Journal of Pakistan Association of Dermatologists. 2019; **29 (1)**: 40-44.

Original Article

Efficacy of Narrow Band UVB in combination with oral acyclovir versus oral acyclovir alone in prevention of post herpetic neuralgia in patients with herpes zoster

Lubna Rani Faysal, Farid-ur-Rehman*

Islamic International Medical and Dental College, Rawalpindi
* Fauji Foundation Hospital/ Foundation University Medical College, Islamabad

Abstract

Background Post-herpetic neuralgia (PHN) is one of the serious complications of herpes zoster and response to available treatment/s is unsatisfactory. A few studies have shown promising effects of narrow band ultraviolet B (NBUVB) in combination with acyclovir in the prevention of PHN. The aim of this study was to determine the efficacy of combination of NBUVB and acyclovir in prevention of PHN in patients with herpes zoster.

Patients and Methods A randomized controlled trial was conducted at Dermatology unit, Fauji Foundation Hospital, Rawalpindi. 60 Patients (age>30years) with herpes zoster were enrolled. The study group (A) was treated with NBUVB; three times a week for a maximum of 15 sessions or before if the pain had completely settled and oral acyclovir (800mg five times a day for 10 days). The control group (B) was treated with only oral acyclovir (800mg five times a day for 10 days). Pain severity was assessed on 4-point verbal rating scale (VRS) before starting treatment, at completion of treatment and 3 months after the end of the trial. The efficacy of treatment was complete pain relief (0-score on VRS) after a 03 month follow up period.

Results After a 03 month follow up period, in group A, 24 patients (92.3%) had complete pain relief while in group B, only 2 patients (7.7%) had achieved the same score. The prevention of PHN was significantly lower ($p < 0.000$) in the control group.

Conclusion NBUVB with oral acyclovir is more effective than oral acyclovir alone in the prevention of PHN in patients of herpes zoster .

Key words
Post-herpetic neuralgia, Narrow band ultraviolet B, acyclovir.

Introduction

Post-herpetic neuralgia is one of the serious and distressing complications of herpes zoster. It is a worldwide problem; more than 30% of patients over 40 years of age who have had herpes zoster suffer from post-herpetic neuralgia.[1] Age is the main predictor of PHN.[2-4]

Herpes zoster is a disease characterized by unilateral, dermatomal grouped vesicles on an erythematous base; as the result of reactivation of varicella zoster virus that had persisted in latent form within sensory ganglia after an earlier attack of varicella.[5] Post herpetic neuralgia is a chronic neuropathic pain lasting

Address for correspondence
Dr. Lubna Rani Faysal
Department of Dermatology
Islamic International Medical College/Pakistan Railways Hospital.Westridge, Rawalpindi.
Ph: +923005282869
Email: lubna.faysal@gmail.com

for more than 06 weeks after the onset of herpes zoster.[1] The precise pathogenesis of PHN is unknown but it is widely considered a multifactorial disease. Generation of spontaneous action potentials in the afferent peripheral neurons, degeneration of peripheral neurons (immunologically mediated) with resultant hyper-excitability of spinal cord neurons, necrosis and possible fibrosis, all contribute to the neuronal damage and development of PHN.[5,6]

PHN has devastating effects on a patient's quality of life (QoL). It affects both physical and psychological aspects of life by causing insomnia, fatigue, depression, interference with daily activities and suicidal ideation.[7,8] The available treatment/s for PHN include antidepressants, anticonvulsants, oral steroids, local anesthetics, topical capsaicin, gabapentin, opioids and Transcutaneous Electrical Nerve Stimulation (TENS). These modalities, especially in combination, may shorten the duration or decrease the severity of symptoms.[9,10] Acyclovir given within 72 hours of eruption has been shown in some studies to reduce the incidence and severity of PHN.[5]

NBUVB is a wave band of electromagnetic radiation with a wavelength of 311nm. UVB has been used to treat a number of dermatological diseases like psoriasis, vitiligo, atopic dermatitis, pruritic disorders, para-psoriasis, and pityriasis rosea.[11,12] Two studies conducted in Tehran and Cairo[13,14] showed significant efficacy of UVB in prevention of PHN. Regional studies on this topic are lacking.

The objective of this study was to compare the efficacy of NBUVB in combination with oral acyclovir versus oral acyclovir alone in prevention of PHN in patients with herpes zoster.

Patients and Methods

This randomized controlled trial was conducted in the Dermatology unit of Fauji Foundation Hospital, Rawalpindi. Patients with diagnosis of Herpes zoster and fulfilling the inclusion criteria (Age>30 years, patients with any severity of pain in the first 07 days of herpes zoster), were enrolled for this study. The trial began after the permission from the Hospital Ethical Review Committee. Patients presenting more than 07 days after the onset of rash and those having history of photosensitivity were excluded from the study. Herpes zoster was diagnosed on the basis of history and clinical examination. Sample size of 60 patients (30 in each group) was calculated with 80% power of test, 1% level of significance. Informed written consent was taken from patients after detailed explanation of purpose of study. Patients were divided in two equal groups by computer generated randomization list. Group allocation was done to group A and group B.

