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MICROFRAGMENTED ADIPOSE TISSUE INJECTION COMPARED TO HYALURONIC ACID FOR TREATMENT OF TEMPOROMANDIBULAR JOINT OSTEOARTHRITIS. (A RANDOMIZED CLINICAL TRAIL)

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ABSTRACT

Objective: This study aimed to evaluate the effectiveness of standard hyaluronic acid (HA) injections following arthrocentesis compared to micro-fragmented adipose tissue derived from the buccal fat pad.

Methods: 26 patients were randomly assigned to two groups: Group A; which received HA injections, and Group B; which received adipose tissue injections. Pain levels were assessed using the visual analog scale, and function was measured by maximum interincisal opening at five intervals: before the procedure, after day one, 1 week, 1 month, and finally after 3 months post-procedure.

Results: Both groups exhibited significant improvements in pain relief and mouth opening compared to their baseline measurements.

Conclusion: Initial results suggest that micro-fragmented adipose tissue injections may offer enhanced benefits in terms of pain reduction and functional improvement compared to the conventional HA treatment.

KEYWORDS: Tmj , Arthrocentesis , Adipose tissue injection , Osteoarthritis .

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INTRODUCTION

Temporomandibular disorders (TMDs) encompass a variety of conditions characterized by pain and/or dysfunction of the temporomandibular joint (TMJ) and associated structures. These disorders often involve muscular and/or skeletal components, with osteoarthritis being the most prevalent joint disease. Osteoarthritis of the TMJ progresses slowly but can lead to significant pain and functional impairments, negatively impacting quality of life. Initial management strategies typically include oral appliances, nonsteroidal anti-inflammatory drugs (NSAIDs), physical therapy, and behavioral adaptations. For patients unresponsive to conservative treatments, arthrocentesis, first described by [1-2] Nitzan *et al* has emerged as a minimally invasive intervention aimed at alleviating joint pain and improving mobility.

Although arthrocentesis is widely used, studies evaluating adjunct therapies have produced conflicting results.[3] Bouloux et al reported no additional benefit from supplementing arthrocentesis with corticosteroids or hyaluronic acid in terms of pain reduction and jaw function. Conversely, [4] Dolwick et al reported improved outcomes with corticosteroid supplementation. Such disparities highlight the need for more robust evidence to determine the optimal treatment approach.

Recently, research has shifted toward biological therapies, including platelet-rich plasma (PRP), which concentrates platelets and growth factors through centrifugation. Systematic reviews have demonstrated the potential benefits of intra-articular PRP injections in managing TMJ disorders. [5]

Furthermore, advancements in tissue engineering and regenerative medicine have introduced the use of stem cells derived from bone marrow for orthopedic applications. Building on this foundation, [6] De Riu et al reported promising outcomes with these novel therapies, paving the way for innovative approaches in TMJ disorder management.

Regenerative dentistry, a dynamic branch of regenerative medicine, harnesses the principles of cell and molecular biology to develop innovative therapies that restore, repair, and regenerate dental tissues. Among the key players in this field are adipose tissue stem cells (ADSCs), a type of mesenchymal stem cell (MSC) enzymatically isolated from fat tissues. ADSCs are remarkable for their ability to express specific surface markers and differentiate into various cell lineages, offering a stem cell concentration 100–500 times greater than bone marrow-derived stem cells (BMSCs). Their versatility allows them to be directly injected or encapsulated in biomaterials for implantation, accelerating healing and differentiating into target cell types. With proven success in repairing critical-sized bone defects and engineering bone grafts, ADSCs have emerged as a powerful and efficient alternative to BMSCs, paving the way for groundbreaking advancements in regenerative therapies. [7 - 8]

MATERIALS AND METHODS

A prospective, randomized clinical trial was conducted at Cairo University's Oral and Maxillofacial Surgery Department. Ethical approval was obtained, and patient enrollment occurred from March 2023 to December 2024.

Preoperative preparation patients initially underwent conservative pharmacological management for two weeks. If unresponsive, 22 randomized patients received physiotherapy for an additional two weeks. Persistently symptomatic patients were treated with semi-invasive Prolotherapy, involving intra-articular injections of 0.5 cc articaine hydrochloride (68 mg/1.7 mL adrenaline) and 1.5 cc 25% dextrose.

