Al-Azhar Journal of Dentistry

Manuscript 1649

Oral Medicine and Surgical Sciences Issue (Oral Medicine, Oral and Maxillofacial Surgery, Oral Pathology, Oral Biology)

Evaluation of the Efficiency of Micro fragmented Adipose Tissue Injection Versus Bone Marrow Aspiration Concentrate Injection in Patient with Temporomandibular Joint Osteoarthritis

Aya Nasser

Susan A Hassan

Emad Hussein

Reem Hossam

Ahmed Farouk

ORIGINAL STUDY

Evaluation of the Efficiency of Micro Fragmented Adipose Tissue Injection Versus Bone Marrow Aspiration Concentrate Injection in Patient With Temporomandibular Joint Osteoarthritis

Aya Nasser, BSc [a,*], Susan A. Hassan [b], Emad Hussein [c], Reem Hossam [d], Ahmed Farouk [e]

[a] Department of Oral and Maxillofacial Surgery, Al Zahraa University Hospital, Egypt
[b] Department of Oral and Maxillofacial Surgery, Faculty of Dental Medicine for Girls, Al-Azhar University, Egypt
[c] Department of Plastic and Reconstructive Surgery, Faculty of Medicine for Girls, Al-Azhar University, Egypt
[d] Department of Oral and Maxillofacial Surgery, Faculty of Oral and Dental Medicine, Cairo University, Cairo, Egypt
[e] Department of Oral and Dental Genetics, Institute of Human Genetics and Genome Research, National Research Center, Giza, Egypt

Abstract

Purpose: This study was performed to evaluate the effect of micro-fragmented adipose tissue (MFAT) injection and bone marrow aspiration concentrate (BMAC) injection in patient with temporomandibular joint (TMJ) osteoarthritis. **Patients and methods:** A total of 18 participants with TMJ osteoarthritis were divided into three groups, six participants in each group, group A: injected with hyaluronic acid (control group), group B: injected with MFAT, group C: injected with BMAC. All patients were assessed preoperatively and postoperatively at 1 day, 1 week, 2 weeks, 1, 3, and 6 months for pain level, maximum interincisal opening, lateral, protrusive movements, joint tenderness, and disk position with MRI after 6 months. **Results:** In the three groups, all clinical variables showed statistically significant discrepancy post-operatively. **Conclusion:** Despite the shortcomings of the current study the following could be concluded: MFAT and BMAC had a promising effect on treatment of TMJD.

Keywords: Bone marrow aspiration, Micro-fragmentation of adipose tissue, Osteoarthritis, Platelet-rich plasma, Temporomandibular disorders

1. Introduction

The proper function of the temporomandibular joint (TMJ) is greatly influenced by the harmony of the TMJ's many elements until external factors such as mechanical, psychological, occupational, or habitual adversely impact the joint function [1].

Myofascial discomfort, internal derangement, and osteoarthrosis are the three temporomandibular disorders (TMDs) that are most frequently seen [2]. The etiology of these TMDs is complex. Occlusal malfunction as well as trauma are usually described as accentuating factors rather than the primary etiological factor [3].

The primary symptoms of TMDs include discomfort, joint sounds, and limited jaw mobility. After acute physical or psychological trauma, the jaw suddenly catches or gets stuck, and the patient experiences extreme anxiety and has trouble doing basic tasks like eating and speaking [4].

Patients with TMDs frequently report a variety of nonspecific symptoms, including neck and shoulder discomfort, tinnitus, headaches, and earaches. The joints that are affected by these degenerative TMDs lack blood arteries, nerves, and lymphatic tissue, and have a limited capacity for self-healing [5].

Physical therapy, occlusal splints, NSAIDs, and arthrocentesis with lubricant or corticosteroid are examples of traditional therapeutic techniques that

Received 23 July 2023; accepted 14 April 2024.
Available online 11 February 2025

* Corresponding author at: Department of Oral and Maxillofacial Surgery, Al Zahraa University Hospital, 11781 Cairo, Egypt.
E-mail address: aya.elshnawy77@gmail.com (A. Nasser).

https://doi.org/10.58675/2974-4164.1649

can temporarily relieve pain but cannot stop the breakdown of articular cartilage [6].

Recently, research has been directed toward the cyto-therapy or cell-based treatment strategy including the injection bone marrow aspirate concentrate (BMAC), micro-fragmented adipose tissue (MFAT), and platelet-rich plasma [5].

Musculoskeletal tissues (chondrocytes or tenocytes) can be formed from mesenchymal stem cells (MSCs) present in MFAT. BMAC, which has become recognized as a secure and dependable source of MSCs, comprises various essential growth factors, such as fibroblast growth factor, bone-morphogenic protein, transforming growth factor beta, and platelet derived growth factor [7]. The study -relevant clinical and radiographic assessment of the effect of MFAT injection and BMAC injection in patient with TMJ osteoarthritis.

2. Patients and methods

To evaluate the effect of (MFAT) and BMAC injection for treatment of osteoarthritis. G power statistical power Analysis program (version 3.1.9.4) for sample size determination was used. A total sample size of 18 (6 in each group) will be sufficient to detect a large effect size (f) ranging from 0.84 to 0.85, with an actual power (1-β error) of 0.8 (80 %) and a significance level (α error) 0.05 (5 %) for the two-sided hypothesis test.

Eighteen individuals with TMJD were randomly selected for a prospective research. They were chosen from the Al-Azhar University Hospital and the Oral and Maxillofacial Surgery Department's outpatient clinic at the Faculty of Dental Medicine for Girls at Al-Azhar University. The Research Ethics Committee (REC), Faculty of Dental Medicine for Girls, Al-Azhar University (code: REC-SU-21-02) gave their approval for this study. The time frame for patient registration was from July 2021 to February 2023.

Cases that were both unilateral and bilateral were included.

2.1. Inclusion and exclusion criteria

The age of all selected patients was above 16 years and generally had good state of health, and did not respond to previous conservative treatment. All of the included patients showed signs of TMJ osteoarthrosis evaluated via clinical examination, and MR. All patients were found to have had TMJ associated manifestations such as restricted mouth opening as well as TMJ-related symptoms including limited mouth opening and arthralgia. Patients with uncontrolled systemic disease and patients who underwent previous arthrocentesis and injection or TMJ surgical treatment were excluded from the study [8].

