Phonophoresis in temporomandibular joint disorders: A clinical trial
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Abstract
Background and Objective: Temporomandibular joint disorders (TMDs) are identified as a major cause of non-dental pain in the orofacial region. An effective drug delivery into this complex joint can result in a good prognosis. Phonophoresis is a novel phenomenon that exponentially increases the absorption of topical pharmacological compounds and achieves effective therapeutic drug concentration at the target site. Hence, this study is designed to assess the feasibility and effectiveness of aceclofenac gel phonophoresis in the management of TMDs.

Methods: Selected 60 patients were randomly divided into two equal groups. Group A were treated with aceclofenac gel phonophoresis and Group B with that of its topical application for 15 days. The scores of visual analog scale (VAS), maximum mouth opening, lateral and protrusive excursion, Helkimo anamnestic and clinical dysfunction index, erythrocyte sedimentation rate, and C-reactive protein were evaluated at baseline and 15 days after treatment.

Results: Statistically significant increase in mean maximum mouth opening, lateral excursion and a significant reduction in scores of VAS, Helkimo anamnestic, and clinical dysfunction index were observed post-treatment in Group A as compared to Group B.

Conclusions: Aceclofenac gel phonophoresis is feasible and effective in reduction of signs and symptoms of TMDs.

Keywords
Phonophoresis, temporomandibular joint disorders, ultrasound

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Introduction
The clinical management of temporomandibular disorders (TMDs) is a difficult task as it has got complex anatomy, multifactorial etiology, and overlapping clinical manifestations. The management of TMD is diverse and extensive involving professionals from different areas and includes several therapies ranging from conservative approaches such as self-care practices, exercises, occlusal corrections, electro-physical modalities to surgical interventions such as intra articular injection and arthrocentesis; however, no therapy has been found to be uniformly superior in the management of TMD pain and dysfunction.\(^1\)

Literature reviews have suggested that an effective drug delivery into this complex joint can result in alleviating TMD symptoms. Phonophoresis is an electro-physical treatment modality where ultrasonic energy enhances the drug permeability through intact skin by a combination of thermal, mechanical, and chemical alterations and achieves effective therapeutic drug concentration at the target site. Deep heat produced by the ultrasound causes local vasodilatation which increases cell permeability. This is accompanied by acoustic pressure wave effect which causes the cells to oscillate at high speed by disrupting the cell membrane resulting in an easy diffusion of the topical agent.\(^2\)

Several studies have reported the use of phonophoresis of topical anti-inflammatory agents to be satisfactory in the management of pain in knee and other joints of the body; however, phonophoresis of a drug in the management of TMD is limited. This has prompted us to design this study with the aims to assess the feasibility and effectiveness of Aceclofenac gel phonophoresis, with that of its topical application in TMDs and to assess the levels of C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) (inflammatory biomarkers) pre- and post-treatment.

Methods
This randomized controlled clinical trial was conducted on 60 subjects who were selected based on the selection criteria. The
study was conducted in full accordance with ethical principles and was reviewed and approved by an ethical board of the institution.

Patients attending to the Department of Oral Medicine and Radiology with a chief complaint of temporomandibular joint (TMJ) pain were evaluated with a detailed history and a thorough clinical examination and findings are recorded in a specially structured case proforma which was designed to evaluate the signs and symptoms of TMJ. Further patients were evaluated with a digital orthopantomograph to rule out any bony pathologies affecting TMJ. Then, patients were categorized according to the Research Diagnostic Criteria (RDC) for TMDs given by Dworkin and LeResche, 1992. 

**Inclusion criteria**

1. Subjects of age 18-70 years with TMJ pain.
2. Subjects with a diagnosis of disc displacement without reduction with limited opening (Group II B), disc displacement without reduction without limited opening (Group II C) and arthralgia (Group III A) according to TMD RDC Axis I.
3. Subjects with TMJ pain of persistent, recurring or chronic nature at least for past 3 months.
4. Subjects with no history of systemic disease or illness.

