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HIGH DOSE ORAL PREDNISOLONE IN PATIENTS WITH HERPES ZOSTER FOR PREVENTING POST HERPETIC NEURALGIA

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ABSTRACT

Background: Post herpetic neuralgia (PHN) is a common, serious, painful neuropathic complication of herpes zoster (HZ), persisting after 30 days of onset of lesions when the cutaneous lesions have healed.. The study was conducted between Jul 2015 to to Jun 2017 in seventy eight patients to study role of high dose oral prednisolne in preventing post herpetic neuralgia. **Methods:** Prospective, randomized, comparative study was carried out in tertiary care hospital. Seventy eight consecutive cases of herpes zoster including indoor, OPD and referred cases were included in the study. The patients were initiated on either Acyclovir plus placebo (A group) or Acyclovir plus oral steroids (B group). The patients were followed up after 30 days, 120 days and 180 days and the results were analysed. **Results:** The incidence of PHN after 30 days was 27.5% in patients treated with acyclovir and 7.89% treated with acyclovir plus prednisolone in the overall age group of 21-80 years. The incidence of PHN was also noted in significantly less no of patients treated with oral prednisolone especially over 50 years of age, however there was no significant difference between two groups after 120 and 180 days. **Conclusion:** PHN is a common serious complication and cause of morbidity in patients with herpes Zoster which requires treatment with oral prednisolone to reduce the incidence of acute PHN especially in patients over 50 years of age.

KEYWORDS: Herpes zoster; post herpetic neuralgia; Acyclovir; Prednisolone.

INTRODUCTION

Post herpetic neuralgia (PHN) is one of the most resistant chronic pain complications, commonly affecting elderly patients, which persists after the resolution of the rash caused by herpes zoster (HZ). Estimates of the incidence of PHN vary widely depending on the population and the definition of PHN used. A variety of definitions of PHN have been used by clinicians and investigators. The definition include severity either clinically meaningful pain i.e., pain intensity of at least 3/10 by Visual Analogue Scale (VAS)[1] and the duration of persistent pain, the results of which from recent studies suggest that the pain associated with herpes zoster has three phases: an acute herpetic neuralgia, where the pain lasts up to 30 days after the onset of rash; sub-acute herpetic neuralgia that lasts for 30 - 120 days after the onset of rash and chronic herpetic neuralgia, where the pain persists beyond 120 days after the onset of rash.[2,3,4] The risk of patients developing PHN increases with age and the incidence rises rapidly after the age of 60 years.[5,6,7] Data show that 10–20% of patients with HZ aged ≥50 years will develop PHN that persists at 3 months[5] Despite numerous treatment advances, many patients remain refractory to the current therapies and continue to have pain, physical and psychological distress.[8,9] This study was undertaken to know the role of high dose of oral prednisolone in preventing the development of PHN.

MATERIAL AND METHODS

A prospective, randomized, comparative, study was carried out in patients attending the skin OPD from Jul 2015 to Jun 2017 after taking clearance from institute ethical committee. The diagnosis of HZ infection was made after detailed history and examination, characterized by a painful maculo-papular or vesicular rash in all or part of the skin territory innervated by a single dorsal root ganglion (Fig. 1). PHN was described as sharp, burning, aching, or shooting pain constantly present in the dermatome that corresponds with the healed earlier rash (Fig. 2). Patients in the age group of 21-80 years of either sex presenting with history or symptoms of herpes zoster (HZ) were included in the study. The following patients were excluded from the study: Patients of herpes zoster of trigeminal nerve, pregnant women, patients with heart disease, renal disease, diabetes, peptic ulcer disease, cerebrovascular disease, hypertension, severe psoriasis, hypersensitivity to acyclovir and patients on anticonvulsant drugs and those who were immunosuppressed due to drug or disease.

