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An observational comparative study to evaluate the efficacy and safety of pregabalin and gabapentin in neuropathic pain- at a Teritiary Care Centre

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Abstract

Background: Millions of people around the world suffer from Neuropathic pain (Nep), a prevalent and debilitating condition. Treatment for NeP typically includes anticonvulsants, antidepressants, opioids, topical medications, and local anesthetics. Although Pregabalin and Gabapentin are commonly used for this purpose, there is a lack of conclusive evidence supporting their efficacy. NeP significantly diminishes patients' quality of life. This study aims to evaluate the safety and effectiveness of Gabapentin and Pregabalin in treating patients with NeP.

Methods: Among a total of 100 patients 50 patients (Group A) were given Gabapentin and 50 Patients (Group B) were given Pregabalin. The efficacy of drug was measured on the basis of decrease in NeP based on Douleur Neuropathique 4 questions (DN4) pain scale measured at baseline, after one month and after two months. Adverse drug reaction (ADR) reported by the patient or observed by the clinician during the study was reported using ADR reporting form.

Result: The mean reduction of the neuropathic pain score in Group A from baseline to 2 months was 2.15, while in Group B it was 3.49. Hence, pregabalin showed comparable pain reduction to gabapentin at the end of the 2-months study.

Conclusion: Pregabalin 100 mg once daily brought better improvement of symptoms and signs than Gabapentin 300 mg administered once daily. The study found that Pregabalin is a better drug for the treatment of neuropathic pain than Gabapentin. Gabapentin had fewer adverse effects than Pregabalin.

Keywords: Neuropathic Pain; Pregabalin; Gabapentin; Adverse drug reaction

1. Introduction

Pain is an unpleasant sensory and emotional experience often resulting from intense or potentially harmful stimuli. Pain thus serves as a warning sign of tissue damage, conveyed through specific receptors and fiber systems spanning from the periphery to the brain. Disruption of these normal pathways due to injury results in immediate loss or reduction of function, often accompanied by pain. However, in certain instances, such as when a lesion occurs, neuropathic pain (NeP) may develop. The International Association for the Study of Pain defines NeP as "an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage." [1]

Neuropathic pain (NeP) results from a lesion or disease affecting the somatosensory nervous system, leading to structural and functional changes that cause spontaneous pain and abnormally amplified responses to both painful and

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non-painful stimuli. Peripheral causes of NeP include conditions such as polyneuropathy, postherpetic neuralgia, postoperative pain, and posttraumatic neuralgia, while central causes include spinal cord injuries and stroke.[2] NeP is commonly described as burning, shooting, pricking, pins and needles, squeezing, or freezing sensations. Spontaneous pain may be occasionally over shadowed by intermittent electric-shock-like paroxysms, either independently or in conjunction with ongoing discomfort.

NeP management primarily focuses on alleviating symptoms, with treatment of the underlying etiological causes being possible only in certain pathological conditions, leading to pain relief. The Special Interest Group on Neuropathic Pain (NeuPSIG) has recommended gabapentinoids, tricyclic antidepressants (TCAs) and selective serotonin–norepinephrine reuptake inhibitors (SNRIs) as first-line drugs for NeP. Lidocaine, Capsaicin, and Tramadol are suggested as second-line treatments, while strong opioids (such as Morphine and Oxycodone) and Botulinum toxin-A (BTX-A) are considered third-line treatments for peripheral NeP. Gabapentin and Pregabalin have received approval from the Food and Drug Administration (FDA) for NeP management. Their structural similarity to the GABA neurotransmitter enables them to bind to the α2-δ subunit of voltage- dependent calcium channels, thereby reducing calcium influx into cells. Both gabapentin and pregabalin have shown significant efficacy in treating Diabetic neuropathy, Post herpetic neuralgia, spinal cord injury (SCI), and phantom limb syndrome.[3]

Pregabalin is a well-established anticonvulsant and analgesic agent and was the first drug approved by the FDA for treating neuropathic pain and postherpetic neuralgia. Preclinical and clinical studies have demonstrated pregabalin's effectiveness in managing neuropathic pain, with animal studies clarifying its anti-hyperalgesic and anti-allodynic mechanisms. Clinical research also supports the efficacy and dose-dependent effects of pregabalin, whether used as monotherapy or alongside other analgesics, in alleviating pain and related symptoms. Its main advantages include reliability, ease of use, and high tolerance in patients with neuropathic pain.