2.1.1. Preoperative phase [9]

The study design, steps, and purpose were clearly described for all study patients. Written informed consent was signed by each patient after their approval to participate in the study.

Before beginning therapy, the selected patients were told about the aim of this investigation and signed a written informed consent.

(a) Patient Assessment: The examiner filled out a questionnaire with all the patient's information, including personal information, the main complaint, medical history, and previous dental history.
(b) Clinical Examination: Recording the sign/symptoms of TMJ osteoarthritis. Presence related symptoms include at least joint pain and limitted mouth opening, examinations of donor sites for (groups B and C) which included: the lower abdomen in (group B) and the iliac crest in (group C)
(c) MRI Examination: MRI was utilized for examination and assessment of all subjects in the three groups. Immediately before the procedure, Unictam (ampicillin, sulbactam, Medical Union Pharmaceuticals) 1.5 mg vial was intravenously administered.

2.2. Clinical diagnosis [10]

Pain was assessed on a visual analog scale (VAS) from 0 to 10 (no discomfort, 1–3 mild pain, 4–6 moderate pain, 7–9 severe pain, and 10 to 10 maximum agony). The vertical space exist between the incisal surfaces of upper and lower central incisors that is termed the maximum inter incisal opening (MIO), was gauged using a Vernier caliper and captured in photographs. Cameras were used to fully document the patient's movements of the jaw to one side and then the other. The vertical distance in millimeters from the mandibular midline to the maxillary midline served as a measure of the range of lateral mandibular excursions. It was noted whether or not there was clicking.

2.3. Patients grouping

Group A: injected with hyaluronic acid (HA) (control group).

Group B: injected with MFAT.

Group C: injected with BMAC.

2.4. Operative procedures

2.4.1. Hyaluronic acid for group A

HA sodium salts (Hyalgan, Fidia Farmaceutical, Italy) were purchased from El Ezaby Pharmacy, Egypt in a pack of 2 ml prefilled syringes.

2.4.1.1. Subcutaneous abdominal fat collection and MFAT for group B [11]. For the collection procedure, patients' evaluation was done in a fully recumbent position and under general anesthetic to establish and mark the area of the abdomen. The local anesthetic was administered via injection at the points of skin specified for cannula entrance. At these points, minor incisions were produced through an 18 gauge needle conjugated to a lipo-suction cannula [L-GI, 13 G*185 mm, A R13/18]. All surgical tools used in the lipo-suction process were supplied by the Lipogems surgical kit [Lipogems, Milan, Italy]. A 120/150 ml tumescent solution (formed of 1000 ml saline, 100 ml lidocaine, 1 ml epinephrine, and 10 ml sodium bicarbonate) was infiltrated through a blunt-tip cannula with a 60 ml syringe. Lipo-aspiration was then performed after 10 min with a cannula positioned through the site of the incision After 10 min, lipoaspiration was then conducted with a cannula placed through the incision site directed toward the umbilicus while a low-pressure vacuum syringe is used posteriorly.

A microfragmenting filter is utilized to get the MFTA (Fig. 1). The equipment is a an inherently sealed tool at which the physical forces is utilized to process the lipo-aspirate while enzymatic additives are not used. Initially, the lipoaspirate is pushed through an inlet-filter to make an initial gross-cluster reduction for the lipo-aspirate which has a yellow liquid appearance while the fat clusters demonstrate a clearly distinguished liquid appearance. Secondly, the rest of the cluster reduction is accomplished through pushing the floating adipose clusters through the second outlet filter. Therefore, the resultant tissue is harvested in 10 ml syringe followed by its transfer to one ml syringe that are then utilized to infiltrate the accurate quantity of adipose tissue inside the TMJ space.

The entire procedure provides a breakdown of fatty tissue clusters as well as a maximum clearance of impurities. Subsequently, the result is a non-expanded, mico-fragmented fatty tissue that comprises an injectable pericyte/stem cell concentrate.

Bone marrow concentrate aspiration for group C (Fig. 2) [5]:

The anterior iliac spine was anesthetized with 1 % lidocaine (10 cc) and 0.25%Marcaine (10 cc), after sterile preparation with betadine and a sterile drape application, under general anesthesia. A 13 gauge disposable bone marrow trocar needle and cannula (Mc Kesson) was introduced in the anterior iliac crest in a clockwise/anticlockwise fashion between the cortices of the crest ~5 cm deep. The trocar was removed and a 50 ml heparin treated syringe was attached to the cannula and a 20 ml of bone marrow aspirate (BMA) was harvested. Punctures were performed through the same cortical hole with the trocar relocated every 10 ml to access different cancellous sites to avoid taking large amounts of bone marrow from one site that would result in excessive dilution with peripheral blood. The syringe was detached from the cannula

Fig. 1. Micro-fragmentation of adipose tissue using microfragmenting filter.

Fig. 2. Bone marrow concentrate.

and shaken in an oscillating manner to ensure a thorough mixing of the bone marrow and the anticoagulant. A bottle of Ficoll Paque Plus (GE Healthcare, Buckinghamshire, UK) was then shaken several times to ensure proper mixing. The bone marrow aspirate was then diluted with an equal amount of saline (1: 1) then layered carefully over Ficoll Paque Plus (GE Healthcare, Buckinghamshire, UK) in a proportion 2: 1. and then processed in centrifuge using a density gradient separation method for 3000 rpm for 20 min at room temperature to separate bone marrow mononuclear cells (BMMNCS). Three layers were formed in the tube the upper layer containing platelets and plasma was aspirated in a sterile syringe and saved for future use. Then the middle cloudy mononuclear layer was collected in a centrifuge tube while avoiding the homogenization between the solutions, saline was added then another centrifugation at 2000 rpm for 10 min. The supernatant was then removed and added to the plasma and platelet poor plasma 0.1 ml of 80 mg gentamycin and 0.1 ml of dexamethasone.

