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Assess the safety and efficacy of amitriptyline, pregabalin, and gabapentin for the management of neuropathic pain at Ayaan Institute of Medical Sciences

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ABSTRACT

Background: The most prevalent neuropathic pain disorders now being treated with tricyclic antidepressants (TCA), gabapentin, and pregabalin are considered first-line treatments for neuropathic pain. Many times, current neuropathic pain treatments are ineffective. Despite the availability of substantial information from numerous recommendations, there is still a significant degree of heterogeneity in treatment patterns. According to recent statistics from the Indian market, the guidelines actually advocate the use (selling) of medications including amitriptyline, pregabalin, and gabapentin.

Methods: This is a single-center, three-arm, prospective, comparative, open-label study conducted at Ayaan Institute of Medical Sciences and Research Center. X-rays, MRIs, and clinical examinations of the lumbosacral spine were used to diagnose 270 individuals with persistent lumbar radiculopathy. The patients were randomly assigned to three groups and given various treatments. Patients in Group A received 300 mg of gabapentine, patients in Group B received 75 mg of pregabaline, and patients in Group C received 10 mg of amitriptyline. Patients' global perception of change scale was used to gauge how much their overall condition had improved and how much pain they had relieved, as measured by a visual analogue scale. Every follow-up visit included a record of adverse medication responses.

Results: In three therapy groups, there was a notable improvement in pain alleviation for all patients. There were seventy patients overall in each group. Within Group A, there were 43 (61.4%) men and 28 (40%) women. Within Group B, there were 39 men (55.7%) and 31 women (44.28%). Within Group C, there were 41 men (58.5%) and 29 women (41.42%). The mean age of the patients in Group A was 53.21 ± 6.41 years. The mean age of the patients in group B was 55.14 ± 6.31 years. The mean age of the patients in group C was 56.31 ± 5.72. According to the p-value of 0.635, there was statistical non-significance.

Conclusions: In light of this, three groups have been demonstrated to be equally effective in reducing pain in NeP patients: amitriptyline, pregabaline, and gabapentine. Pregabalin has the same advantages as gabapentine and amitriptyline in terms of Numeric Pain Rating Scale (NPRS) scores.

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Keywords: Gabapentine, Amitriptyline, Pregabalin, Neuropathic pain

Introduction:

By employing a multimodal strategy, neuropathic pain therapy aims to enhance function, lessen discomfort, and enhance the patient's quality of life. These are some common strategies used to manage neuropathic pain. Neuropathic pain is frequently treated with tricyclic antidepressants (amitriptyline, nortriptyline), selective serotonin-norepinephrine reuptake inhibitors (SNRIs), such as duloxetine. Pregabalin and gabapentin are two common drugs used to treat neuropathic pain because they reduce pain signals and stabilize nerve cell membranes.

Techniques such as massage, stretching, and exercises can help improve mobility, reduce muscle tension, and alleviate pain associated with neuropathy. Adopting a healthy lifestyle, including regular exercise, maintaining a balanced diet, avoiding alcohol and tobacco, and getting adequate sleep, can help manage neuropathic pain symptoms. Some patients may find relief from neuropathic pain through therapies such as herbal supplements, biofeedback, or meditation. However, evidence supporting the effectiveness of these approaches is limited, and they should be used cautiously and under the guidance of a healthcare professional.

The main purpose of the drug gabapentin is to alleviate neuropathic pain, seizures, and restless legs syndrome. It belongs to the class of drugs called anticonvulsants. anti-epileptic drugs. Gabapentin works by affecting the way nerves send messages to the brain, thus reducing abnormal electrical activity in the brain that can lead to seizures or nerve pain. The FDA has approved gabapentin for the management of postherpetic neuralgia, or pain in the nerves following shingles, neuropathic pain resulting from diabetic neuropathy or spinal cord injury, and partial seizures. Common side effects of gabapentin may include dizziness, drowsiness, fatigue, headache, blurred vision, dry mouth, and weight gain. Some individuals may also experience mood changes, including anxiety or depression.

Amitriptyline is a medication belonging to the class of tricyclic antidepressants (TCAs). While it's primarily known as an antidepressant, it is also used to treat various other conditions, including neuropathic pain, migraines, and insomnia. Here are some key points about amitriptyline. The FDA has approved amitriptyline for the management of serious depressive illness. But it's also frequently used off-label for neuropathic pain conditions like fibromyalgia, diabetic neuropathy, and postherpetic neuralgia as well as for preventing migraines and managing certain sleep disorders.

