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EFFECTIVENESS OF STEM CELLS INJECTION FOR TREATMENT OF TEMPOROMANDIBULAR JOINT ADVANCED INTERNAL DERANGEMENT

Hatem Ismael Mattar[1]*, Dr. Mohsen Fawzy Abo Elhassan[2],Dr. Abdel Aziz Baiomy Abdullah[3], Hussein Elrawy [4], Mustafa G Khallaf [5]

Paper extracted from doctoral thesis titled:Effectiveness of Stem Cells injection for treatment of Temporomandibular Joint advanced internal derangement

1.Oral and Maxillofacial Surgeon, Ministry of Health, Egypt
2. Professor of Oral and Maxillofacial Surgery, Faculty of Dental Medicine, Al- Azhar University - Assiut
3. Professor of Oral and Maxillofacial Surgery, Head of Oral and Maxillofacial Surgery Department, Faculty of Dental Medicine, Al- Azhar University – Assiut
4. Chairman, cleveland dental institute
5.Lecturer of Oral and Maxillofacial Surgery, Al-azhar University, Cairo, Egypt

ABSTRACT

Purpose: Thisstudy aimed to evaluate the effectiveness of bone marrow injection for treatment of Temporomandibular Joint advanced internal derangement.**Subjects and methods:**Twenty patients requiringtreatment of Temporomandibular Joint advanced internal derangementwere included in this retrospective study. Ten patients receivedinjections with bone marrow concentrate and the other ten injected with bone marrow aspirate. Postoperative efficacy of the technique was evaluatedby monitoring the patients over a period of 6 months.Additionally, MRI were used as a radiographical parameter at the end of the follow-up period.**Results:**Bone marrow rich stem cells injection for treatment of Temporomandibular Joint advanced internal derangement resulted in significant decreases inpain and significant improvement in maximum interincisal at the end of the 6-month observation period. **Conclusion**: Injecting the TMJ with bone marrow-derived stem cells is a reliable and technically applicable method for the treatment of Temporomandibular Joint (TMJ) advanced internal derangement.

Keywords: Stem Cells injection, Temporomandibular Joint, Advanced Internal Derangement

INTRODUCTION

Internal derangement of the temporomandibular joint is one of the most prevalent issues within temporomandibular disorders. This refers to an abnormal positioning of the disc in relation to the mandibular condyle and the glenoid fossa, often termed "disc displacement." When the disc is forced out of its proper place, it can lead to direct contact between bones, resulting in increased joint wear and tear and subsequent pain.[(1)]

The most frequent form of TMJ disorder is the displacement of the TMJ articular disc, which is followed by gradual degenerative changes in the joint, potentially leading to osteoarthritis.[2–4]

Recent advancements in stem cell-based treatments and tissue engineering have opened up new avenues for alleviating symptoms and even replacing damaged tissue in TMJ disorder therapy. These stem cells aid in healing, reduce inflammation, and contribute to the restoration of injured tissue. Additionally, mesenchymal stem cells (MSCs) exhibit immune-regulating properties, adjusting the activation of natural killer cells, macrophages, and T and B lymphocytes. This gives MSCs beneficial anti-inflammatory and antifibrotic characteristics that enhance their therapeutic impact.[5–11]

Research has demonstrated that cultured stem cells derived from bone marrow, pre-conditioned with osteogenic and chondrogenic media, can generate bone-like and cartilage-like structures in vitro. These structures mimic the properties of a joint-like structure when introduced into the affected area. Some clinical trials have proposed these techniques for addressing internal derangement, involving the direct injection of stem cells into the synovial fluid within the joint

To concentrate harvested bone marrow, a centrifugation process with a separating medium can be utilized. This step concentrates the layer containing mononuclear cells, thereby increasing the number of MSCs relative to the baseline [12]

Therefore, the purpose of this study was to assess the impact of injecting a concentrate of bone marrow-derived stem cells into the upper space of the temporomandibular joint as a treatment for advanced internal derangement, specifically disc displacement without reduction.

MATERIAL AND METHODS

Study Setting:

This study was performed for treatment of Temporomandibular Joint advanced internal derangement was carried out in patients who reported to the Department of Oral and Maxillofacial Surgery, Faculty of Dental Medicine, Al- Azhar University (Assiut).

Study Design:

Sample size was determined to be 20 patients in two groups 10 in each. Patients who suffering from internal derangement without reduction as approved by clinical and radiographic examination were included in the study. All the patients were informed about the study after ethical committee of Al-AzharUniversity (Assiut) approved the study design. Oral surgery informed consentwas explained and taken from all the patients including photography and video consents. Preoperative Magnetic Resonance Imaging were taken. All the patients in the same group were subjected to the same treatment protocol.

