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An In-vivo Study to Evaluate the Onset of Relief from Ibuprofen, Placebo and Occlusal Splint in Patients with Acute Myalgia in Muscles Related to Temporomandibular Joint: A Comparative Pilot Study

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Abstract

Purpose: The treatment priority in management of Temporomandibular Joint (TMJ) pain is directed towards the causative factor along with symptomatic treatment. In this process many times psychological aspect is overlooked. Hence with this pilot study, importance of psychological aspect of Temporomandibular Joint Disorder (TMD) is emphasised. **Methods and Material:** 15 patients suffering from pain in TMD region who qualify under myalgia pain in DC/TMD Axis I category were selected. Patients were divided into 3 groups; Ibuprofen, placebo and occlusal splint with 5 patients in each group. Pain assessment was done at the first visit, 7th day visit and 14th day visit using a VAS scale. **Statistical Analysis Used:** Friedman Test was applied to determine overall relief from pain in the three groups. Wilcoxon sign rank test evaluated pain relief between each time interval. Kruskal Wallis Test compared different groups for relief from pain at each time interval. **Key Finding:** Wilcoxon sign rank test showed a significant pain relief in all three groups from I day to I follow up day and I day to II follow up day. However Pain relief from I follow up to II follow up day was significant only in placebo group. **Conclusions:** Management of TMD myalgia requires a comprehensive understanding of physical and psychological aspect. This will aid us in formulating a treatment plan comprising pharmacotherapy, placebo or physical therapy or combination of any of these.

Keywords: Myalgia, NSAIDs, Occlusal Splint, Placebo, Temporomandibular Disorder

1. Introduction

Orofacial pain disorders are debilitating conditions prevalent in about 10% population, involving the head, face and neck. Owing to their multi-factorial aetiology, they are a challenge for the doctor. The orofacial pain as classified by Okeson is divided into physical (Axis 1) and psychological (Axis 2) conditions explained later in text.

Physical conditions involving Temporomandibular Disorders (TMD), include:

- Disorders of the Temporomandibular Joint (TMJ)

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- Disorders of the musculoskeletal structures (eg. Masticatory muscles and cervical spine);
- Neuropathic pains, which include episodic (eg. Trigeminal neuralgia)
- Continuous (eg. peripheral/centralized mediated) pains
- Neurovascular disorders (eg. migraine).

Psychological conditions include anxiety and mood disorders[1].

Temporomandibular Disorder (TMD) is a heterogeneous term which encompasses a variety of signs and symptoms. History, clinical examination and appropriate conservative management should precede further investigations as indicated by an appropriate treatment plan to achieve a good overall outcome[2]. TMD cases have always been considered crucial in diagnosing and treating; however, with a standardized classification patients can be treated with a broad spectrum of treatment options with a good success rate[1].

The Research Diagnostic criteria for Temporomandibular Disorders (RDC/TMD) by E. Schiffman[3] are a comprehensive protocol for TMD research since1992, which was later renamed as DC/TMD criteria. This criterion was compelled to develop into a system for examining, diagnosing and classifying the need to provide clinical researchers with standardized and most common subtypes of Temporomandibular Disorders.

RDC/TMD is explained under 2 axes.

Axis 1

- Basically a pain screener.
- Based on a questionnaire that includes questions on history of pain.
- Examination by palpation of pain locations.
- Interpretation and diagnosis.

Axis 2

- Recognizing cognitive, emotional and behavioural responses to pain.
- Employs various instruments like PHQ, GCPS, JLFS, and OBC.

The treatment goals for TMD are decreasing pain, restoring normal range of motion and restoring normal masticatory and jaw function. Many TMDs can be cyclical and self-limiting, with periods of complete remission of symptoms[1].

The first line of treatment preferred by many clinician and researchers is supportive therapy (conservative). It is further divided in two types: Pharmacological and Physical. Supportive therapy is directed towards altering the patient's symptoms and often has no effect on the aetiology of disorder. The recorded success rates of conservative and non conservative seems to be same (75%-80%). Thus it would be logical to attempt conservative treatment and evaluate its results before non conservative line of treatment[4].

Pharmacologic intervention in the management of chronic orofacial pain should be considered an adjunct to a more definitive treatment. This combined therapy will eventually correct the underlying pathophysiologic process[5]. Being a large group, NSAID shave been most commonly prescribed for pain in the orofacial region. NSAIDs are indicated for mild to moderate acute inflammatory conditions in the TMJ. D. A. Hass[6] states that "To achieve an anti-inflammatory effect in TMD, these medications should be taken for a minimum of 2 weeks".