Pregabalin is a drug used to treat generalized anxiety disorder, fibromyalgia, partial-onset seizures (as an adjunctive treatment), and neuropathic pain. It's classified as an anticonvulsant or anti-epileptic medication. Pregabalin inhibits the release of neurotransmitters involved in pain transmission by attaching to calcium channels in the central nervous system.

Material and Methods:

This single-center, three-arm, prospective, comparative trial is open-label and conducted at the Medicine OPD at Ayaan Institute of Medical Sciences and Research Center.

Inclusion criteria: - Patients in the age bracket of over 18 years old, regardless of gender. instances of spinal cord damage, post-herpetic neuroglia, fibromyalgia, low back pain, and diabetic peripheral neuropathy that have been diagnosed as neuropathic pain.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 1, 2024

Exclusion criteria: individuals with a background of TB, heart disease, liver disease, or renal sickness. ladies who are nursing or pregnant. individuals with impaired immune systems. Individuals whose known sensitivity to the study medications.

Study Design: Two hundred and ten patients, each with a diagnosis of neuropathic pain, were randomly assigned.
Group A patients received Gabapentine 300 mg
Group B patients received Pregabalin 75 mg
Group C patients received Amitriptyline 10 mg

Efficacy assessment
Numerical pain rating scales (NPRS) were used to measure pain at study onset (0 day), 15 days, and 30 days.

ADR Reporting: -
Using the ADR reporting form, adverse drug reactions that were noticed by the doctor or reported by the patient during the trial were recorded.

Statistical Analysis: -
An Excel document with the gathered data was created, along with a master chart. Qualitative data was expressed as percentages and values. The means and SDs were used to depict the quantitative data. An ANOVA was utilized to compare the mean pain on a numerical pain rating scale across the three groups. The Tukey Post Hoc test was employed to compare two groups at varied time periods as well. The three research groups' adverse medication responses were assessed using the chi square test. P-value was examined at the 5% significance level.

Results:

Table 1: Patient distribution based on gender

Gender	Group A	Group B	Group C
Male	43 (61.4 %)	40 (57.1 %)	42 (60 %)
Female	27 (38.5 %)	30 (42.85 %)	28 (40 %)
Total	70 (100 %)	70 (100%)	70 (100%)

There were ninety patients overall in each group. Within Group A, there were 43 (61.4%) men and 28 (40%) women. Within Group B, there were 39 men (55.7%) and 31 women (44.28%). Within Group C, there were 41 men (58.5%) and 29 women (41.42%).

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 1, 2024

Table 2: Patient distribution based on age group

Age-group	Group A	Group B	Group C
17-41	13	12	9
42-61	24	26	27
>60	33	32	34
Total	70 (100 %)	70 (100 %)	70 (100 %)
Mean SD	53.21 ± 6.41	55.14 ± 6.31	56.31 ± 5.72
p-value	0.635^{ns}		

The mean age of the patients in Group A was 53.21 ± 6.41 years. The mean age of the patients in group B was 55.14 ± 6.31 years. The mean age of the patients in group C was 56.31 ± 5.72. According to the p-value of 0.635, there was statistical non-significance.

Table 3: Clinical Diagnosis of the patients

Clinical Diagnosis	Group A	Group B	Group C
Diabetic peripheral neuropathy	13	16	14
Trigeminal neuralgia	9	8	9
Peripheral neuropathy	29	32	30
Post herpetic neuralgia	3	3	2
Central pain after stroke	7	6	8
Central neurogenic pain	2	2	1
Myelopathy pain	2	1	2
Reflex sympathetic dystrophy	1	1	2
Others	3	1	2

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 1, 2024

Table 4: Comparing the baseline, 15-day, and 30-day scores on the Numeric Pain Rating Scale (NPRS) for each of the three groups (ANOVA).

		Mean±SD	p-value
Baseline	**Group A**	7.84 ± 1.53	0.435[ns]
	Group B	7.96 ± 1.62	
	Group C	7.96 ± 1.62	
After 15 days	**Group A**	5.12 ± 1.42	0.061 [ns]
	Group B	5.23 ± 1.32	
	Group C	6.23 ± 1.43	
After 30 days	**Group A**	3.11 ± 1.04	0.001 [s]
	Group B	3.63 ± 1.02	
	Group C	4.25 ± 1.03	

(P<0.05 is statistically significant, S-significant, NS-not significant, NPRS-Numeric Pain Rating Scale)

At baseline, Group A, B, and C had NPRS scores of 7.84±1.53, 7.96±1.62, and 7.92±1.62, respectively. With a p-value of 0.435, the findings could not be considered statistically significant. Following a 15-day period, Group A's mean±SD NPRS score was 5.12 ± 1.42, whereas Group B and Group C scored 5.23 ± 1.32 and 6.23 ± 1.43, respectively. There was no statistical significance in the data, as demonstrated by the p-value of 0.061. Group A had a mean±SD of 3.11 ± 1.04 after 30 days, while Group B and Group C had scores of 3.63 ± 1.02 and 4.25 ± 1.03, respectively, on the NPRS. There was a 0.001 statistically significant p-value found.

