Venlafaxine Extended Release in the Treatment of Post Herpetic Neuralgia: A Quasi-Experimental Study

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Abstract

Background: Anti depressant drugs are sometimes used to treat neuropathic pain like Postherpetic Neuralgia (PHN) however, their analgesic efficacy is unclear. Venlafaxine is a reasonably well tolerated anti depressant and is a Serotonin Norepinephrine Reuptake Inhibitor (SNRI) and weak noradrenaline reuptake inhibitor. Although not licensed for the treatment of chronic or neuropathic pain in most countries, it is sometimes used for this indication. The present study evaluated the efficacy, tolerability and Quality of Life (QoL) of venlafaxine use for 12 weeks in patients with PHN.

Materials and methods: This quasi-experimental (Pre-test-posttest design) was conducted in the department of Neurology, Dhaka Medical College Hospital, from July 2012 to June 2013. Four hundred and fifty two patients were included in the study and Venlafaxine extended release tablet (75 to 150 mg) were administeredfor 12 weeks. Pain severity score, pain interference score and QoL score were assessed by a self-rated questionnaire before treatment and at 12 weeks follow-up.

Results: Majority of the patients were male (63.7%) with a mean age of 48.1 years. After 12 weeks of Venlafaxine treatment, 330 (73%) patients reported at least 50% relief in pain, whereas three (0.7%) patients did not report any pain relief. Pain was relieved completely in 32 (7.0%) patients. There was a significant decrease in the mean pain severity score, (5.8±2.0 versus 3.6±2.2) and meanpain interference score (4.5±2.0 versus 3.1±1.9) from baseline to 12 weeks. The mean QoL scale score improved significantly from 5.9±1.6 at baseline to 8.0±1.7 at week 12. Only 2.8% (13/452) patients experienced at least one adverse effect during the study period.

Conclusion: Venlafaxine was found to be effective, safe and well tolerated in the patients of PHN for relieving pain and improving QoL. Further double blinded randomize study is needed to validate these findings.

Key words : Herpes Zoster; Postherpetic neuralgia; Quality of life; Venlafaxine.

Introduction

Herpes zoster is accompanied in the majority of patients by intense pain that is variously described as burning, deeply aching, tearing or lancinating. Abnormalities of sensation in affected dermatomes are common, including hyperpathia or allodynia.[1] While herpes zoster associated pain tends to resolve spontaneously with time, some patients suffer from chronic, debilitating neuropathic pain that persist beyond the resolution of visible cutaneous manifestation of the underlying viral eruption termed as Postherpetic Neuralgia (PHN). PHN occur in the area affected by herpes zoster at least 3 months after crusting of the herpes zoster rash and may persist for many years.[2]

PHN is usually refractory to simple analgesic therapies and treatment most often is pharmacologic, including a wide variety of drugs and routes of delivery.[3] Most commonly used medications are oral medication such as TCAs, Gabapentin, Carbamazepine, Oxcarbazepine, Duloxetine, Opioids.[4] Unfortunately, pain relief was achieved in only about 50% of patients treated with these medication.[5] Moreover, these medications have significant side effect which limits its use.[6]

One particular medication for neuropathic pain is venlafaxine. Venlafaxine immediate release was the first Serotonin Norepinephrine Re-uptake Inhibitor (SNRI) to be marketed in the United States and was approved by the US Food and Drug Administration (FDA) in1993. In 1997, the Extended Release (XR) version of the medication was approved by the FDA and is dosed once per day. While proving to be an efficacious medication for neuropathic pain, venlafaxine's adverse effect profile should be noted. Cardiac conduction abnormalities and hyponatremia have been reported in a small number patients.[7]

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It should be stated that literature and research give evidence that balanced inhibition of the uptake of both serotonin and noradrenaline is considered to be important also for its analgesic effect. From this concept venlafaxine can be very effective for the treatment of PHN.[8] The present study was designed to evaluate the efficacy, tolerability and Quality of Life (QoL) change by venlafaxine in patients with postherpetic neuralgia.

Materials and methods

This was a single center quasi-experimental (Pretest posttest design) study conducted in the department of Neurology, Dhaka Medical College Hospital, from July 2012 to June 2013. Prior approval was obtained from the Ethical Review Committee of DMC and informed consent was attained from all participants.

Diagnosed cases of PHN as per the criteria given by Nalamachu et al included in the study from the Outpatient department if they presented minimum 3 months after the occurrence of herpes zoster.[9] Patients associated with other cause of neuropathic pain e.g. cervical spondylosis, Diabetes Mellitus and Hypothyroidism were excluded. Out of the 550 patients screened, 500 patients were enrolled. Venlafexine extended release tablet were administered once daily from 75 mg to 150 mg. The daily dose was titrated from 75 mg to 150 mg day 1 to day 7. Each patient was followed up after a period of 12 weeks.

