Efficacy of TENS versus Conservative Pain Control Measures in Post Herpetic Neuralgia: A Retrospective Observational Study.

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Abstracts: Background & Objective: To evaluate the effectiveness of transcutaneous electrical nerve stimulation (TENS) in treatment of post herpetic neuralgia (PHN) compared with conservative pain control measures. Methodology: A retrospective institution based observational study was conducted evaluating the records of patients visiting the dermatology OPD during last 6 consecutive months for herpes zoster and PHN. 152 out of 6240 new cases had herpes zoster and 50 of these patients had PHN which was defined as persistence of pain at the involved site one month after subsidence of rash. Pain was quantitatively noted in these patients on a visual analogue scale (VAS) from 0-10.Three treatment groups were compared: only TENS therapy, TENS with analgesics (most commonly NSAIDS) and tab gabapentin along with tab amitriptyline as tricyclic antidepressant. ANOVA test was applied to study the statistical difference in treatment response between the three groups. Results: Mean baseline VAS in the groups was 6.6, 7.06 and 6.78 respectively. At the end of treatment the mean VAS was 2.1, 2.39 and 2.86 respectively. We found that there was 68.1%, 66.1% and 57.8% improvement in VAS in the individual groups respectively. The improvement was found to be statistically significant ($p<0.05$) in all the three treatment groups. Intergroup analysis, however, did not reveal any statistically significant difference between the groups. Conclusion: TENS is a safe and effective measure for pain control in post herpetic neuralgia patients. However, its efficacy over conventional pain control measures like NSAIDs and tab gabapentin and tricyclic antidepressants could not ascertained. Our study also revealed that initiation of antiviral therapy within 72 hours did not affect the severity of PHN. [Mistry A NJIRM 2015; 6(4):14-19]

Key Words: TENS, PHN, VAS

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Introduction: Post-herpetic neuralgia (PHN) is the most challenging and debilitating complication of herpes zoster. Reactivation of varicella zoster virus in the dorsal root ganglia leads to inflammation of nerve endings and hence the pain. No consensus has been reached regarding the duration of pain after subsidence of herpes zoster rash to label it as PHN. Some authors suggest it as more than one month while others suggest more than 3 months and some even more than 6 months after the rash has resolved.[1-4]

It is characterized mainly by constant or intermittent burning, itching or aching, with paroxysmal shooting pain. Numbness, tingling and allodynia, also contribute to the burden of PHN. Predictors of PHN are: greater age, acute pain and rash severity, prodromal pain, the presence of virus in peripheral blood as well as adverse psychosocial factors.[1,2]

The reported incidence of PHN is age dependent: the risk is low (2%) in patients younger than 50 years of age, 20% in those older than 50 years and35% in those over the age of 80 years.[4-7] More than5% of elderly patients have PHN at 1 year after acute Herpes Zoster.[2,6]

The usual treatment of herpes zoster with orally administered antiviral drugs (acyclovir or valcyclovir) is most effective when started within 72 hours after the onset of the rash.[1,8,9] It has been believed till now that initiation of therapy within this window period reduces acute pain, hastens rash healing, and reduces the risk of PHN. However, meta-analyses have shown no oronly a partial effect on the incidence of PHN.[1,6,10,11]

Treatment of PHN is known as a challenge. Symptoms vary among patients and may be resistant to common analgesics. Various modalities have been tried for treatment of this debilitating disease. Current evidence supports that multiple medications are effective in reducing the PHN including tricyclic antidepressants (TCA), antiepileptics, opioids, as well as topical lidocain and capsaicin; sympathetic blockade may assist in treating the pain of herpes zoster or PHN; transcutaneous electrical nerve stimulation (TENS)

or per cutaneous electrical nerve stimulation (PENS) may be effective in some cases.[1,2,9,12-16]
Only few studies have been published on PHN treatment with alternative treatment regimens as TENS or PENS .[12,17-19]

The aim of this study was to compare the efficacy of TENS in treatment of PHN as a single modality; in combination with analgesics and against other drugs.

