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Effectiveness of Tricyclic Antidepressants (TCA'S) in Management of Chronic Orofacial Pain

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ABSTRACT

Orofacial pain (OFP) diagnosis and management are challenging because of their complex histories, pathophysiology and are usually associated with psychosocial co-morbidities such as depression, stress and anxiety. TCAs are selective serotonin reuptake inhibitors resulting in increased activity of descending inhibitory pain pathways. Thus, the aim of this study is to assess the effectiveness of low dose amitriptyline in management of OFP.

This prospective study included 50 OFP patients who visited the university dental hospital from February 2018 to December 2019. These patients were treated with 10mg of amitriptyline and their VAS score was measured at baseline, 15 days, 30 days, and 45 days. The most prevalent age group and gender of the study population was 31-40 years (32%) with a female predilection (52%). The most common OFP was disc-condyle disorder (46%). Drowsiness (46%) was most reported adverse effect to TCA's. A paired t test performed to assess the mean difference at 15,30 45 days after using TCA's revealed p<0.01 with mean and SD as 4.400 ± 1.050; 1.956 ± 0.917; 0.577 ± 0.667, respectively. Low dose amitriptylines are more effective in management of OFP and its associated symptoms. It is more economical and less adverse effects reported.

Key words: Amitriptyline, BMS, Disc-condyle disorder, OFP

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INTRODUCTION

International Association for Study of Pain (IASP) defines pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage. Pain associated in the head and neck regions are referred to as Orofacial pain. Orofacial pain is divided into physical (axis 1) and psychological (axis2) by Okeson [1]. Physical conditions include Temporomandibular disorders (TMD), Musculoskeletal disorders (Myofacial pain dysfunction syndrome MPDS), dental and pulpal pain of somatic origin, neuropathic pain including trigeminal neuralgia, glossopharyngeal neuralgia, post herpetic neuralgia and neurovascular disorders/headaches (eg. Migraine and temporal arteritis) [1,2].

Burning mouth syndrome is a condition characterised by burning sensation or discomfort affecting the mouth, occurring in presence of clinically healthy mucosa [3]. They are broadly classified into Primary and Secondary. Primary BMS occurs when organic cause for oral burning cannot be identified, whereas Secondary BMS may arise because of any local [4] or systemic pathology [3]. It may be aggravated on consumption of hot and spicy foods. Studies have reported BMS in patients with diabetes mellitus [5,6], antihypertensive drugs [7]. To identify the systemic causes of BMS, patients should receive hematological and biochemical investigations to exclude anemia and hematinic deficiency [8]. BMS is reported to affect 0.7-15% of the population [9].

Atypical orofacial pain has been defined by International Classification of Headache Disorders (ICHD) as a persistent facial and/or oral pain, with varying presentations, but recurring daily for more than 3 months in the absence of

neurological deficit. Pain is characterized as dull, aching poorly localized with or without sharp exacerbations [10]. Primary diagnosis is based on pain history and clinical examination.

TMDs refer to conditions affecting the temporomandibular joint (TMJ), and/or the muscles of mastication [11]. Diagnosis of TMD follows a thorough history and examination. History includes pain character, precipitating and exacerbating factors, habits, and previous trauma [12,13]. Clinical examination includes assessment of mouth opening, palpation of TMJ and auscultation of joint sound [13]. Palpation of muscles of mastication to elicit tenderness or hypertrophy. Etiology of TMD is multifactorial including anatomical, psychological, and physiological factors. The most common Disc- condyle disorders constitutes internal derangements which includes disc displacements with and without reduction. Myofascial pain is usually dull and continuous with trigger points localized to muscles which are often tender when palpated [14].

The main aim of treatment of orofacial pain is to educate the patient about their condition and ensuring reassurance and hope. Psychological approach of treating orofacial pain using a Cognitive behavioural therapy (CBT) has been seen in reducing the pain intensity [15]. TMDS can be managed conservatively with occlusal splints, jaw exercises and with limited opening [16]. Topical management of OFP includes anesthetics such as lidocaine patches [17], proparacaine [18], capsaicin [19]. Systemic management includes NSAIDs [20], sympathomimetics [21], anticonvulsants [22] and antidepressants [23]. Botulinum A toxins have also proved its efficacy in managing TMDs [24].

