

## **Comparative study of clinical efficacy with amitriptyline, pregabalin, and amitriptyline plus pregabalin combination in postherpetic neuralgia**

Sir,

The most common and most intractable sequel of herpes zoster is postherpetic neuralgia (PHN). There is no universally accepted definition of postherpetic neuralgia. The duration of PHN was evaluated by using two definitions: Pain that persisted after healing of rash and pain that persisted for more than 30 days from the time of enrollment.<sup>[1]</sup> Some authors also described PHN as pain persisting for at least three months after healing of rash.<sup>[2]</sup> The overall incidence of PHN is 8 to 15%, using the first two definitions. Patients of age 50 years or older had a 14.7-fold higher prevalence of pain, 30 days after onset of rash, than patients younger than 50 years of age.<sup>[3]</sup> PHN is thought to be due to nerve damage caused by the varicella virus.

Many patients, however, are refractory to these treatments because of inadequate pain relief or intolerable side effects. The objective of the present study is to see the comparative clinical efficacy with monotherapy, either with amitriptyline or pregabalin and combined therapy with amitriptyline plus pregabalin.

A randomized comparative study of the clinical efficacy in PHN patients with the following treatment—amitriptyline, pregabalin, and amitriptyline plus pregabalin combination was carried

out in the Midnapore Medical College and Hospital. Inclusion criteria were as follows: (1) PHN of more than one month duration (2) pain at least moderately severe (disagreeable, unpleasant, uncomfortable) (3) patients aged 40 years or older and not pregnant. Patients with history of serious illness were excluded.

Patients were randomized into three groups comprising of 15 patients per group. Amitriptyline 25 mg was given once daily at night and pregabalin 75 mg twice daily. For the combined therapy group, both the medicines were given at the same doses.

Total period of study was eight weeks and the study was conducted from April 2008 to September 2008. The patients were reviewed after the second, fourth, and eighth weeks, to see the degree of improvement of pain perception and to check for any adverse reactions. Pain relief was assessed with a percentage rating, with patients being asked to estimate on a scale of 0 to 100%, how much better they were.

We considered it a satisfactory improvement if there was >50% improvement of pain perception after four weeks and >75% improvement after eight weeks of treatment. The differences of clinical efficacy of the three different groups were compared using the chi-square test.

A total of 45 patients with PHN were included in the study. They were randomized into three groups (i) amitriptyline (n = 15), (ii) pregabalin (n = 15), and (iii) amitriptyline plus pregabalin (n = 15).

Thirty males (66.7%) and 15 females (33.3%) participated in the present study.

Statistically, no significant differences in satisfactory improvement were seen in any group at the end of four weeks ( $\chi^2 = 1.56$  and  $P$  value = >05). At the end of eight weeks, statistically significant satisfactory improvement (>75%) in pain perception was noticed in the combined group, with amitriptyline plus pregabalin, compared to the monotherapy groups, with either amitriptyline alone or only pregabalin ( $\chi^2 = 11.23$  and  $P$  value = <0.05) [Table 1]

Dryness of the mouth was the most common adverse reaction in the amitriptyline group (7/15), drowsiness and dizziness in the pregabalin group (4/15 in each) and dizziness and dryness in combined group (5/15 in each). Intensity of these adverse reactions was mild-

**Table 1: Improvement of phn after eight weeks of combined and monotherapy**

Therapy group	≥75% improvement (%)	≤75% improvement (%)
Amitriptyline	2 (13.4)	13 (86.6)
Pregabalin	8 (53.3)	7(46.7)
Amitriptyline plus pregabalin	11 (73.3)	4 (26.7)

$\chi^2 = 11.23$   $P$  value = <0.05

to-moderate and no patient stopped treatment due to adverse reactions.

The present study demonstrates that the combination therapy is more efficacious in relieving pain, compared to monotherapy, in patients with PHN, at the end of eight weeks of treatment.

Various studies with amitriptyline, nortriptyline or desipramine to placebo showed significant benefit when associated with tricyclic antidepressant therapy.<sup>[4]</sup> Two parallel group placebo-controlled trials in which the analgesic efficacy of pregabalin was investigated, showed superiority over placebo.<sup>[5]</sup> However, there is no study that compares combination therapy with monotherapy like the present study.

The present study shows that combination therapy reduces the perception of pain sensation significantly compared to monotherapy. The side effects of the combination therapy are almost the same as for monotherapy. Therefore, we concluded that in a PHN patient, a combination therapy with amitriptyline or pregabalin, may be more beneficial than monotherapy, after completion of eight weeks of treatment.

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