Table 5: Tukey Post Hoc Test comparison of NPRS scores in two groups at baseline, 15 days, and 30 days

		Mean± SD	p-value
Baseline	**Group A Vs Group B**	0.12	0.632[ns]
	Group A Vs Group C	0.11	0.538 [ns]
	Group B Vs Group C	0.23	0.502 [ns]
After 15 days	**Group A Vs Group B**	0.11	0.438 [ns]
	Group A Vs Group C	1.11	0.023 [s]
	Group B Vs Group C	1.00	0.481 [ns]
After 30 days	**Group A Vs Group B**	0.52	0.432 [ns]
	Group A Vs Group C	1.14	0.007 [s]
	Group B Vs Group C	0.62	0.004 [s]

(p<0.05 is statistically significant. S-significant. NS-not significant. NPRS-Numeric Pain Rating Scale)

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 1, 2024

Table 6: Comparison of the three groups' baseline and 30-day NPRS (Numeric Pain Rating Scale) score reduction percentages

Group	Mean reduction
Group A at baseline Vs Group A at 30 days	**4.61**
Group B at baseline Vs Group B at 30 days	**4.31**
Group C at baseline Vs Group C at 30 days	**3.46**

Table 7: Adverse Drug reaction in each of the three groups of patients

	Group A		**Group** B		**Group C**		**Chi-square**	**p-value**
	n	**%**	**n**	**%**	**n**	**%**		
Sedation	17	24.2	23	32.8	17	24.2	6.58	0.021
Dizziness	9	12.8	17	24.2	2	2.85	4.39	0.036
Constipation	0	00	0	00	6	8.5	8.58	0.000
Dry mouth	0	00	0	00	7	10.	11.39	0.000

In the current study, group B had a significantly greater incidence of dizziness than group A and group C, with 17 patients, or 24.2% and 12.8% and 2.85%, respectively [p=0.036]. Compared to group A (9 patients; 12.8%) and group C (17 patients; 24.2%), group B showed a significantly higher percentage of sedation—23 patients (32.8%) [P=0.021]. Constipation affected six patients (8.58%) in group C, which is a significantly greater percentage than the 0 patients (0%%) in groups A and B (p=0.000). The incidence of dry mouth was significantly higher than that of Groups A and B, which had 0 patients(0%), and Group C, which included 7 patients (11.39%) [p=0.000].

Discussion:

Although gabapentin does not directly interact with GABA receptors, certain research indicates that GABA, the brain's primary inhibitory neurotransmitter, may have its inhibitory effects enhanced indirectly by it. This modulation of GABAergic activity may contribute to gabapentin's anti-seizure effects. Gabapentin may also exert effects on neuroplasticity, influencing the adaptive changes that occur in the nervous system in response to injury or disease. By modulating synaptic transmission and neuronal excitability, gabapentin may help normalize aberrant neural signaling associated with conditions such as neuropathic pain.

Amitriptyline works by blocking the reuptake of neurotransmitters such as serotonin and norepinephrine in the brain, leading to increased levels of these neurotransmitters. This action is thought to contribute to its antidepressant effects as well as its ability to modulate pain perception. Amitriptyline frequently results in weight gain, constipation, dizziness, dry mouth,

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poor vision, and tiredness and urine retention as adverse effects. These side effects are often dose-dependent and may improve over time as the body adjusts to the medication

Pregabalin works by attaching itself to the central nervous system's voltage-gated calcium channel alpha2-delta subunit. This reduces the production of neurotransmitters such substance P, norepinephrine, and glutamate that are involved in the transmission of pain signals. Side effects of pregabalin might include weight gain, impaired vision, dry mouth, drowsiness, and dizziness and edema (swelling). These side effects are usually mild to moderate in severity and may improve over time as the body adjusts to the medication

Conclusion:

In light of this, three groups have been shown to be equally effective in alleviating pain in NeP: gabapentine, pregabaline, and amitriptyline. When it comes to Numeric Pain Rating Scale (NPRS) scores, Pregabalin outperforms Amitriptyline and Gabapentine. When treating patients, it's crucial to remember that amitriptyline is more affordable than pregabalin.

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ISSN: 0975-3583,0976-2833 VOL15, ISSUE 1, 2024

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