Gabapentin (GBP) is commonly used for postherpetic neuralgia (PHN). Its mechanism of action involves binding with high affinity to the alpha-2-delta subunit of voltage-gated calcium channels in the peripheral and central nervous system, modifying neurotransmitter release and reducing nerve cell excitability. This action likely contributes to its analgesic effect in neuropathic pain patients.[4]

2. Methods

- Study design: Present study was prospective, observational, comparative study, single centre study.
- Study centre and duration: Study was conducted at outpatient and inpatient of Neurology department at SH medical centre, Kottayam, Kerala for a period of 6 months.
- Study design: Total patients were 100 and were randomised into 2 groups. Group A patients received Gabapentin 300 mg. Group B patients received Pregabalin 100 mg.
- Inclusion criteria: Patients of either sex with age >18 years, Inpatients and out patients of neurology department with NeP based on clinical presentation, Those who are receiving Pregabalin 100 mg or Gabapentin 300 mg for NeP, Those who are willing to give consent were included in the study.
- Exclusion criteria: In patient with other types of pain not confirmed to be NeP, Patients who previously did receive any of the drug that will be used in the study, Patient with histories of liver disorders, heart conditions, renal disorders, pregnancy /lactation.
- Procedure: The patients were evaluated on basis of proper history, presenting complaints and past symptoms. Patients diagnosed as a case of NeP attending inpatient and outpatient department of neurology, SH medical center. Patients were enrolled in the study after signing the consent form which were provided in Malayalam and English. After getting enrolled and prior to the commencement of the treatment, the following were recorded in the case record form-physical examination, past medical history, concomitant medications if any if any, clinical test for neuropathic pain, diagnosis and pain assessment was done using Douleur Neuropathique 4 questions.

Table 1 Douleur neuropathic 4 questionnaire (DN4)

DOULEUR NEROPATHIC SCALE 4 QUESTIONS
Please complete this questionnaire by ticking one answer for each item in the Questions below
INTERVIEW OF THE PATIENT
QUESTION NO 1: Does your pain present by one or more of the following characteristics. Pain feels like burning Sensation of painful cold Pain feels like electric shocks
QUESTION NO 2: Is the pain associated with one or more of the Following symptoms in same area? Tingling Pins and needles Numbness Itching
PATIENTEXAMINATION
QUESTION NO3: Is the pain located in an area where the physical Examination had one or both of the following characteristics? 1.Hypoesthesia to touch? 2.Hypoesthesia to pinprick?
QUESTION NO 4: Is the pain provoked or increased by? 1.Brushing?
Yes=1/No= 0 patient's Score: /10Scores≥4/10indicate NeP

- ADR reporting: Adverse drug reaction reported by the patient or observed by the clinician during the study was reported using the ADR reporting form.
- Statistical analysis: For analysis of this data Statistical package for social science (SPSS) software version 20th was used. Qualitative data were represented in the form of values and percentages. Quantitative were represented in the form of mean±Standared Deviation (SD). An ANOVA test was conducted to compare the mean scores of the Douleur Neuropathique 4 questionnaire between the two groups. Additionally, a Chi-square test was used to assess adverse drug reactions in the two study groups.