3. Operative phase

3.1. Preparation of the surgical field

The ethyl-alcohol cotton swab was used to disinfect the surgical field. A cotton pellet is utilized to protect the exterior auditory canal form the collection of liquids and blood. The Holmund-Hellsing line was drawn (a line in front of the ear midtragus till the eye outer canthus) while 1 ml Mepevecaine L [2%-Mepevecaine HCl/1 : 200 000 Levonordefrine; Alexanderia Company for pharmaceutical products, Alex, Egypt].

3.2. TMJ drug delivery

The mouth was opened and pulled forward in the protruded position to permit the forward movement of the condyles and the creation of a pyramidal hollow in front of the tragus. An 18 gauge needle (inlet needle) was inserted at point A 10 cm in front of the tragus 2 mm down angling it superiorly and medially. The needle was advanced approximately 2.5 cm within the upper joint space. Afterward, the joint was distended with 2 ml of Ringer lactate solution. The accurate needle placement was checked by confirmation of the movement of the needle when the joint was manipulated. The second needle (outlet needle) was inserted at point B 20 cm in front of the tragus and 10 mm below and approximately 2.5 cm into the upper joint space. The joint was then washed with 200 ml of irrigating solution [12].

The outlet needle was removed at the end of the arthrocentesis. For group A 2 ml of High molecular weight HA was dispensed into the joint via the inlet needle. For group B 3 mm of MFAT was introduced into the joint and for group C BMMNCS was injected. This was followed by needle withdrawal as well as slight and gentle jaw manipulation in lateral, protrusive, and vertical motion to split any adhesions, release the disc, and re-establish the normal movement of the mandible. The area was covered with sterile gauze.

The procedure for each group usually lasted for around 30 min.

Postsurgical instructions: [1].

(i) Medicaments: Panadol tablets/8 h for 3 days.
(ii) Application of cold fomentation (ice packs) for 1 day postsurgical then warm packs for 4 days four times a day.
(iii) Soft diet for the first week.
(iv) Exercises of range of movement started after operation and continued for several days. Exercises were performed five times per day for 5 min for a week.
  (a) Patients were advised to open mouth widely and place the index finger on the lower teeth and the thumb on the upper teeth with firm pressure in a scissors like manner.
  (b) Shift the lower jaw as far as possible to the right and also to the left.
  (c) Shift the lower jaw forward as far as possible and return it to the rest position.
(v) Use soft toothbrush to maintain the oral and dental health and hygiene.

3.3. Follow-up phase

Patients returned for follow-up Baseline, 1 day, after 1 week, 1, 3, and 6 months intervals for clinical assessment of maximum inter incisal opening, pain on VAS, lateral jaw movements, protrusive movement and detection of any tenderness on palpation a postoperative MRI was ordered after 6 months (Fig. 3).

3.4. Statistical analysis

It was carried out through the use of SPSS version 19 statistical package [SPSS v.19: SPSS, Chicago, USA]. The data followed nonparametric distribution, and were compared by χ^2 test.

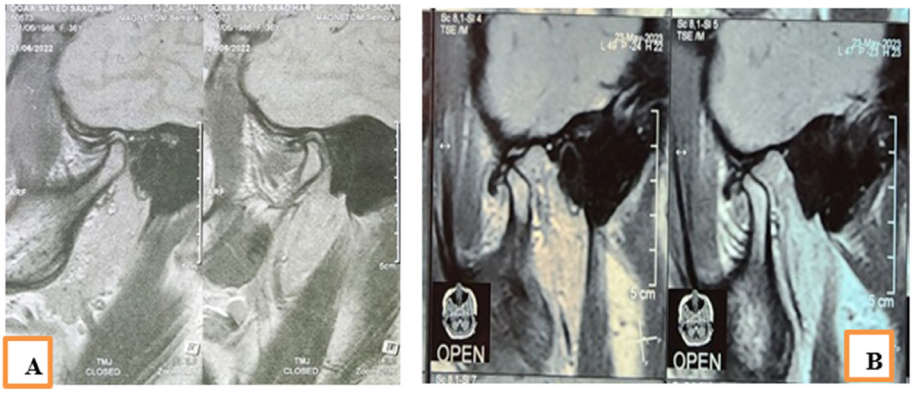

Fig. 3. (A) Preoperative T1 MRI show closed cut of temporomandibular joint shows flatting in the condyle, osteophyte and anterior Disc displacement. (B) Postoperative T1 MRI shows right open cut shows flatting in condyle, osteophyte.

4. Results

4.1. VAS pain between the three groups at different time intervals

At baseline (immediate following injection/same day): The greatest mean of VAS was achieved in the HA group (9.67 ± 0.52) and the lowest one achieved in BMAC group (8.17 ± 1.83), there was no significant difference between the three groups, and the overall *P* value was not statistically significant ($P > 0.05$).

After 1 day: The greatest mean of VAS was achieved in the HA group (8.33 ± 1.37) and the lowest one was achieved in MFAT group (3.83 ± 3.54), there was no significant difference between MFAT and BMAC groups, while there was a significant difference between HA group and the other groups, and the overall *P* value was statistically significant ($P < 0.05$).

After 1 week: The greatest mean of VAS was achieved in the HA group (7.33 ± 1.03) and the lowest one achieved in MFAT group (0.5 ± 1.22), there was no significant difference between MFAT and BMAC groups, while there was significant difference between HA group and the other groups, and the overall *P* value was statistically highly significant ($P < 0.001$).

Other follow-ups from 2 weeks to 6 months: The greatest mean of VAS was achieved in the HA group, then changed to zero in the MFAT and BMAC groups, there was no significant difference between MFAT and BMAC groups (the VAS value was zero), while there was a significant difference between HA group and the other groups, and the overall *P* value was statistically highly significant ($P < 0.001$) (Fig. 4, Table 1).

4.2. Palpation of tmj pain at different time intervals

At baseline: The greatest mean of palpation of TMJ pain was achieved in the HA group (9.67 ± 0.52) and the lowest one achieved in BMAC group (8.83 ± 0.75), there was no significant difference between the three groups, and the overall *P* value was not statistically significant ($P > 0.05$).

