

Efficacy of Dosulepin in Tension Type Headache and Midfacial Pain a Randomised Controlled Study

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Abstract

Introduction:

Patients presenting with pain in the facial region are commonly referred to Otorhinolaryngologist. Due to the various causative factors causing pain in the facial region, the proper diagnosis and more importantly the skill to rule out the sinogenic pain plays an important role in management. Tension type headache and midfacial pain are often misdiagnosed and treated wrongly and thus add to the morbidity of patients. Of all the medications that are used for the treatment, most provide minimal, short term relief with side effects on prolonged use. Dosulepin a Tricyclic Antidepressant helps in relieving pain with minimal side effects as compared to other Tricyclic Antidepressants.

Aims and Objective:

To study the efficacy of dosulepin in patients attending outpatient Department of otorhinolaryngology of Silchar Medical College and Hospital

Methods:

130 patients attending outpatient Department of ENT and Head and Neck Surgery of Silchar Medical College & Hospital, from September 2017 to August 2018 with complaints of headache diagnosed as tension type headache and midfacial pain were evaluated. Neurological and radiographic examinations were performed prior to therapy and local cause of pain in the facial region were ruled out. Together with this we also performed psychic evaluation for those patients who could not be withdrawn from current medication and then to start them on our current medication. Patients were randomly divided into two groups, one group receiving dosulepin and the other group receiving only placebo. Patients were followed on 1 week, 4 weeks and 8 weeks. Post treatment pain was assessed with a 10cm visual analogue scale (VAS), and McGill Pain Questionnaire (MPQ). Relief of pain was estimated with a separate VAS at the end of completion of treatment. Quantification of depression was done with Hamilton Depression Inventory.

Then the statistical analysis of the various pain and mood scale were done with a paired t test for within the subject comparisons and with independent t test for between-subject comparison.

Results:

Data from 114 patients were then analysed, as 4 dropped out after one month, 8 subjects failed to comply with the treatment and 4 subjects took analgesic and benzodiazepines together with dosulepin. From the study it has been found that subjects receiving dosulepin had more effective pain control and mood elevation than the subjects receiving placebo.

Keywords: TCA- tricyclic antidepressant, VAS- visual analogue scale, MPQ- mcgill pain questionnaire

Date of Submission: 25-02-2020

Date of Acceptance: 09-03-2020

I. Introduction

Pain is subjective, personal experience that is influenced by cultural learning, the meaning of situation, attention and other psychological variables¹. Any injury or disease process produces neural signals that enters the nervous system, these acts as the substrate upon which the past experience, culture, anxiety and depression acts and thus produce the pain response. Majority of pain stimulus from face that are myelinated nerve reaches spinal cord of brain via afferents of trigeminal nerve. Neurophysiological model of Olesen² explains the interaction of various nociceptive inputs causing tension headache and facial pain. Thus pain is dynamic complex process that involves continuous interactions among complex ascending and descending systems. Orofacial region is made of lots of musculoskeletal, dental, vascular and neural structures and together with the various disease process affecting it, the interpretations of pain in these region becomes complicated. Tension type headache described as feeling of tightness pressure or constriction, with varying intensity, frequency and duration, presenting at the vertex, forehead, eyes, temple or occipital region while midfacial segment pain is similar except that it is symmetrical and involves midface and retro-orbital region.

In management of chronic pain of various conditions Tricyclic Antidepressant were in use for a long time, such as in migraine^{3,4}, tension headache^{5,6}, atypical facial pain^{7,8,9} and myofascial pain-dysfunction syndrome¹⁰. But there were conflicting opinions regarding the analgesic effects and antidepressant activity, suggesting that pain relief is associated with antidepressant treatment.^{3,6,8,9,11}. Amitriptyline has been used for a long time but there are certain drawbacks to the use of it as its dosages which is different for analgesic effect and antidepressant effects^{4,5,10,12,13}, slow onset of action, high anticholinergic effects, poor tolerability in elderly and high cardiotoxicity. On the other hand dosulepin which is also a TCA but having high efficacy¹⁴, prompt mode of action, superior anxiolytic and antidepressant efficacy, well tolerability¹⁴ and lesser side effects can be used in the treatment of chronic facial pain and midfacial pain.

European Federation of Neurological Societies Guidelines, Canadian Pain Society and Neuropathic Pain Special Interest group of International Association for the study of pain in the management of neuropathic pain have recommended dosulepin as the first line therapy. National Institute for Health and Care Excellence (NICE) guidelines have also demonstrated favourable results and have suggested dosulepin for postherpetic neuralgia, diabetic neuropathy, painful polyneuropathy. Feinmann et al. have also found that dosulepin as superior to placebo in relieving psychogenic facial pain¹⁵. Further Pilowsky et al.¹³ saw no significant effect for amitriptyline in comparison to placebo in a double blind crossover study.

In our present study we have evaluated the efficacy of dosulepin in comparison to placebo in tension type headache and midfacial pain.

