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Effectiveness of Bone Marrow Concentrate Injection for Treatment of Temporomandibular Joint Advanced Internal Derangement

Hatem Ismael Mattar*[1], Mohsen Fawzy Aboelhasan [1], Abdel Aziz Baiomy Abdullah [1]

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Aadj@azhar.edu.eg

ABSTRACT

Aim: This study sought to assess the effectiveness of using bone marrow concentrate injections to treat advanced internal derangement of the Temporomandibular Joint (TMJ). **Subjects and methods:** Ten patients diagnosed with advanced internal derangement of the TMJ were included in this retrospective analysis. All ten patients underwent treatment with bone marrow concentrate injections. The post-treatment effectiveness was assessed by monitoring the patients for six months. Additionally, MRI scans were used to evaluate the outcome at the end of the follow-up period. **Results:** The use of bone marrow concentrate injections for treating advanced internal derangement of the TMJ led to significant reductions in pain and notable improvements in maximum interincisal opening after the six-month observation period. **Conclusion:** Injecting bone marrow concentrate into the TMJ proves to be a dependable and technically feasible approach for managing advanced internal derangement of the Temporomandibular Joint.

KEYWORDS

Bone marrow concentrate injection, Temporomandibular Joint, Advanced Internal Derangement

INTRODUCTION

Disruption of the temporomandibular joint's internal alignment is a common problem encountered in temporomandibular disorders. This condition, known as "disc displacement," involves an abnormal positioning of the disc relative to the mandibular condyle and the glenoid fossa. When the disc is displaced from its normal position, it can cause bones to come into direct contact, leading to heightened joint degradation and consequent discomfort.[1]

The most common type of TMJ disorder involves the displacement of the articular disc within the TMJ, followed by progressive degenerative alterations in the joint, which could eventually lead to osteoarthritis.[2–4]

Recent progress in stem cell-based therapies and tissue engineering has introduced fresh possibilities for mitigating symptoms and potentially replacing impaired tissue in TMJ disorder treatment. These stem cells

1. Department of Oral and Maxillofacial Surgery, Faculty of Dental Medicine, Al-Azhar University, Assuit, Egypt.

* Corresponding Author e-mail: dr.hatem.mattar@hotmail.com

play a role in promoting healing, diminishing inflammation, and participating in the repair of damaged tissue. Furthermore, mesenchymal stem cells (MSCs) demonstrate immune-modulating abilities, regulating the activation of natural killer cells, macrophages, and T and B lymphocytes. This imparts beneficial anti-inflammatory and anti-fibrotic properties to MSCs, thereby amplifying their therapeutic effectiveness.[5–11]

Studies have shown that stem cells cultured from bone marrow, and prepared with osteogenic and chondrogenic media, can produce bone-like and cartilage-like formations in laboratory settings. These structures replicate the characteristics of joint-like tissues when implanted into the affected region. Several clinical trials have suggested utilizing these methods to tackle internal derangement by directly injecting stem cells into the synovial fluid within the joint.

To enhance the concentration of collected bone marrow, a centrifugation process employing a separating medium can be employed. This process concentrates the layer containing mononuclear cells, thereby augmenting the quantity of MSCs compared to the initial baseline level. [12]

Hence, the aim of this research was to evaluate the effects of injecting a bone marrow concentrate into the superior space of the temporomandibular joint as a therapeutic approach for advanced internal derangement, particularly focusing on disc displacement without reduction.

MATERIAL AND METHODS

Study Setting:

This investigation was conducted at the Department of Oral and Maxillofacial Surgery, Faculty of Dental Medicine, Al-Azhar University (Assiut), to address Temporomandibular Joint advanced internal derangement in patients seeking treatment.

Study Design:

A sample size of 10 patients was determined for the study. Patients diagnosed with internal derangement without reduction based on clinical and radiographic assessments were included. Ethical approval from the Al-Azhar University (Assiut) ethical committee was obtained, and informed consent, including consent for photography and video recording, was obtained from all patients. Preoperative Magnetic Resonance Imaging (MRI) scans were conducted, and all patients were subjected to the same treatment protocol, using identical materials, techniques, and performed by the same operator.

Inclusion criteria:

- Patients with MRI evidence of disc displacement without reduction in the open mouth position.
- Patients exhibiting clinical signs and symptoms of disc displacement, including limited mouth opening, temporomandibular joint pain during jaw movements, joint sounds (clicking), and anhedonia (inability to enjoy life).
- Patients without systemic conditions that could affect treatment.
- Patients with both anterior and posterior occlusion.