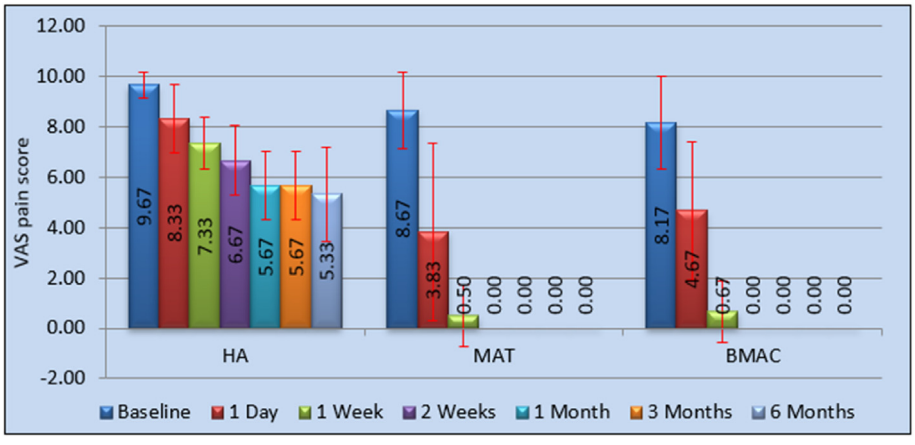

Fig. 4. Bar chart representing the mean and SD of visual analog scale pain score for all groups at different time intervals.

Table 1. Mean ± SD and visual analog scale pain score for all groups at different time intervals.

	HA	MFAT	BMAC	*P* value[a]
Baseline	9.67 ± 0.52^{A}	8.67 ± 1.51^{A}	8.17 ± 1.83^{A}	**0.146**^{NS}
1 day	8.33 ± 1.37^{A}	3.83 ± 3.54^{B}	4.67 ± 2.73^{B}	**0.011**^{S}
1 week	7.33 ± 1.03^{A}	0.5 ± 1.22^{B}	0.67 ± 1.21^{B}	**0.001**^{HS}
2 weeks	6.67 ± 1.37^{A}	0±0^{B}	0±0^{B}	**0.000**^{HS}
1 month	5.67 ± 1.37^{A}	0±0^{B}	0±0^{B}	**0.000**^{HS}
3 months	5.67 ± 1.37^{A}	0±0^{B}	0±0^{B}	**0.000**^{HS}
6 months	5.33 ± 1.86^{A}	0±0^{B}	0±0^{B}	**0.000**^{HS}

Capital letters for inter-group comparison (Mann–Whitney test) and the means with different superscripts are statistically significant different at *P* less than or equal to 0.05.
S= Statistically significant at *P* less than or equal to 0.05 - NS= Nonsignificant *P* greater than 0.05.
HS= Highly significant at *P* less than or equal to 0.001.
[a] Overall *P* value for intra-group comparing under the same (Kruskal–Wallis test).

Table 2. Mean ± SD of palpation of temporomandibular joint pain for all groups at different time intervals.

	HA	MFAT	BMAC
Baseline	9.67 ± 0.52^{a}	9.00 ± 0.63a	8.83 ± 0.75a
1 day	9.33 ± 0.52a	8.00 ± 1.26a	7.00±2a
1 week	7.33 ± 1.03 ab	1.5 ± 1.05^{b}	3 ± 2.53^{b}
2 weeks	6.67 ± 1.37b	0±0^{b}	1.5 ± 2.35^{bc}
1 month	6.33 ± 1.03^{b}	0±0^{b}	0.17 ± 0.41^{c}
3 months	6.33 ± 1.86^{b}	0±0^{b}	0±0^{c}
6 months	6.33 ± 1.86^{b}	0±0^{b}	0±0^{c}
P value[a]	0.000^{HS}	0.000^{HS}	0.000^{HS}

Small letters for intra-group comparison (Mann–Whitney test) and the means with different superscripts are statistically significant different at *P* less than or equal to 0.05.
S= Statistically significant at *P* less than or equal to 0.05 - NS= Nonsignificant *P* greater than 0.05.
HS= Highly significant at *P* less than or equal to 0.001.
[a] Overall *P* value for intra-group comparing under the same (Kruskal–Wallis test).

After 1 day: The greatest mean of TMJ pain was achieved in the HA group (9.33 ± 0.52) and the lowest one achieved in BMAC group (7.00 ± 2.00), there was no significant difference between MFAT and BMAC groups, while there was a significant difference between HA group and the other groups, and the overall *P* value was statistically significant (*P* 0.05).

After 1 week: The greatest mean of TMJ pain was achieved in the HA group (7.33 ± 1.03) and the lowest one achieved in MFAT group (1.5 ± 1.05), there was no significant difference between MFAT and BMAC groups, while there was significant difference between HA group and the other groups, and the overall *P* value was statistically significant ($P < 0.05$).

Other follow-ups from 2 weeks to 6 months: The greatest TMJ pain was achieved in the HA group, and the least result was zero in the MFAT group, there was no significant difference between MFAT and BMAC groups, while there was a significant difference between HA group and the other groups, and the overall *P* value was statistically significant ($P < 0.05$) (Table 2).

4.3. Maximum mouth opening at different time intervals

At baseline: The greatest mean of mouth opening was achieved in the BMAC group (28.17 ± 8.95 mm) and the lowest one achieved in MFAT group (712.33 ± 4.08 mm), there was no significant difference between HA and BMAC groups, while there was a significant difference between MFAT group and the other two groups, and the overall *P* value was statistically significant ($P < 0.05$).

After 1 day: The greatest mean of mouth opening achieved in the BMAC group (34.5 ± 4.14 mm) and the lowest one achieved in MFAT group (27.83 ± 6.46 mm), there was no significant difference between HA and MFAT groups, while there was a significant difference between BMAC group and the other two groups, and the overall *P* value was statistically significant ($P < 0.05$).

Other follow-ups from 1 week to 6 months: The greatest mean of mouth opening was achieved in the BMAC group and the lowest one was achieved in HA group, there was no significant difference between HA and MFAT groups, while there was a significant difference between BMAC group and the other two groups, and the overall *P* value was statistically highly significant ($P < 0.001$).