TCAs are selective serotonin reuptake inhibitors which effectively blocks the reuptake of neurotransmitters norepinephrine (noradrenaline) and serotonin which are usually released from the central pain modulating system descending from brainstem to spinal cord. Thus, there is increased concentration of neurotransmitters and duration of action in synaptic cleft there by prolonging the inhibitory action on spinal cord neurons involved in transmitting pain [25]. In turn reduces the pain signaling in CNS and pain transmission. The common adverse effects are dizziness, sedation, orthostasis and cardiac rhythm changes thus contraindicated in cardiac patients [26]. TCA's are non-habituating and at a very lower risk for organ toxicity [27]. Orofacial pain being a chronic condition with a predominant psychogenic cause TCA's can be the drug of choice.

Thus, this study aims to assess the effectiveness of low dose amitriptyline in patients with chronic orofacial pain. Our recent research portfolio slides numerous articles in reputed journals [28-32]. Based on this experience we planned to pursue Effectiveness of Tricyclic antidepressants (TCA's) in chronic orofacial pain.

MATERIALS AND METHOD

The study was conducted in an university dental hospital setting covering patients visiting with management for various orofacial pain conditions. The research was approved by the institutional ethical committee and scientific review board (SRB). The study was carried out by 2 members, the primary researcher, and a department faculty. This prospective study was carried out from February 2018 - December 2019.

INCLUSION CRITERIA

Burning mouth syndrome, Disc-condyle disorders, Myofascial pain dysfunction syndrome (MPDS) and atypical facial pain patients.

These orofacial pain patients who did not respond other management.

EXCLUSION CRITERIA

Pain caused due to dental cause.

Neuralgias.

TMJ osteoarthritis and subluxation.

TMD's which require surgical management.

Pain caused due to systemic disease.

Pregnancy.

Cardiac disorder.

Known intolerance to amitriptyline.

In this study 50 orofacial pain patients were included in the final analysis. All demographic details and duration of symptoms were included. These patients were treated with 10mg of

amitriptyline and their VAS score was measured at baseline, 15 days, 30 days and 45 days.

The internal validity was maintained as set diagnostic criteria was followed and this methodology can be replicated at other centres also, maintaining the external validity also.

The study data was formulated on an excel sheet then later transferred to a SPSS file. IBM SPSS 20 was used in our study. The qualitative variables used in the study are gender, orofacial pain disorders like Burning mouth syndrome (BMS), atypical facial pain, disc condyle disorders, Myofascial pain dysfunction syndrome (MPDS). Quantitative variables include the age duration of pain and VAS score. The independent variables were age, sex, type of orofacial pain and dependant variables were VAS score. Correlation and association were analysed using Chi-square test for age, sex and type of orofacial pain. A paired t test for assessing the VAS score both preoperatively and postoperatively (15,30,45 days).

RESULTS AND DISCUSSION

In this prospective study 50 orofacial pain patients were included and were treated with low doses of TCA's.

The most prevalent age group and gender of the study population was 31-40 years (32%) followed by 21 to 30 years (28%); 41 to 50 years (18%); 51 to 60 years (12%); 11 to 20 years (8%) and 61 to 70years (2%) (Figure 1) and was predominant in females (52%) and males (48%) (Figure 2).

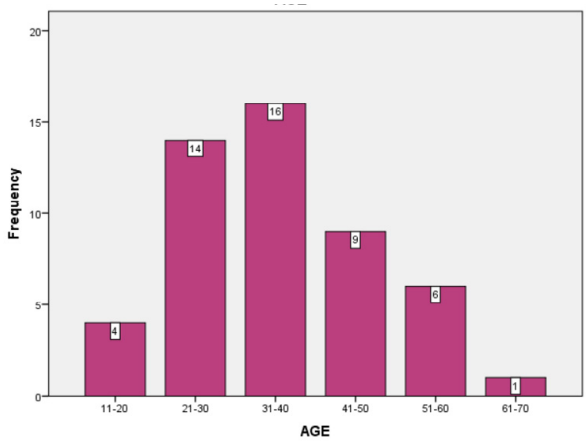

Figure 1: This bar graph represents the age distribution of our study population where the X axis represents the age in years and Y axis represents the frequency in number of OFP patients. In our study the maximum patients (n=16) belonged to the age group of 31 to 40 year (32%).