**Exclusion criteria**

Patients with history of allergy to topical application of aceclofenac gel or any other drug, prior TMJ surgery or trauma to jaw in last 3 months, pacemakers, intra articular injections in preceding year, radiation treatment to head and neck region, undergoing dental procedure or with a history of dental treatment in last 3 weeks, presence of skin lesion, atrophic or scarred skin at the site of application or with history of any other dermatological problems, such as psoriasis, urticaria, taking antidepressant, narcotic medication, steroids, and muscle relaxants, are excluded from the study.

All the selected subjects were explained about the aims and methodology of this study, risks, and benefits of participation in this study in their own language. A formal written informed consent was obtained from each patient before inclusion into the study.

**Pain assessment by visual analog scale (VAS) scores**

The selected 60 subjects were evaluated for the degrees of pain in TMJ using 0-10 cm horizontal VAS scores, where 0 denotes no pain, and 10 cm denotes pain as bad as could be.

**Assessment of mandibular movements**

A repeated three consecutive measurements are taken, and an average of three measurements is recorded as respective measurements of jaw movements.

**Maximum active mouth opening (AMO)**

Maximum AMO was measured in mm by asking the subjects to open their mouth as much as possible without pain. The vertical distance from the labioincisal embrasure between the mandibular central incisors to the labioincisal embrasure of the opposing maxillary central incisors were measured using the digital Vernier caliper and recorded in mm.

**Maximum passive mouth opening (PMO)**

Maximum PMO was measured in mm by asking the subjects to open their mouth as much as possible with pain by placing the thumb on the maxillary incisors and application of moderate downward pressure on the mandible by the second and third finger of the examiner. The vertical distance from the labioincisal embrasure between the mandibular central incisors to the labioincisal embrasure between the opposing maxillary central incisors were measured using the digital Vernier caliper and recorded in mm.

**Lateral excursive and protrusive jaw movements**

Right lateral excursion (RLE) and left lateral excursion (LLE) were measured by asking the subjects to open their mouth slightly and move the mandible as far as possible on the right side first and then left side, protrusive movement was measured asking the patient to open and protrude the jaw slightly and measurement from the labioincisal embrasure between the mandibular central incisors to the labioincisal embrasure between the maxillary central incisors were recorded with digital Vernier caliper in mm.

**Helkimo index assessment**

All the selected subjects were evaluated for the different symptoms of dysfunction of TMJ using Helkimo anamnestic index and functional evaluation of the TMJ using clinical dysfunction index at the baseline and 15 days post-treatment.

**Scores of Helkimo anamnestic index**

- 0 - No symptoms
- 1 - Mild symptoms (sensation of jaw fatigue, jaw stiffness, and TMJ sounds)
- 2 - Severe symptoms (difficulty in mouth opening, jaw locking, mandible dislocation and its painful movement, painful TMJ region and/or masticatory muscles).

**Scores of clinical dysfunction index**

- 0 - No dysfunction
- I - Mild dysfunction (1-4 points)
- II - Moderate dysfunction (5-9 points)
- III - Severe dysfunction (>9 points).

**Collection of serum/blood sample**

A disposable sterile 10 ml syringe and 26 gauge needle were used to draw venous blood sample from the median cubital vein in the antecubital fossa from which 2 ml is stored in test tube mixed with anticoagulant to prevent it from clotting on ESR assessment, and the rest 8 ml is stored in test tube mixed without anticoagulant at room temperature for several hours until the complete formation of clot. The serum is then separated and
Phonophoresis in TMJ disorders Vijayalakshmi, et al.


stored at 2-4°C for CRP assessment. Assessment of ESR is done by Westergrens method and CRP by slide test.

Allergy test
A patch test on the ventral surface of the forearm was done 24 h prior to the treatment with aceclofenac gel to rule out the drug allergy.