4.4. Lateral and protrusive movements at different time intervals

At baseline: The greatest mean of movements was achieved in the HA group (5 ± 0.89 mm) and the lowest one achieved in BMAC group (3.4 ± 1.82 mm), there was not any statistically significant difference among the whole study groups, and the overall *P* value was not statistically significant ($P > 0.05$).

After 1 day: The greatest mean of movements achieved in the MFAT group (5.5 ± 1.52 mm) and the lowest one achieved in BMAC group (4.2 ± 1.3 mm), there was not any statistically significant difference among the whole study groups, and the overall *P* value was not statistically significant ($P > 0.05$).

Other follow-ups from 1 week to 6 months: The greatest mean of movements was achieved in the BMAC group and the lowest one was achieved in HA group, there was no significant difference between BMAC and MFAT groups, while there was a significant difference between HA group and the other two groups, and the overall *P* value was statistically significant ($P < 0.05$) (Fig. 7).

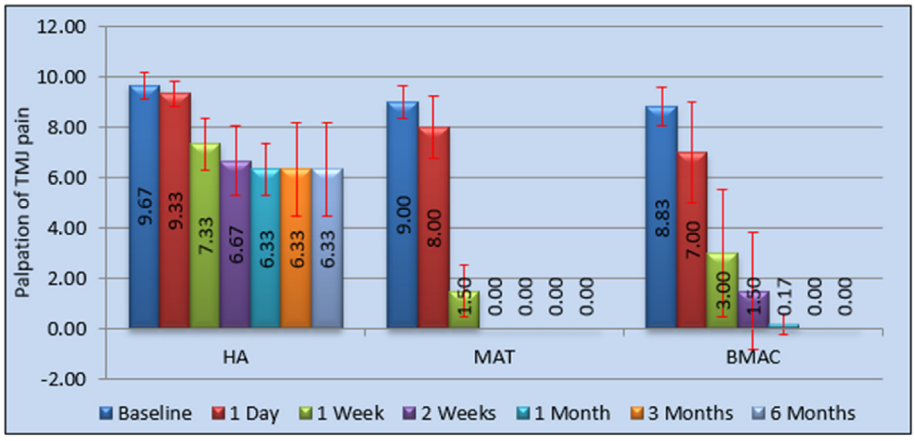

Fig. 5. Bar chart representing the mean and SD of palpation of temporomandibular joint pain for all groups at different time intervals.

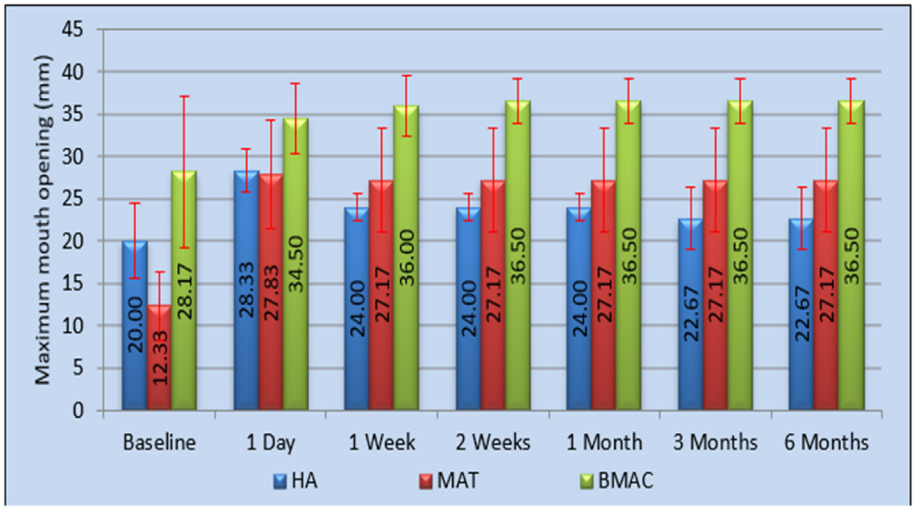

Fig. 6. Bar chart representing the mean and SD of maximum mouth opening for all groups at different time intervals.

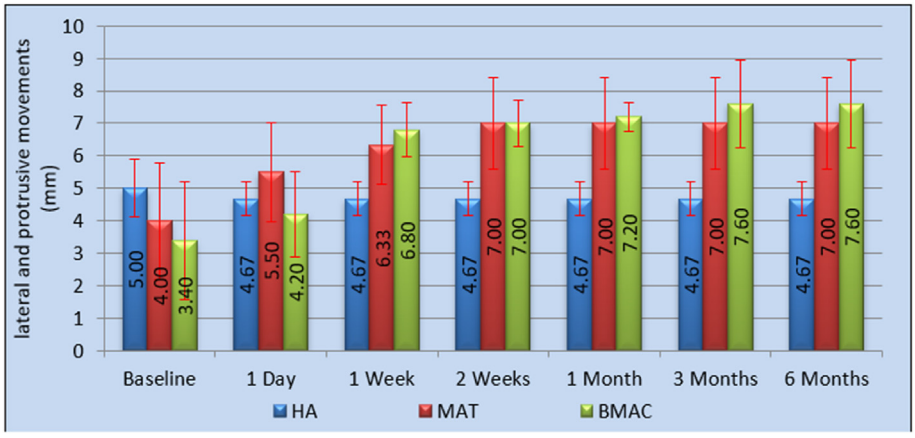

Fig. 7. Bar chart representing the mean and SD of lateral and protrusive movements for all groups at different time intervals.

4.5. Pain of muscles of mastication at different time intervals

At baseline: The greatest mean of masticatory muscles pain was achieved in the HA group (7.67 ± 0.52) and the lowest one was achieved in MFAT group (7.33 ± 0.52), there was no significant difference between the three groups, and the overall *P* value was not statistically significant ($P > 0.05$).

After 1 day: The greatest mean of pain was achieved in the HA group (6 ± 0.89) and the least result was zero in the MFAT group, there was a statistically significant difference among the whole study groups, and the overall *P* value was statistically highly significant ($P < 0.001$).

After 1 week: The greatest mean of pain was achieved in the HA group (5.33 ± 1.86) and the least result was zero in the MAFT group, there was no significant difference between MFAT and BMAC groups, while there was significant difference between HA group and the other groups, and the overall *P* value was a statistically highly significant ($P < 0.001$).