All patients have been treated according to the group they were assigned to using the same materials, same technique within the same group and same operator for all groups.

Inclusion criteria:

- Patient with MRI evidence of disc displacement without reduction in open mouth position.

- Patient presenting with clinical signs & symptoms of disc displacement that include the following:

a) Limited mouth opening
b) Pain in the temporomandibular joint on jaw movements
c) Temporomandibular joint sounds (clicking)
d) Anhedonia (inability to enjoy the life)

- Patient are free from any systemic condition may alter the treatment.
- Patient with anterior and posterior occlusion.

Exclusion criteria:

- Patient presenting with non-inflammatory conditions of the temporomandibular joint (fracture, joint ankylosis, tumors… etc).
- Patient with oral and paraoral habits.
- Completely edentulous patient.
- Patient with sever malocclusion or canting on occlusion.
- Patient with previous (TMJ) surgery.

Once they are selected to be enrolled in the study; All the patients underwent through the same clinical and radiographic protocol as following:

- Extraoral examination as a general exam for head and neck including the lymph nodes and facial deformities.
- Standard pain scoringwas carried out before treatment through a visual analogue scale (VAS)
- Maximal mouth opening was measured inter- incisally with a digital caliper.
- Joint sounds as clicking or crepitation were evaluated preoperatively by oscillation with stethoscope.
- Preoperative CBCT done for all patients to exclude any osseous disorderandMagnetic resonance imaging (MRI) done for each patient to confirm the diagnosis and to document the disc position before arthrocentesis.

Surgical procedures

The operations were performed under Generalanesthesia by a single qualified surgeon. The patient was ideally positioned in a supine or reclined posture, with their head turned away from the injection site.Lavage was performed using Ringer's lactate solution. Initially, a single-needle technique was employed to administer Ringer's lactate solution with the patient in a mouth-open position, creating under-pressure to expand the joint cavity. Subsequently, a second needle was inserted, and the joint was flushed with 160 ml of Ringer's lactate using two plastic syringes, each containing 20ml; one served as the inflow needle, and the other as the outflow needle (Fig. 1).

Figure 1 - Lavage performed for the patients in the two groups using Ringer's lactate solution

Afterwards,iliac crest bone marrow aspirate was primarily collected (fig. 2). Using a gauge 13 bone marrow trocar, a puncture was made penetrating the anterior superior iliac spine with a watch wind movement. 20 ml of bone marrow aspirate was obtained in a heparin-treated 50 ml syringe. A minor repositioning of the trocar was done for each 10 ml to access different areas of cancellous bone marrow through the same cortical access hole.

Figure 2 - iliac crest bone marrow aspirate

For the bone marrow concentrate group A : Aspirate was then diluted (1 ml for each 5ml aspirate) with saline or Ringer lactate and then carefully layered very slowly onto lymphocyte separating medium (Pancoll® Paque Plus ,PAN Biotech, Buckinghamshire, UK) in silicon falcon tube and avoiding mixing the two solutions (6ml diluted aspirate on 3ml Pancoll in the tube). (Fig 3).

Figure 3 - The bone marrow aspirate with Ficoll then centrifuged at 2000 rpm for 20 minutes at room temperature using a multi-speed 4000 rpm vertical rotor

Then centrifuged at 2000 rpm for 20 minutes at room temperature using a multi-speed 4000 rpm vertical rotor. The upper layer containing plasma and platelets was then collected using a sterile pipette with the mononuclear cell layer then carefully transferred to a sterile tube and centrifuged at 2000 rpm for 10 min (Fig 4), the supernatant was then removed, and the cell pellet was resuspended in 3 ml of the previously obtained platelet poor plasma, then injected in the superior joint space. (Fig. 5)

Figure 4 - Cell isolate was then washed using balanced salt solution and centrifuged at 2000 rpm for 10 min