On the other hand various placebo-controlled studies suggested that NSAIDs are ineffective for chronic orofacial pain. Studies by Singer[7] and G. V. Pramod[8] suggest that the placebo can give near similar results as other pain medications. Hence the role of placebo should also be considered as one of the important management strategies in reduction in the masticatory muscle tenderness and significant improvement in the mouth opening.

Another type of supportive treatment modality is Oral Splints. These are acrylic devices that come under different classification and indications and have been used for TMD management successfully. Klasser[9] has advocated for splints, as an effective therapy in TMD cases in his review article.

This study aims at streamlining the TMD patient of myalgia group as classified under International Classification of Disease (9th and 10th revision) by E. Schiffman[3] and treating them with three conservative modalities randomly and later evaluating them on the basis of faster onset of relief from symptoms. Diagnostic criteria by E. Schiffman explain how myalgia in TMJ muscles can be diagnosed based on history and examination. When the patient presents with muscular pain that is affected by jaw movement, function or parafunction and this pain replicates with provocation testing of masticatory muscles, patient should be asked for history of present illness and examination performed (Table 1).

Since the evidence based data of success in various lines of treatment is sparse this pilot study can help in establishing foundation for further studies in this line.

Table 1. Diagnostic criteria by Eric Schiffman et al[3].

History	Examination
1. Positive for pain in jaw, temple, in the ear or front of the ear and 2. Pain is modified (but persists) with jaw movement, function or parafunction	1. Confirmed pain location in masseter or temporalis muscle and 2. Reporting familiar pain in masseter or temporalis muscle with any of the below mentioned provocation tests: A] palpation of temporalis or masseter muscle or B] maximum assisted or unassisted mouth opening movement

2. Materials and Methods

The study was conducted on the patients visiting the outpatient department of a Dental College and Hospital in Gujarat, India within a time period of 6 months. Subjects within age group of 21 to 55 years who complained of Temporomandibular pain were evaluated by the DC/TMD protocol Axis 1. 15 of those who qualified under the myalgia group symptoms were considered part of the study.

The exclusion criteria comprised of pregnant or lactating females, people on anti-inflammatory or antibiotic therapy within the previous 3 months, malocclusion or improper prosthesis, smokers or individuals with any systemic condition that could influence pain management. All subjects were explained about the treatment and a written consent was obtained from those who willingly accepted to become a part of the study. Subjects were divided into 3 groups:

Group I: 5 selected subjects were prescribed Ibuprofen (Tab Brufen 400 mg tid) by an assistant and recalled after 7 days and next after 14 days and their pain were evaluated at first day, 7th day and 14th day using VAS.

Group II: 5 selected subjects were prescribed Placebo (Cap Becosules od) by an assistant and recalled after 7 days and next after 14 days and their pain were evaluated at first day, 7th day and 14th day using VAS.

Group III: 5 selected subjects were given Centric stabilizing occlusal splint of permissive type (DPI heat cure acrylic resin) and were asked to wear it during night time (approx. 8 hours) and recalled after 7 days and next after 14 days and their pain was evaluated at first day, 7th day and 14th day using VAS.

All the participants were ruled out for any gastric related disease because of the nature of the interventional mode. Approval from the Institutional Ethics Committee was also obtained before starting with the study. The lab procedures were done in the department laboratory by one operator only.

VAS (Visual Analogue Scale) was used to quantify the pain by the subject on the three subsequent visits. Subjects were instructed to mark on a VAS strip (Figure 1) the pain

