Original Article

DOI: 10.17354/ijss/2016/53

Comparative Study of Gabapentin in Combination with Valacyclovir and Valacyclovir Alone in Herpes Zoster

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Abstract

Background: In herpes zoster, during the acute illness, the rash is often accompanied by intense pain in the majority of patients which can interfere with sleep and routine daily activities affecting the quality of life. Many studies have shown that gabapentin administered in acute phase reduces the incidence of post-herpetic neuralgia, but the evidence of its efficacy and safety in the acute phase is scarce.

Objective: The aim of the present study was to compare and evaluate the effects of adding gabapentin with valacyclovir and valacyclovir alone in the acute phase of herpes zoster.

Materials and Methods: A total of 40 patients were enrolled in the study and were divided into two groups. Group 1 (n = 20): Gabapentin given in successive escalating doses for 28 days + valacyclovir 1 g tds for 7 days. Group 2 (n = 20): Valacyclovir 1 g tds for 7 days. Efficacy of the therapy was assessed by the time needed for healing of rash and improvement in pain intensity which was evaluated by using a 10 cm visual analog scale (VAS) at each visit, i.e., on the day of enrollment (0 day), 3, 7, 14, 21, and 28 days. A checklist was used to enquire about adverse effects at each visit. The results were analyzed using Student's *t*-test (paired and unpaired).

Result: The herpetic rash healed in about 5-8 days in both the groups. Improvement in VAS score was significantly higher in Group 1 at each visit except on days 3 and 7.

Conclusion: Gabapentin in combination with valacyclovir is safe and effective for the management of herpes zoster and the pain associated with it.

Key words: Gabapentin, Herpes zoster, Valacyclovir

INTRODUCTION

Herpes zoster results from reactivation of the varicella-zoster virus, which remains latent in the sensory ganglia after primary infection.[1] Unlike varicella (chickenpox), herpes zoster is a sporadic disease with an estimated lifetime incidence of 10-20%. The incidence of herpes zoster increases sharply with advancing age, roughly doubling in each decade past the age of 50 years. During the acute illness, the rash is often accompanied by intense pain in the majority of patients that can be described as burning, deeply aching, tearing, electric shock-like or lancinating which can interfere with sleep and routine daily activities affecting the quality of life.[2]

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www.ijss-sn.com

Month of Submission : 12-2015
Month of Peer Review : 01-2016
Month of Acceptance : 01-2016
Month of Publishing : 02-2016

Though in majority of cases, the zoster-associated pain resolves spontaneously with time, but as it is also the chief complaint for which patient seeks medical care, the pain management has important status in acute condition. Therefore, the treatment of herpes zoster should include drugs for managing pain in addition to controlling the acute viral infection. Antiviral agents, oral corticosteroids, and

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adjunctive individualized pain management modalities are used to achieve these objectives.[3,4]

Evidence-based strategies for the management of acute herpes zoster include the use of antiviral agents (acyclovir, famciclovir, and valacyclovir) with or without analgesics. These are effective in reducing the severity and duration of acute illness when given within 72 h of rash onset. In addition to this, some studies have also demonstrated that their use in immunocompetent patients is associated with significant improvements in the severity of the acute pain of herpes zoster.[5,6]

Numerous treatment algorithms list trials of common analgesics such as ibuprofen or acetaminophen, topical treatment such as capsaicin cream or lidocaine patches, tricyclic antidepressants, or other antidepressants (e.g. amitriptyline hydrochloride, desipramine hydrochloride), and anticonvulsants (e.g., carbamazepine, gabapentin, lamotrigine) as first-line therapy for neuropathic pain.[7-9] These medications may be used alone or in combination. The choice of medication should be directed toward the type of painful symptom described.

Gabapentin has been proposed as one the of several first-line treatments for neuropathic pain, which is structurally related to gamma-aminobutyric acid, a pain-modulating neurotransmitter. Numerous studies have shown that gabapentin administered in acute phase reduces the incidence of post-herpetic neuralgia (PHN), but the evidence of its efficacy and safety in the acute phase is scarce. Therefore, the present study was planned with the objectives to compare and evaluate the effects of adding gabapentin with valacyclovir and valacyclovir alone in the acute phase.

MATERIALS AND METHODS

This was a prospective observational comparative study for the evaluation of efficacy and safety of gabapentin in combination with valacyclovir and valacyclovir alone for acute herpes zoster. The patients enrolled for the study were adults aged 50 years or more, presenting with signs and symptoms suggestive of localized herpes zoster within 72 h of the onset of rash accompanied with at least moderate pain.