Other follow-ups from 2 weeks to 6 months: The greatest mean of pain of muscles of mastication was achieved in the HA group, and the lowest result was zero in the MFAT group, there was no significant difference between MFAT and BMAC groups, while there was a significant difference between HA group and the other groups, and the overall *P* value was statistically highly significant ($P < 0.001$) (Fig. 8, Table 5).

Table 3. Mean ± SD and inter-group comparison of maximum mouth opening (mm) for all groups at different time intervals.

	HA	MFAT	BMAC	*P* value[a]
Baseline	20 ± 4.47^{A}	12.33 ± 4.08^{B}	28.17 ± 8.95^{A}	**0.002**^{S}
1 day	28.33 ± 2.58^{B}	27.83 ± 6.46^{B}	34.5 ± 4.14^{A}	**0.047**^{S}
1 week	24 ± 1.55^{B}	27.17 ± 6.11^{B}	36 ± 3.58^{A}	**0.000**^{HS}
2 weeks	24 ± 1.55^{B}	27.17 ± 6.11^{B}	36.5 ± 2.66^{A}	**0.000**^{HS}
1 month	24 ± 1.55^{B}	27.17 ± 6.11^{B}	36.5 ± 2.66^{A}	**0.000**^{HS}
3 months	22.67 ± 3.61^{B}	27.17 ± 6.11^{B}	36.5 ± 2.66^{A}	**0.000**^{HS}
6 months	22.67 ± 3.61^{B}	27.17 ± 6.11^{B}	36.5 ± 2.66^{A}	**0.000**^{HS}

Capital letters for inter-group comparison (Tukey post hoc test) and the means with different superscripts are statistically and significantly different at *P* less than or equal to 0.05.
S= Statistically significant at *P* less than or equal to 0.05 - NS= Nonsignificant *P* greater than 0.05.
HS= Highly significant at P less than or equal to 0.001.
[a] Overall *P* value for intra-group comparing under the same (ANOVA test).

Table 4. Mean ± SD of lateral and protrusive movements (mm) for all groups at different time intervals.

	HA	MFAT	BMAC	*P* value[a]
Baseline	5 ± 0.89^{A}	4 ± 1.79^{A}	3.4 ± 1.82^{A}	**0.250**^{NS}
1 day	4.67 ± 0.52^{A}	5.5 ± 1.52^{A}	4.2 ± 1.3^{A}	**0.214**^{NS}
1 week	4.67 ± 0.52^{B}	6.33 ± 1.21^{A}	6.8 ± 0.84^{A}	**0.003**^{S}
2 weeks	4.67 ± 0.52^{B}	7 ± 1.41^{A}	7 ± 0.71^{A}	**0.001**^{HS}
1 month	4.67 ± 0.52^{B}	7 ± 1.41^{A}	7.2 ± 0.45^{A}	**0.001**^{HS}
3 months	4.67 ± 0.52^{B}	7 ± 1.41^{A}	7.6 ± 1.34^{A}	**0.002**^{S}
6 months	4.67 ± 0.52^{B}	7 ± 1.41^{A}	7.6 ± 1.34^{A}	**0.002**^{S}

Capital letters for inter-group comparison (Tukey post hoc test) and the means with different superscripts are statistically significantly different at *P* less than or equal to 0.05.
S= Statistically significant at *P* less than or equal to 0.05 - NS= Non-significant *P* greater than 0.05.
HS= Highly significant at *P* less than or equal to 0.001.
[a] Overall *P* value for intra-group comparing under the same (ANOVA test).

5. Discussion

The most typical kind of joint illness is thought to be TMJ osteoarthritis. Osteoarthritis often advances slowly. Articular cartilage, subchondral bone, ligaments, synovium, and even nearby muscles are all affected by OA in the whole joint. Patients with TMJ OA frequently experience discomfort, joint noises, limited mouth opening, and mandibular deviation toward the afflicted side when opening the mouth

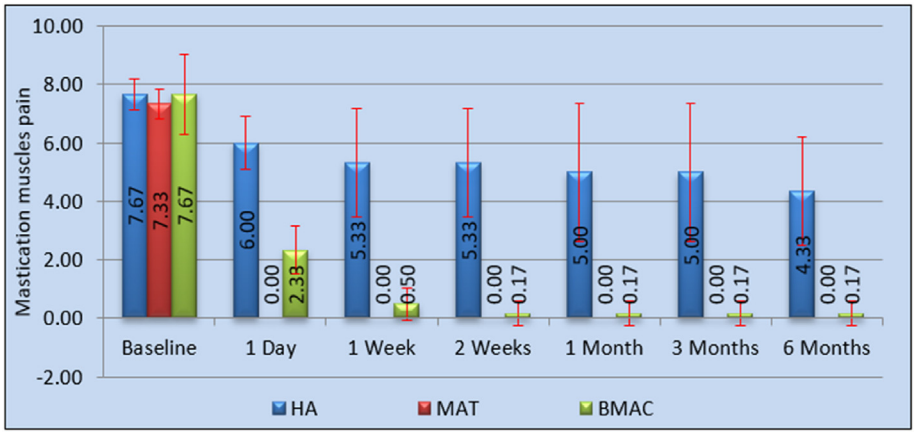

Fig. 8. Bar chart representing the mean and SD of mastication muscles pain for all groups at different time intervals.

Table 5. Mean ± SD and inter-group comparison results of mastication muscles pain for all groups at different time intervals.