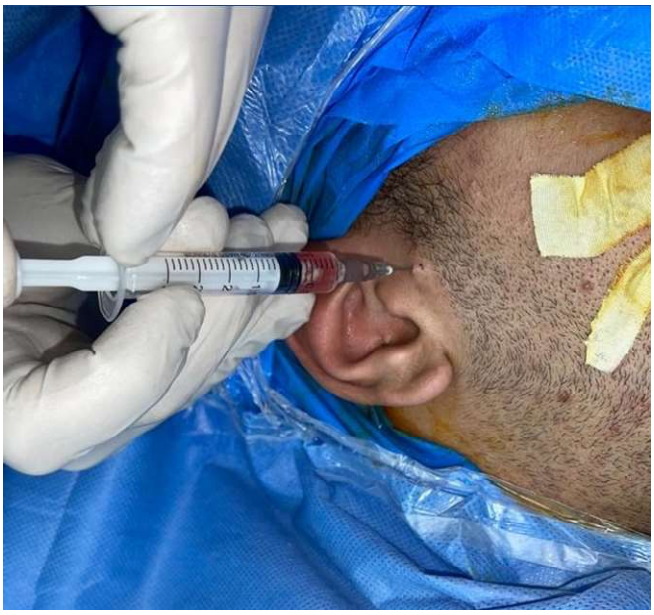

Figure 5- cell pellet was resuspended in 2 ml of the previously obtained platelet poor plasma and injected in the joint space.

For patients in the second group B bone marrow aspirate was injected directly in the upper joint space.

RESULTS

The current study included 10 patients (3 males and 7 females with an average age of 26.9±9.43 years) at the time of the procedure.

The maximum mouth opening of the patients were evaluated along six months follow up as. The Mean ± standard deviation preoperative calculations was (23.7±3.83). While after one month, it was (30.7±3.97). After three months, it was (34.7±2.83). Finally, after six months, it was (39.4±2.46)(Fig. 6). This demonstrates a substantial reduction in pain levels, with a significant decrease observed at each follow-up point.

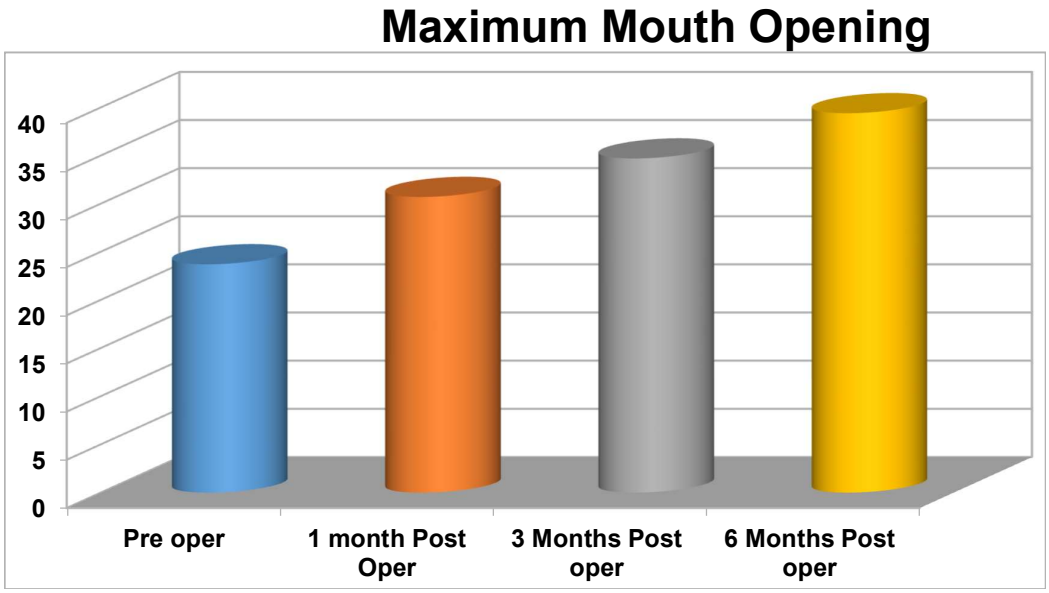

Figure 6- Column chart showing mean maximum mouth opening in different observation times

Patients` pain were evaluated along six months follow up.The Mean ± standard deviation preoperative calculations was (8.3±1.16). While after one month, it was (6.00±0.82). After three months, it was (3.6±0.7). Finally, after six months, it was (1.7±0.95). The data shows a substantial reduction in pain levels, with a significant decrease observed at each follow-up point.

Patients` condylar size were evaluated along six months follow up. The Mean ± standard deviation preoperative calculations was (5.39±1.06). After six months, it was (5.41±1.07).The patients exhibited a slight or no increase in condylar size after six months, although the change was not statistically significant.

Patients` interarticular space were evaluated along six months follow up as preoperative, and after six months. The Mean ± standard deviation preoperative calculations was (3.00±0.69). After six months, it was (3.08±0.76).The interarticular space showed no change after six months.

