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Original Article

Comparison of amitriptyline and carbamazepine effectiveness in the treatment of postherpetic neuralgia

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Abstract

Intoduction Postherpetic neuralgia (PHN), a chronic and debilitating pain condition, is caused by acute herpes zoster lesions. It affects the patient's daily activities, sleep, social well-being, and quality of life (QoL). The mainstays of its treatment are systemic medications such as tricyclic antidepressants and antiepileptics.

Objective To determine the effectiveness of carbamazepine and amitriptyline in the management of PHN.

Methods In this study, amitriptyline and carbamazepine were given to PHN patients who met the inclusion criteria at Khyber Teaching Hospital in Peshawar. Patients were separated into two groups after written informed consent, a physical examination, and relevant investigations. Group A received 25mg amitriptyline at night time and Group B received 200 mg carbamazepine two times daily for eight weeks. The severity of the pain and the effectiveness of the therapy was assessed using a visual analogue scale (VAS score). SPSS 23 was used to analyzed the data.

Results There was no significant difference statistically in the age of patients (p=0.41), gender (p=0.40), duration of PHN (P=0.40), and pre-treatment VAS score (p=0.11). The effectiveness (good to excellent) of amitriptyline and carbamazepine was 86% and 80% respectively (p=0.66). Upon intragroup comparison, amitriptyline (p<0.001) and carbamazepine (p<0.02) were statistically significant in the reduction in PHN.

Conclusion Amitriptyline and carbamazepine reduce PHN-associated pain and discomfort. Both medications improve PHN patients' QoL, well-being, and physical functioning.

Key words
Postherpetic neuralgia, Herpes zoster, visual analog scale, carbamazepine, amitriptyline.

Introduction

After the herpes zoster lesions have healed, a chronic neuropathic pain condition known as post-herpetic neuralgia (PHN) develops.[1-3] Herpes zoster is caused by the varicella-zoster virus (VZV) reactivating in a sensory ganglion (shingles). It develops as an excruciatingly painful vesicular rash that lasts a few weeks.[4] After the rash has healed, intense pain is the most frequent side effect of HZ, which affects 18 to 41% of these patients.[1,5] Older age, diabetes, SLE, trauma, and immunosuppression enhance the incidence of PHN.[6,7] Topical therapy (capsaicin and lidocaine) and systemic

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therapy (analgesics, antiepileptics, antidepressants, antipsychotics, anti-dementia medications, and magnesium sulphate) are the principal pharmacological treatments for post-herpetic neuralgia.[1,8-10] Using zoster vaccines can lower PHN.[11] Amitriptyline is a tricyclic antidepressant (TCA) often used in PHN patients.[1] Its pain-relieving effects in post-herpetic neuralgia are unrelated to its serotoninergic actions and distinct from its effects on depression.[12] Carbamazepine is an antiepileptic medicine used to treat individuals with acute and chronic pain, including trigeminal neuralgia.[13,14]

Pakistan struggles to treat postherpetic neuralgia. PHN doctors and patients have many constraints. Amitriptyline and carbamazepine haven't been compared locally. This study will compare the effectiveness of various medications in PHN for future investigations. This study will update PHN management guidelines for local health authorities.

Patients and Methods

This comparative study of clinical efficacy was carried out in the Department of Dermatology, Khyber Teaching Hospital, Peshawar with amitriptyline and carbamazepine administered to PHN patients during the period from 25th June 2022 to 24th October 202. Inclusion criteria were as follows: (i) Patients with pain on the dermatomal distribution, who have experienced herpes zoster in the last three months (ii) both genders were included (iii) patients aged ≥20 years. PHN patients with cardiac disease, urinary obstructive disorders those on immunosuppressive therapy or who had a history of taking amitriptyline or carbamazepine in the last month were excluded.