Exclusion criteria:

- Patients with non-inflammatory temporomandibular joint conditions (fracture, joint ankylosis, tumors, etc.).
- Patients with oral or paraoral habits.
- Completely edentulous patients.
- Patients with severe malocclusion or occlusal canting.
- Patients with a history of previous TMJ surgery.

Upon enrollment, all patients underwent the same clinical and radiographic assessments, including:

- Extraoral examination for head and neck, including lymph nodes and facial deformities.
- Pre-treatment pain assessment using a visual analogue scale (VAS).
- Measurement of maximal mouth opening with a digital caliper.
- Evaluation of joint sounds (clicking or crepitation) preoperatively with a stethoscope.
- Preoperative cone-beam computed tomography (CBCT) for osseous disorder exclusion, and MRI to confirm diagnosis and document disc position before arthrocentesis.

Surgical procedures

The surgeries were conducted under general anesthesia by a single experienced surgeon. The patient was positioned ideally either in a supine or reclined position, with the head turned away from the injection site. Lavage was carried out using Ringer's lactate solution. Initially, a single-needle technique was utilized to administer Ringer's lactate solution while the patient's mouth was open, creating negative pressure to expand the joint cavity. Subsequently, a second needle was inserted, and the joint was flushed with 160ml of Ringer's lactate using two plastic syringes, each containing 20ml; one syringe served as the inflow needle, and the other as the outflow needle (Fig. 1).

Subsequently, bone marrow aspirate from the iliac crest was primarily collected (see fig. 2). A gauge 13 bone marrow trocar was used to make a puncture, penetrating the anterior superior iliac spine with a watch wind movement. Twenty milliliters of bone marrow aspirate was collected in a 50 ml syringe treated with heparin. Minor repositioning of the trocar was performed after every 10 ml to access various regions of cancellous bone marrow through the same cortical access hole.

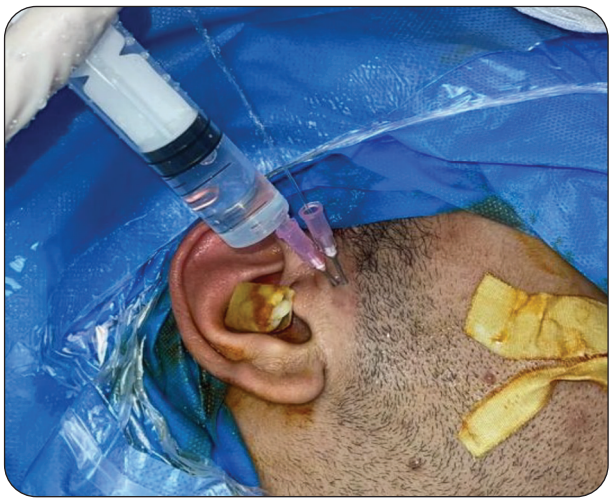

Fig. (1) Lavage performed for the patients using Ringer's lactate solution

Fig. (2) Iliac crest bone marrow aspirate

The aspirate was subsequently diluted, with 1ml of diluent for every 5ml of aspirate, using either saline or Ringer lactate. This mixture was then carefully layered very slowly onto lymphocyte separating medium (Pancoll® Paque Plus, PAN Biotech, Buckinghamshire, UK) in a silicon Falcon tube, ensuring that the two solutions were not mixed. Specifically, 6 ml of diluted aspirate was layered onto 3 ml of Pancoll in the tube (Fig 3).

Next, the mixture was centrifuged at 2000rpm for 20 minutes at room temperature using a multi-speed

4000rpm vertical rotor. The upper layer, consisting of plasma and platelets, was then collected using a sterile pipette. Subsequently, the mononuclear cell layer was carefully transferred to a sterile tube and centrifuged at 2000 rpm for 10 minutes (Fig. 4). The supernatant was then removed, and the cell pellet was resuspended in 3 ml of the previously obtained platelet-poor plasma before being injected into the superior joint space (Fig. 5).

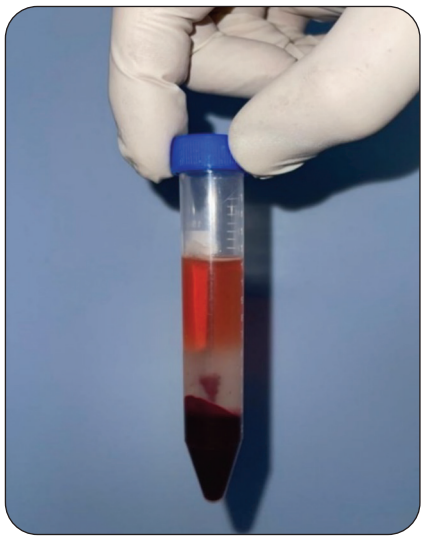

Fig. (3) The bone marrow aspirate with Ficoll then centrifuged at 2000 rpm for 20 minutes at room temperature using a multi-speed 4000 rpm vertical rotor