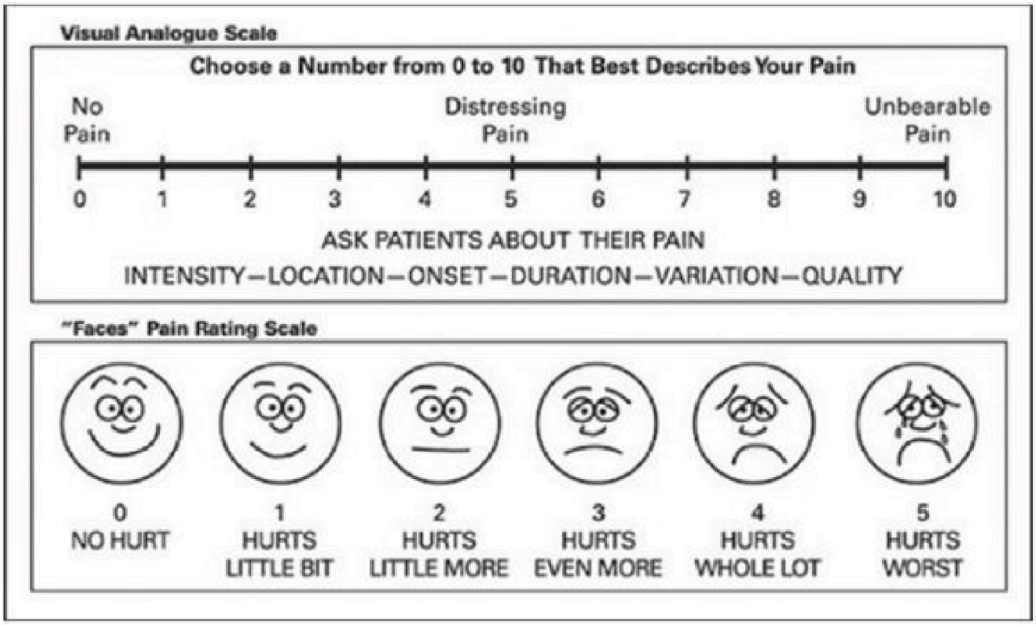


Figure 1. VAS scale.

intensity from '0' (absence of pain) up to '10' (the worst pain ever).

The study was double blinded as an assistant was used to prescribe the medication to prevent operator bias in the study during VAS recordings.

The study was registered with the Clinical Trial Registry India with reference no. REF/2016/05/011404.

3. Results

Since the data followed an asymmetrical data distribution, non-parametric tests were applied. Friedman Test was applied to determine the onset of relief from pain between different time intervals in the three groups. It demonstrated a significant 'p' value for all three groups (p = 0.04) at three time intervals.

Wilcoxon sign rank test evaluated pain relief between each interval. It was seen that 'p' value was significant between examination day and 1st follow up and examination day and 2nd follow up for all three groups (p = 0.04). It was also seen that between 1st and 2nd follow up 'p' value was not significant for Ibuprofen group (0.19) and splint group (0.27) but was significant for the placebo group (0.04) (Table 2).

Kruskal Wallis Test compared different groups for relief from pain at each time interval (Table 3). Although mean difference was greater in splint group between the examinations day (8.6) and 2nd follow up (2.4) than

Table 2. Comparison between different time intervals for each group

Rx		N	Mean (SD)	Range	Median (Q1-Q3)	Friedman Test		Wilcoxon sign rank test(p-value)		
						Chi Square Value	p-value	I day vs I follow up	I day vs II follow up	I follow up vs II follow up
Ibuprofen	Ist day	5	8.4 (1.14)	7 – 10	8 (7.5 - 9.5)	8.32	0.02*	0.04*	0.04*	0.19(NS)
	Ist follow up	5	4.6 (3.05)	1 – 8	5 (1.5 - 7.5)					
	IInd follow up	5	3.8 (2.17)	2 – 7	3 (2 - 6)					
Placebo	Ist day	5	7.4 (0.55)	7 – 8	7 (7 - 8)	10.00	0.007*	0.04*	0.04*	0.04*
	Ist follow up	5	4.2 (1.64)	2 – 6	5 (2.5 - 5.5)					
	IInd follow up	5	2.6 (1.82)	0 – 5	3 (1 - 4)					
Splint	Ist day	5	8.6 (0.89)	8 – 10	8 (8 - 9.5)	8.32	0.02*	0.04*	0.04*	0.27(NS)
	Ist follow up	5	4 (2.24)	1 – 7	4 (2 - 6)					
	IInd follow up	5	2.4 (3.05)	0 – 7	1 (0 - 5.5)					

*p<0.05 statistically significant

Table 3. Comparison between different groups at each time interval

	Rx	N	Mean (SD)	Range	Median (Q1-Q3)	Kruskal Wallis Test	
						Chi Square Value	p-value
Ist day	Ibuprofen	5	8.4 (1.14)	7 - 10	8 (7.5 - 9.5)	4.82	0.09(NS)
	Placebo	5	7.4 (0.55)	7 - 8	7 (7 - 8)		
	Splint	5	8.6 (0.89)	8 - 10	8 (8 - 9.5)		
Ist follow up	Ibuprofen	5	4.6 (3.05)	1 - 8	5 (1.5 - 7.5)	0.19	0.91(NS)
	Placebo	5	4.2 (1.64)	2 - 6	5 (2.5 - 5.5)		
	Splint	5	4 (2.24)	1 - 7	4 (2 - 6)		
IInd follow up	Ibuprofen	5	3.8 (2.17)	2 - 7	3 (2 - 6)	1.11	0.57(NS)
	Placebo	5	2.6 (1.82)	0 - 5	3 (1 - 4)		
	Splint	5	2.4 (3.05)	0 - 7	1 (0 - 5.5)		

