A Clinical Assessment of Mesotherapy as a Therapeutic Intervention for Myofascial Pain Syndrome: A Randomized Controlled Trial

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A Clinical Assessment of Mesotherapy as a Therapeutic Intervention for Myofascial Pain Syndrome: A Randomized Controlled Trial

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Introduction

Statement of the problem:

Temporomandibular joint disorders represent a complex and heterogeneous group of musculoskeletal conditions affecting the temporomandibular joint, masticatory muscles, and associated structures, frequently manifesting as chronic orofacial pain (Mohl & Dixon, 1994; Chan et al., 2022; Garstka et al., 2023) [1, 2, 3]. These disorders present a significant clinical challenge due to their multifaceted etiology, overlapping clinical presentations, and the potential for co-occurrence with other pain conditions, requiring meticulous differential diagnosis to ensure appropriate management (Farook, 2014) [4].

Thorough clinical examination is paramount to accurately localize the source of pain, discerning whether it originates primarily from the joint itself or from the surrounding musculature. The intricate interplay between the temporomandibular joint, myofascial muscles, and related structures underscores the importance of considering the broader context of orofacial pain and cervical spine disorders in the diagnostic and therapeutic process (Mannheimer, 2007) [5].

The reported treatments range from physical therapy and manual therapy to occlusal splints, laser therapy, oral and injectable pharmacotherapy, and in severe cases, surgery (Regulski et al., 2023) [6]. Pain intensity and maximum mouth opening are critical variables assessed, alongside patient-reported outcomes concerning the impact of mandibular impairment on daily life and psychosocial well-being, offering a comprehensive understanding of the patient's experience (Vos et al., 2013) [7].

Rationale for carrying out the trial:

Temporomandibular joint (TMJ) disorders are a common source of significant pain and functional impairment, yet conventional treatment approaches often yield inconsistent outcomes (Yost et al., 2020; Lu & Du, 2024) [8, 9]. Mesotherapy, a minimally invasive technique involving microinjections of pharmacological agents or other bioactive substances into the mesodermal layer of the skin, has shown potential in managing chronic pain (Patel et al., 2023)

[10]. However, its application in TMJ disorders remains underexplored.
Trigger point injections have emerged as a valuable therapeutic modality in the management of orofacial pain, especially when the pain is caused by myofascial pain syndrome (Koszela et al., 2024) [11].

Literature Review

Temporomandibular joint (TMJ) disorders encompass a group of conditions affecting the jaw joint and associated musculature, leading to pain, impaired function, and a diminished quality of life. These disorders arise from various etiologies, including trauma, degenerative conditions such as osteoarthritis, and systemic inflammatory diseases, emphasizing their multifactorial nature (Cruz et al., 2015; Lee, 2024) [12, 13].

The temporomandibular joints (TMJs) are among the most frequently used joints in the body, opening and closing approximately 2,000 times a day. These joints are essential for various critical activities, including verbal and nonverbal communication, the challenging movements involved in chewing, and even the more subtle action of breathing. Healthy functioning of both the TMJs and the surrounding tissues is crucial for these activities. Additionally, the joints play a vital role in interpersonal interactions and contribute to facial expressions that convey emotions such as joy or sadness, as well as impacting self-esteem and self-identity (Lee, 2024; Mohl & Dixon, 1994) [13, 1].

Temporomandibular disorders are recognized as the most common chronic orofacial pain condition, with no significant differences found between racial groups. As previously defined, TMD refers to a group of pain conditions and dysfunctions, and not all epidemiological studies have used the same classification or differentiated between muscle and joint disorders. Indeed, inclusion criteria employed in studies before modern classifications encompassed some disorders into one entity. This questions the validity of much of the epidemiologic research performed before criteria and diagnoses were standardized. This prevalence highlights the widespread impact of these conditions and underscores the critical need for effective diagnostic and therapeutic strategies (Chan et al., 2022) [2].

The pathophysiology of TMJ disorders is complex, involving factors such as mechanical stress, inflammation, and genetic predisposition. These disorders typically affect the masticatory muscles, the TMJ itself, and the dentition, reflecting their multifaceted nature (Ribeiro et al., 2018) [14].