Fig. (4) Cell isolate was then washed using balanced salt solution and centrifuged at 2000 rpm for 10 min

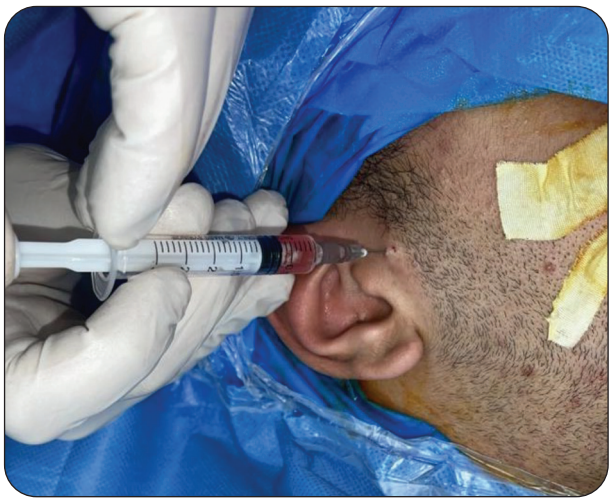

Fig. (5) Cell pellet was resuspended in 2 ml of the previously obtained platelet poor plasma and injected in the joint space.

RESULTS

The study enrolled a total of 10 patients, comprising 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 was assessed over a six-month follow-up period. The preoperative mean ± standard deviation measurement was 23.7±3.83. After one month, it increased to 30.7±3.97. At three months, it further improved to 34.7±2.83, and finally, after six months, it reached 39.4±2.46 (see Fig. 6). These findings indicate a notable decrease in pain levels, with a significant improvement observed at each follow-up interval.

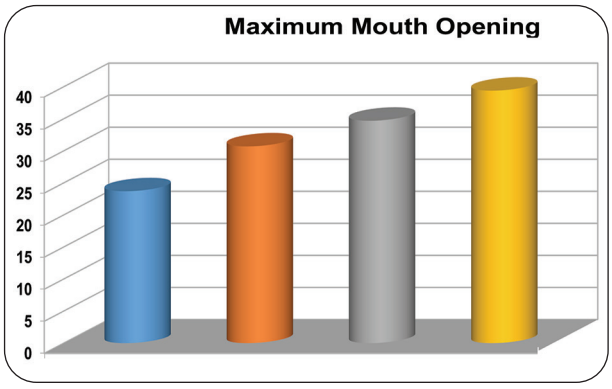

Fig. (6) Column chart showing mean maximum mouth opening in different observation times

Patients' pain levels were assessed over a six-month follow-up period. The preoperative mean ± standard deviation was 8.3±1.16. After one month, it decreased to 6.00±0.82. At three months, it further decreased to 3.6±0.7, and finally, after six months, it reached 1.7±0.95. These results indicate a significant reduction in pain levels, with a noticeable decrease observed at each follow-up interval.

The size of patients' condyles was evaluated over a six-month follow-up period. The preoperative mean ± standard deviation was 5.39±1.06. After six months, it was 5.41±1.07. Patients exhibited a slight or no increase in condylar size after six months, although this change was not statistically significant.

The interarticular space of patients was assessed over a six-month follow-up period, comparing preoperative measurements to those taken after six months. The preoperative mean ± standard deviation was 3.00±0.69. After six months, it was 3.08±0.76. The interarticular space showed no change after six months.

DISCUSSION

Nonsurgical methods are typically effective in improving TMJ internal derangement. Painless clicking usually doesn't require treatment. However, for moderate to severe persistent pain or dysfunction that doesn't respond to conservative treatments, surgery is recommended. Surgical options include arthrocentesis and arthroscopy. Arthrocentesis is preferred for cases of disc displacement due to its minimally invasive nature, especially with recent technological advancements.[13,14]

The most common TMJ disorder is disc displacement without reduction, which, if left untreated, can result in joint degeneration and osteoarthritis. Prompt diagnosis and intervention are essential to prevent complications and improve the quality of life for individuals affected by this condition.[2-4]

Recent advancements in stem cell therapies and tissue engineering have provided new avenues for addressing TMJ disorders. Stem cells play a crucial role in promoting healing, reducing inflammation, and potentially repairing damaged tissue. Additionally, mesenchymal stem cells (MSCs) have been found to possess immunosuppressive properties, modulating different types of immune cells and thereby enhancing their anti-inflammatory and tissue-repairing capabilities.[5-11]

