A Comparative Pilot Study to Evaluate the Adjunctive Role of Levosulpride with Trigger Point Injection Therapy in the Management of Myofascial Pain Syndrome of Orofacial Region

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Abstract

Purpose To evaluate the effect of therapy with levosulpride combined with conventional trigger point injection therapy in terms of pain and depression in the chronic myofascial pain syndrome patients.

Materials and Methods This was a comparative prospective study in which subjects with at least one trigger point and symptom duration of at least 3 months were recruited and randomized into two groups. Group A subjects received trigger point injections with 0.5 % bupivacaine and tablet levosulpride and group B received trigger point injections and a placebo. Subjects were assessed for pain with visual analog scale (VAS) and depression with Beck's depression inventory (BDI) at the follow-up periods of 1, 4, 6 and 12 weeks. The treatment effect was measured in terms of mean difference of BDI and VAS scores at various studied intervals from the baseline values.

Results The sample was composed of 15 subjects with 8 in group A (6 females and 2 males, with a mean age of 41.88 ± 15.13 years, disease duration of 12.37 ± 16.11 months) and 7 in group B (6 females and 1 male, with a mean age of 43.86 ± 12.34 years, disease duration of 9.64 ± 9.34 months). The mean baseline VAS score and BDI score

was 6.75 ± 1.03 in group A and 6.86 ± 1.06 in group B and 24.25 ± 10.20 in group A and 24.43 ± 11.16 in group B respectively. The mean difference of VAS scores at 12th week interval from the baseline values was highly significant. Although the mean difference of VAS scores at all the other intervals and mean difference of BDI scores at all the intervals was statistically nonsignificant, there was improvement in the mean differences at all the follow-up intervals in terms of both pain as well as depression.

Conclusions The combined therapy with conventional trigger point injection and levosulpride as antidepressant significantly reduce pain and depression in the study subjects suffering from chronic myofascial pain with moderate to severe depression in the orofacial region.

Keywords Myofascial pain syndrome · Orofacial pain · Trigger points

Introduction

Myofascial pain associated with trigger points has been studied by the medical and dental profession for more than a century [1, 2]. However, various aspects of its pathophysiology, clinical manifestation and treatment remain unclear. Myofascial pain constitutes a major contribution to the spectrum of orofacial pain. Literature data on temporomandibular disorders (TMD) has clearly demonstrated the highest prevalence of myofascial pain among all the TMDs. The exact etiopathogenesis of trigger points is unknown till now, however the integrated trigger point hypothesis is the most accepted.

Since these active trigger points are the key etiological factors for the pain symptoms in myofascial pain syndrome (MPS) patients along with other contributing factors that

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perpetuate the problem. The primary goal of treatment is to break this “pain-spasm-pain” cycle. Trigger point (TrP) injection is one of the most effective methods in treatment of MPS. Local anesthetic, saline, steroid, botulinum toxin, and dry needling techniques are different injection techniques that can be used to inactivate activated trigger points.

The biopsychosocial model of pain has pointed out the necessity of assessing psychological status of chronic pain patients; therefore anxiety, depression, and somatization should be routinely evaluated in TMD patients [3]. Despite abundant work on the association of chronic pain and depression, paucity of data exists about the efficacy of antidepressant in combination with conventional trigger point injection therapy.

A pilot study was done to compare the adjunctive role of tablet levosulpride as antidepressant combined with trigger point injection therapy versus placebo with the hypothesis that adjunctive antidepressant therapy helps in better treatment outcome in the management of MPS of the orofacial region.

Patients and Methods

Study Design

This was a prospective, comparative pilot study conducted by the Department of Oral and Maxillofacial Surgery, Post Graduate Institute of Dental Sciences, Rohtak. An informed written consent was taken from all the patients enrolled in this study.

Patient Population

The subjects were assessed for the presence of trigger points in the muscles of mastication. Subjects with at least one trigger point and symptom duration of at least 3 months were recruited in the study. All patients' routine hematological and biochemical parameters were determined.

Patients with fibromyalgia, cervical disc lesion, major systemic disease and pregnant patients; those having undergone neck and shoulder surgery; with drug allergy history, and abnormal laboratory results and those diagnosed with group III TMD according to Research diagnostic criteria for TMD were excluded from the study.