The study included 100 patients randomized into two groups of 50 patients to receive 25 mg amitriptyline daily at night or 200 mg carbamazepine twice daily for eight weeks. The two drugs were allocated upon blocked randomization. It is important to note that there were no analgesics provided to study patients during the period of study. Each patient's written informed consent was obtained at the time of enrollment. Prior to the start of the treatment, a general physical, neurologic, and other systematic examinations were performed. Prior to beginning treatment, the study protocol was approved by the institutional review board (IREB).

The total study period was 04 months and patients were assessed on monthly basis to observe the effectiveness of the treatment. A VAS scale was used to assess the severity of pain with 100 representing severe intolerable pain, a score more than 70 suggesting severe pain, and a score of 30 indicating clinically significant pain **(Figure 1)**. Complete pain relief was defined as no pain or occasionally nonpainful sensations (VAS<10), very good pain relief was defined as occasional pains primarily of trigger origin and relief was satisfactory to the patient (VAS<30 but >10), fair pain relief was defined as improved but unsatisfactory to the patient (VAS<50 but >30), and no response was defined as VAS>70.

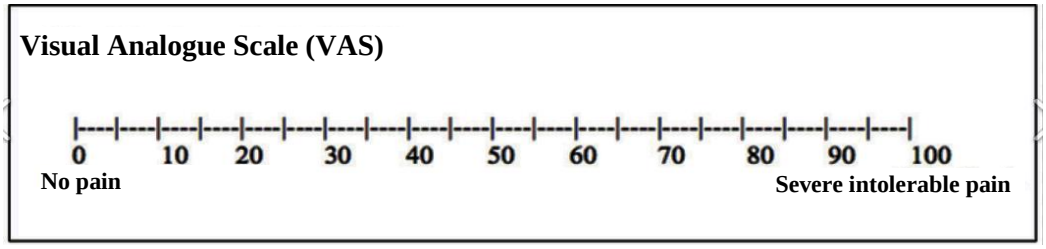

Figure 1 Visual analog scale (VAS) in PHN.

Remissions were classified as complete when the patient was pain-free and taking no medication, and partial when minor discomfort only occasionally required treatment.

The SPSS version 22 was used to analyze the data. The frequencies and percentages were computed for categorical variables, the mean and standard deviation were computed for numerical variables. The student t-test was used to compare numerical variables, while the chi-square test was used to compare categorical variables. A p-value<0.05 was considered statistically significant.

Results

A total of 100 patients were enrolled in this study (50 PHN in each group). Male patients made up the majority in Group A (the amitriptyline group) with 26 patients (52%), whereas male patients made up the majority in Group B (the carbamazepine group) as well, with 30 patients (60%) overall. The visual analogue scale score (p=0.11), the mean age (p=0.41), and the duration of PHN (P=0.40) were not significantly different between the two groups **(Table 1)**.

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Thus, the overall effectiveness (good-excellent) in amitriptyline carbamazepine groups was 86% and 80% respectively with a statistically insignificant difference (p=0.66) **(Table 2)**. Between pre- and post-treatment, there was a statistically significant difference in VAS in both of these groups (p<0.001 for the amitriptyline group and p<0.02 for the carbamazepine group) **(Table 3)**.

Discussion

The unilateral rash of Herpes zoster is typically limited to the distribution of a single dermatome and is caused by latent varicella-zoster virus (VZV) reactivation, which is acquired through primary varicella zoster infection.[15,16]

Table 1 Basic parameters of patients (n=100).

Parameters	*Amitriptyline group (n=50)*	*Carbamazepine group (n=50)*	*p-value*
Gender	Male 26 (52%) Female 24 (48%)	Male 30 (60%) Female 20 (40%)	P =0.40
Age (in years)	48.39 ± 13.71 SD	67.51 ± 1.66218	P =0.41
Duration of PHN	3.7800± 1.40393	4.8200 ± 11.54 SD	P =0.40
The VAS score	65.66 ± 17.87	59.56 ± 19.78	0.11

Table 2 Post treatment parameters (n=100).