For the purpose of study, the patients were recruited and allocated to receive one of the two regimens by basic method of simple randomization after flipping a coin by the patient [i.e.,

heads(Group A):Acyclovir plus placebo , tails(Group B) :Acyclovir plus oral Prednisolone). A total of 87 patients were recruited, out of which 44(Group A) were treated by tab Acyclovir 800 mgs 05 times a day for 07 days and 43(Group B) were treated by tab Acyclovir 800 mgs 05 times a day for 07 days followed after 07 days by tab Prednisolone 01 mg/kg body weight for 07 days with a maximum of 60 mgs followed by 0.5 mgs/kg body weight with maximum of 30 mgs for 07 days followed by tapering in the third week according to following schedule; 0.25mgs/kg body weight with maximum of 15 mgs for 03 days, 10 mgs for 02 days and 05 mgs for 02 days. The group A patients were also treated with matched placebo for 03 weeks after treatment with acyclovir. The outcome was assessed by another clinician in the centre and the results were analyzed. Before treatment the patients were explained and the written informed consent were taken. Post treatment follow up was done either on due date or immediately after 30 days, 120 days and 180 days and the therapeutic results were clinically assessed for pain by visual analogue scale (VAS) using horizontal scale. The patient treatment response was evaluated as having PHN if pain >3/10 by VAS. Analytical comparison of the two modalities of treatment was done by *p* value using Fisher's exact test by two tailed method.

Table 1: Baseline characteristics of patients included in the study.

Characteristics	Group A(Acyclovir Plus Placebo) Average(Range)	Group B(Acyclovir Plus oral prednisolone) Average(Range)
Age of patients(years)	52.1(21-80)	51.9(22-77)
Duration of symptoms(days) before recruitment of patients	3.9(2-6)	3.8(1-7)
No of patients treated age group 51-80	17	18
No of patients treated age group 21-50	23	20
Total No of patients treated	40	38

Table 2: Comparison of incidence of PHN between Group A & Group B patients in 21-80 years age group.

Post Herpetic Neuralgia (PHN)	Group A (n=40)	Group B (n=38)	*p* Value
30 days	11/40 (27.5%)	03/38 (7.89%)	0.0373
120 days	04/40 (10%)	01/38 (2.63%)	0.3593
180 days	01/40 (2.5%)	01/38 (2.63%)	1.0000

Table 3: Age wise comparison of incidence of PHN between Group A & B patients.

Age Groups : 51-80 years			
Post Herpetic Neuralgia (PHN)	**Group A (n=17)**	**Group B (n=18)**	***p* value**
30 days	8/17 (47.05%)	2/18 (11.11%)	0.0275
120 days	3/17 (17.64%)	01/18 (5.55%)	0.3377
180 days	01/17 (5.88%)	1/18 (5.55%)	1.0000
Age Groups : 21-50 years			
Post Herpetic Neuralgia (PHN)	**Group A (n=23)**	**Group B (n=20)**	***p* value**
30 days	03/23 (13.04%)	1/20 (5%)	0.6105
120 days	1/23 (4.34%)	0/20 (0%)	1.0000
180 days	0/23 (0%)	0/20 (0%)	1.0000

Illustrations

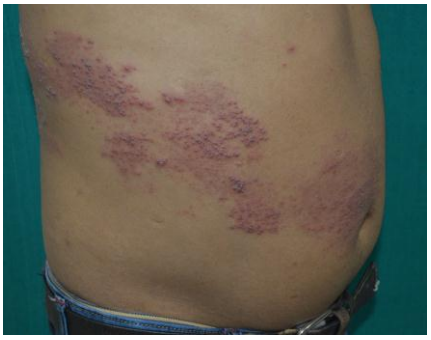

Fig. 1: Grouped vesicular lesions on erythematous base in patient with Herpes zoster.