	HA	MFAT	BMAC	*P* value[a]
Baseline	7.67 ± 0.52^{A}	7.33 ± 0.52^{A}	7.67 ± 1.37^{A}	0.761^{NS}
1 day	6 ± 0.89^{A}	0 ± 0^{C}	2.33 ± 0.82^{B}	0.001^{HS}
1 week	5.33 ± 1.86^{A}	0 ± 0^{B}	0.5 ± 0.55^{B}	0.001^{HS}
2 weeks	5.33 ± 1.86^{A}	0 ± 0^{B}	0.17 ± 0.41^{B}	0.000^{HS}
1 month	5 ± 2.37^{A}	0 ± 0^{B}	0.17 ± 0.41^{B}	0.000^{HS}
3 months	5 ± 2.37^{A}	0 ± 0^{B}	0.17 ± 0.41^{B}	0.000^{HS}
6 months	4.33 ± 1.86^{A}	0 ± 0^{B}	0.17 ± 0.41^{B}	0.001^{HS}

Capital letters for inter-group comparison (Mann–Whitney test) and the means with different superscripts are statistically significantly different at *P* less than or equal to 0.05.
S= Statistically significant at *P* less than or equal to 0.05 - NS= Nonsignificant *P* greater than 0.05.
HS= Highly significant at *P* less than or equal to 0.001.
[a] Overall *P* value for intra-group comparing under the same (Kruskal–Wallis test).

[13]. Most patients with OA can be treated successfully with nonsurgical therapy as pharmacotherapy, physical therapy, and TMJ splints. Invasive treatments such arthrocentesis, arthroscopy, intra-articular injections of HA, corticosteroids, and prolotherapy with platelet-rich plasma or PRGF may be necessary for patients who do not respond to nonsurgical treatment. In case of failure of minimally invasive techniques, more invasive procedures are required as disc repositioning, discectomy and modified condylotomy [1].

The TMJ is injected with MFAT in the current study because MFAT originating from humans and animals has lately received more attention because to their availability and abundance. These multipotent cells have the ability to differentiate into mature adipocytes as well as chondrocytes, osteoblasts, myocytes, hepatocytes, neuronal-like, and endothelial cells, according to in vitro, ex vivo, and in vivo data. This ability might be used to restore tissues that have been injured. Through the production of numerous bioactive molecules that function in a paracrine manner, MFATs start and maintain angiogenic, antifibrotic, antiapoptotic, and immunomodulatory reactions in target tissue [14].

Because systemically administered stem cells may migrate to the lung, kidney, and other organs, direct and local implantation of stem cells has always been the preferred method of treating OA. Clinical trials have demonstrated that intra-articular injections of MSCs significantly reduced pain, stiffness in the joints, and physical impairment in individuals with OA. Another focus was on BMAC, which has become a crucial biological tool for orthopaedic surgeons as one of the few methods of administering stem cells and growth factors that has been given FDA approval at this time [15].

The feasibility and safety of injecting BMMCS into the TMJ are this study's two significant outcomes. The procedure could be carried out via the use of local anesthetic similar to outpatient operations. In BMMCS group patients, no complications were found at either the donor or the receiving sites. The entrance position on the iliac crest must be carefully chosen and should be positioned at least 2 cm posterior to the antero-superior iliac spine to prevent damage to the lateral femoral cutaneous nerve [1].

Standard products used with arthrocentesis in the literature are injections of HA, local anesthetics like bupivacaine and mepivacaine, morphine, and steroids. The bulk of research detailing these techniques are inconsistent in their superiority to the basic technique represented by arthrocentesis alone, demonstrating the lack of information about which approach yields the greatest outcomes. As the gold standard medication for the treatment of TMJOA, HA was employed in the current study. All the participants in our trial had arthrocentesis, which removes chemical inflammatory mediators from the synovial fluid and lowers levels of inflammatory cytokines, degraded proteins, and arachidonic acid metabolites in the synovial fluid, allowing the joint to benefit most from the medication delivery. Additionally, by removing the negative pressure within the joint, releasing joint adhesions through the irrigation's hydraulic pressure, and enabling nutrient perfusion for the disc's free sliding movement, mandibular mobility is increased [8].

Ringer's solution is more tolerable than saline in the fibrous tissue of the articular disc, making it more physiological during arthrocentesis treatments. In our study, 100 cc of TMJ lavage solution was utilized to get rid of certain proteins, proteases, and denatured hemoglobin [5].

To determine if an arthrocentesis treatment was successful, the American Association of Oral and Maxillofacial Surgeons established the following criteria: at 12 months after treatment, the presence of mild or no pain (VAS score #3) and an MMO of 35 mm [16].

Statistical analysis of pain on VAS showed gradual decrease the pain score post-operatively through follow up period in BMAC and MFAT groups. This discrepancy was extremely statistically significant ($P < 0.0001$) as after 1 day the greatest mean of VAS achieved in the HA group was (8.33 ± 1.37) and the lowest one achieved in MFAT group was (3.83 ± 3.54) and also at the other follow-ups from 2 weeks to 6 months the greatest mean of VAS was

achieved in the HA group, then changed to zero in both the MFAT and BMAC groups.

Statistical analysis of palpation of TMJ pain showed a gradual decrease postoperatively in both groups BMAC and MFAT through follow-up period till two weeks then no pain on palpation was detected at one month while the greatest mean of palpation of TMJ pain was achieved in the HA group at all time intervals, which continued till the end of follow-up period.

Statistical analysis of the maximum mouth opening showed gradual increase in HA while an immediate improvement in mouth opening achieved at the first postoperative day in both BMAC and MFAT through all the different time intervals, this discrepancy was extremely statistically significant ($P < 0.0001$). It increased from (28.17 ± 8.95 mm) at base line to (34.5 ± 4.14 mm) after 1 day and (36.5 ± 2.66) after 6 months (Table 3, Fig. 5).

Statistical analysis of lateral and protrusive movements showed the greatest mean of movements achieved in the BMAC group and MFAT group while the lowest one achieved in HA group from 1 week to 6-month intervals (Table 4, Fig. 6).

Statistical analysis of mastication muscles pain showed that the greatest mean of mastication muscles pain was achieved in the HA group at all time intervals while MFAT group showed the lowest one (7.33 ± 0.52) at baseline and (0 ± 0) after 6 months.

Absence of pain at first operative day till the end of the follow-up period. The findings of this study showed that both the MFAT and BMAC groups were successful in lowering pain and muscle pain.

Because the harvesting phase is significantly less invasive than the lipoaspiration procedure, MSCs derived from adipose tissue have a marginally significant advantage over MSCs derived from bone marrow [17] and this findings is in agreement with a previous study [18]. MSCs isolated from adipose tissue and bone marrow share similar characteristics [4].