Material and Methods: A retrospective institution based observational study was done in a tertiary care centre. The records of patients visiting the dermatology OPD during last 6 months were analysed for the herpes zoster and PHN. There were a total of 6240 new cases, out of which 152 had Herpes Zoster. The diagnosis of herpes zoster was made on clinical basis of typical unilateral vesicular exanthem in a single dermatome. PHN was considered as pain remaining in the affected dermatome, 1 month after the subsidence of the Herpes zoster rash. 50 patients fit into this criterion and were further analysed for age, sex, duration of PHN, presence of antiviral treatment and treatment received for the present condition. Pain was quantitatively noted in these patients on a visual analogue scale (VAS) from 0-10. History of antiviral treatment taken at the beginning of rash was not available in 22 cases as they had not visited a specialist at the onset of the rash. Rest 28 cases, which came within 72 hours of onset of rash, were given antiviral treatment in form of tab acyclovir in dose of 800mg five times a day or tab valacyclovir 1000mg three times a day for one week. A total of 36 patients received TENS. Three groups could be made on the analysis of the data. Group 1 was where patient received TENS as the only modality of treatment, group 2 received analgesics (paracetamol, NSAIDS or tramadol) along with TENS, and group 3 received tab gabapentin along with tab amitriptyline as tricyclic antidepressant. Some patients received topical treatment also in form of calamine lotion for its soothing effect. A single session of TENS therapy consisted of the placement of two patches on the skin at the dermatome infected: one patch placed at paravertebral region, another patch on the other side along the nerve for 30 minutes five times a week for 2 or 3 weeks. The patches were connected to a low output (1–5 mA) electrical generator and stimulated at frequencies ranging from 20 to 40 Hz. The patients were followed up for one year. Additional sessions of TENS were given on request of some of the patients during the follow-up. Statistical analysis of data was done using ANOVA test to study the difference between the responses in the three groups.

Results:
Data of 50 patients was analysed. Incidence of herpes zoster came out to be 2.4 per 1000 patients while incidence of PHN occurring in these patients was 32%. Males were affected more than females (1.4:1) but there was no sex difference in case of frequency of PHN (1:1). Youngest patient was 29 years old and oldest was 80 years, thus the mean age was 57.36 years. 24 % patients were less than 50 years of age. Most common site affected was thorax (44%) with T4 dermatome being the most common, followed by abdomen and lumbar area (22%), extremities (18%) and lastly head and neck area(16%). As majority of the patients were more than 50 years old, we also looked into coexisting comorbid illnesses. 11 patients suffered from diabetes, 2 had both diabetes and hypertension while 5 had hypertension only.

Group 1 had 21 patients who were treated with TENS only. Group 2 and 3 had 15 and 14 patients respectively. The demographic data of the patients is summarised in table 1.

Table 1: Demographic data of patients in the three groups

	Group 1 (TENS only)	Group 2 (TENS + analgesics)	Group 3 (Gabapentin + TCA)
Patients (n)	21	15	14
Male: Female	12:9	7:8	6:8
Age (mean) (years)	54.6	58.86	59.78
< 50 years	5	5	2
>50 years	16	10	12
Comorbid illness (n)	3	7	8
Location of rash			
Face	4	4	0
Thorax	8	4	10
Extremities	4	4	1
Abdomen and lumbar area	5	3	3

Pain was measured on a visual analogue scale where 0 was equivalent to no pain and 10 was

maximum as unbearable pain. Minimum baseline VAS was 5 and maximum was 9.We noticed that there was increase in baseline VAS with increasing age only in Group 1, while in the other groups no specific pattern was seen.(Table 2) It was seen that there was a highly significant improvement ($p<0.01$) in VAS in all the treatment groups in various age distributions. However, in group 3 among the patients aged 30-45 years, the difference in baseline and end VAS was significant ($p<0.05$) only.

