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ORIGINAL ARTICLE

Comparative Study to Evaluate Efficacy and Safety for Management of Neuropathic Pain with Gabapentin, Pregabalin, and Amitriptyline

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ABSTRACT

Background: Current treatments for neuropathic pain (NeP) are tricyclic antidepressants (TCA), such as pregabalin and gabapentin are first-line drugs for the management of NeP complaints. Current treatment for the management of neuropathic pain is often sub-standard.

Methods: It's a three-arm, prospective, comparative, open-label study. A total of 270 patients with persistent lumbar radiculopathy were randomized into three groups based on clinical examination, symptoms, X-rays, and MRI scans of the lumbosacral spine. Patients in Groups A and B got Gabapentine 300 mg, Pregabaline 75 mg, and Amitriptyline 75 mg, respectively.

Results: The mean NPRS score at two months was 3.72 ± 2.65 for Group A, 3.63 ± 2.65 for Group B, and 5.21 ± 2.65 for Group C. The F-value was 6.63, and the p-value was 0.001, which was statistically significant. As compared to the other two treatment groups, the subjects in Group 3 saw a significant difference. The adverse effects reported occurrence of dizziness was significantly more in group B with 21 patients (23.33%) as compared to group A with 11 patients (12.22%) and group C with 4 patients (4.44%), [p=0.041). The sedation occurred in 28 patients of group B (31.11%), which was significantly more than group A i,e, in 23 patients (25.55%) and group C, i.e., 22 patients (24.44%), [P=0.036].

Conclusions: In patients with NeP Thus, in conclusion, three groups Gabapentine, Pregabaline, and Amitriptyline, are equally efficacious in relieving pain in NeP. Pregabalin has advantages in terms of Numeric pain rating scale (NPRS) score over the Gabapentine and Amitriptyline. Gabapentine has fewer reported adverse effects and hence better patient compliance on long-term use.

Keywords: Gabapentine, Amitriptyline, Pregabalin, Neuropathic pain

INTRODUCTION

Neuropathic pain is triggered by an injury or infection of the somatosensory system, comprising peripheral fibers (Aβ, Aδ, and C strands) and central neurons and influences 7–10% of the population. [1] The burden of ongoing neuropathic pain is related to the complexity of neuropathic side effects, helpless results, and troublesome treatment choices. [2] Importantly, personal satisfaction is impeded in patients with neuropathic torment attributable to expanded medication solutions and visits to medical care suppliers, just as the dismalness from the actual aggravation and the inducing infection.

Pregabalin is a well-established anticonvulsant and pain-relieving drug. Pregabalin is the principal medication to get supported marking from the Food and Drug Association (FDA) to treat neuropathic agony and post-herpetic neuralgia. [6] Preclinical and clinical investigations have shown the adequacy of pregabalin in dealing with neuropathic torment. [7] Clinical investigations have additionally shown the viability and portion subordinate impacts of pregabalin either as monotherapy or in blend with analgesics in calming torment and related side effects. The significant benefit of pregabalin is its relative dependability, simple use, and high resistance in patients with neuropathic torment. [8]

Gabapentin (GBP) is usually utilized for post-herpetic neuralgia (PHN). The instrument of activity for GBP identifies with its capacity to tie with high-partiality to the alpha-2-delta subunit of voltage-gated calcium channels situated all through the fringe and focal sensory system; along these lines, it alters the arrival of synapses and diminishes the edginess of nerve cells. [9] It is this component of activity that might deliver the pain-relieving result in patients encountering neuropathic torment. [10]

Amitriptyline is a tricyclic stimulant that is broadly used to treat persistent neuropathic torment. The instrument of activity of amitriptyline in the treatment of neuropathic torment stays dubious, despite the fact that it is known to hinder both serotonin and noradrenaline reuptake. [11] The instrument will probably vary from that in sadness since the absence of pain with antidepressants is frequently accomplished at lower measurements than the beginning of any stimulant impact. [12, 13]

MATERIAL AND METHODS

This is a comparative, prospective, open-label, three-arm study carried out at the Neurology OPD in King Khalid General Hospital, Majmaah, Hawtat Sudair general hospital, Zulfi general hospital and Kingdome hospital Riyadh, Saudi Arabia from January 2020 to December 2020.