Change in neuropathic pain at week 12 compared with baseline was assessed by the pain severity score and pain interference scores of the BPI-SF, a self-rated questionnaire. The pain severity score was calculated by taking the mean of scores for pain at its worst, pain at its least, pain on average and pain experienced at a particular time point. The pain interference score was calculated by taking the mean of scores for the interference of pain with general activity, mood, walking, normal work, relations, sleep and enjoyment of life. The QoL was evaluated at baseline and week 12, using the American Chronic Pain Association QoL scale. Data were analyzed using SPSS version 22.0. Categorica data were expressed as frequency %) and continuos data were expressed as mean (±SD). Mean differences of pre and post intervention values of pain severity score, pain interference score and QoL score were tested by paired sample t test. p value < 0.05 was considered as significant statistically.

Results

Out of 500 enrolled patients 452 (90.4%) patients were available in the 12 weeks follow-up and included in the analysis. Mean age was 48.1±11.3 years and majority of the patients were male (63.7%) (Table I).

Table I : Baseline demographic characteristics of the patients (n=452)

Characteristics	Frequency (%)/Mean ±SD
Age, years	48.1±11.3
Sex	
Male	288 (63.7)
Female	164 (36.3)

After 12 weeks of treatment with venlafaxine there was significant reduction of both pain severity score and pain interference score from baseline. Similarly, QoL score improved significantly from baseline to 12 weeks after treatment (Table II). These indicated that, venlafaxine was effective as an analgesic and also to improve QoL in the study.

Table II : Change in neuropathic pain and QoL score at 12 weeks FU from baseline

Parameters	Mean ±SD values at Baseline	At 12 weeks FU	Mean difference (95% CI)	p value*
Pain severity score	5.8±2.0	3.6±2.2	-2.2 (1.01-3.11)	<0.001
Pain interference score	4.5±2.0	3.1±1.9	-1.4 (1.03-2.99)	<0.001
Quality of life score	5.9±1.6	8.0±1.7	2.1 (1.30-4.01)	<0.001

CI: Confidence Interval; *p values were obtained from paired sample t test.

In the study, out of 500 enrolled patients 48 (9.6%) were lost to follow-up. Adverse events were reported infrequently and most frequent was drowsiness (0.9%), followed by headache (0.7%), nausea (0.4%), hyponatremia (0.4%), dizziness (0.2%) and hypertension (0.2%)(Figure 1).

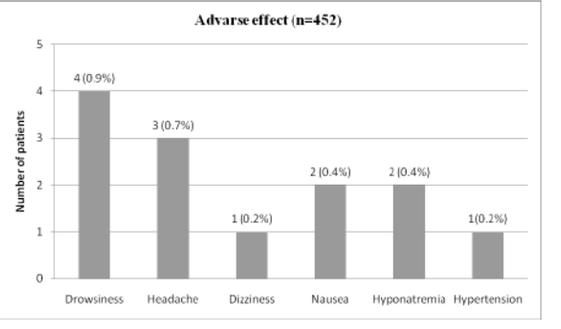

Fig 1: Adverse events during the study period

Discussion

This study assessed the efficacy, tolerability and impact on QoL of treatment with Venlafaxine in the PHN patients. The study demonstrated a promising effect in such patients' regarding pain severity reduction and improving QoL with 12 weeks of treatment.

After 12 weeks of Venlafaxine treatment, about 330 (73%) of the patients reported at least 50% relief in pain, whereas three (0.7%) patients did not report any pain relief. For 32 (7.0%) patients, 100% pain relief was observed. Moreover, at 12 week, there was a significant ($p < 0.001$) decrease in the mean (± SD) pain severity score, from 5.8±2.0 at baseline to 3.6±2.2 at week 12 and mean(± SD) pain interference score from 4.5±2.0 at baseline to 3.1±1.9 at week 12. This findings are in similarity with Sindrup et al and Rowbotham et al.[10,11]. The mean (± SD) Quality of life scale score was significantly ($p < 0.001$) improved from 5.9±1.6 at baseline to 8.0±1.7 at week 12. Kadiroglu et al also finds that Venlafaxine significantly improves quality of life in diabetic peripheral neuropathy.[12] Previous several study also suggested that Venlafaxine significantly improves sleep quality, mobility, general activity and mood of peripheral neuropathy patients.[13,14]

Thirteen patients (2.8%) experienced at least one adverse effect during the study period. The most common adverse effect was drowsiness, followed by headache, mild dizziness, nausea, hyponatremia and hypertension. Most of the adverse effects were mild in severity. No deaths or other serious adverse effect were reported. Sumpton et al found hyponatremia and hypertension are common side effect of Venlafaxine.[13,15]

Limitation

This study has several limitations. Entire sample was selected from a single public tertiary care hospital. Quasi-experimental design was another major limitation.

Conclusion

Venlafaxine 75 to 150 mg for 12 weeks significantly relieved pain and improved QoLin patient with PHN. Venlafaxine had a promising safety profile and well tolerated.

Recommendation

Further multi center, double-blind randomized trials are needed to validate our findings.

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Contribution of authors

SA-Conception, design, drafting & final approval.

NHM-Interpretation of data, critical revision & final approval.

MMR-Data collection & data analysis, critical revision & final approval.

AKMHK-Data analysis, critical revision & final approval.

NFA-Data collection, drafting & final approval.

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Disclosure

All the authors declared no competing interest.

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