Management of TMJ disorders often requires a multidisciplinary approach, incorporating both conservative and invasive treatments tailored to the condition's severity and underlying causes (Yost et al., 2020) [8]. Among conservative treatments, mesotherapy has gained attention as a minimally invasive technique. This method involves intradermal or subcutaneous injections of pharmacological agents. The localized delivery allows for a time-released therapeutic effect, minimizing systemic exposure (Lu & Du, 2024) [9].

The trigger points, the most sensitive points within a contracted muscle band, elicit pain upon compression and may be accompanied by referred pain. These points are considered active or latent based on their clinical characteristics (Benoliel & Sharav, 2008) [15]. Active trigger points cause spontaneous pain and alter sensations in predictable pain patterns associated with that specific muscle. Latent trigger points, on the other hand, do not cause spontaneous pain but can restrict movement or cause muscle weakness. Myofascial pain is often misdiagnosed because the trigger point causing pain is often distant to where the pain is felt (Özkan et al., 2021) [16].

Myofascial trigger points can be found in any muscle group, but they have a higher prevalence in postural muscles, such as the upper trapezius (Shah et al., 2015) [17]. Trigger point injections have emerged as a valuable therapeutic modality in the management of orofacial pain, especially when the pain is caused by myofascial pain syndrome (Ribeiro et al., 2018) [14]. Orofacial pain can stem from inadequate positioning of the stomatognathic system structures, such as the hyoid bone or cervical spine (Müggenborg et al., 2023) [18].

Temporomandibular disorders and myogenous temporomandibular disorders, also known as masticatory myalgia, are the most common condition, affecting 45.3% of TMD cases (Kalladka et al., 2021) [19].

Trigger point injections involve the direct injection of a local anesthetic, either with or without corticosteroids, into the identified trigger point, aiming to alleviate pain and muscle tension (Appasamy et al., 2022) [20].

Mesotherapy has been used in managing various musculoskeletal conditions, including TMJ disorders, due to its potential to target underlying inflammatory processes. By modulating inflammation, mesotherapy may reduce pain and enhance joint functionality, aligning with the current focus on personalized, localized therapies (Lu & Du, 2024) [9]. Some studies have reported positive outcomes, such as reduced pain and improved range of motion in patients with TMJ disorders (Yost et al., 2020) [8]. However, the current evidence base is limited, necessitating further research to establish the effectiveness of mesotherapy as a treatment option.

Although the mechanism of action of mesotherapy in TMJ disorders involves delivering anti-inflammatory and analgesic agents directly to the affected area, the literature reveals a significant research gap regarding its efficacy and long-term benefits (Mohl & Dixon, 1994) [1].

Database research

A search was performed on electronic databases (PubMed, Scopus, and Cochrane Library).

Aim of the study

A-PICO format:

Patient/Population:

Patients diagnosed with Myofascial Pain Dysfunction Syndrome (MPDS).

Intervention:

Study Group: Mesotherapy (microinjections of NSADs, local anesthesia, and corticosteroid into the Masseter and Temporalis Muscle Bilateral)

Control/Comparatore:

Trigger Point Injections of of NSADs, local anesthesia, and corticosteroid into the Masseter and Temporalis Muscle Bilateral)

Outcome measure:

Outcome measure		Measure unit	Measure device
1ry Outcome	Improvement in TMJ Pain	Pain (VAS) (0 to10)	Visual Analog Scale (VAS) (0 to10)
2ry Outcome	maximal mouth opening	Jaw Function MMO	Mouth Ruler (for maximum opening)

B-Research question:

Is mesotherapy more effective than trigger point injections in managing pain and dysfunction in patients with Myofascial Pain Dysfunction Syndrome?

Objectives of the study

Research hypothesis:

The null hypothesis is Mesotherapy does not significantly improve clinical outcomes, reduce orofacial pain, or enhance mouth opening in patients with Myofascial Pain Dysfunction Syndrome (MPDS) compared to trigger point injections.

Primary objective:

To evaluate and compare the efficacy of mesotherapy versus trigger point injections in alleviating clinical symptoms—particularly orofacial pain and restricted mouth opening—in patients diagnosed with Myofascial Pain Dysfunction Syndrome (MPDS).