3. Results

Table 2 Distribution of patients according to age group

Age in years	GROUP A (Gabapentin) (n=50)		GROUP B (Pregabalin) (n=50)		Total (N=100)	
	Frequency	Percentage (%)	Frequency	Percentage (%)	Frequency	Percentage (%)
≤50	4	8.0	4	8.0	8	8.0
51-60	14	28.0	11	22.0	25	25.0
61-70	18	36.0	14	28.0	32	32.0
71-80	12	24.0	18	36.0	30	30.0
>80	2	4.0	3	6.0	5	5.0

In this study, patients were more in the age group 61-70 years followed by 71-80 and 51-60. The mean age of patients in the study is 65 years. In group A, patients were more in the age group 61- 70 years and the mean age is 64 years. In group B, patients were more in the age group 71 -80 years and the mean age is 66 years.

In each group total 100 patients were there. In group A total females were 42 (84%) and 8 (16%) were males and in group B, females were 22 (56%) and males were 28 (44%).

Table 3 Distribution of patients according to gender

Sex	Group A Gabapentin (n=50)		(Group B) Pregabalin (n=50)		Total (N=100)	
	Frequency	Percentage (%)	Frequency	Percentage (%)	Frequency	Percentage (%)
Male	8	16.0	28	56.0	36	36.0
Female	42	84.0	22	44.0	64	64.0

At baseline, the mean±SD of DN4 score in Group A was 6.57±0.81and Group B was 7.14±0.74 respectively with t value of 3.486 and p value of <0.001 which was statistically significant. At one month, the mean±SD of DN4 pain score in Group A was 5.70±0.70 and Group B was 5.23±0.77 respectively with an t value of 2.689 and p value of 0.009 which was not statistically significant. At two months, the mean±SD of DN4 pain score in Group A was 4.41±1.15 and Group B were 3.65±1.00 respectively with t value of 3.335 and p value of <0.001 which was statistically significant.

Table 4 Comparison of neuropathic pain score in Group A and Group B at baseline, after one month and after 2 months

Time	Group	Mean	SD	Mean difference	t value	p value
Baseline	Group A (Gabapentin) (n=46)	6.57	0.81	0.57	3.486	<0.001***
	Group B (Pregabalin) (n=43)	7.14	0.74			
First follow up	Group A (Gabapentin) (n=46)	5.70	0.70	0.42	2.689	0.085
	Group B (Pregabalin) (n=43)	5.28	0.77			
Second follow up	Group A (Gabapentin) (n=46)	4.41	1.15	0.76	3.335	<0.001***
	Group B (Pregabalin) (n=43)	3.65	1.00			

In Group A, the mean difference in DN4 score from baseline to one month of treatment was 0.89, with a p-value of <0.001, indicating statistical significance. From baseline to the second follow-up, the mean difference in DN4 score was 2.15, with a p-value of 0.01, which was statistically significant. The mean difference in DN4 score between the first and second follow-up was 1.28, with a p-value of 0.001, which was also statistically significant as shown in table 8.5 and figure 8.5.

Table 5 Comparison of neuropathic pain score in Group A at baseline, after one month and after two months

Group	Mean	SD	Mean difference	t value	p value
Baseline	6.57	0.81	0.89	10.882	<0.001***
First follow up	5.70	0.70			
Baseline	6.57	0.81	2.15	13.857	0.01**
Second follow up	4.41	1.15			
First follow up	5.70	0.70	1.28	8.668	0.001***
Second follow up	4.41	1.15			

In Group B, the mean difference in DN4 score from baseline to one month was 1.86, with a p-value of <0.001, which was statistically significant. From baseline to the second follow-up, the mean difference in DN4 score was 3.49, with a p-value of <0.001, which was statistically significant. The mean difference in DN4 score from the first follow-up to the second follow-up was 1.63, with a p-value of <0.001, indicating statistical significant.

Table 6 Comparison of neuropathic pain score in Group B at baseline, after one month and after two months

Group	Mean	SD	Mean difference	t value	p value
Baseline	7.14	0.74	1.86	12.034	<0.001***
First follow up	5.28	0.77			
Baseline	7.14	0.74	3.49	20.036	<0.001***
Second follow up	3.65	1.00			
First follow up	5.28	0.77	1.63	11.523	<0.001***
Second follow up	3.65	1.00			

The mean reduction of the neuropathic pain score in Group A from baseline to 2 months was 2.15, while in Group B it was 3.49. Hence, pregabalin showed comparable pain reduction to gabapentin at the end of the 2-months study.