In the present study BMAC proved to be effective in management of function of symptomatology secondary to TMJ OA, yet it is still unclear how BMAC can be used most effectively for the treatment of various conditions, but the quantity of MSCs in bone marrow aspirates is often low and dependent on the site of collection, the patient's sex, and their age; in contrast, MFAT is abundant in micro-vessels and pericytes, which are immature MSC progenitors [16].

5.1. Conclusion

MFAT injection and BMAC injection is an emerging treatment option for patients with TMJ osteoarthritis, with several studies reporting significant improvements in pain, function, and quality of life. Future research is needed to fully understand the optimal dosing and timing of MFAT and BMAC injection and to evaluate its long-term effects. However, the available evidence suggests that MFAT and BMAC injection is a safe and effective treatment option for eligible patients with TMJOA.

6. Recommendations

Further studies are warranted to gain more insight into the performance and the synergetic effect of using both cell-based therapeutic materials together.

Conflict of interest

There are no conflicts of interest.

Acknowledgments

I'm greatly honored to express my deepest love and appreciation to my family for their continuous support and motivation.

References

[1] Boulos RT, Najjoum CF, El Asmar EA, Abi Chahine NH. Degenerative disorder of the temporomandibular joint treated with autologous bone marrow-derived stem cells using the regen time technique: a Case Report. Cureus 2023;15:11–5.
[2] Gutiérrez IQ, Sábado-Bundó H, Gay-Escoda C. Intraarticular injections of platelet rich plasma and plasma rich in growth factors with arthrocenthesis or arthroscopy in the treatment of temporomandibular joint disorders: a systematic review. J Stomatol Oral Maxillofac Surg 2022;123:e327–35.
[3] Akçay Köprücü S, Uzun T. Magnetic resonance imaging and fractal analysis findings in temporomandibular joints with disk perforation. Oral Surg Oral Med Oral Pathol Oral Radiol 2023;00:0–12.
[4] Ahmed SO, Shamaa A, Mohammed SS. The effect of intra-articular injections of high molecular weight hyaluronic acid, botox, and therir combination on complete freunds adjuvant-induced TMJ osteoarthiritis in rats. Egypt Dent J 2023;69:7084.
[5] Boffa A, Perucca Orfei C, Sourugeon Y, Laver L, Magalon J, Sánchez M, et al. Cell-based therapies have disease-modifying effects on osteoarthritis in animal models. A systematic review by the ESSKA Orthobiologic Initiative. Part 2: bone marrow-derived cell-based injectable therapies. Knee Surg Sports Traumatol Arthrosc 2023;10:16–23.
[6] Klasser GD, Goulet JP, Moreno-Hay I. Classification and diagnosis of temporomandibular disorders and temporomandibular disorder pain. Dent Clin N Am 2023;67:211–25.
[7] Keeling LE, Belk JW, Kraeutler MJ, Kallner AC, Lindsay A, McCarty EC, et al. Bone marrow aspirate concentrate for the treatment of knee osteoarthritis: a Systematic Review. Am J Sports Med 2021:1–8.
[8] Elkholy A, Abd El-Moniem N, Hassan S, Enite A. Effect of plasma rich in growth factors intra articular injection in management of patients with internal derangement of tmj using ct guided puncture versus conventional technique. Al-Azhar Dent J Girls 2019;6:427–35.
[9] Mecott GA, Gonzalez-Cantu CM, Moreno-Peña PJ, Flores PP, Castro-Govea Y, de Oca-Luna RM, et al. Effect of diameter and fenestration area of the liposuction cannula on the viability of the adipocytes. Aesthetic Plast Surg 2022;46:912–9.

[10] Bayramoglu Z, Yavuz GY, Keskinruzgar A, Koparal M, Kaya GS. Does intra-articular injection of tenoxicam after arthrocentesis heal outcomes of temporomandibular joint osteoarthritis? A randomized clinical trial. BMC Oral Health 2023;23:131.
[11] Han C, Weng XS, Cui Y. Microfragmented adipose tissue and its initial application in articular disease. Chin Med J (Engl) 2019;132:2745−8.
[12] Marzook HAM, Abdel Razek AA, Yousef EA, Attia AAMM. Intra-articular injection of a mixture of hyaluronic acid and corticosteroid versus arthrocentesis in TMJ internal derangement. J Stomatol Oral Maxillofac Surg 2020;121:30−4.
[13] Okikiade A, Osharode A, Oyewole A, Ogunesan D, Oladejo D, Oshobu I, et al. Understanding the role of inflammation in secondary osteoarthritis. Asian J Med Heal 2022;20:60−74.
[14] Mautner K, Bowers R, Easley K, Fausel Z, Robinson R. Functional outcomes following microfragmented adipose tissue versus bone marrow aspirate concentrate injections for symptomatic knee osteoarthritis. Stem Cells Transl Med 2019;8:1149−56.
[15] De Riu G, Vaira LA, Carta E, Meloni SM, Sembronio S, Robiony M. Bone marrow nucleated cell concentrate autograft in temporomandibular joint degenerative disorders: 1-year results of a randomized clinical trial. J Cranio-Maxillo-Fac Surg 2019;47:1728−38.
[16] Sembronio S, Tel A, Tremolada C, Lazzarotto A, Isola M, Robiony M. Temporomandibular joint arthrocentesis and microfragmented adipose tissue injection for the treatment of internal derangement and osteoarthritis: a Randomized Clinical Trial. J Oral Maxillofac Surg 2021;79:1447−56.
[17] Pintore A, Notarfrancesco D, Zara A, Oliviero A, Migliorini F, Oliva F, et al. Intra-articular injection of bone marrow aspirate concentrate (BMAC) or adipose-derived stem cells (ADSCs) for knee osteoarthritis: a prospective comparative clinical trial. J Orthop Surg Res 2023;18:350.
[18] Ulivi M, Meroni V, Viganò M, Colombini A, Lombardo MDM, Rossi N, et al. Micro-fragmented adipose tissue (mFAT) associated with arthroscopic debridement provides functional improvement in knee osteoarthritis: a randomized controlled trial. Knee Surg Sport Tr A 2022;67: 1−50.