Secondary objective:

To evaluate the duration of pain relief achieved with mesotherapy compared to trigger point injections.

Study design:

Trigger Point Injections of of NSADs, local anesthesia, and corticosteroid into the Masseter and Temporalis Muscle Bilatera)

Methods (-participants, interventions, and outcomes)

Study settings:

Our patients are from the clinic of Oral & maxillofacial Surgery department in the Faculty of Oral and Dental Medicine, Future University in Egypt, who are seeking treatment for temporomandibular joint disorder (TMDJ) symptoms.

Eligibility criteria:

A- Inclusion criteria:

1) patients between 18 - 60 years.
2) Patients who had a Diagnosis of TMD, with chronic pain, muscle spasms, myofascial pain syndrome lasting at least 3 months, and challenges while chewing.
3) Patients who have difficulty opening their mouths, cases where conservative treatment methods (physical, medical, or appliances) have failed.
4) Patients who have Bruxism

B- Exclusion criteria

1) Systemic Diseases such as uncontrolled Diabetes, uncontrolled hypertension disorders of coagulation (hemophiliacs, undergoing therapy with anticoagulants or antiplatelet agents, and cancer patients undergoing chemotherapy.

2) Patients with a history of Muscular dystrophies, Myasthenia Gravis, Polymyositis, Rheumatoid arthritis, Hypothyroidism, and Sarcoidosis

3) Patients with active Infections around the injection site.

4) Females who are pregnant or breastfeeding are excluded.

5) A patient who had a history of severe mental health disorders or neurological conditions affecting pain perception or compliance.

6) Patients with allergies to the components used in mesotherapy.

Intervention:

1) Full medical and dental history will be taken from the patient participating in this study.

2) The patient will sign a written consent form for the potential of operative and postoperative complications.

3) Physical examination for TMJ Visual Inspection

Inspect preauricular area for Swelling and erythema

TMJ Palpation

Place fingers over the TMJ (just anterior to the tragus).

Ask patient to open and close the mouth slowly.

During slow closure, feel for posterior movement of the condyle.

Muscle Palpation (Masticatory & Cervical Muscles)

Cervical Muscles:

Sternocleidomastoid, Trapezius and Posterior cervical muscles

Masticatory Muscles:

Masseter: At zygomatic arch and mandibular angle.

Temporalis: Palpate Over temporal fossa and intraorally along ascending ramus

Medial pterygoid: Bimanual palpation:

One finger externally at mandibular angle

One intraorally in retromolar region

Lateral pterygoid: Intraoral palpation posterior to maxillary tuberosity

Measure interincisal distance (in mm):

Normal: 35–60 mm

<35 mm = restricted opening

Observe mandibular deviation

4) The skin is prepared with an antiseptic solution, and topical anesthesia is applied.

5) Record baseline data for pain (VAS), jaw function (mouth opening), muscle tenderness, and joint sounds.

Study group:

1. Preparation of the mesotherapy agent by mixing (30mg/1ml Ketolac + 100mg/1ml Hydrocortisone + 60mg/1ml xylocaine dissolve in 2 ml normal saline)
2. Preparation of mesotherapy gun (EZ Injector™) using disposable 5cc syringe, Negative Pressure Needle (EZ-5- 5 Pin 31G-1.5mm/2.0mm/2.5mm)
3. Injection of 1,25ml at the masseter muscle and temporalis muscule bilateral in total of 5 ml \ once per week for one month and follow up for 3 months and six months)

Control group:

1. Preparation of the medication agent by mixing (30mg/1ml Ketolac + 100mg/1ml Hydrocortisone + 60mg/1ml xylocaine dissolve in 2 ml normal saline)
2. Palpate and confirm trigger point.
3. Slowly inject **0.2–0.3 mL** of the solution per trigger point (typically 2–3 sites per side).
4. Inject **0.2 mL** per site (usually 2–3 points on each side) \ once per week for one month and follow up for 3 months and six months).

6) Ice pack and topical antibiotics) Fucidin)

7) Postoperative instructions and medications:

- Cold Compress
- Avoid Touching or Massaging the Area
- Hydration
- Analgesic
- Topical antibiotic
- 30% Arnica Cream

Criteria for discontinuing intervention:

Occurrence of any harmful side effect from either of the treatment modalities.