Table 7 Comparison of mean reduction of neuropathic pain score in group A and group B at baseline vs after 2 months

GROUP	MEAN REDUCTION
Group A at baseline Vs Group A at 2 months	2.15
Group B at baseline Vs Group B at 2 months	3.49

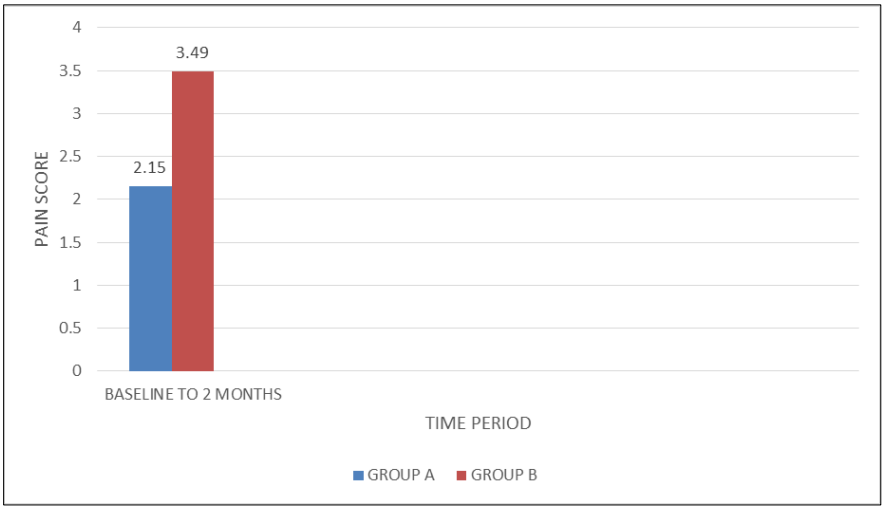

Figure 1 Comparison of mean reduction of neuropathic pain score in group A and group B at baseline vs after 2 months

Table 8 Adverse drug reaction in patients in group A and group B

Adverse effects	Groups		P value	Chi-square
	GROUP A	GROUP B		
Sedation	4	8	0.202 (NS)	1.613
Dizziness	0	1	0.309 (NS)	1.033
Drowsiness	0	2	0.148 (NS)	2.088
Somnolence	0	1	0.309(NS)	1.033

The occurrence of sedation was higher in Group B, with 8 patients, compared to Group A, with 4 patients. However, this difference was not statistically significant. Additionally, dizziness and somnolence was observed in one patient in Group B, and drowsiness was observed in two patients in Group B, none of which were statistically significant.

4. Discussion

A prospective observational comparative study was conducted at the department of Neuro-medicine, SH Medical Center, Kottayam, over a period of six months from 2023 to 2024. The study focused on evaluating the efficacy and safety of pregabalin and gabapentin, which are commonly used for NeP in both the OPD and inpatient departments of neuro-medicine at the aforementioned hospital. Patients attending the OPD and inpatient departments at SHMedical Center, Kottayam, were diagnosed with NeP based on the criteria established by the DN4 questionnaire, developed by the French NeP Pain Group. The DN4 questionnaire aids in distinguishing NeP from non-NeP and is a straightforward, objective tool that includes both an interview and a patient examination.

The efficacy of the drug was evaluated based on the decrease in neuropathic pain (NeP) using the DN4 scale, measured at specific intervals. The participants were randomly assigned to two groups. Group A received Gabapentin (300 mg) and Group B received Pregabalin (100 mg) as a single daily dose for a period of two months. Observations were made at baseline, one month, and two months.