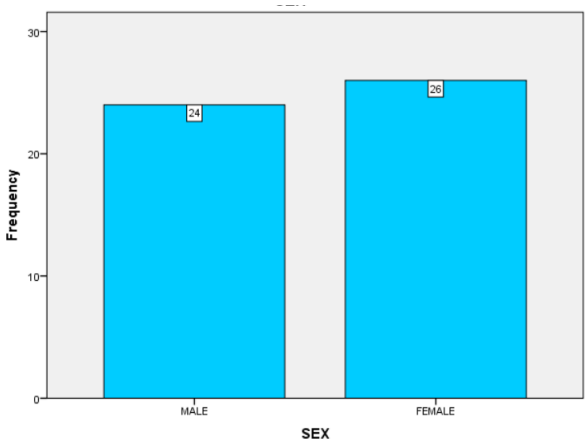

Figure 2: This bar graph represents the sex distribution of our study population where the X axis represents the sex and Y axis represents the frequency in numbers of OFP patients. This graph shows that females (52%) were more affected than males (48%).

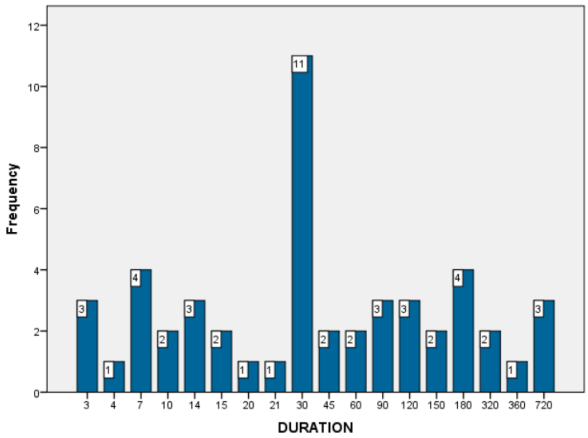

Figure 3: This bar graph represents the duration of symptoms reported in our study population, where the X axis represents duration in days and Y axis represents the frequency in numbers of OFP patients. In our study the maximum duration of symptoms was reported in 30 days (22%).

Frequency distribution of duration of symptoms revealed minimum duration of 3 days (6%) and a maximum duration of 720 days (6%) with a most frequent duration observed was 30 days (22%) (Figure 3). The most common orofacial reported was disc-condyle disorder (46%) followed by MPDS (32%); BMS(18%) and atypical facial pain(4%) (Figure 4). Most common adverse effect observed was drowsiness in 46% followed by dry mouth (20%), combination of dry mouth and drowsiness (20%) and no adverse effects reported in 14% (Figure 5). A chi-square test performed to assess the association between age and type of orofacial pain revealed disc-condyle disorder was more prevalent in 31 to 40 years while MPDS in 21 to 30 years; BMS in 51 to 60 years and atypical facial pain in 41 to 50 years and $p>0.05$ (Figure 6). Association between gender and type of orofacial pain revealed disc-

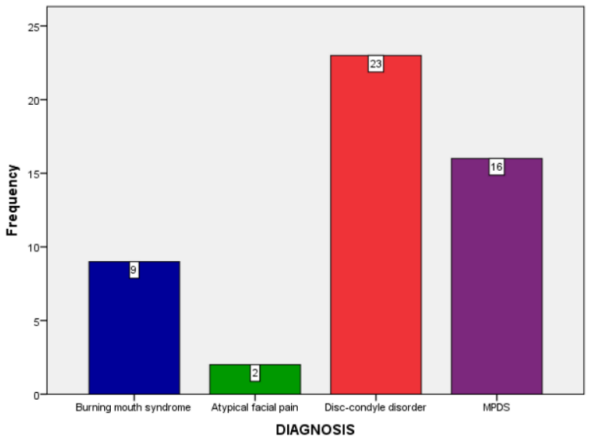

Figure 4: This bar graph represents the type of orofacial pain reported in our study population where the X axis represents the type of orofacial pain (Disc- condyle, MPDS- Myofascial pain syndrome, degenerative disorder, BMS- Burning mouth syndrome and atypical facial pain) and Y axis represents the frequency in number of orofacial pain patients. In our study the maximum reported was Disc-condyle disorder (46%) followed by MPDS (32%).