Inclusion criteria: - Patients of either sex with the age group of more than 18 years. Diagnosed cases of neuropathic pain due to diabetic peripheral neuropathy, low back pain, post-herpetic neuroglia, fibromyalgia, and spinal cord injury.

Exclusion criteria: Patients with a history of liver diseases, cardiac illness, renal disease, diabetes, tuberculosis. Pregnant and lactating women. Patients who are immunocompromised. Patients with known hypersensitivity to the study drugs.

Study Design: A total of 300 patients were diagnosed with neuropathic pain and were randomized into three groups.

Group A patients received Gabapentine 300 mg

Group B patients received Pregabalin 75 mg
Group C patients received Amitriptyline 10 mg

Efficacy assessment: Pain assessment was done using a numeric pain rating scale (NPRS) at the start of the study (0 days), 15 days, and 30 days.

ADR Reporting: Adverse drug reaction reported by the patient or observed by the clinician during the study was reported using ADR reporting form.

Statistical Analysis: The collected data was compiled in an EXCEL sheet, and a Master chart was prepared. For analysis of this data, SPSS (Statistical Package for Social Sciences) software version 20th was used. Qualitative data were represented in form values and percentages. Quantitative was described in the form of mean and SD. For comparison between three groups, mean pain on the numerical pain rating scale, ANOVA was used. Also, for comparison between two groups at different time intervals Tukey Post Hoc test was used. A Chi-square test was used to evaluate adverse drug reactions in all three study groups. p-value was checked at a 5 % level of significance

RESULTS

In each group total of 90 patients were there. In Group A: 42 (60 %) were males, and 28 (40 %) were females. In Group B: 39 were males (55.7 %), and 31 (44.28 %) were females. In Group C: 41 were males (58.5 %) and 29 (41.42 %) were females. (Table 1)

Table 1: Distribution of patients according to Gender

Gender	Group A	Group B	Group C
Male	42 (60 %)	39 (55.7 %)	41 (58.5 %)
Female	28 (40 %)	31 (44.28 %)	29 (41.42 %)
Total	70 (100 %)	70 (100%)	70 (100%)

Table 2: Distribution of Patients according to Age group

Age-group	Group A	Group B	Group C
18-40	16	14	11
41-60	23	27	26
>61	31	29	33
Total	70 (100 %)	70 (100 %)	70 (100 %)
Mean SD	54.38 ± 6.38	53.24 ± 6.48	54.48 ± 6.33
F-value	0.326		
p-value	0.635^{ns}		

In Group A: the Mean age of patients was 54.38 ± 6.38 years. In group B: Mean age of patients 53.24 ± 6.48 years. In group C: The mean age of patients was 54.48 ± 6.33. The F-value was 0.326 and the p-value 0.635, which was statistically not significant. (Table 2) In able 3, Peripheral neuropathy was the most common clinical diagnosis of pain among patients in group A, B and C.

Table 3: Clinical Diagnosis of the patients

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

Table 4: Comparison of Numeric pain rating scale (NPRS) score in all three groups at baseline after 15 days and after 30 days (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, the Mean±SD of NPRS score in Group A was 7.84±1.53 in Group B and Group C were 7.96 ± 1.62 and 7.96 ± 1.62 respectively and p-value of 0.435 which was not statistically significant. At 15 days, the Mean±SD of NPRS score in Group A was 5.12 ± 1.42, in Group B and Group C were 5.23±1.32 and 6.23±1.43 respectively and p-value of 0.061 which was not statistically significant. At 30 days, the Mean±SD of NPRS score in Group A was 3.11 ± 1.04, in Group B and Group C were 3.63 ± 1.02 and 4.25±1.03 respectively and p-value of 0.001 which was statistically significant. (Table 4)

At baseline, the Mean±SD of NPRS score of Group A versus Group B was 0.12 and Group B versus Group C were 0.23 and p-value of 0.538 which was not statistically significant. At 15 days, the Mean±SD of NPRS score of Group A versus Group C 1.11 and p-value of 0.023 which was statistically significant. At 30 days, the Mean±SD of NPRS score in Group A versus Group C 0.62, in Group B and Group C were 0.62 and p-value of 0.004 which was statistically significant. (Table 5 and 6)