Inclusion Criteria

- Clinical and MRI-confirmed TMJ internal derangement and osteoarthritis.

- Symptoms include limited mouth opening and joint pain.
- Previous conservative treatment failure.
- Age ≥16 years.
- No history of TMJ surgery.
- Written informed consent and complete pre-and post-operative data.

Exclusion Criteria

- Hematological or neurological disorders.
- Malignant head and neck neoplasms.
- Fat harvesting contraindications.
- Uncooperative behavior.

Surgical steps

1. Arthrocentesis Technique

Standard arthrocentesis was performed following the Nitzan DW technique. Local anesthesia (2-4 mL articaine hydrochloride, 68 mg/1.7 mL adrenaline) was administered for auriculotemporal nerve block and periarticular infiltration. Additional anesthetic was used as needed in the upper joint compartment during lavage. A 19-gauge needle was inserted into the articular fossa for saline injection and aspiration, followed by a second needle placement in the articular eminence. The joint space was irrigated with 80 mL saline to ensure free fluid flow.

2a. Group 1 (Control Group): ***Following the arthrocentesis, 2 mL of Hyalgan 20mg ® (Hyaluronic acid/ Sodium 20mg/2ml; IBN SINA FARAMA) was injected into the superior compartment.***

2b. Group 2 (Experimental Group):

Following the arthrocentesis protocol, micro-fragmented adipose tissue was obtained from the buccal fat pad. A small intraoral incision was made above the second molar, Fig (2-A) followed by blunt dissection to access the buccal pad of fat. Fig (2-B).

Fig (1) The landmarks and the positions of the syringes used during arthrocentesis of TMJ (solution in and out).

The harvested fat was manually processed using two syringes to fragment the tissue and then centrifuged at 3000 rpm for 13 minutes. Fig (2 C & D) The final product, a concentrated micro-fragmented adipose tissue rich in pericytes and mesenchymal stem cells, Fig (2-E) then injected into the superior joint compartment Fig (2-F) using a 1 mL syringe.

Outcome Measures

The following outcome measures were evaluated and recorded (baseline, 1 week, 1 month, and 3 months postoperatively).

Primary Outcome

Pain Assessment: Pain levels were assessed using a visual analog scale (VAS) ranging from 0 to 10 (0:no pain and 10: the most severe pain). Patients were asked to rate their pain both at rest and during functional activities.

Secondary Outcomes

Maximum Mouth Opening (MMO): The maximum interincisal distance (in millimeters) was measured between the upper and lower central incisors using a polygauge caliper.

Jaw Movement: Jaw movement was evaluated clinically to identify any deviation or deflection during mandibular motion.