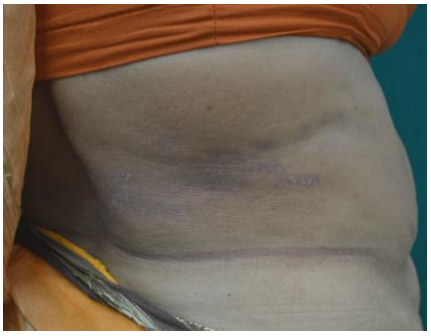

Fig. 2: Grouped scars in patient with healed Herpes zoster.

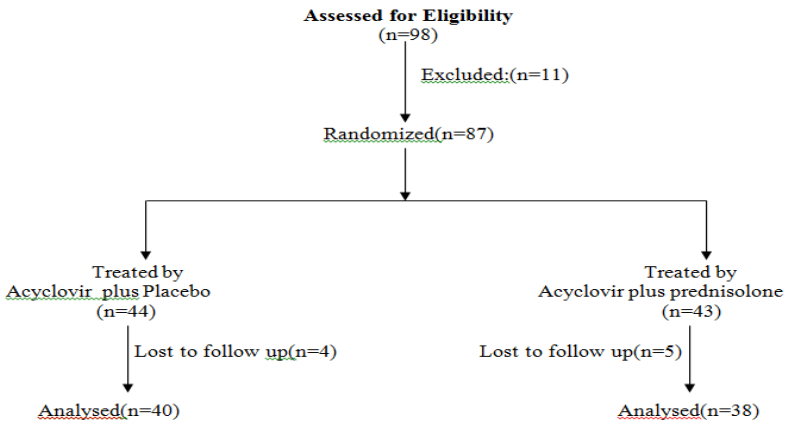

Fig. 3: Consort statement for study.

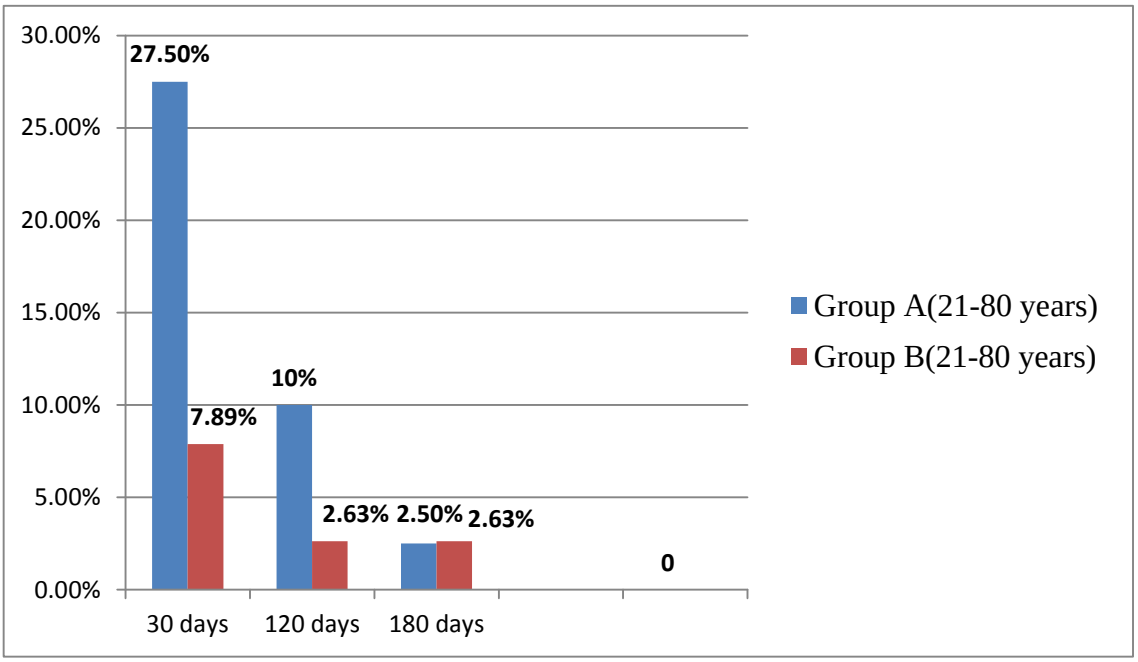

Fig. 4: Comparison of incidence of PHN in percent between Group A & Group B patients.