Patients allocated in Group-A (study group) were given oral acyclovir (800mg five times a day for 10 days), analgesics (paracetamol only) and NBUVB to the affected dermatome. Patients in Group-B (control group) were treated only with oral acyclovir in the same dose and same analgesics. In the study group, NBUVB was delivered only to the affected dermatome while the rest of body was covered with clothing. The starting dose of NBUVB was 0.21 J/cm^2 and it was increased by increment of 10% on every session as long as no adverse effects including persistent erythema, burning or itching were reported by the patient. The sessions were repeated 03 times per week to a maximum of 15 sessions or less if the pain had completely settled. All the patients were evaluated subjectively for pain relief using VRS at the end of treatment sessions and after 03 months follow-up period.

Pain severity was assessed by using 4-point VRS as reported by the patient: 0-no pain, 1-mild pain that does not interfere with daily activities, 2-moderate pain that interferes with daily activities but does not cause sleeplessness, 3-severe pain that causes sleeplessness and 4-very severe unbearable pain that is extremely incapacitating. Efficacy was defined in terms of complete pain relief at the end of 3 months interval i.e. 0 score on VRS.

Data was entered and analyzed by statistical package for social sciences (SPSS) version 12. Quantitative data was calculated in the form of mean and standard deviation. Qualitative data was calculated in the form of frequencies and percentages. Chi-square test was used to compare the efficacy in two groups. A probability (*p*) value of less than 0.05 was considered statistically significant. Data was stratified for severity of pain at baseline i.e. mild, moderate and severe to address effect modifiers.

Results

A total of 60 patients suffering from herpes zoster were enrolled in the study, with 30 patients in each group, A and B respectively. The overall mean age of study population was 52.60 years and there was no significant difference between the mean ages of study population between the two groups. There were 16 (53%) males and 14 (47%) females in group A and 19 (63%) and 11 (37%) respectively in group B.

The distribution of patients in all grades of pain (moderate, severe and very severe) was comparable between the two groups **(Table 1)**. Majority of patients in both groups had VRS 04 (very severe pain).

At the end of 03 months follow up period, in group A, 24 (92.3%) patients achieved complete pain relief and 0 pain score on VRS, while only 02 (7.7%) patients achieved the same score in group B, p-value < 0.000 **(Table 2)**.

Discussion

The present study clearly shows the advantage of combining NBUVB with acyclovir in the prevention of PHN. Acyclovir inhibits viral replication which in turn decreases neuronal damage and consequently decreases the

Table 1 Stratification of patients on the basis of pain at baseline

Pain at base line		*Treatment groups*		
		Acyclovir +UVB (A)	*Acyclovir alone (B)*	*Total*
1.	Moderate	1	3	4
2.	Severe	9	8	17
3.	Very severe	20	19	39
	Total	30	30	60

Table 2 Chi- Square Tests showing significant difference

	Value	*df*	*Asymp. Sig. (2-sided)*	*Exact Sig. (2-sided)*	*Exact Sig. (1-sided)*
Pearson Chi-Square	32.851[a]	1	.000		
Continuity Correction[b]	29.932	1	.000		
Likelihood Ratio	37.388	1	.000		
Fisher's Exact Test				.000	.000
N of Valid Cases	60				

[a.] 0 cells (.0%) have expected count less than 5. The minimum expected count is 13.00.
[b.] Computed only for a 2x2 table

incidence of PHN.[15] Systematic review on the treatment of acute herpes zoster with 800 mg of acyclovir five times a day for 7-10 days revealed that it may reduce the incidence of PHN at 1-3 months.[16] But the largest of the 04 RCTs in this systematic review found no benefit in this context. In this study, only 7.7% of patients, who had acyclovir alone (Group B) achieved VRS 0, i.e. complete pain relief at the end of 03 months follow up period.

UVB affects the course of PHN through its suppressing effect on inflammation, converting Th-1 cytokine profile to Th-2 cytokine profile, which has an important role in its pathogenesis.[17] One of the probable targets is the Langerhans cells, which sensitize nociceptors and effect immune response through release of various cytokines. UVB stimulates keratinocytes and mast cells to secrete immunosuppressive cytokines which inhibit the antigen presenting function of Langerhans cells and also causes their depletion in the epidermis.[18]

The present study, both groups had majority of patients in the fifth decade of life with either very severe or severe pain at baseline **(Table 2)**. At 03 months after the follow up period, in group A, 24 patients had VRS 0. This score was achieved by only 2 patients in group B.

Jalali et al. conducted an RCT with same treatment protocol as present study, but using broad band UVB, found similar result (88.3% vs. 53.8%) at the end of 03 months follow up period.[13] The possible explanation of better efficacy in our study is use of narrow band UVB which is more selective and has greater immunosuppressive effects.[18] Jalali et al. compared the severity of pain between the two groups, which was low in phototherapy group as compared to control group (mean VRS 2.50 vs. 3.28 at 3 months).