The pain reduction in patients treated with pregabalin was 3.49 and gabapentin it was 2.15 at the end of 2 months. Hence pregabalin shown statistically significant pain reduction as compared to gabapentin at the end of 2 months of the study. Mohit Shukla *et al.* reported that results from a randomized trial support the superior efficacy of pregabalin compared to gabapentin, which is consistent with the findings of the present study.[3]

The results of the present study indicate a female preponderance in both treatment groups, which contrasts with other studies that have reported male predominance. This discrepancy could be due to geographical variations or the lower pain threshold and greater emotional lability of females.[7]

During the study, it was observed that ADR were more prevalent in the pregabalin treated group compared to the gabapentin group. Specifically, the occurrence of sedation was higher in group B, with 8 patients affected, compared to group A, which had 4 patients affected. Only a few patients who took pregabalin reported drowsiness, and just 1 out of 46 patients experienced dizziness and somnolence.

Various studies on the efficacy and safety of drugs for NeP have been conducted. Attal *et al.* found that pregabalin is more efficacious than gabapentin in patients with spinal cord injury experiencing chronic NeP.[8] A prospective, randomized, double-blind, placebo-controlled study conducted by Mishra *et al*. on 120 patients compared the efficacy of amitriptyline, gabapentin, and pregabalin in neuropathic cancer pain, demonstrating that all three drugs are effective in relieving cancer-related NeP.[9] Pregabalin showed a statistically and clinically significant morphine-sparing effect in relieving neuropathic cancer pain and symptoms compared to other anti-neuropathic drugs. Kiss *et al.* published an article summarizing, presenting, and evaluating national and international guidelines issued in the past five years.[10]

The most frequently recommended drugs in all guidelines are amitriptyline, duloxetine, gabapentin, and pregabalin. Pregabalin is the only drug recommended as a first-line treatment in all referenced guidelines. Markman *et al.* analyzed data from 18 randomized, double-blind, placebo-controlled trials of pregabalin in patients with NeP previously treated with gabapentin and concluded that pregabalin can successfully treat patients who are refractory, respond inadequately, or are intolerant to gabapentin.[11] Kopel *et al*. published a case report describing a patient successfully treated for PHN with pregabalin after failing gabapentin. Pregabalin is suggested as an effective first-line therapy for PHN and other forms of neuropathic and chronic pain.[12] Tong *et al.* completed a network meta-analysis of eight randomized controlled trials examining pregabalin, gabapentin, carbamazepine, and amitriptyline.[13] The analysis found that, based on average pain intensity after treatment, the efficacy order from highest to lowest was pregabalin, gabapentin, amitriptyline, carbamazepine, and placebo in patients with spinal cord injury-related NeP.

Limitations

The current study was conducted over a limited period of 6 months. Some dietary and lifestyle parameter changes might have influenced the results. There may also be concerns about compliance with the study drugs among some subjects. Another limitation of this study is the variability in individual pain perception due to the subjective nature of pain. Primary outcomes in terms of efficacy and adverse effects should be assessed by conducting long-term studies, using

different doses of pregabalin and gabapentin, and considering the recurrence of disease after discontinuation of medication, as recurrence is a major factor in current treatment options for neuropathic pain

5. Conclusion

In summary, the observational comparative study, conducted at a tertiary care center, evaluated the efficacy and safety of pregabalin and gabapentin in treating NeP. Our findings suggest that while pregabalin demonstrated superior efficacy compared to gabapentin, it also showed a higher incidence of ADR, particularly sedation. Conversely, gabapentin exhibited a lower incidence of ADR, rendering it a potentially safer option for certain patients. Furthermore, our results revealed a female preponderance in both treatment groups, contrasting with studies reporting male predominance. This incongruity may stem from geographical variations or differences in pain threshold and emotional response between genders. The subjective nature of pain and individual variances in pain perception present limitations to our study. Additionally, the study's duration limits our ability to ascertain the long-term effects and safety of these medications. Consequently, future research with larger patient cohorts and prolonged follow-up periods is imperative to offer more comprehensive insights into the sustained efficacy and safety of pregabalin and gabapentin for NeP management.

Compliance with ethical standards

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Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of ethical approval

The study was approved by the Institutional Ethics Committee

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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