II. Methods:

The study subjects were 130 outpatients attending ENT and Head & Neck Surgery Department of Silchar Medical College & Hospital with tension type headache and midfacial pain. Inclusion criteria were (1) chronic tension type headache, (2) headache with or without symptoms continuous or for 15 days a month, (3) 20 years of age or older. Certain specific exclusion criteria were (1) pain attributable to local well defined cause as sinusitis, dental abscess, malignancy or trigeminal neuralgia or temporomandibular joint pathology, (2) associated cardiac morbidities, severe liver disease and diagnosed psychiatric illness, (3) high risk of suicide. After thorough history and clinical (general, local and neurological) examination, radiological examination was done to rule out any local cause for pain and finally the patients were subjected to psychiatric evaluation.

Estimation of pain was done with a 10-cm visual analogue scale (VAS) and the McGill Pain Questionnaire (MPQ). Relief of symptoms i.e. pain was estimated with a separate VAS at the end of each drug regime period. Quantification of Depression was done with the help of Hamilton Depression Inventory

III. Results:

Out of 130 patients, 114 of them were analysed based on the data provided by them, as there were 4 drop out after one month, 8 subjects failed to comply with the treatment and 4 subjects took analgesic and benzodiazepines together with dosulepin. The study sample had 88 males and 26 females from age group 20 to 45 years who have been suffering from pain for last 2 years.

Table 1 distribution of sex and age groups

Parameters (age in years)	Male	Female	total
20-29	26(22.8%)	8(7%)	34(29.8%)
30-39	46(40.3%)	14(12.2%)	60(52.6%)
40-45	16(14%)	4(3.5%)	20(17.5%)
Total	88(77.1%)	26(22.8%)	114(100%)

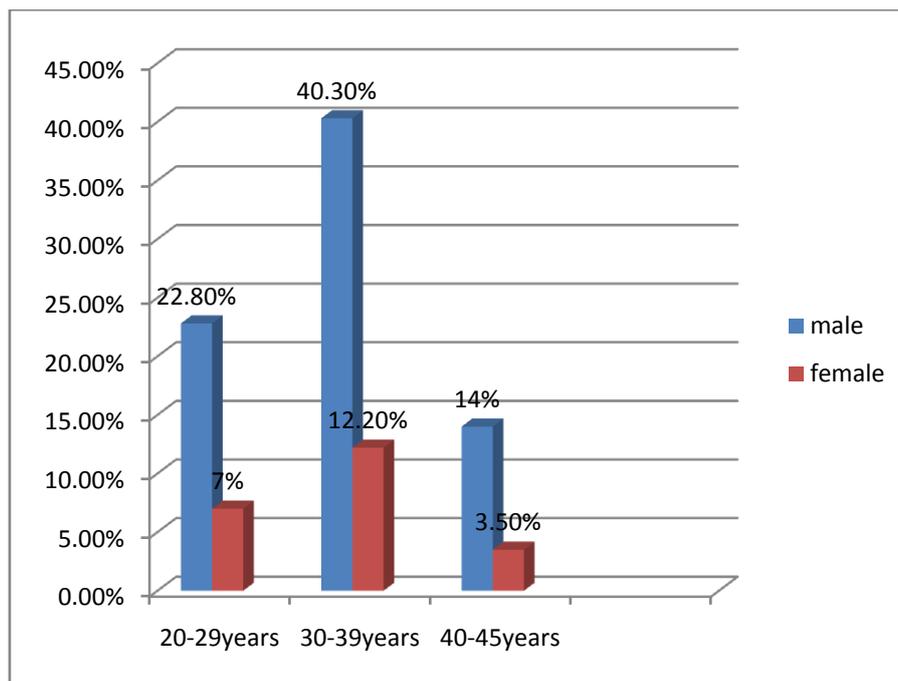


Figure 1: distribution of patients as per age group and sex

Table 2: effect of dosulepin on 3 pain scales: pain score difference from base line on visual analogue scale (VAS) and the McGill pain questionnaire (McG) and pain relief on the visual analogue scale (PR-VAS)

Test	Time (weeks)	dosulepin	Placebo
△ VAS	1	26.8 ± 7.6	12.8 ± 11.1
	4	27 ± 7.1	2.6 ± 7.9
	8	26 ± 2.1	1.4 ± 8.1
△ McG	1	7.4 ± 3.2	2.9 ± 2.7
	4	8.3 ± 2.1	1.1 ± 3.1
	8	9.7 ± 2.1	0.9 ± 3.1
△ PR- VAS	1	36.7 ± 13.1	18.3 ± 12.5
	4	33.1 ± 11.2	19.5 ± 11.5
	8	31.1 ± 14.6	17.5 ± 11.5

p value was found <0.01 at 4 weeks and 8 weeks of treatment, and is statistically significant

Clinical pain

Comparison of pain was done within subjects and their change in pain from the base line to each of the drug period was calculated. There was no significant difference in pain at the end of 1 week but there was significant reduction in pain after 4 weeks and 8 weeks and p value is <0.01 which is statistically significant

Depression

Subjects were divided into two groups according to their Hamilton score into depressed and non depressed. It has been found that VAS pain score for depressed group differ significantly (p <0.01) than the non depressed group. It was observed that the patients who were having depression together with pain and had received dosulepin had mood elevation together with significant pain reduction in comparison to patients receiving only placebo.