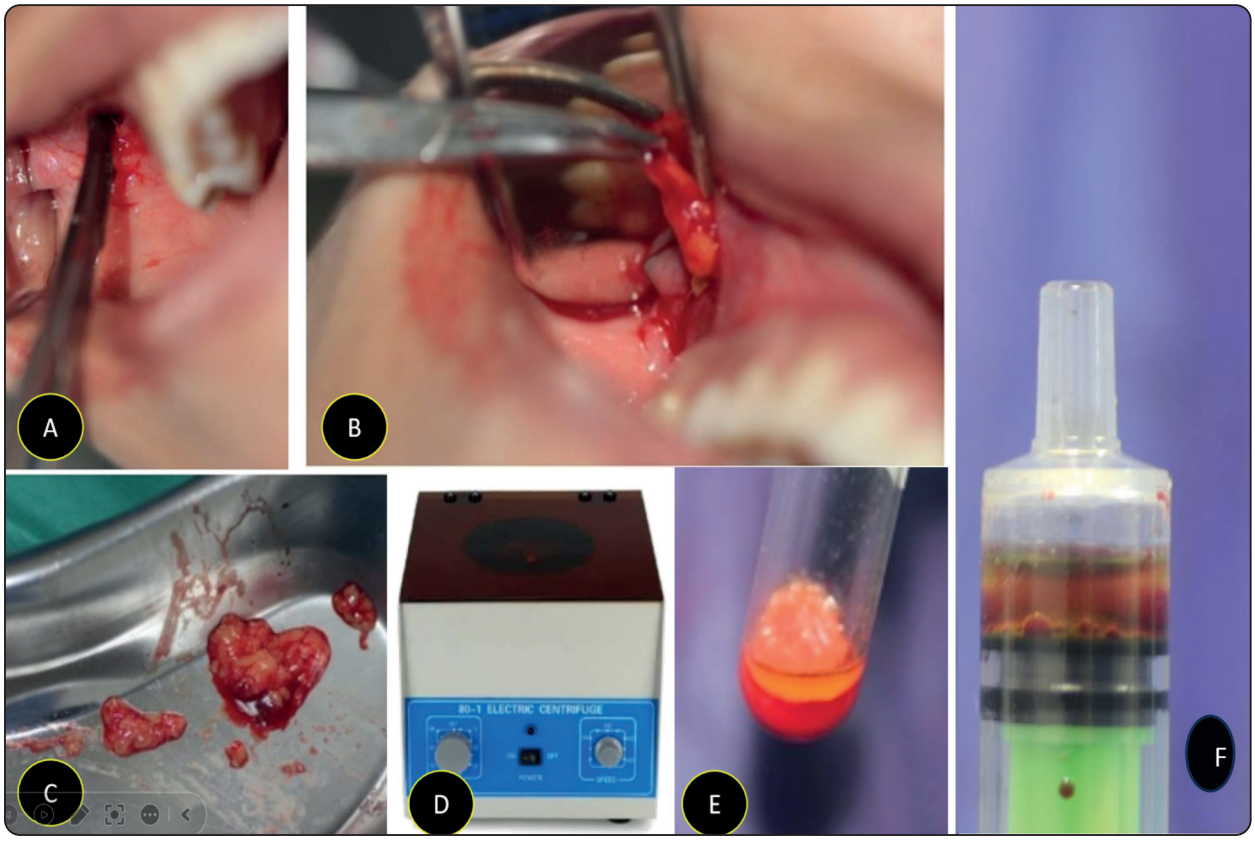

Fig. (2) A : Intra oral incision for lipids harvest. B : Dissecting the incision for collection of lipids. C : Collected lipids pre fragmentation. D : Centrifuge device used for preparation of lipids. E : Final product after centrifuge . F: Loaded 1 ml final product ready for injection.

RESULTS

The procedures went uneventful for the 26 candidates who participated in this study. All the patients completed the study follow up intervals.

Primary Outcome:

1. Pain Incidence (Fig 3):

- **Day 1:** Both groups reported severe pain (p = 1).
- **1 Week:** Group A showed less severe pain (30.8% mild, 69.2% moderate) compared to Group B (23.1% severe, 76.9% moderate), with a significant difference (p = 0.029).
- **1 Month:** Both groups reported moderate pain in 76.9% of cases, with no significant difference (p = 1).
- **3 Months:** Pain distribution was similar across groups (76.9% moderate in Group A vs. 61.5% in Group B), with no significant difference (p = 0.39).

2. Pain Intensity:

- **Day 1:** No statistically significant difference (p = 0.1) in pain intensity between groups (Group A: 8.0 ± 0.8, Group B: 8.46 ± 0.66).
- **1 Week:** Group A had statistically significantly lower pain intensity (3.9 ± 0.75) compared to Group B (5.69 ± 0.85) (p < 0.001).
- **1 Month:** No statistically significant difference in pain intensity (Group A: 5.69 ± 1.18, Group B: 5.76 ± 1.16) (p = 0.8).
- **3 Months:** Pain intensity remained similar (Group A: 5.53 ± 1.33, Group B: 6.38 ± 0.96) with no statistically significant difference (p = 0.07).