DISCUSSION

TMJ internal derangement usually improves with nonsurgical approaches. No treatment is necessary for painless clicking. Surgery is recommended for moderate to severe persistent pain or dysfunction when conservative treatments fail. Surgical options include arthrocentesis and arthroscopy, with arthrocentesis being favored for its minimally invasive nature in cases of disc displacement, due to recent technologicaladvancements. [13,14]

The prevalent TMJ disorder is disc displacement without reduction, which can lead to joint degeneration and osteoarthritis if not addressed. Timely diagnosis and intervention are crucial to prevent complications and enhance the quality of life for affected individuals.[2-4]

In recent years, advancements in stem cell therapies and tissue engineering have offered alternative approaches to alleviate symptoms and replace damaged tissue in treating TMJ disorders. Stem cells aid in healing, reduce inflammation, and potentially restore injured tissue. Moreover, MSCs exhibit immunosuppressive properties by regulating various immune cell types, enhancing their anti-inflammatory and tissue-repairing effects.[5-11]

Researches indicates that bone marrow-derived stem cells, cultured and prepared with specific growth media to promote bone and cartilage formation, can develop structures resembling bone and cartilage within joint-like environments. Clinical trials have explored using these approaches, including intra-articular injections to introduce stem cells directly into the synovial fluid, for the treatment of internal derangement in TMJ disorders.[15-18]

There were no significant differences between the two treatment groups in terms of these outcomes. This finding seems to confirm the fact that the presence of MSCs with chondrogenic differentiating capacities is very low in marrow concentrates. However, isolated bone marrow nucleated cells implanted into degenerated human peripheral joints have shown some promise for joint repair. Despite the significant increases in condylar size, it's worth noting that the study did not detect evidence of cartilage regeneration by the 6-month MRI assessment. Discussion Several studies indicate repairing or regenerating cartilage tissue in the joint can be a slow and gradual process that may extend beyond the 6-month timeframe allotted for the follow up. This suggests that while the interventions had positive effects on the joint's structure, complete cartilage regeneration may take longer than the 6- month observation period provided in the study.[19-20]

The results also showed that the TMJ injection in both groups led to a significant improvement in maximum interincisal opening over the 6-month observation period. MIO improved after the procedure, with significantly better scores at all the postoperative follow-up stages. Values for the two groups were significantly different at 6 months. This improvement in MIO aligns with the general goal of TMJ disorder treatments, which aims to restore normal jaw function. The fact that both groups demonstrated significant improvements suggests that these interventions have a positive impact on the joint's functional capacity. This finding also aligns with previous studies and research that shown significant improvement in MIO.[19-22]

Furthermore, the study assessed pain perception as improvement in pain perception is particularly crucial as TMJ disorders can be associated with chronic pain and discomfort in the jaw region, affecting a person's quality of life. Managing pain is a primary goal in the treatment of TMJ disorders, and the study's results indicate that both stem cell and bone marrow injections may be effective in achieving this objective.[19-22]

Age may play a role in treatment outcomes. In this study, it was noticed clinically a slightly more improvement in mouth opening and pain score in younger age patients than older patients in group B. However, in group A the improvement was noticed equally in all age groups. Several previous studies agreed with these outcomes which may be due to the abundance of the MSCs in younger patients. Studies have suggested that the regenerative capacity of stem cells decreases with age, which could affect treatment responses. However, this area of research is still evolving, and more investigations are needed to understand the relationship between age and stem cell therapy efficacy for TMJ disorders.[19-22]

One limitation is the difficulty of separation technique in stem cells concentrate group. The process of isolating and concentrating stem cells from bone marrow aspirate can be technically complex. Also, Bone marrow contains various cell types, and the concentration of stem cells can vary between individuals. Obtaining a sufficient number of viable stem cells from the bone marrow aspirate for therapeutic purposes might be challenging, particularly in some patients with low stem cell yield.

CONCLUSION

In conclusion, injecting the TMJ with bone marrow-derived stem cells is a reliable and technically applicable alternative method for the treatment of Temporomandibular Joint (TMJ) advanced internal derangement. Furthermore, this technique reduced the treatment period to only 6 months, from the beginning of surgery.Injecting the TMJ with bone marrow-derived stem cells is expected to provide anti-inflammatory effects, reduce pain, and enhance joint lubrication. Also, Stem cell therapy has the potential to offer long-term benefits, as the injected cells can continue to promote tissue repair and regeneration over time.

RECOMMENDATIONS

Further researches are needed to validate the findings. More comprehensive studies with a larger sample size and longer follow-up periods would help establish the long-term effectiveness and safety of stem cell therapy for TMJ derangement.

Clinicians should carefully evaluate each patient's medical history, condition severity, and other factors before recommending stem cell therapy. Patient selection is crucial to ensure that stem cell injections are appropriate and safe for the individual's specific case.

CONFLICT OF INTEREST

Authors hereby declare no conflict of interest.

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