Outcomes:

Primary Outcome:1. Improvement in TMJ clinical symptoms, Pain intensity will be assessed using the Visual Analog Scale (VAS), which is a 10-point scale where 0 represents "no pain" and 10 represents "worst imaginable pain.

Secondary Outcome: Improvement in Maximum Interincisal opening, using a MMO Ruler for Measurement

Sample size:

The required sample size for this study is 24 participants12 in each group. The sample size was determined based on a previous study titled 'Effectiveness of Mesotherapy on Temporomandibular Joint Disorders.' The significance level and statistical power in that study were higher than those used in the current study. A 95% confidence interval was applied the confidence interval was 95%, and the actual power was 95.20%. The sample size and the effect size g = 0.4001 were calculated using a computer program G Power version 3.1.9.

The formula of sample size

$$samplesize = \frac{Z^2 \hat{P}(1 - \hat{P})}{C^2}$$

Where:

Z = Z value (1.96 for 95% confidence level)
p = percentage picking a choice, expressed as decimal
c = confidence interval, expressed as decimal.

To calculate the dropout rate (0.20%) by using the formula below:

$$N = \frac{n}{(1 - \frac{DR}{100})}$$

Statistical analyses will be performed using Statistical Package for Social Sciences (SPSS version 26). Numerical variables will be expressed by descriptive statistics as mean, standard deviation, and range; nominal data will be represented by frequency, percent, and median, P value <0.05(*) was considered a significant difference & P-value <0.001(**) was considered a highly significant difference.

Plans to promote participant retention and complete follow-up:

Telephone numbers of all enrolled patients will be recorded as a part of the written consent. All patients will be given a phone call at the time of the pre-determined follow up appointments.

Data management:

All data will be entered and saved electronically.

Patient files are to be stored in numerical order and stored in secured file.

Data will be encrypted using a password.

All data will be maintained in storage for 1 year after completion of the study.

Statistical analysis:

The obtained data will be tabulated and statistically analyzed to interpret the results of the proposed study.

Harms:

Any temporary or permanent adverse effect will be recorded and documented.

Auditing:

Auditing of the study design will be done by the Ethics Committee, Faculty of Oral and Dental Medicine- Future University.

Research ethics approval:

This protocol and the template informed consent form will be reviewed by the Ethics Committee of Scientific Research –Faculty of Oral and Dental Medicine-Future University.)

Protocol amendments:

Any modification to the protocol which may have an impact on the conduct of the study, potential benefit of the patient or may affect patient safety will require a formal amendment to the protocol. Such amendment will be agreed upon by the Council of Oral & Maxillofacial Surgery Department.

Consent:

The entire procedure will be explained to the patients and a written consent will be obtained.

Confidentiality:

Participants 'study information will not be released outside of the study without the written permission of the participant.

Declaration of interests:

If there will be any conflict of interest, it will be declared.

Ancillary and Post Trial Care:

All patients will be followed up for 6 months after the clinical trial is over.

Dissemination policy:

The study results will be published as partial fulfillment of the requirements for master's degree in oral & maxillofacial surgery.

Topics suggested for presentation or publication will be circulated to the authors.

▪ References

1. *Journal of the American Dental Association, 125*(1), 56. https://doi.org/10.14219/jada.archive.1994.0014

2. Chan, N. H. Y., Ip, C. K., Li, D. T. S., & Leung, Y. Y. (2022). Diagnosis and treatment of myogenous temporomandibular disorders: A clinical update. *Diagnostics, 12*(12), 2914. https://doi.org/10.3390/diagnostics12122914

3. Garstka, A. A., et al. (2023). Accurate diagnosis and treatment of painful temporomandibular disorders: A literature review supplemented by own clinical experience. *Pain Research and Management, 2023*, 1002235. https://doi.org/10.1155/2023/1002235

4. Farook, S. A. S. (2014). Current management of temporomandibular joint (TMJ) disease. *Journal of Arthritis, 3*(3), 1000138. https://doi.org/10.4172/2167-7921.1000138

