombam Ratan Singh *et al.*^{11,19} There is significant difference between three groups regarding time of first rescue analgesia and tramadol consumption. The mean amount of dose of tramadol requirement was also less in pregabalin and gabapentin group. Yu L, Ran B, Li M, Shi Z *et al.* has concluded that gabapentin and pregabalin were efficacious in reduction of postoperative pain and narcotic requirements after lumbar spinal surgery. Liu B, Liu R, Wang L *et al.* has concluded that Preoperative use of gabapentinoids was able to reduce postoperative pain, total morphine consumption, and morphine-related complications following spine surgery.^{20,21} This two study supports our finding. Somnolence and dizziness was common in pregabalin and gabapentin group but frequency of nausea and vomiting was more in control.

Finding of Khalid G Abd El-Maksoud, Mokhtar M Younes, Sherif A Elokda *et al.* supports our study.¹⁴

CONCLUSION

The VAS score was significantly higher in control then pregabalin and gabapentin group. Both pregabalin (group P) and gabapentin (group G) are comparable to each other regarding VAS score at different time interval in post operative period. Ramsay sedation score was significantly higher in pregabalin and gabapentin group up 4 hour post operatively but after that there was no significant difference between two groups. Both pregabalin (group P) and gabapentin (group G) are comparable to each other regarding Ramsay sedation score at different time interval in post operative period. There is significant difference between three groups regarding time of first rescue analgesia and tramadol consumption. The mean amount of dose of tramadol requirement was also less in pregabalin and gabapentin group. Somnolence and dizziness was common in pregabalin and gabapentin group but frequency of nausea and vomiting was more in control.

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