Studies have shown that bone marrow-derived stem cells, when cultured and prepared with specialized growth media to stimulate bone and cartilage formation, can generate structures resembling bone and cartilage within environments similar to joints. Clinical trials have investigated the application of these methods, including intra-articular injections to deliver stem cells directly into the synovial fluid, for treating internal derangement in TMJ disorders.[15-18]

The research findings suggest that the presence of mesenchymal stem cells (MSCs) with chondrogenic differentiation capabilities is relatively low in marrow concentrates. However, isolated bone marrow nucleated cells implanted into degenerated human peripheral joints have shown promise for joint repair. Despite significant increases in condylar size, it's important to note that the study did not observe evidence of cartilage regeneration during the 6-month MRI assessment. Several studies suggest that repairing or regenerating cartilage tissue in the joint can be a gradual process that may extend beyond the 6-month follow-up period. This indicates that while the interventions had positive effects on the joint's structure, complete cartilage regeneration may require a longer timeframe than the 6-month observation period provided in the study.[19-20]

The study results revealed a notable enhancement in maximum interincisal opening (MIO) throughout the 6-month observation period following Bone Marrow Concentrate injection. MIO

showed consistent improvement post-procedure, with significantly better scores recorded at all subsequent follow-up stages. Notably, there was a significant disparity in values between the two groups at the 6-month mark. This improvement in MIO is consistent with the overarching objective of TMJ disorder treatments, which seek to restore normal jaw function. The significant improvements observed following Bone Marrow Concentrate Injection suggest a favorable impact on the joint's functional capacity. This finding is also consistent with prior research indicating substantial enhancement in MIO post-treatment. [19-22]

Moreover, the study evaluated pain perception, considering that improvement in pain perception is especially vital given the association of TMJ disorders with chronic pain and discomfort in the jaw region, which significantly impacts an individual's quality of life. Effectively managing pain is a primary objective in treating TMJ disorders, and the study's findings suggest that bone marrow concentrate injections could be efficacious in accomplishing this goal. [19-22]

Age may indeed influence treatment outcomes, but in this study, clinically equal improvements in mouth opening and pain scores were observed across all age groups. While previous studies have indicated that the regenerative potential of stem cells may decline with age, potentially impacting treatment responses, this field of research is still developing. Further investigations are necessary to elucidate the connection between age and the efficacy of bone marrow concentrate injection for TMJ disorders. [19-22]

One limitation of the study is the complexity of the separation technique. The process of isolating and concentrating stem cells from bone marrow aspirate can be technically challenging. Additionally, bone marrow contains diverse cell types, and the concentration of stem cells may vary among individuals. Obtaining an adequate number of viable stem cells from the bone marrow aspirate for therapeutic purposes might be difficult, especially in patients with low stem cell yield.

CONCLUSION

In conclusion, injecting bone marrow concentrate into the TMJ proves to be a dependable and technically feasible alternative method for treating advanced internal derangement of the Temporomandibular Joint (TMJ). Moreover, this technique shortens the treatment duration to just 6 months from the initiation of surgery. Injecting bone marrow concentrate into the TMJ is anticipated to deliver anti-inflammatory effects, alleviate pain, and improve joint lubrication. Additionally, bone marrow holds the potential to provide long-term advantages, as the injected cells can persist in promoting tissue repair and regeneration over time.

RECOMMENDATIONS

Further research is warranted to validate the findings of this study. More extensive studies with larger sample sizes and longer follow-up periods would contribute to establishing the long-term effectiveness and safety of Bone Marrow Concentrate injection for TMJ derangement.

Clinicians should exercise caution and carefully assess each patient's medical history, severity of condition, and other relevant factors before considering stem cell therapy. Patient selection is paramount to ensure that stem cell injections are suitable and safe for the individual's particular circumstances.

Conflict of interest

Authors hereby declare no conflict of interest.