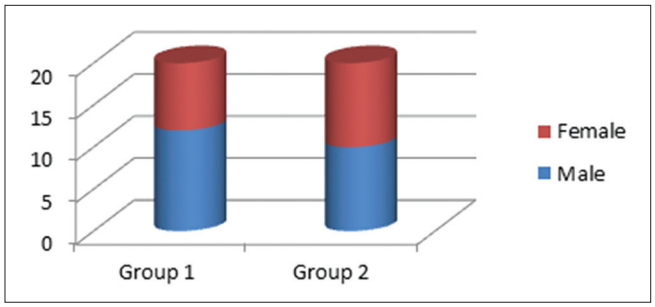

Figure 1: Sex distribution

The exclusion criteria for the study were herpes zoster ophthalmicus, pregnancy, lactation, and patients who had received cytotoxic or immunosuppressive drug therapy within the 3 months before presentation. Patients who had received topical or systemic antiviral medications or immunomodulatory agents for varicella zoster virus infections, for example, interferon or capsaicin, within the previous 4 weeks and those receiving tricyclic antidepressant drugs or other pain medication immediately before presentation were also excluded.

A total of 40 patients fulfilling the inclusion criteria were enrolled in the study and were divided into two groups according to the medications they received.

Group 1 ($n = 20$): Gabapentin given in successive escalating doses starting from 300 mg HS for first 3 days, 300 mg BD for next 3 days, and finally 300 mg tds which were continued till 28th day of the study + valacyclovir 1 g 3 times daily for 7 days.

Group 2 ($n = 20$): Valacyclovir 1 g 3 times daily for 7 days.

Main outcome measures: Resolution of zoster-associated pain, rash healing, and safety of therapy.

Efficacy of the therapy was assessed by the time needed for healing of rash and improvement in pain intensity. Pain was evaluated by using a 10 cm visual analog scale (VAS) with the end points of 0 cm rated as no pain and the points of 10 cm as intolerable pain at each visit, i.e., on the day of enrollment (0 day), 3, 7, 14, 21, and 28 days.

A checklist was used to enquire about adverse effects at each visit by the patients.

Statistical Analysis

The results were analyzed using Student's *t*-test (paired and unpaired) and were expressed as mean ± standard error.

RESULTS

Out of the 40 patients enrolled in the study, 22 were male and 18 were female (Figure 1). Demographic parameters and other baseline characteristics including age, sex, age, severity of rash, pain, and VAS score were similar in both the groups and there was no significant difference in any parameter (Table 1).

The herpetic rash healed in about 5-8 days in both the groups. The average pain score was significantly reduced in both the groups after 28 days. Comparative analysis between the groups shows that improvement in pain score was more in Group 1 (Table 2). This difference was significant ($P < 0.05$) at all follow-up visits except for the first two visits, i.e. at 3 day and 7 day still the improvement was higher in Group 1 (Table 2).

Intragroup comparison shows that significant reduction in VAS score was seen after 7 days in Group 1 ($P < 0.05$) and it further improved and was maintained thereafter while in Group 2 significant reduction in VAS score ($P < 0.05$) was observed only after 14 days and was maintained thereafter (Figures 2 and 3).

Table 3 shows the adverse effects encountered in different groups during follow-up visits. Adverse effects were more common among the patients who received the combination treatment. Most common adverse effect reported was sedation and dizziness in Group 1, but these side effects were tolerable, and none of the patients withdrew from the study because of adverse effects. Moreover, these adverse effects reduced both in incidence and severity with the duration of the study. In Group 2, the only complaint reported by the patients was gastrointestinal side effects.

Table 1: Demographic profile and disease characteristics at baseline

Characteristics	Group 1 (*n*=20)	Group 2 (*n*=20)	*P* value
Age			
Mean±SD	57.35±5.79	60.1±7.03	NS
Sex			
Male	12	10	NS
Female	8	10	NS
SES			
High	1	0	NA
Middle	18	18	NS
Low	1	2	NS
Diet			
Veg	7	8	NS
Non-veg	13	12	NS
Area of lesion			
Thoracic	6	6	NS
Lumbosacral	7	6	NS
Trigeminal	4	7	NS
Cervical	3	1	NS
Mean VAS score			
Mean±SD	7.45±1.39	7.25±1.45	NS

SD: Standard deviation, VAS: Visual analog scale, SES: Socioeconomic status, NS: Nonsignificant

Table 2: Comparison of VAS scores at each visit between Group 1 and Group 2

Days	Group 1	Group 2	*P* value
0	7.45±1.39	7.25±1.45	NS
3	6.55±1.23	6.6±1.27	NS
7	5.3±1.17	5.75±1.29	NS
14	3.45±1.14	4.25±1.55	<0.05
21	2.05±0.94	3.15±1.53	<0.05
28	1.15±0.87	2.35±1.46	<0.05