Then, selected 60 subjects were assigned randomly in two groups of 30 patients in each group:
1. Group A (experimental group): 30 subjects were treated with application of aceclofenac gel phonophoresis for a total of 6 setting on an alternate day for a period of 2-week for 10 min by making them seat comfortably in a dental chair. The pre-auricular skin of the affected TMJ was cleansed with sterile cotton roll dabbed in spirit containing 70% isopropyl alcohol before application of therapy. 5 mm thickness of ultrasound gel was evenly spread over the transducer head, and 3-4 mm of 1.5% aceclofenac gel was applied over the sound head. The ultrasound unit was preset to deliver a 1 MHz, continuous waveform, at between 0.8 and 1.5 W/cm² for 10 min [Figure 1]. The sound head was applied with a light touch and moved slowly in a continuous circular motion by keeping it flat against the skin of the affected joint [Figure 2].

2. Group B: 30 subjects were instructed to gently apply 3-4 mm of aceclofenac gel over the pre-auricular skin of the affected TMJ for 3 min in a circular motion thrice daily for a period of 2-week. Each subject was provided with written instruction on gel application. The subjects were asked to report on an alternate day for evaluation of TMJ signs and symptoms.

All the obtained values of the assessed parameters were tabulated and statistically analyzed.

Statistical analysis

Statistical software
The statistical software, namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0, and R environment ver.2.11.1, were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables.

Results

After a thorough statistical analysis, the results of the study are presented as tables.

Among all the subjects 23 (38.4%) were males and 37 (61.6%) were females. Group A consisted of 10 (33.3%) males and 20 (66.7%) female, with a mean age of subjects 35.03 years [Table 1]. 18 subjects (60%) were categorized into disc displacement without reduction with limited opening (Group II B), 11 (36.7%) into disc displacement without reduction without limited opening (Group II C), and 1 (3.3%) into arthralgia (Group III A). Whereas Group B consisted of 13 (43.3%) males and 18 (56.7%) females. With a mean age of the subjects 35.10 years [Table 1] and 15 subjects (50%) were categorized into disc displacement without reduction with limited opening (Group II B), 14 (46.7%) into disc displacement without reduction without limited opening (Group II C) and 1 (3.3%) into arthralgia (Group III A). Table 2 shows the details and observations of the parameters evaluated.

Discussion

TMD symptoms have always been considered to have a broad prevalence peak between 20 and 40 years of age. Studies conducted by Österberg et al.41 De Kanter et al.5 have reported lower frequencies of symptoms with increasing age and have shown that the highest prevalence of TMD occurs among adults under 45 years of age. Similarly, in this study out of 60 subjects, 78.33% were <45 years of age. Manfredini et al.6 reported that disc displacements disorders occur around the age of 30 years and inflammatory-degenerative joint disorders over...
the age of 50 years which is in accordance with observations of this study where mean age for disc displacement disorders was 35 ± 3.99 years and 51.5 ± 0.44 years for inflammatory and degenerative disorders.

This study comprised 61.6% of females as compared to 38.3% of males. The high prevalence of TMD in women is supported by studies conducted by Huang et al.\[7\] Rantala et al.\[8\] and LeResche et al.\[9\] However, no statistically significant difference is noticed with the treatment response with respect to gender in the present study.

The parameters that were used to evaluate the prognosis of TMD in this study are maximum mouth opening (active and passive), lateral and protrusive excursion (PE) VAS scores on cm scale, ESR values in mm/h by Westergrens method, CRP by rapid latex slide test and Helkimo anamnestic and clinical dysfunction index.