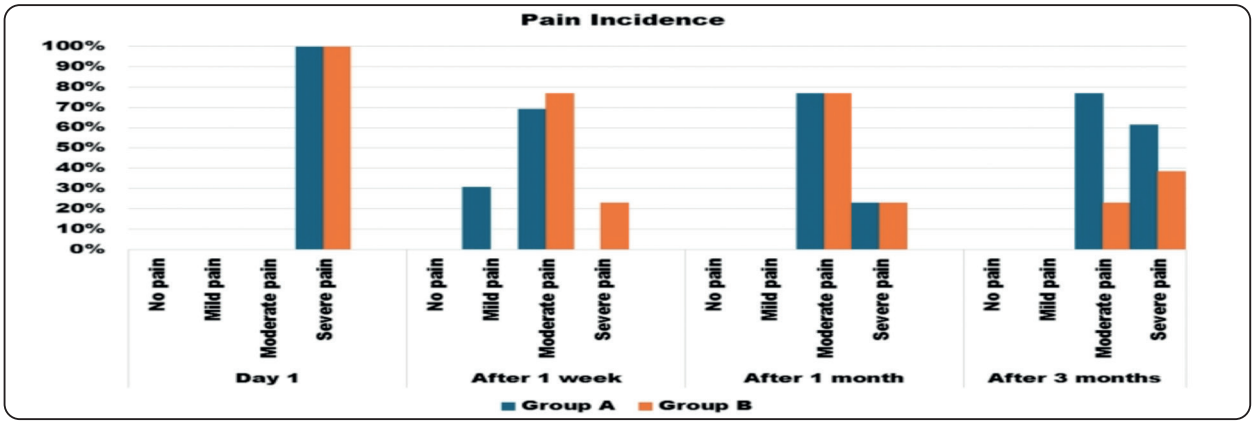

Fig. (3) Bar chart representing the incidence of pain at the follow up intervals for both groups.

Mouth Opening (fig 4)

- **Day 1:** No statistically significant difference in mouth opening (Group A: 23.23 ± 2.50 mm, Group B: 23.84 ± 1.86 mm, p = 0.4).
- **1 Week:** No statistically significant difference (Group A: 35.92 ± 3.50 mm, Group B: 33.60 ± 4.50 mm, p = 0.1).
- **1 Month:** Minimal difference (Group A: 33.90 ±4.55 mm, Group B: 34.23 ± 4.00 mm) with no statistically significant difference (p = 0.005).

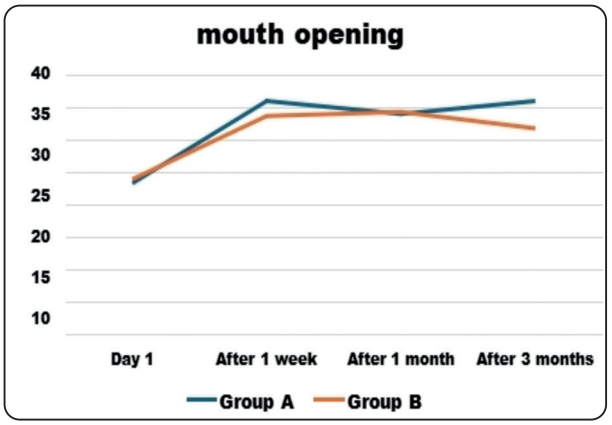

Fig. (4) Line chart representing the mouth opening at the follow up intervals for both groups.

DISCUSSION

Temporomandibular joint osteoarthritis (TMJ OA) is a progressive, multifactorial degenerative disease marked by cartilage degradation, subchondral bone remodeling, synovitis, and chronic pain, which significantly impacts patients' quality of life. Traditional treatments, such as physical therapy, occlusal splints, NSAIDs, and arthrocentesis with lubrication or corticosteroids, primarily focus on symptom relief and functional restoration, though diagnostic and therapeutic approaches remain controversial. [9-10]

The present study was aimed to evaluate pain management and improve the quality of life in patients with TMJ dysfunctions via using adipose tissue injection, use of lipid cells because of their anti-inflammatory effects, reducing pain and swelling and enhancing healing by releasing growth factors. as mentioned by Storti G, et al and Hunter D.J., et al. [11-12]

Regarding to present study clinical results, both groups reported severe pain at the baseline measurement (beginning of our thesis). After 1 week, 30.8% of patients in Group A had mild pain, while none in Group B reported mild pain. A statistically significant difference was observed between the groups (p = 0.029). After 1 month, both groups reported moderate pain in 76.9% of

cases, with no statistically significant difference (p = 1). After 3 months, 76.9% of Group A and 61.5% of Group B reported moderate pain, with no statistically significant difference (p = 0.39). this was possibly due to anti-inflammation effect of both the lipids cells and the hyaluronic acid. [13-14-15-16-17]