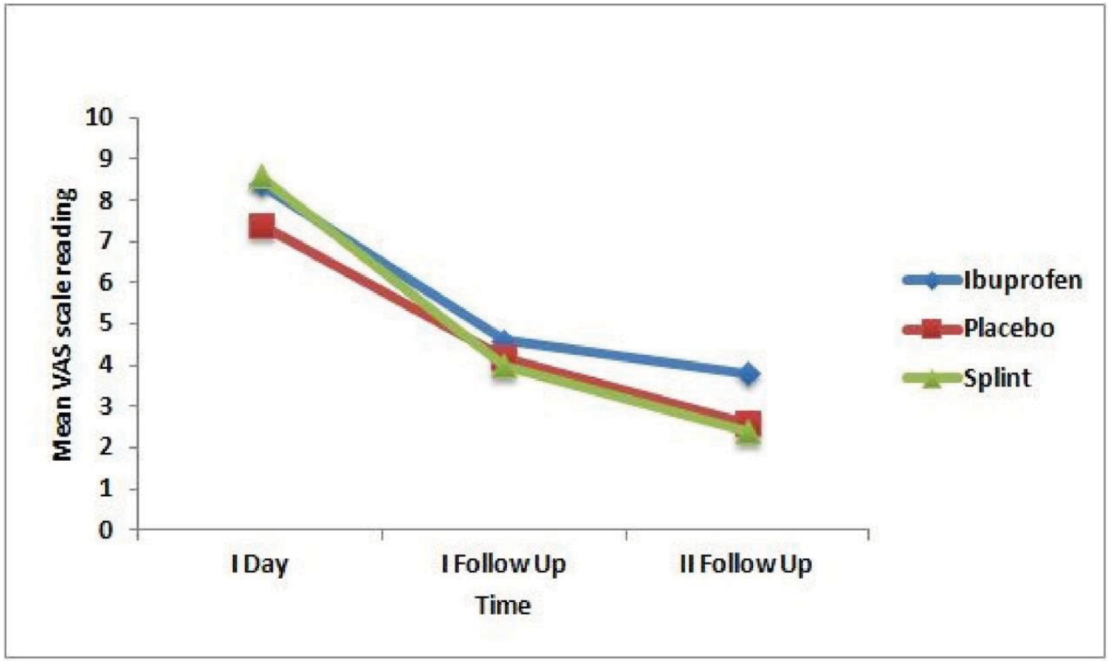


Figure 2. Comparing 3 different groups at each time interval.

other groups, statistically no significant difference was appreciated. (Figure 2).

4. Discussion

It was recognized that many putative dental and surgical therapies for TMDs have not withstood scientific scrutiny, and were being used as the drugs/treatments for primary intervention for some forms of chronic orofacial pain[5]. Curing TMJ-related pain remains a challenge, despite plethora of analgesic medication. Due to the lack of documented randomized controlled trials, NSAIDs are the most frequently prescribed drugs for pain for TMDs[6],

The NSAIDs group of drugs, prescribed for mild to moderate acute inflammatory conditions in the TMJ, inhibit cyclo-oxygenases and prevent the formation of prostaglandins[10]. For achieving relief from inflammatory symptoms in TMD, these medications are administered for a minimum of two weeks period[6].

The present study shows significant reduction ($p = 0.04$) of symptoms in all three groups from first day of appointment to the II follow up day. Ibuprofen reduced the pain symptoms significantly for first seven days. However data for next seven days was not statistically significant.

This can be supported by the conclusions of Ta and Dionne[11] from their randomized, double-blind trial, ho stated that "when associated with other substances, such as muscle relaxant (carisoprodol), analgesic (acetaminophen) and central analgesic and adjuvant (caffeine), the effects of NSAIDs could be improved and prolonged".

However NSAIDs are also known to have adverse effects on prolonged use. The most important one to know is that it causes gastric erosion leading to ulceration and gastric bleeding[10]. D. A. Haas mentions in his paper that "NSAIDs may also reduce renal blood flow, tubular excretion of drugs and renal prostaglandin production and when given for extended periods (N5 days), they may attenuate the effect of antihypertensive drugs". In addition; various drug interactions with NSAIDs can result in adverse effects[12].