Table 2: Baseline VAS in the three groups

Age (yrs)	Baseline VAS (mean)	VAS at end of treatment (mean)	p value	improve-ment in VAS (%)
Group 1				
29-49(n=5)	6.4	1.8	0.00002	68.1
50-65(n=15)	6.7	2.2	0.00 00000006	
66-79(n=1)	8	4	-	
Group 2				
35-50(n=5)	6.8	2.6	0.00003	66.1
51-65(n=4)	7.5	2.7	0.011	
66-80(n=6)	7	3.1	0.000003	
Group 3				
30-45(n=2)	7	3.2	0.042	57.8
46-60(n=5)	6.2	1.8	0.0003	
61-75(n=7)	7.2	2.5	0.0001	

VAS after treatment ranged from 1 to 5 in various groups. Mild allodynia remained in most of the cases while some still had moderate pain. The improvement in mean VAS from baseline to end of treatment in all three groups is given in Fig 1.

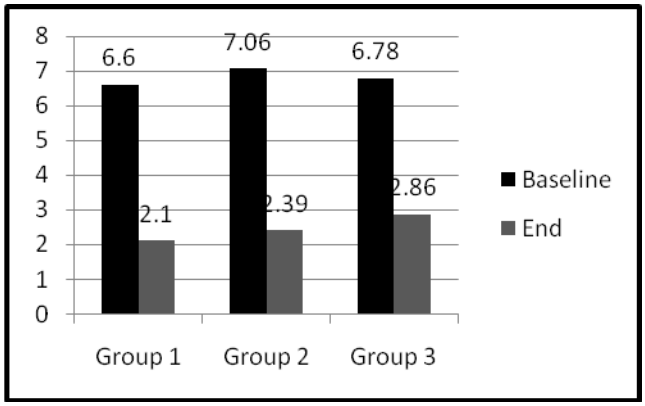

Figure 1: VAS at baseline and treatment end

ANOVA test was applied to study the difference in the treatment response between the three groups. It was observed that the difference in baseline and end VAS was not statistically significant.

In those patients who did not receive any antiviral treatment at the onset of disease, average baseline VAS was 6.7 and at the end of treatment, it was 2.3. In the other set of patients who had received antiviral treatment within 72 hours of eruption of exanthem, average baseline VAS at beginning and end was 6.9 and 2.5 respectively.

Out of the 36 patients who received TENS, 5 requested a repeat session during first three months of follow up. (Table 3) After the second session, we were able to manage all of them on analgesics only.

Table 3: Profile of patients who had repeat TENS session during follow up

SN	Age (yrs) / Sex	Comorbid illness	Modality of treatment	Base-line VAS	VAS at end of first session	Repeat TENS session	VAS at end of second session
1.	56/M	DM	TENS + Analgesics	9	4	2 months	2
2.	77/F	DM	TENS + Analgesics	8	5	1.5 month	2
3.	80/F	-	TENS + Analgesics	8	4	1 month	1
4.	50/F	-	TENS	8	4	2 months	2
5.	79/M	HT	TENS	7	4	2.5 months	1

Discussion: Herpes zoster is a very common cutaneous disorder with considerable effect on quality of life of the patients. It is caused by reactivation of the varicella zoster virus which becomes latent in the dorsal root sensory ganglia after primary infection usually during childhood (clinically manifested as varicella). On becoming

active again, it spreads along the corresponding dermatome, and generates the characteristic unilateral vesicular rash. The accompanying inflammation of the sensory nerve and skin damage are supposedly responsible for the associated significant acute pain.[1]Mostimmunocompetent patients experience spontaneous and complete recovery within a few weeks, but some will develop complications, and the most common is postherpetic neuralgia in the affected dermatome.