In the present study it was found that group (A) which received HA injections, and Group (B) which received adipose tissue injections after arthrocentesis, they ended up with the same outcome as pain reduction in the agreement with finding of [11] Haigler et al. who reported that 10 patients were treated with temporomandibular lavage (arthrocentesis) alone (Group A) and next 10 patients were treated with arthrocentesis with sodium HA (Group B). The patients were followed up to 12 weeks. Improvement in pain was assessed in VAS. statistically Significant reduction in pain was observed in both groups by 12th postoperative week, but the reduction in pain was more in Group B. In Group A, nine patients reported moderate pain and one patient reported severe pain preoperatively. On day 1, day 5, and day 7 follow-up, nine patients had moderate pain, and one had no to mild pain. In 4th week, only 4 patients had moderate pain. By the 12th week, all patients had no to mild pain, i.e., the pain was statistically significantly decreased. In Group B, two patients had severe pain, eight patients had moderate pain preoperatively, and by 4th week, nine patients had no to mild pain. By the 12th week postoperatively, all patients were relieved of pain.

Additionally, in the present study it was found that there was a statistically significant improvement in mouth opening observed in both groups, but Group B (arthrocentesis plus HA) showed faster recovery. Similar to the findings of the study performed by [3] Bouloux et al; they assumed that the washout of inflammatory mediators during arthrocentesis helps clear adhesions in the joint, making it an effective surgical method which has a positive on mouth opening later on. In comparison, research on lipid-based therapies for TMJ pain management is still emerging. Preliminary studies suggest that adipose tissue injection can reduce joint friction, decrease pain, and improve joint function in experimental models.

Washing out of inflammatory and bonding mediators to clean any adhesions on the joint disc and fossa is a simple and effective surgical method. Although intraarticular irrigation is a reliable method, complications can be observed due to joint anatomy, arthrocentesis technique and surgeon experience. Many complications have been reported after arthrocentesis under local anesthesia agreed with the study of De Riu et al. [6] complications were reported during the bone marrow aspirate injection after arthrocentesis and mainly occurred due to joint anatomy. On the other hand, regarding the complication of the present study, it was found that all patients in group (A) that treated with HA after lavage recorded fewer complications list than group (B) who were treated with lipids injection collected from the buccal pad of fat were as they suffered postoperatively from pain on the working side that we collect lipids from as incision line and suture with localized swelling for two to three weeks. All patients were treated with medication post-operative to control the pain of the operation.

It was found some serious complications that unfortunately occurred for both groups, they were associated with TMJ arthrocentesis and lavage, as mechanical damage caused by the cannula or allergic reactions to local anesthesia. More severe complications include facial paralysis, vertigo, dizziness, and hearing issues. Similar to the findings of the study performed by [18] Vaira LA et al and [19] Carroll et al. who reported that a 59-year-old woman who remained drowsy case post operatively of arthrocentesis and developed left hemiparesis following right TMJ arthrocentesis and lavage for TMJ dysfunction. After the operation, computed

tomography (CT) revealed that an extradural hematoma occurred where the cannula passed the TMJ and pricked the intracranial portion of the middle meningeal artery. With a brain surgeon's intervention, the hematoma was removed, and no perforation of the dura nor damage to the bone of the central cranial fossa, and a 48-year-old female suffered from an independently regressing short term vertigo attack after local anesthesia (mepivacaine 2% and 1:200,000 epinephrine) was given before arthrocentesis.

CONCLUSION

Arthrocentesis, particularly when combined with hyaluronic acid injections, statistically significantly reduces pain and improves mouth opening in TMJ OA patients, though careful management of complications is necessary. These results highlight the growing role of minimally invasive treatments for TMJ disorders and the importance of personalized approaches for optimal management of TMJ OA.

Recommendation for future research:

- A longer observation period for outcomes of treatment protocols will add a greater value in presenting and comparing the long-term effect of each TMJ-OA treatment protocol.
- Some studies have proposed combining lipids with HA will enhance the therapeutic effects, leveraging the complementary roles of these molecules in restoring joint health.

Competing interest:

No conflict of interest.

Ethical approval:

The ethics and research committee, Faculty of Dentistry, Cairo University approved the study and patients' consent was obtained (no. 18324)

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