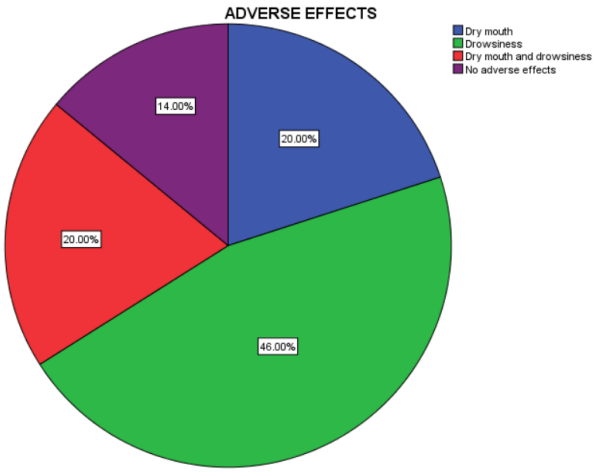

Figure 5: This pie graph represents the adverse effects reported in our study population.Blue denotes dry mouth; Green denotes drowsiness; Red denotes dry mouth and drowsiness; Violet denotes no adverse effects. In our study the drowsiness (46%) was maximum reported.

condyle disorder was predominant in males, MPDS and BMS in females while atypical facial pain reported were reported equally in both gender and p>0.05 (Figure 7).

Mean and standard deviation (SD) of VAS score at baseline, first review (15 days), second review (30 days) and third review (45 days) is 7.08 ± 1.007; 2.68 ± 1.236; 0.73 ± 0.598; 0.15 ± 0.364 respectively. A paired t test performed to assess the mean difference at 15,30 45 days after using TCA's revealed p<0.01 with mean and SD as 4.400 ± 1.050; 1.956 ± 0.917; 0.577 ± 0.667 respectively (Table 1).

Orofacial pain is the term used to describe pain arising from regions of the face and mouth and

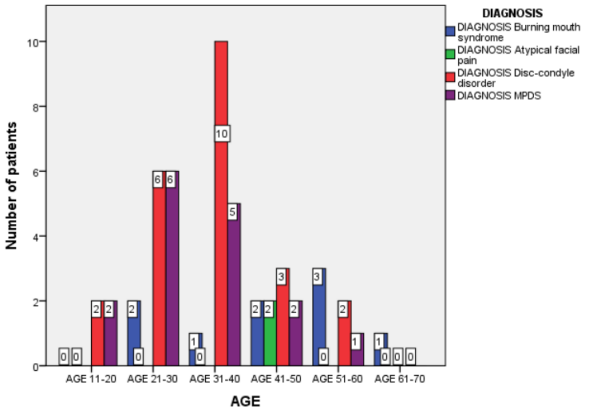

Figure 6: This bar graph represents the association of age and type of orofacial pain where the X axis represents age of patients in years and Y axis represents number of OFP patients. Disc-condyle disorder was more prevalent in 31 to 40 years while MPDS in 21 to 30 years; BMS in 51 to 60 years and atypical facial pain in 41 to 50 years. Pearson chi square= 22.321 p=0.099 (p>0.05)(chi-square) which was statistically not significant .

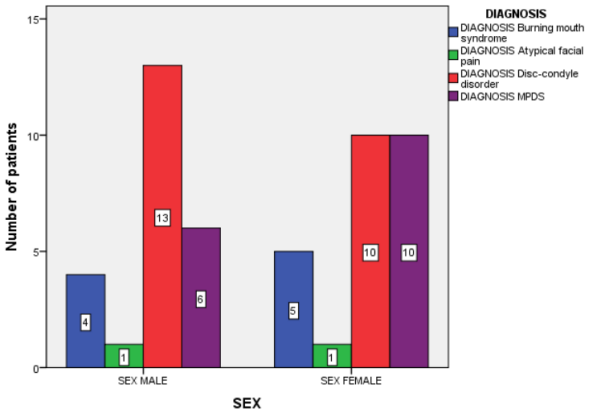

Figure 7: This bar graph represents the association of gender and type of orofacial pain where the X axis represents the gender of orofacial pain patients and Y axis represents number of OFP patients. Disc-condyle disorder was predominant in males, MPDS and BMS in females while atypical facial pain was reported equally in both genders. Pearson chi square= 1.425 p=0.700 (p>0.05) (chi-square) which was statistically not significant.