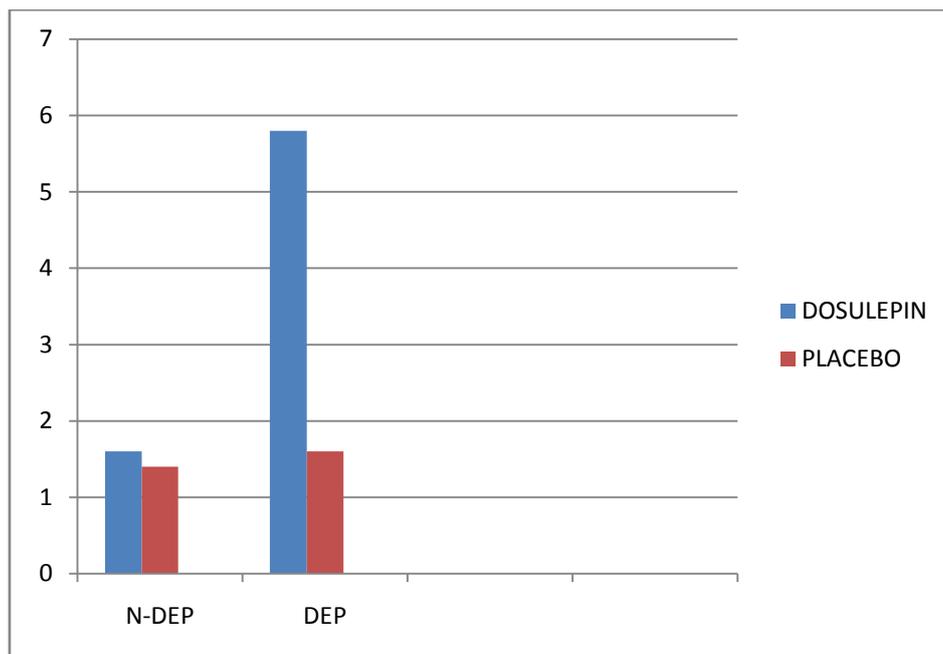


Figure 3: effect of dosulepin after 4weeks on reduction from baseline on the Hamilton depression score (HAM-D) in non-depressed (N-DEP) and depressed (DEP) subjects. P<0.01

IV. Discussion

In our present study it can be seen that dosulepin has effective pain control in tension type headache and mid facial pain. It has also been found in our study that the patients with depression and facial pain also responded well with dosulepin. Though both the depressed and non depressed patients responded equally to pain relief, depressed patients had added benefit of mood elevations.

Deslandes PN et al. (2016) in their study have found that that the trend in usage of dosulepin has altered significantly after the introduction of National Prescribing Indicator¹⁶

Kenneth A et al. in their study a found that tricyclic antidepressant as the first choice of drug in chronic tension type headache.¹⁷

Study done by Ramakrishnan K et al. and colleagues have found that there was significant (90%) improvement of severity of illness in patients suffering from anxiety depressive illness in Asian patients, right from the fourth day of starting treatment¹⁸

Badhri P et al have found in their study that dosulepin resulted in significant improvement in depressive symptoms and total score, from week 1 of therapy, with 95.4% of the patients treated for depression and associated anxiety showing overall clinical improvements.¹⁹

Dhavale, et al. in his study also found that, their was clinical improvement in anxiety disorders within 1 week of starting the treatment with dosulepin.²⁰

Dowrkin RH et al. has also suggested dosulepin as the first choice to treat anxiety in general practice.²¹

Donovan S et al., Zusky P et al., Claghorn JL et al., all of them in their study have stated that dosulepin as well tolerated and has a low incidence of cardiotoxicity.^{22,23,24}

N. Shah et al in his study have found that Sertraline, a Selective Serotonin Reuptake Inhibitor does not offer any therapeutic superiority over Tricyclic Antidepressant (dosulepin) in terms of efficacy.²⁵

Corne SJ et al in their study have found that improvement in sleep with dosulepin was always better than fluoxetine.²⁶

A study by Lambourn and Ress comparing the efficacy and safety of dosulepin and amitriptyline has found the incidence and severity of side effects were significantly less in dosulepin compared to amitriptyline.²⁷

There were various other study that have also depicted the superior effect of dosulepin over amitriptyline in pain controlled. Dosulepin also has superior effect to Selective Serotonin Reuptake Inhibitor , chlorthalidopoxide, sertraline, fluoxetine in emotional disturbance as depression.

V. Conclusion

Tension type headache and midfacial pain are two chronic condition that severely affects day to day life and greatly reduces the productivity of a person. Moreover there are various causes of headache, which needs to be diagnosed accurately so that appropriate treatment can be started. In our study we have found that headache has a psychosomatic factor, so medications that has anti depressant action plays a significant role. We

have seen that dosulepin a Tricyclic Antidepressant has both analgesic effect and antidepressant action thus reducing the chronic facial pain and midfacial pain, with minimal side effect.

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XXXXXX,etal. "Efficacy of Dosulepin in Tension Type Headache and Midfacial Pain a Randomised Controlled Study." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 19(3), 2020, pp. 10-14.