Table 5: Comparison of NPRS score in two groups at baseline, 15 days, and 30 days [Tukey Post Hoc Test]

		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 S Vs Group C	1.11	0.023^{s}
	Group BS 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 BS Vs Group C	0.62	0.004^{s}

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

Table 6: Comparison of percent reduction of NPRS (Numeric Pain Rating Scale) score baseline VS after 30 days in all three groups

Group	Mean reduction
Group A at baseline Vs Group A at 30 days	4.73
Group B at baseline Vs Group B at 30 days	4.33
Group C at baseline Vs Group C at 30 days	3.48

Table 7: Adverse drug reaction in patients in all three groups

	Group A		Group B		Group C		Chi-square	p-value
	N	%	n	%	n	%		
Dizziness	9	12.8	17	24.2	2	2.85	4.39	0.036
Sedation	17	24.2	23	32.8	17	24.2	6.58	0.021
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 present study, the occurrence of dizziness was significantly more in group B with 17 patients (24.2%) as compared to group A with nine patients (12.8%) and group C with two patients (2.85%), [p=0.036). The sedation occurred in 23 patients of group B (32.8%), which was significantly more than group A i,e, in 9 patients (12.8%) and group C, i.e., 17 patients (24.2%), [P=0.021]. The occurrence of constipation was seen in 6 patients of group C (8.58%), which was significantly more than in Group A and B with 0 patients (0%) [p=0.000]. The occurrence of dryness of mouth was significantly more in group C with seven patients (11.39%) as compared to that of Group A and B with 0 patients (0%) [p=0.000].(Table 7)

DISCUSSION

Back pain, diabetes (painful diabetic neuropathy), post-surgical pain, HIV/AIDS, and herpes zoster (post-herpetic neuralgia) are all common causes of pain, but they can also be caused by a range of other diseases or traumas. [13] Paraesthesia, searing or shooting pains, changed sensation (numbness, allodynia, or hyperalgesia), and locally altered autonomic function are all clinical features. [14-17]

After two months, there was a significant reduction in mean pain scores in all three groups in this study. The mean pain score decreased dramatically in gabapentin-treated patients, from 8.31 to 3.72. This result was comparable to that of Gilron et al. investigations [18]. Patients on pregabalin experienced a significant reduction in pain, dropping from 8.42 to 3.63. This finding was comparable to that of Holbech et al. [19] The mean pain score in patients receiving amitriptyline was lowered from 8.29 to 5.21. No trial showed the same results as amitriptyline in reducing chronic lumbar radiculopathy pain as this one did.

There was no significant difference in pain scores comparison between Group A and Group B with a mean difference of 0.09 [p-value-0.523], a significant difference in pain scores comparison between Group A and Group C with a mean difference of 1.49 [p-value of 0.006], and significant difference in pain scores comparison between Group A and Group D with a mean difference of 1.49 [p-value-0.006].

During the study, it was found that the adverse drug reactions were found more in pregabalin and amitriptyline treated groups as compared to the Gabapentin group. In the present study, the occurrence of dizziness was significantly more in group B with 17 patients (24.2%) as compared to group A with nine patients (12.8%) and group C with two patients (2.85%), [p=0.036). The sedation occurred in 23 patients of group B (32.8%), which was significantly more than group A i, e, in 9 patients (12.8%) and group C, i.e., 17 patients (24.2%), [P=0.021]. The occurrence of constipation was seen in 6 patients of group C (8.58%), which was significantly more than in Group A and B with 0 patients (0%) [p=0.000]. The occurrence of dryness of mouth was significantly more in group C with seven patients (11.39%) as compared to that of Group A and B with 0 patients (0%) [p=0.000].

CONCLUSION

As a result, three sets of drugs, Gabapentine, Pregabaline, and amitriptyline, are equally effective in reducing pain in NeP patients. Pregabalin outperforms Gabapentine and Amitriptyline in terms of the Numeric Pain Rating Scale (NPRS) score. Gabapentine has fewer reported side effects, resulting in higher long-term patient compliance. Amitriptyline is less expensive than pregabalin, which is a crucial consideration when treating patients.

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