Parameters	*Amitriptyline group (n=50)*		*Carbamazepine group (n=50)*		*p-value*
VAS2	30.42 ± 21.64		34.9800 ± 23.26		0.31
Efficacy	Excellent 32(64%)	Good-excellent 43 (86%)	Very good 28(56%)	Good-excellent 38 (80%)	P =0.66
	Good 11 (22%)		Good 12(24%)		
	No response 7 (14%)		No response 10(20%)		

Table 3 Intra-group comparison of V.A.S (pre- and post-therapy) (n=100)**.**

Parameters	*Pre-treatment VAS*	*Post-treatment VAS*	*p-value*
Amitriptyline Group (n=50)	65.66 ± 17.87	30.42 ± 21.64	P =0.001
Carbamazepine group (n=50)	59.56 ± 19.78	34.98 ± 23.26	P =0.02

Approximately 10-15% of HZ patients experience PHN.[13,17] Nearly half of individuals with PHN recover within three months, but about 22% of these people continue to feel pain after a year.[18] Refractory and ongoing neuropathic pain has been associated with PHN. Various types of pain, including continuous, deep, burning, agonizing, and lancinating pain, paroxysmal pain, hyperalgesia (painful stimuli are more painful than predicted), and allodynia (pain often related to non-painful stimuli) can be experienced by PHN patients.[19]

Capsaicin and lidocaine are examples of topical treatments used in the pharmacological therapy of PHN. Systemic therapies include various options such as tricyclic antidepressants (amitriptyline), and antiepileptic drugs (carbamazepine). This study compared the therapeutic efficacy of amitriptyline and carbamazepine in treating PHN.

The VAS score was employed in our study to assess the effectiveness of therapy for post-herpetic neuralgia. The clinical efficacy of therapeutic agents was assessed using the same scale across numerous trials on the treatment of PHN.[20-22]

Amitriptyline had an overall good to excellent efficacy of 86% in our study, compared to carbamazepine's 80% (P=0.66). Amitriptyline was shown to be highly successful in relieving PHN pain in 81% of instances, according to Max MB *et al.* study, which is comparable with the findings of our investigation.[23]

In 64% of the cases in our study, amitriptyline was found to be excellently effective. According to Watson CP *et al.* study, 66.67% of their patients with PHN experienced good to excellent alleviation[24] which is similar to our study's findings. At the end of the first month of treatment, Achar A *et al.* found that 64% of their patients had a PHN improvement of at least 50%.[25] Amitriptyline was found to significantly reduce PHN in 38% of instances and to somewhat reduce it in 53% of cases, according to Rowbotham MC *et al*.[26]

Both trigeminal neuralgia and postherpetic neuralgia were successfully treated with carbamazepine, according to Abhinaya LM *et al*.[27] In their systematic review, Wiffen PJ *et al.* found that carbamazepine, at any dose, reduced the incidence of both acute and chronic neuropathic pain, including PHN, by 70%, as compared to 12% in the placebo group.[12]

There hasn't been a recent comparison research on the effectiveness of amitriptyline and carbamazepine for treating PHN. This study serves as the foundation for that approach because both of these therapeutic drugs significantly decreased VAS scores (amitriptyline, $p<0.001$, and carbamazepine, $p<0.02$) without significantly differing in their effectiveness in treating PHN (P=0.66).

Conclusion

Postherpetic neuralgia is an important and devastating clinical condition secondary to herpes zoster. Amitriptyline or carbamazepine are both effective pharmacological treatments for PHN, and both have a positive impact on patients' general health, functioning, and quality of life. Either of these agents may be prescribed in patients with PHN depending on the clinician's clinical expertise, the patients' co-morbid illnesses, and the drugs' tolerability.

Recommendations

Multiple centered open labeled large sample-sized studies are recommended to evaluate the efficacy of these agents in the PHN, particularly at the national level and generally at the

international level are recommended.

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