Evaluation of pain over TMJ was based on subjective measurement using 0-10 horizontal VAS, which was found to be feasible, easily understood and answered by all subjects of our study. The pre-treatment mean VAS scores in Group A was 7.57 ± 1.04 and in Group B was 7.33 ± 1.47 and 15 days post-treatment it was reduced to 3.10 ± 2.77 and 6.70 ± 1.29, respectively. It was also observed that the VAS score was significantly reduced immediately after the first visit in Group A and gradual reduction thereafter on the subsequent visits in both the groups. Similar observations of pain reduction were found in studies conducted by Shin and Choi\[10\] and Gray et al.\[11\] in the management of TMDs. This may be attributed to phonophoresis technique, as ultrasound waves increase the kinetic energy of a drug molecule and increase circulation to the area, enhancing drug molecule to diffuse through the stratum corneum and achieve therapeutic drug concentration at the target thereby reducing inflammation and pain. Yang et al.\[12\] investigated for the effective ultrasound frequency, intensity, and the duty cycle using a 0.5% triamcinolone acetonide gel to enhance drug penetration through mouse skin. They concluded that the 1 MHz frequency showed a relatively higher transport than either 3 MHz or its topical application of the drug. Mitragotri et al.\[13\] also reported that phonophoretic enhancement varies inversely with ultrasound frequency as frequency increases, the vibration amplitude decreases and absorption increases. Therefore, 1 MHz frequency ultrasound for aceclofenac gel phonophoresis was considered to be effective and adapted in this study.

Statistically significant improvement with regard to mean maximum AMO in mm pre- and post-treatment (30.7 ± 7.86, 36.2 ± 8.67), mean maximum PMO in mm pre- and post-treatment (32.2 ± 8.42, 37.5 ± 9.30), mean maximum RLE in mm pre- and post-treatment (3.83 ± 1.14, 5.23 ± 1.832), mean maximum LLE in mm pre- and post-treatment (4.17 ± 1.41, 5.50 ± 1.67), and mean maximum PE in mm pre- and post-treatment (3.90 ± 1.44, 5.00 ± 1.61) with a P < 0.001 in

| Table 2: Mean ESR, VAS, maximum active and PMO, RLE and LLE, PE, Helkimo anamnestic and clinical dysfunction index in males and females pre- and post-treatment between the groups |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Parameters                      | Gender          | Group A          | P value         | Group B          | P value         |
|                                 | Pre             | Post             |                 | Pre             | Post             |
| ESR in mm/h                     | Males           | 41.9±7.78        | 33.4±5.62       | 0.001**         | 35.0±5.23       | 31.2±4.81       | 0.001**         |
|                                 | Females         | 32.9±4.23        | 29.0±4.50       | 0.000**         | 31.0±4.60       | 26.9±4.39       | 0.000**         |
| VAS                             | Males           | 7.00±1.05        | 2.1±1.85        | 0.000**         | 6.76±1.42       | 6.07±1.18       | 0.006           |
|                                 | Females         | 7.85±0.93        | 3.6±3.05        | 0.000**         | 7.76±1.39       | 7.17±1.18       | 0.004           |
| AMO in mm                       | Males           | 33.5±8.44        | 39.7±7.85       | 0.000**         | 32.4±7.17       | 33.8±7.64       | 0.000**         |
|                                 | Females         | 29.2±7.35        | 34.3±8.81       | 0.000**         | 27.2±8.01       | 28.3±8.44       | 0.000**         |
| PMO in mm                       | Males           | 35.3±9.25        | 41.6±8.02       | 0.000**         | 33.2±7.27       | 34.9±7.93       | 0.000**         |
|                                 | Females         | 30.5±7.72        | 35.4±9.40       | 0.000**         | 27.6±8.02       | 28.6±8.44       | 0.000**         |
| RLE in mm                       | Males           | 4.2±1.39         | 5.9±1.37        | 0.000**         | 4.23±1.36       | 4.61±1.50       | 0.018           |
|                                 | Females         | 3.6±1.18         | 4.9±1.97        | 0.000**         | 3.52±0.87       | 3.82±1.18       | 0.136           |
| LLE in mm                       | Males           | 4.80±1.30        | 6.50±0.97       | 0.001**         | 4.61±1.50       | 4.92±1.25       | 0.040           |
|                                 | Females         | 3.80±1.49        | 5.00±1.74       | 0.000**         | 4.00±1.22       | 4.35±1.05       | 0.009           |
| PE in mm                        | Males           | 4.20±0.91        | 6.10±0.87       | 0.001**         | 3.69±1.03       | 4.15±1.57       | 0.111           |
|                                 | Females         | 3.20±0.95        | 4.40±1.63       | 0.000**         | 3.23±1.20       | 3.70±1.45       | 0.002           |
| Helkimo anamnestic index        | Males           | 1.60±0.51        | 0.20±0.63       | 0.000**         | 1.69±0.48       | 1.46±0.51       | 0.082           |
|                                 | Females         | 1.80±0.36        | 0.80±0.89       | 0.000**         | 1.82±0.39       | 1.70±0.46       | 0.163           |
| Clinical dysfunction index      | Males           | 6.30±1.25        | 1.50±2.06       | 0.000**         | 7.00±0.91       | 6.76±0.92       | 0.082           |
|                                 | Females         | 6.75±1.20        | 2.75±2.46       | 0.000**         | 7.11±0.69       | 7.00±0.70       | 0.163           |