In a 3 month period from October 2010 to January 2011, among the 26 patients referred to our pain clinic for assessment, 15 patients met the inclusion criteria and were enrolled for the study. After physical examination, all the necessary laboratory investigations were evaluated. Patients were randomly assigned into 2 groups. Randomization was computer generated. Group A received combined trigger

point injection therapy with 0.5 % bupivacaine and 50 mg of tablet levosulpride per orally B.I.D for an initial period of 2 weeks followed by increasing to a maximum of 150 mg daily for a maximum period of 6 weeks and Group B received local anesthetic injection (0.5 % bupivacaine) on trigger points and a placebo according to the technique described by Travell and Simons [4].

The severity of pain was assessed by linear visual analog scale (VAS). The Turkish version of the Beck depression inventory (BDI) [5, 6] was administered to assess the depression. Severity of depression was interpreted from scores as : 0–9, minimal; 10–16, mild; 17–29, moderate; and 30–63, severe [7]. BDI scoring of all the patients was done by one psychiatrist from the department of psychiatry.

Patients were followed-up at 1, 4, 6 and 12 weeks interval to evaluate the treatment outcome in terms of pain and depression.

Observations

Fifteen patients were enrolled in this comparative pilot study over a period of 3 months and were randomized into 2 groups. Group A comprised of 8 patients (6 females and 2 males, with a mean age of 41.88 ± 15.13 years, disease duration 12.37 ± 16.11 months) and group B comprised of 7 patients (6 females and 1 male, with a mean age of 43.86 ± 12.34 years, disease duration of 9.64 ± 9.34 months).

The mean baseline VAS score was 6.75 ± 1.03 in group A and 6.86 ± 1.06 in group B. The mean baseline BDI score was 24.25 ± 10.20 in group A and 24.43 ± 11.16 in group B (Table 1). All patients completed the study. No side effects were observed during the injections. There were no statistically significant differences in the pre-treatment evaluation parameters of the patients.

Statistical Assessment of Clinical Parameters Assessed

When the relative efficacies of two interventions were compared between the two groups in terms of reduction of VAS scores in comparison to the baseline VAS scores it was found that the mean difference between the VAS scores of Groups A and B was statistically significant (p value- 0.045) at the 12th week interval while it was non-significant at all the other follow-up intervals (Table 2).

Similarly when the relative efficacies of two interventions were compared between the two groups in terms of reduction of BDI scores in comparison to the baseline BDI scores the mean difference between BDI scores of Groups A and B was non-significant at all the follow-up intervals (Table 3).

Table 1 Socio-demographic and baseline clinical characteristics of study subjects

Characteristic observed	Group A (N = 8)	Group B (N = 7)	χ^2/T statistic	Df ***	P value
Mean age (in years)	41.88 $\pm$ 15.132	43.86 $\pm$ 12.348	−0.275	13	0.787*
Gender					
Female	6	6	0.268	1	0.605**
Male	2	1			
No. of trigger points					
1	2	0	2.277	4	0.685**
2	1	1			
3	3	3			
4	1	1			
5	1	2			
Mean no. of trigger points	3.216 $\pm$ 1.057	3.166 $\pm$ 1.383	−1.242	13	0.236*
Mean duration (in months)	12.375 $\pm$ 16.115	9.643 $\pm$ 9.348	0.393	13	0.700*
Side affected					
Bilateral	1	3	2.746	2	0.253**
Left	4	1			
Right	3	3			
Depression level					
Mild	1	1	1.741	2	0.418**
Moderate	4	6			
Severe	3	0			
Baseline BDI score (mean)	24.25 $\pm$ 10.20	24.43 $\pm$ 11.16	−0.032	13	0.975*
Baseline VAS score (mean)	6.75 $\pm$ 1.03	6.86 $\pm$ 1.06	−0.197	13	0.847*

* t- test, ** χ^2 test, *** Degrees of freedom

Table 2 Relative efficacies of the two interventions in reduction of VAS scores in comparison to baseline scores in the two Groups