Despite advances in antiviral therapy during acute HZ and the more recent introduction of vaccination against Varicella-zoster virus (VZV)[20], PHN continues to be a significant clinical problem, with up to 25% of patients over 60 years developing persistent neuropathic pain following acute HZ.[21-23] The estimated incidence of PHN varies with its definition.[24-29] PHN can persist, in some individuals, for months or years after the HZ rash has healed, causing suffering for the patient and a burden of economic cost on patient, care givers, and healthcare providers. Studies vary widely in the reporting of the duration of persistent pain.[30]Helgasonet al[31] found that of 13 subjects with persistent pain 12 months after HZ, 6 still reported pain after 6.3 years. In one study of patients aged over 65 years, the mean duration of pain was 3.3 years, and ranged from 3 months to more than 10 years.[32]In detail, Bouhassira et al. [33] reported the presence of zoster-related pain in 6% of 1032 patients12 months after HZ. McKendrick et al.[36] This is the reason why, in the last years, PHN is emerging as a preferred clinical trial model for chronic neuropathic pain.[35]

TENS or transcutaneous electrical nerve stimulation (TENS) is a useful adjunctive treatment for PHN. TENS delivers a low voltage electrical current to nerves via conductive pads called electrodes which are placed over specific areas of skin. The mechanism of TENS in pain- relief is based on the gate control theory. While stimulating large afferent fibers, the input of small pain afferent fibers will be inhibited on the dorsal horn neurons before projecting to the spinal cord.[36]

This retrospective study suggests that TENS may be a good modality for treatment of patients with PHN. Use of TENS provided symptomatic pain relief in the patients with the advantage of having no harmful side effects. TENS also the added benefit of having almost no contraindications for its use except implanted pacemaker and skin malignancy, none of which were seen in our patients.

The incidence of herpes zoster in our study population was 2.4 per 1000 people which is similar to some studies (3.6 [37], 2.3 [38])but higher than one of the earlier studies from Slovenia-1.8.[39] The incidence of PHN (32%) was also higher than which has been reported previously.[5,9,39] In our study males had a higher incidence of herpes zoster which is in contrast to other studies where there was a female preponderance.[9,39] Our study showed that there was no difference in PHN in males and females. This has been by other authors also including Volpi et al.[40] Similarly, Dworkin and Schmader[41] did not find sex differences to be associated with the various aspect of herpes zoster, with the only exception being the intensity of acute pain which is higher in women than in men, as also confirmed by Volpi et al in their study about acute herpetic pain previously.[42] It can be assumed that the earlier reported association between gender and long-term pain may have been a consequence of the fact that more women were in the higher age strata.[43]

Mean age(in years) of the patients in various groups were 54.6, 58.86 and 59.78 respectively. A higher baseline VAS was seen in Group 3 where the mean age was also highest. One may presume that this is in accordance with the accepted theory that PHN is higher in older age groups.[4-7]But when we did an intragroup evaluation of baseline VAS in various age groups, it did not suggest the same. Increasing VAS with increase in age was evident only in group 1, whereas in the other two groups this was not seen. This discrepancy can possibly be explained by difference in pain tolerance threshold among the individuals.

There was a statistically significant difference in the baseline and end VAS in the three groups. Only a single age group (66-79 year) in first treatment group could not be analysed as there was only one patient. However, when we compared the difference in response between the groups, it was not found to be significant.

Conclusion: TENS alone is effective as a treatment modality for pain control, it does not fare better than TENS combined with analgesics or tab gabapentin along with tricyclic antidepressants. Absence of any side effects is an added advantage in TENS, though we could not study the adverse effect profile in the patients as there were only non specifics complaints in the patients. Another finding of our study was absence of role of early initiation of antiviral therapy over the severity of PHN as we found VAS to be higher in the patients who had received oral antiviral within 72 hours of the exanthema.

Limitation: Relatively small sample size, small number of people in various groups, absence of baseline data about severity of exanthem and distribution of patients in various groups according to patient convenience are some of the weak points of this study. A randomised prospective study with a greater sample size and longer follow up period is needed to evaluate the efficacy of TENS in PHN in long term.

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