**Strongly significant, ESR: Erythrocyte sedimentation rate, VAS: Visual analog scale, AMO: Active mouth opening, PMO: Passive mouth opening, RLE: Right lateral excursion, LLE: Left lateral excursion, PE: Protrusive excursion.**
Group A as compared to Group B where mean maximum AMO in mm pre- and post-treatment (29.5 ± 7.97, 30.7 ± 8.43), mean maximum POM in mm pre- and post-treatment (30.1 ± 8.08, 31.3 ± 8.68), mean maximum RLE in mm pre- and post-treatment (3.80 ± 1.27, 3.80 ± 1.27), mean maximum LLE in mm pre- and post-treatment (4.27 ± 1.36, 4.60 ± 1.16), and mean maximum PE in mm pre- and post-treatment (3.43 ± 1.13, 3.53 ± 1.04) with a P = 0.01 which is of moderate statistical significance is noted in our study. Similar observations were made by Shin and Cho(10) using indomethacin phonophoresis in TMDs. Similar results with respect to maximum mouth opening, protrusive opening were found in a study conducted by Kaya et al.(11) with a P < 0.001 in group with combination of treatment modalities (phonophoresis + low level laser treatment + HEP).

The functional capabilities of the TMJ were evaluated by means of the Helkimo anamnestic dysfunction index (Ai) and the Helkimo clinical dysfunction index (Di). Studies conducted by Fricton and Schiffman,(12) Wänman and Salonen(13) considered these indices to be useful and has recommended for epidemiological research, the Helkimo anamnestic dysfunction index (Ai), and the Helkimo clinical dysfunction index (Di) are used to assess the functional capabilities and found to be consistent in this study with the mean pre-treatment scores of 1.77 ± 0.43 and 6.6 ± 1.22 and mean post-treatment scores 0.60 ± 2.33, respectively. However, no other clinical trials have assessed these parameters.

The present study incorporated assessment of inflammatory biomarkers levels such as ESR and CRP before and after post-treatment. In our study, the comparison of mean ESR pre- and post-treatment in Group A showed a strong statistical significance with a P = 0.001 in comparison to Group B. It is noticed that the mean ESR scores among female were low in comparison with mean ESR scores of men, in spite of the normal range of ESR is lower in males than females by Westergen methods. CRP did not show any statistically significant difference between Group A and B pre- and post-treatment. The probable reason attributed to this could be the inclusion of subjects into this study with a chronic nature of pain, and as CRP shows a more rapid response; hence, CRP test values did not show any statistical significance.

**Conclusion**

Aceclofenac gel phonophoresis was found to be feasible in the management of TMDs. Signs and symptoms of TMDs have shown strong statistical significant improvement in relieving the pain (P < 0.0001) and increasing the maximum active and PMO (P < 0.0001) and mandibular movements in the Group A in comparison to Group B. However, studies with larger sample size including other RDC/TMD groups are required to recommend aceclofenac gel phonophoresis as an effective electro-physical modality in the management of TMDs.

**References**