A pilot study, with same treatment protocol as the present study, but without a control group was conducted in Cairo. 17 patients were enrolled in this study. The mean age of the patients was 52.06 years and out of the 12 patients, 10 had VRS score 4 at baseline. The age and baseline VRS scores are comparable to our study. In the Egyptian study, 42% patients achieved VRS score 0, after 3 months of follow up period.[14] The results are not comparable to our study, as 92.3% of our patient population achieved VRS 0 score. This disparity may be explained as the pilot study had a small sample size (17 patients).

Conclusion

Narrow band UVB in combination with oral acyclovir is more effective in prevention of post herpetic neuralgia in patients with herpes zoster as compared to oral acyclovir alone.

References

1. Sterling JC. Viral infections. In Griffiths CEM, Barker J, Bleiker T, Chalmers R and Creamer D eds. Rook's Textbook of Dermatology. West Sussex: Wiley Blackwell 2016: 25: 27-31.
2. Satyaprakash A, Ravanfar P, Tyring SK and Seigafuse S. In: Hall BJ, Hall JC eds. "Infectious diseases in skin". Sauer's Manual of Skin Diseases. Philadelphia: Lippincott Williams & Wilkins 2010: 232.
3. Gauthier A, Breuer J, Carrington D, Martin M. Epidemiology and cost of herpes zoster and post-herpetic neuralgia in the United Kingdom. Epidemiol Infect 2008; 9: 1–10.
4. Coen PG, Scott F, Leedham-Green M, Nina T, JamilA et al. Predicting and preventing post-herpetic neuralgia: are current risk factors useful in clinical practice? Eur J Pain 2006; 10: 695–700.
5. Schamader KE, Oxman MN. Varicella and herpes zoster. In: LA, Katz SI, Gilchrest BA, Paller AS, Leffell DJ and Wolff K eds. Fitzpatrick's Dermatology in general medicine. USA: Goldsmith McGraw-Hill companies 2012:194; 2386-90.

6. Cohen JI, Straus SE, Arvin Am: varicella-zoster virus replication pathogenesis and management. In: Knipe DM, Howley PM, Griffin DE, Lamb RA, Martin MA et al eds Fields Virolog, Philadelphia: Lippincott, William &Willikins, 2007: 2744 -50.
7. Katz J, Cooper EM, Walther RR, Sweeney EW, Dworkin RH: Acute pain in herpes zoster and its impact on health-related quality of life. Clin Infect Dis 2004; 39: 342-348.
8. Volpi A, Gatti A, Pica F, Bellino S, Marsella LT, Sabato AF: Clinical and psychosocial correlates of post-herpetic neuralgia. J Med Virol 2008; 80:1646-1652.
9. Cristopher L. Wu, Srinivasv N. Raja. An update on the treatment of post herpetic neuralgia. The journal of pain 2008; 9: 19-30.
10. Dubinsky RM, Kabbani H, El-ChamiZ, Boutwell C and Ali H. Practice Parameters: Treatment of postherpetic neuralgia: an evidence based report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 2004; 63 (6): 959-65.
11. Dogra S, Kanwar AJ. Narrow band UVB phototherapy in dermatology. Indian J Dermatol Venereol Leprol 2004; 70: 205-9.
12. Hjerppe M, Hasan T, Sakasa I, Reunala T. Narrow band UVB treatment in atopic dermatitis. Acta Derm Venereol 2001; 81: 439-40.
13. Jalali MHA, Ansarin H, Soltani-Arabshahi R. Broad- band UVB phototherapy in zoster patients may reduce the incidence and severity of post herpetic neuralgia. Photodermatol Photoimmunol and Photomed 2006; 22: 232-7.
14. EI-Nabarawy E. The use of narrow band UVB in prevention and treatment of post herpetic neuralgia (A pilot study). Indian J Dermatol 2011; 56: 44-7.
15. Dworkin RH, Johnson RW, Judith Breuer J, Gnann JW, Myron J. et al. Recommendations for the Management of Herpes Zoster. ClinInf Dis 2007; 44 Suppl: S1-26.
16. Alper BS, Lewis PR. Does treatment of acute herpes zoster prevent or shorten postherpetic neuralgia? A systematic review of the literature. J Fam Pract. 2000 Mar; 49: 255-64.
17. Zhang M, Wu N, Yang L, Zhang J, Sun X et al. Study on the T-helper cell 1/2 cytokine profile in blister fluid of patients with herpes zoster and its clinical significance. J of Dermatol 2011; 38: 1158-62.
18. Amerio P, Carbone, Auriemma M, Varraati S and Tulli A. UV induced skin immunosuppression. Anti-Inflammatory & Anti-Allergy Agents in Medicinal Chemistry 2009; 8(1): 3-13.