Table 1: Showing mean difference of VAS score assessed using a paired t-test.

	Baseline	First review (15 days)	Second review (30 days)	Third review (45 days)
Mean and Std dev	7.08 ± 1.007	2.68 ± 1.236	0.73 ± 0.598	0.15 ± 0.364
Mean difference and Std dev	0	4.400 ± 1.050	1.956 ± 0.917	0.15 ± 0.364
p value	0	0	0	0

they are caused due to diseases of regional structures, nervous system disorders, referral from distant sources or sometimes an unknown etiology [33]. They are described as acute when present less than 3 months and chronic when present more than 3 months.

BMS is a complex multifactorial complex process resulting due to an interaction between local, systemic, and psychosocial factors [9]. Studies

have reported secondary neuropathic changes to perimenopausal hormonal dysregulation [34]. Atypical orofacial pain patients exhibit higher incidence of comorbidities such as depression and obsessive- compulsive personality characteristics [35]. TMDs are caused due to both peripheral and central sensitization mechanisms [36]. They are referred to as central sensitization pain syndrome where the peripheral nociceptors produce a reversible, prolonged, and increased activity in central nociceptive pathways which results in pain hypersensitivity and hyperalgesia [37]. Orofacial pain diagnosis and management are challenging because of their complex histories, pathophysiology and are usually associated with psychosocial co-morbidities such as depression, stress, and anxiety.

In our study orofacial pain was more common in 31 to 40 years with a female predilection (52%). Akshay shetty et al. reported a mean age of 33.5 with a female prevalence of 59% [38]. A study conducted by Easter et al in 2018 in the United Kingdom reported a mean age of 38.3 years with a male predilection of 48.2% [39]. The pain onset duration varied from 3 days to 2 years in our study population whereas Derafshi et al. in 2019 reported a pain duration of 11 days to 3.4 years [40]. Disc condyle disorder (46%) was the more prevalent OFP in our study and the results agree with the study conducted by Badel et al. [41]. The most common adverse effect reported in our study was dry mouth and drowsiness which were similar in a study conducted by Guler et al. [42]. Association between age and type of orofacial pain revealed disc-condyle disorder was more prevalent in 31 to 40 years while MPDS in 21 to 30 years; BMS in 51 to 60 years and atypical facial pain in 41 to 50 years. Association gender and type of orofacial pain revealed disc-condyle disorder was predominant in males, MPDS and BMS in females while atypical facial pain reported were reported equally in both genders.

Shirish Ingawale reported the TMD were more prevalent in females between 20 to 40 years and Kohorst et al. [43] stated that BMS was more common in women older than 50 years while atypical facial pain was prevalent in females with a mean age of 46.6 years as reported by Guler et al. [42-44]. Amitriptyline has been used in management of chronic pain conditions and studies have reported that their analgesic effects are independent of their antidepressant effects. In our study VAS measured at regular intervals showed a progressive reduction in pain and burning sensation assessed using a paired t test revealed $p<0.001$ proving it to be statistically significant. Amitriptyline has proved its effectiveness in management of OFP with less adverse effects and the results are like studies conducted by Aurilo et al. CMR Barbosa et al. and Cavalcanti et al. [45-47]. Limitations of the study are reduced sample size; long term follow up including withdrawal of medication must be assessed.

CONCLUSION

Orofacial pain conditions occur due to complex pathophysiology and are often associated with psychosocial co-morbidities. Chronic orofacial pain has a significant impact upon quality of life and daily functioning. A biopsychosocial approach for the diagnosis and management may address the multifactorial etiology of orofacial pain conditions whilst limiting the economic and health related burden associated with these conditions. The study concludes that low dose amitriptylines are more effective in management of OFP and its associated symptoms, more economical and less adverse effects reported.

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AUTHOR CONTRIBUTIONS

Manivasagam Deepigaa has made substantial contributions to the research design, acquisition, and analysis of data, and to drafting the paper and revising it critically. Muthukrishnan Arvind has made substantial contributions to the research design, acquisition, and analysis of data, and to drafting the paper and revising it critically.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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