	Mean difference (A–B)	Standard error	P value	95 % Confidence interval	
				Lower bound	Upper bound
0 and 1 wk	0.196	0.445	0.666	−0.764	1.157
0 and 4 wks	0.321	0.852	0.712	−1.519	2.162
0 and 6 wks	1.161	1.038	0.288	−1.082	3.403
0 and 12 wks	1.786	0.854	0.057	−0.60	3.632

Table 3 Relative efficacies of the two interventions in reduction of BDI scores in comparison to baseline scores in the two Groups

	Mean difference (A–B)	Standard error	P value	95 % Confidence interval	
				Lower bound	Upper bound
0 and 1 wk	−0.482	1.865	0.800	−4.510	3.546
0 and 4 wks	5.089	4.256	0.253	−4.106	14.285
0 and 6 wks	4.071	3.899	0.315	−4.351	12.494
0 and 12 wks	5.036	4.001	0.230	−3.608	13.679

Discussion

Myofascial pain is the most common form of musculo-skeletal pain affecting the head, neck and face [8, 9]. Source of symptoms and findings in myofascial pain syndrome is the trigger points within taut band. Trigger point formation mechanism is not fully known. Overload of muscles, damage, and stress are accepted as the most important factors. Trigger point injections or dry needling are a highly effective way to reduce the local pain and contraction of the taut band. This does not, however, constitute the whole treatment of MPS and MTrPs. The causes that led to the condition must be corrected, when possible. Mechanical, medical, and psychological perpetuating factors must also be eliminated

or alleviated in order to reduce the chance of recurrence. Inadequate attention to these aspects of treatment leads to failure to relieve pain and restore function [10, 11].

Velly et al. [12] investigated the contributing factors for chronic masticatory myofascial pain. The results revealed that a higher score of depression and anxiety were associated with masticatory myofascial pain, as well as other psychological symptoms, compared with the controls selected from the non-specialized temporomandibular disorders clinic. Altindag et al. [13] found higher levels of depression and physical disability in patients with MPS and a relationship between pain intensity and the level of depressive symptoms as measured by BDI in MPS patients. But there is still dilemma present as to whether chronic pain causes depression or

depression causes pain [14]. Esenyel et al. [15] reported that depression showed improvement by the treatment of MPS. Various trials have been done to evaluate the improvement in pain and depression with trigger point injection therapy with local anesthetic as well as dry needling. These trials showed that depression and pain have close relationship, and as pain decreases, depression decreases as well [16]. One point worth noted in these studies is that they have included majority of patients with mild depression. Whereas in our study, the mean baseline depression score was 24.25 ± 10.20 in group A and 24.43 ± 11.16 in group B with majority of patients suffering with moderate and severe depression. We feel that in patients of chronic pain with moderate to severe depression, the depression component should also be addressed to relieve pain and contribute to the patients' quality of life. The analgesic role of antidepressants in chronic pain has also been well documented in the literature [17, 18]. However to the best of our knowledge, the role of antidepressants in treatment outcome in terms of pain as well as depression of chronic myofascial pain has not been studied in the literature. Therefore we designed this study to evaluate the effect of adjuvant therapy with levosulpride as antidepressant combined with trigger point injection therapy in the treatment outcome of MPS.

In this study levosulpride has been used as antidepressant over conventional antidepressants such as Tricyclic Antidepressants (TCAs) because of the lack of anticholinergic and cardiovascular side effects of TCAs in levosulpride. In a comparative study with Amitriptyline, it was found that levosulpride has rapid onset of action with equivalent long term response and fewer adverse effects [19]. No side effects were observed in our study.

In this study, we found that there was statistically significant improvement in pain at the 12th week follow-up in the study group treated with combined therapy. There was decline in the mean differences of depression scores at all the follow-up intervals in both the treatment as well as placebo group with higher mean difference in the treatment group; however the improvement in depression scores was statistically non-significant when the treatment group was compared with the placebo group. This can be explained by the small sample size and short duration of the study.

In summary, the significant contributory role of depression in the chronic myofascial pain and the promising results of levosulpride as an antidepressant gives us a future insight to study the role of levosulpride as adjunctive therapy combined with conventional trigger point injection therapy with larger sample size in long term treatment outcome and thus contributing to relieve human sufferings.

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