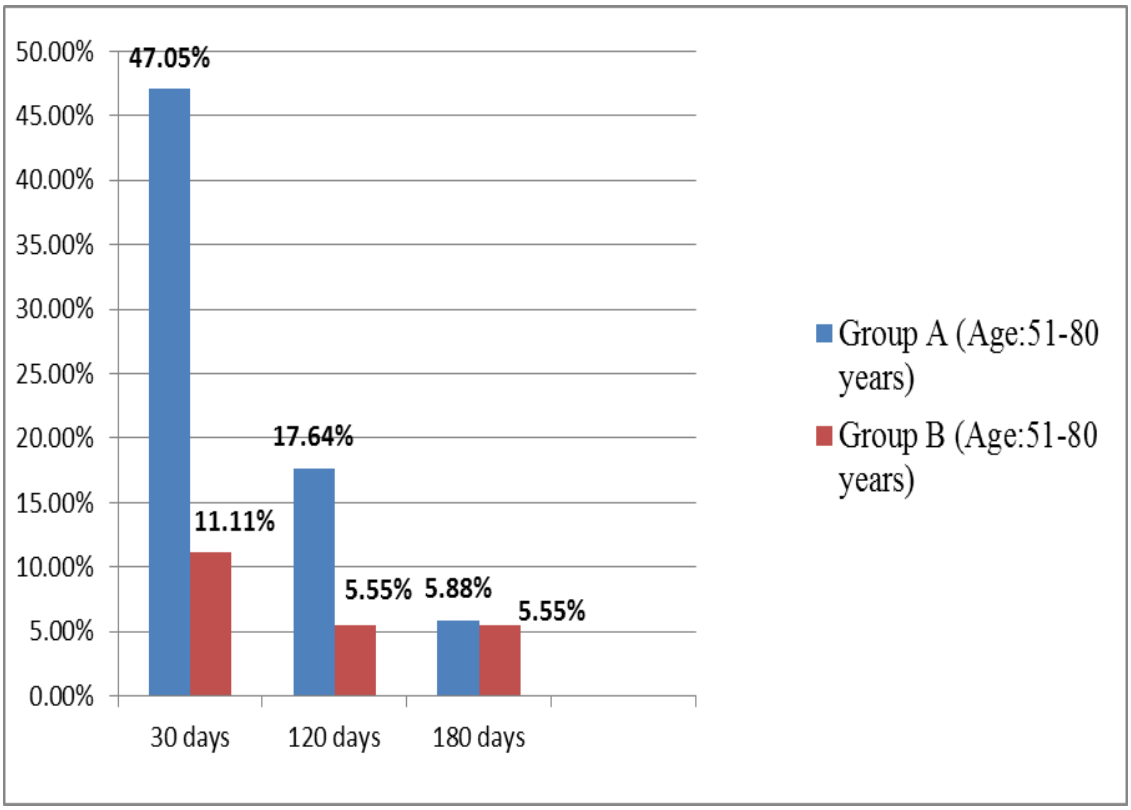

Fig. 5: Comparison of incidence of PHN in percent between Group A & B in 51-80 years age group.