Clinically, the decision to prescribe an NSAID is based on correlating signs with the symptoms noted by the patient. Since TMD is a multifactorial disease, risk–benefit ratio needs to be evaluated through research in pharmacotherapy for TMD patient[6].

In the present study, Table 2 demonstrated that there was no statistically significant difference observed in pain relief by the various groups from first (examination) day to second follow up day. This concurs with the

study by Fernando et al.[13] in which NSAID therapy achieved analgesia on the third day and placebo only by the eighth day. Hence no significant difference between medicaments was observed for VAS analysis in their study. However when the mean values were compared in the present study, splint groups showed maximum difference (examination day mean = 8.6) (II follow up day mean = 2.4). This indicates, though not statistically but clinically, towards the importance of acknowledging the local factors (loss of vertical length, parafunction, interference, etc.) responsible in TMDs.

Klasser et al[9], J. Friction[14], Clark et al[15] and Dube C[16] also stated in their individual studies that occlusal splint is an essential therapy for some TMD cases wherein they prevent excessive tooth wear decreasing the frequency, duration and intensity of para-function. Rahul[17] et al., explained "Splint therapy unloads the joint by disarticulating the dentition and increasing the vertical dimension of occlusion. By unloading the joint, there will be a reduction in both synovitis and masticatory muscle hyperactivity, hence relieving the fatigued muscle. If the hyperactivity is stopped, the pain caused due to it will usually disappear."

Manfredini et al.,[18] in his review addressed the association between pain and psychosocial involvement in TMD patients. He suggested that psychological suffering need not depend on the pain location. He affirmed longer the pain persists, greater the potential for emergence and amplification of cognitive, psychosocial and behavioural risk factors leading to enhanced pain sensitivity and reduced probability of success from standard treatments. Therefore, both treatment protocols, physical and psychological, should be considered while treating a TMD patient to assure treatment success.

Hence it is prudent on our part to tend to the psychological aspect of myalgia also. But most clinical studies documented in this field have compared two different potentially effective therapies and very few of them have used a placebo control[19], and the clinical studies available are underpowered due to lack of patients with TMD[20],

In the present study relief in symptoms between the first follow up day and second follow up is seen to be significant only for placebo (p = 0.04) (Table 3). Thus from this study it can be inferred that there was statistically significant pain relief from placebo during the full course of the study.

Earlier literatures also support use of placebo. Gale C Dixon[21] employed 7 questionnaires for depression and anxiety and found a correlation among depression, anxiety and TMD. This correlation was also verified by Pereira et al[22] in teenagers using RDC axis I and II.

Ekberg E[23] in a short, placebo-controlled, randomized clinical trial for TMJ pain compared diclofenac with placebo and concluded with no significant greater effect of diclofenac compared to placebo.

Also literature suggests that pain or suffering is composed of two phases: The original pain sensation, and the reaction to it or the processing of it by the central nervous system[24]. The placebo, Beecher[25] wrote, exerts its action on the processing component of pain, and this processing or reaction phase is greater in painful situations where stress is also at a high level. If true, this would explain why placebos seem to be more effective when patient anxiety is high.

Hence from this study all three groups quantify to give significant result within seven days, however placebo group continued to give statistically significant results over next seven days also ('p' = 0.04). Here it should be considered that the base line VAS values were not the same for all groups since the patients were randomly allotted in the group.

Also being a pilot study the sample size is very small hence the distribution of data cannot be predicted properly. Thus further studies are required in same league to quantify the results. But at the same time it should be mentioned here that the role of placebo in muscle pain should not be overlooked.

Thus above all the patient selection criteria should be standardized, as different TMDs experience relief from different treatment modalities. Further comparative studies in each category of TMD, with acceptable sample size should be conducted and the comparison spectrum should be broadened to have a wider comparison between the groups.

5. Conclusion

From the present study we can conclude that all three groups effectively reduced the pain symptoms. Thus management of myalgia cannot be restricted to pharmacotherapy and splint therapy alone. Measures should be taken to assess the psychological output on the TMD.

Within the limitations of this study we can say that

- Correct and procedural diagnosis is mandatory to determine the category of Temporomandibular Disorder before prescribing treatment this should be followed in clinical set up to maintain standardization in treatment protocol.
- Determining the case for application of placebo should be outlined through further studies.
- The treatment should cater to the causative factors for a faster relief and not just follow the contemporary pharmacological trend.

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