VAS: Visual analog scale

Table 3: Adverse drug effects

Drug effects	Group 1	Group 2
Sedation	15	0
Dizziness	11	0
Vertigo	8	0
Gastrointestinal side effects	4	5

DISCUSSION

The majority of patients with herpes zoster experience pain. Antiviral agents have been shown to decrease the duration of herpes zoster rash and the severity of pain associated with the rash.[10] However, these benefits have only been demonstrated in patients who received antiviral agents within 72 h after the onset of rash. Moreover, antiviral agents may be beneficial as long as new lesions are

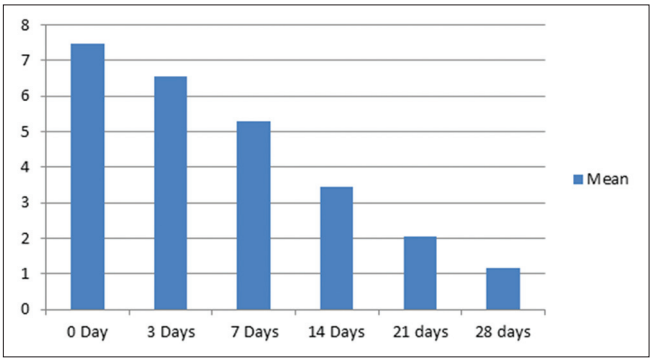

Figure 2: Mean visual analog scale score at each visit in Group 1

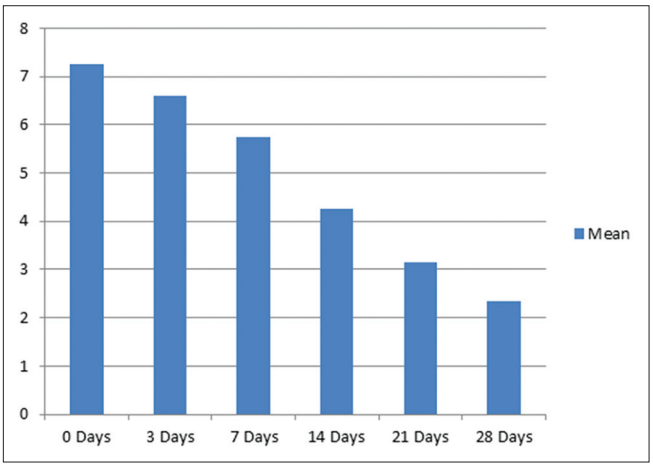

Figure 3: Mean visual analog scale score at each visit in Group 2

actively being formed, but they are unlikely to be helpful after lesions have crusted.

The primary treatment for acute zoster-associated pain includes narcotic and non-narcotic analgesics (both systemic and topical), neuroactive agents, and anticonvulsant agents. While the efficacy of these treatments for general neuropathic pain has been well established, only a few of these modalities have been evaluated specifically for acute zoster-associated pain in controlled studies.[11]

The role of gabapentin in reducing the pain of PHN is well established.[7,12,13] In most of the earlier studies, gabapentin was started after 30 days to 3 months from the onset of zoster. These studies showed significant role of gabapentin in the chronic pain of PHN. In our study, gabapentin was started within 72 h of rash onset. The results of the present study demonstrate that gabapentin in combination with valacyclovir was more effective ($P < 0.05$) in reducing the pain of acute herpes zoster when compared with valacyclovir alone. A study done by Sanjay Kanodia *et al.* observed that gabapentin in a dose of 600 mg is effective in acute herpetic neuralgia.[14] In other study, Berry and Petersen observed 66% reduction of pain as compared to placebo by using single dose 900 mg of gabapentin.[15] The results of our study are in accordance with the previous studies.

The present study shows that some patients experienced somnolence, dizziness, and gastrointestinal side effects in the gabapentin group but it was tolerable. Few earlier studies have also demonstrated the similar type of tolerability and safety profile, but the incidence of side effects was more in the present study.[14] This variation could be because of the smaller sample size of our study.

Limitation of the Study

The sample size of the study was small, and it included only the elderly people, thus caution must be exercised while extrapolating the results.

CONCLUSION

The results of this study show that early initiation of gabapentin in combination with valacyclovir is safe and effective for the management of herpes zoster and the pain associated with it. Further trials can be done in future enrolling more number of patients to confirm the findings of the present study.

ACKNOWLEDGMENT

The authors are thankful to the volunteer patients who have participated in the study.

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How to cite this article: Singh S, Madhwar A, Singh JP. Comparative Study of Gabapentin in Combination with Valacyclovir and Valacyclovir Alone in Herpes Zoster. Int J Sci Stud 2016;3(11):37-40.

Source of Support: Nil, **Conflict of Interest:** None declared.