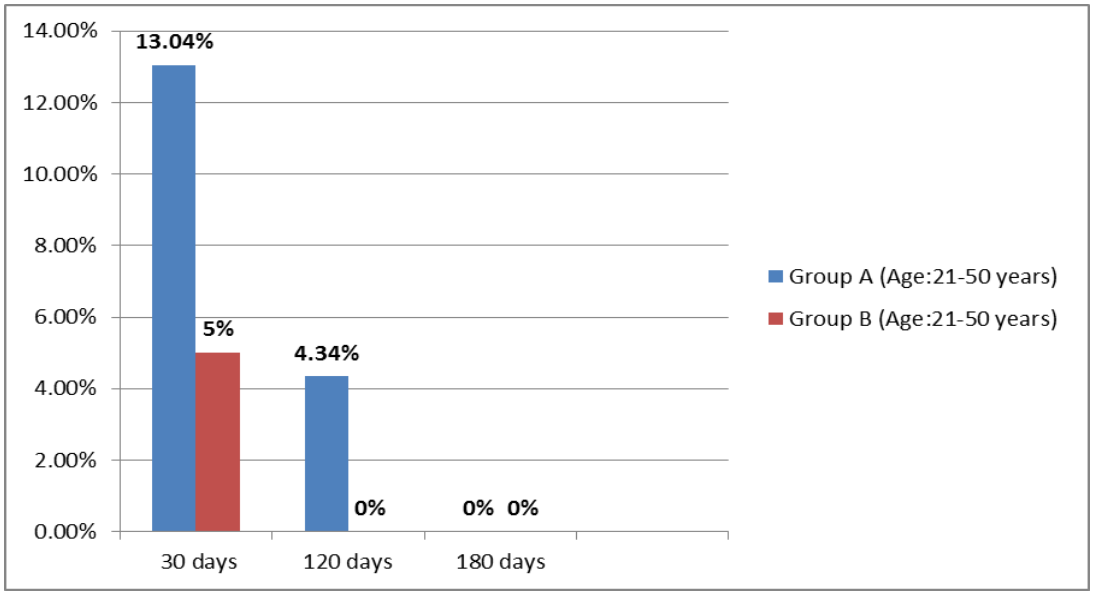

Fig. 6: Comparison of incidence of PHN in percent between Group A & B in 21-50 years age group.

RESULTS

Over the period of two years (Jul 2015-Jun 2017), 87 patients aged 21-80 years after exclusion were recruited for the study, Out of which, 04 in group A and 05 in group B were lost to follow up and remaining 40 and 38 in group A and B respectively were followed successfully for analysis as shown in consort flow diagram (Fig. 3). Baseline characteristics of patients included in the study are given in Table 1. The patients were randomly subjected to two kinds of treatment as shown in Table 1.The overall incidence of PHN noted in the age group of 21-80 years in two groups of patients after 30,120 and 180 days with tab Acyclovir plus placebo(group A) and Tab Acyclovir plus oral Prednisolone(group B) is given in Table 2. The incidence of PHN after 30 days is observed in 11 (27.5%) and 03 (7.89%) of the patients treated in A and B group respectively. The incidence of PHN after 120 days and 180 days are noted in 04 (10%) and 01 (2.5%) of the patients respectively treated in A group where as it found in 01(2.63%) and 01(2.63%) respectively in B group. The incidence of PHN noted in age group of 51- 80 years and 21-50 years of age between A and B group after 30,120 and 180 days is given in Table 3.

DISCUSSION

The most common complication of HZ is PHN and the treatment is often challenging. Various therapeutic modalities that have been used for treating it have not been successful every time. Seventy eight patients aged 21- 80 years, diagnosed as HZ were treated with

either of two drug regimens and followed after 30,120 and 180 days for the incidence of PHN. The average age and duration of symptoms before the study were 52.1 years and 3.9 days in group A patients and 51.9 years and 3.8 days in group B patients respectively (Table 1). The two groups of patients were comparable in their age and duration of disease.