5. Mannheimer, J. S. (2007). Limited evidence to support the use of physical therapy for temporomandibular disorder. *Evidence-Based Dentistry, 8*(4), 110. https://doi.org/10.1038/sj.ebd.6400528

6. Regulski, P., Szopiński, K., & Levičnik-Höfferle, Š. (2023). Photobiomodulation therapy for the symptoms related to temporomandibular joint disk displacement. *Case Reports in Dentistry, 2023*, 5947168. https://doi.org/10.1155/2023/5947168

7. Vos, L. M., Slater, J. J. R. H., & Stegenga, B. (2013). Arthrocentesis as initial treatment for temporomandibular joint arthropathy: A randomized controlled trial. *Journal of Cranio-Maxillofacial Surgery, 42*(5). https://doi.org/10.1016/j.jcms.2013.07.010

8. Yost, O., Liverman, C. T., English, R., Mackey, S., & Bond, E. C. (Eds.). (2020). *Temporomandibular disorders: Priorities for research and care*. National Academies Press.

9. Lu, G., & Du, R. (2024). Temporomandibular joint disorder: An integrated study of the pathophysiology, neural mechanisms, and therapeutic strategies. *Archives of Oral Biology, 164*, 106001.

10. Patel, K., Eley, K. A., Cascarini, L., Watt-Smith, S., Larkin, M., Lloyd, T., ... & McMillan, R. (2023). Temporomandibular disorders—Review of evidence-based management and a proposed multidisciplinary care pathway. *Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology, 136*(1), 54–69.

11. Koszela, K., Słupiński, M., & Woldańska-Okońska, M. (2024). The role of rehabilitation after spinal mesotherapy in a three-stage treatment concept. *Journal of Clinical Medicine, 13*(11), 3195.

12. **Cruz, A. P. O., das Neves, A. F. R., Ramires, I., & Mendonça, M. (2015). Effectiveness of mesotherapy on temporomandibular joint disorders. *Journal of Physical Science and Application, 5*(4), 249–254.**

13. **Lee, Y. H. (2024). Functional anatomy of the temporomandibular joint and pathologic changes in temporomandibular disease progression: A narrative review. *Journal of Korean Dental Science, 17*(1), 14–35.**

14. **Ribeiro, D. C., Belgrave, A., Naden, A., Fang, H., Matthews, P., & Parshottam, S. (2018). The prevalence of myofascial trigger points in neck and shoulder-related disorders: A systematic review of the literature. *BMC Musculoskeletal Disorders, 19*(1), 252. https://doi.org/10.1186/s12891-018-2157-9**

15. **Benoliel, R., & Sharav, Y. (2008). Masticatory myofascial pain and tension-type and chronic daily headache. In *Orofacial pain and headache* (pp. 109–128). Elsevier.**

16. **Özkan, F., Çakır Özkan, N., & Erkorkmaz, Ü. (2021). Trigger point injection therapy in the management of myofascial temporomandibular pain. *Agri: The Journal of the Turkish Society of Algology, 33*(1), 30–36. https://doi.org/10.14744/agri.2020.05959**

17. **Shah, J. P., Thaker, N., Heimur, J., Aredo, J. V., Sikdar, S., & Gerber, L. (2015). Myofascial trigger points then and now: A historical and scientific perspective. *PM&R, 7*(7), 746–761. https://doi.org/10.1016/j.pmrj.2015.01.024**

18. **Müggenborg, F., de Castro Carletti, E. M., Dennett, L., de Oliveira-Souza, A. I. S., Mohamad, N., Licht, G., ... & Armijo-Olivo, S. (2023). Effectiveness of manual trigger point therapy in patients with myofascial trigger points in the orofacial region—A systematic review. *Life, 13*(2), 336.**

19. **Kalladka, M., Young, A., & Khan, J. (2021). Myofascial pain in temporomandibular disorders: Updates on etiopathogenesis and management. *Journal of Bodywork and Movement Therapies, 28*, 104–113.**

20. **Appasamy, M., Lam, C., Alm, J., & Chadwick, A. L. (2022). Trigger point injections. *Physical Medicine and Rehabilitation Clinics of North America, 33*(2), 307.**