In this study, 27.5% patients treated with acyclovir (group A) and 7.89% treated with acyclovir plus prednisolone (group B) had PHN after 30 days(Fig. 4) in the overall age group of 21-80 years. The incidence of PHN after 30 days in group A patients was 47.05%, where as in B group it was 11, 11% in age group 51-80 years(Fig. 5), whereas it was 13.04% and 5% in group A and B in the age group of 21-50 years respectively(Fig. 6). Statistical analysis in this study have shown that there was significant difference between the two types of treatment in overall age group with *p* values of 0.0373(< 0.05%) as shown in Table 2 and the pain was significantly higher in acyclovir treated group compared to acyclovir plus prednisolone treatment group. It was also found out that the incidence of PHN after 30 days in the age group of 51-80 years was 47.05% in group A patients versus 11.11% in group B patients which was statistically significant with p value of 0.0275(< 0.05%),where as in the age group of 21-50 years it is higher in Acyclovir than acyclovir plus prednisolone group but it is statistically insignificant. In the previous study conducted by Keczkes K et al[10] in 20 patients, reported PHN incidence of 15% after 06 months over the age of 50 years, who received 40 mgs prednisolone daily with gradual reduction over a period of 4 weeks which was slightly lower in our study where it is 11.11 %. The incidence of PHN study by Helgason S et al[11] without treatment at 30 and 90 days were 40.8% and13% in patients having more than 60 years of age and 8.8% and 2% under 60 years of age. In another placebo group study by McKendrick et al[12] prevalence of PHN among 181 patients 60 years and older was 62.4% at one month and 24.2% at three months after zoster. Both studies cannot be compared as these studies were recorded in patients without any medication.

Two double-blind, randomized, controlled trials by Wood MJ and Whitley RJ, concluded that corticosteroids given for 21 days did not prevent PHN. Wood MJ et al found that patients treated with corticosteroids and acyclovir had a greater reduction in pain on days 7 and 14, but at day 21 there was no difference.[13] The second study by Whitley RJ et al found that corticosteroids combined with acyclovir result in a significant benefit in quality of life at day 30 including less time returning to normal activity and uninterrupted sleep.[14]

After 120 days, 10% in group A and 2.63% in group B noted to have PHN in the age group of 21-80 years (Fig. 4). It was also found to have PHN in 17.64% and 5.55% in age group 51-80 years (Fig. 5), whereas it was 4.34% and 0% in age group 21-50 years in group A and B respectively (Fig. 6). In both age group 51-80 and 21-50 years, the incidence of PHN was higher in acyclovir group than acyclovir plus prednisolone group but was statistically insignificant in both with *p* value < 0.05%(Table 3). In the study by McKendrick et al, prevalence of PHN in 181 patients 60 years and older was 24.2% at three months after zoster.[12] In a population based study using medical records by Yawn BP et al,[15]in the United States, 10% of patients reported incidence of PHN after 90 days compared to this study where it is 2.63% in corticosteroid treated group.

The overall incidence of PHN after 180 days was 2.5% and 2.63% in group A and B patients respectively. In this study it was also found that 5.88 % and 5.55% of the patients in group A and B developed PHN respectively in the age group of 51-80 years where as none have developed pain in both groups A and B in the age group of 21-50 years. Statistical analysis showed that there was no significant difference between the two in both age groups. In the landmark placebo group zoster vaccine study, which included almost 40,000 people aged 60 years or older and where PHN was defined as pain intensity of 3/10 or more, 30% of patients who developed HZ had PHN at 1 month, 12% at 3 months, and 5% at 6 months.[16]

In this study it was observed that incidence of PHN was higher in the age group of 51-80 years of age in both A and B groups of patients indicating the the risk of developing PHN increases with age. Similar results were seen in a study by Yawn BP et al in united states, where PHN at 03 months was found in 18% in persons older than 50 years and 33% in those older than 80 years of age.[17]

CONCLUSION

The results of this study suggest that the addition of prednisolone to acyclovir confer additional benefit in reducing incidence of PHN after 30 days, especially after the age of 50 years, however it has no appreciable influence in reducing incidence of subacute and chronic PHN. If the use of orally administered prednisolone is not contraindicated, adjunctive treatment with this agent is justified on the basis of its effects in reducing pain in acute PHN, despite questionable evidence for its benefits in decreasing the incidence of pain in subacute and chronic cases. It is recommended that oral prednisolone should be used in patients more than 50 years of age who are at greater risk of developing PHN.

Conflict of Interest: There are no conflicts of interest.

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