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REFERENCES

1. Guarda-Nardini L, Piccotti F, Mogno G, Favero L, Manfredini D. Age-Related Differences in Temporomandibular Disorder Diagnoses. 2012.
2. Rajapakse S, Ahmed N, Sidebottom AJ. Current thinking about the management of dysfunction of the temporomandibular joint: a review. British Journal of Oral and Maxillofacial Surgery. 2017;55:351–6.
3. Chen D, Shen J, Zhao W, Wang T, Han L, Hamilton JL, et al. Osteoarthritis: toward a comprehensive understanding of pathological mechanism. Bone Res. 2017 Jan 17;5.
4. Hylander W. Functional Anatomy of the TMJ. 2006.
5. Uccelli A, Pistoia V, Moretta L. Mesenchymal stem cells: a new strategy for immunosuppression? Trends in Immunology. 2007;28:219–26.
6. Wang Y, Chen X, Cao W, Shi Y. Plasticity of mesenchymal stem cells in immunomodulation: pathological and therapeutic implications. Nat Immunol. 2014 Oct 25;15(11):1009–16.
7. Wei CC, Lin AB, Hung SC. Mesenchymal stem cells in regenerative medicine for musculoskeletal diseases: bench, bedside, and industry. Cell Transplant. 2014;23(4–5):505–12.
8. Fong ELS, Chan CK, Goodman SB. STEM CELL HOMING IN MUSCULOSKELETAL INJURY. Biomaterials. 2011 Jan;32(2):395.
9. Acharya C, Adesida A, Zajac P, Mumme M, Riesle J, Martin I, et al. Enhanced chondrocyte proliferation and mesenchymal stromal cells chondrogenesis in coculture pellets mediate improved cartilage formation. J Cell Physiol. 2012 Jan;227(1):88–97.
10. Pers YM, Ruiz M, Noël D, Jorgensen C. Mesenchymal stem cells for the management of inflammation in osteoarthritis: state of the art and perspectives. Osteoarthritis Cartilage. 2015 Nov 1;23(11):2027–35.
11. Oliver K, Awan T, Bayes M. Single- Versus Multiple-Site Harvesting Techniques for Bone Marrow Concentrate: Evaluation of Aspirate Quality and Pain. Orthop J Sports Med. 2017 Jan 1;5(8).
12. Hernigou P, Mathieu G, Poignard A, Manicom O, Beaujean F, Rouard H. Percutaneous autologous bone-marrow grafting for nonunions. Surgical technique. J Bone Joint Surg Am. 2006;88 Suppl 1 Pt 2:322–7.
13. Young AL. Internal derangements of the temporomandibular joint: A review of the anatomy, diagnosis, and management. The Journal of the Indian Prosthodontic Society.2015 Jan 1;15(1):2.
14. Ahmad M, Schiffman EL. Temporomandibular Joint Disorders and Orofacial Pain. Dent Clin North Am. 2016 Jan 1;60(1):105.
15. Brady MA, Sivananthan S, Mudera V, Liu Q, Wiltfang J, Warnke PH. The primordium of a biological joint replacement: Coupling of two stem cell pathways in biphasic ultrarapid compressed gel niches. Journal of Cranio-Maxillofacial Surgery. 2011 Jul;39(5):380–6.
16. Barry F, Murphy M. Mesenchymal stem cells in joint disease and repair. Nature Reviews Rheumatology. 2013;9:584-94.
17. Chen K, Man C, Zhang B, Hu J, Zhu SS. Effect of in vitro chondrogenic differentiation of autologous mesenchymal stem cells on cartilage and subchondral cancellous bone repair in osteoarthritis of temporomandibular joint. Int J Oral Maxillofac Surg. 2013 Feb;42(2):240–8
18. Abdelazeem AF, Hassib NF, Elmasry M, Mattar HI, Ahmed NE. Regenerative Approach for Repairing Large Odontogenic Cystic Defects: Three Case Reports and a Review of Literature. J Stem Cells. 2021;16(2/3):49-58.
19. Al-Ahmady HH, Abd Elazeem AF, Bellah Ahmed NE moataz, et al. Combining autologous bone marrow mononuclear cells seeded on collagen sponge with Nano Hydroxyapatite, and platelet-rich fibrin: Reporting a novel strategy for alveolar cleft bone regeneration. Journal of Cranio-Maxillofacial Surgery. 2018 Sep 1;46(9): 1593–600.
20. Chahla J, Mannava S, Cinque ME, et al. Bone Marrow Aspirate Concentrate Harvesting and Processing Technique. Arthrosc Tech . 2017 Apr 1;6(2):e441.
21. De Riu G, Vaira LA, Carta E, et al. Bone marrow nucleated cell concentrate autograft in temporomandibular joint degenerative disorders: 1-year results of a randomized clinical trial. J Craniomaxillofac Surg. 2019 Nov 1;47(11):1728–38.
22. Hauser RA, Orlofsky A. Regenerative injection therapy with whole bone marrow aspirate for degenerative joint disease: A case series. Clin Med Insights Arthritis Musculoskelet Disord. 2013 Sep 4;6.

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فعالية الحقن المركزة بنخاع العظم في علاج الاختلال الداخلي المتقدم للمفصل الصدغي الفكي

حاتم اسماعيل مطر* ، محسن فوزى ابو الحسن، عبدالعزيز بيومى عبدالله

1. قسم جراحة الفم والوجه والفكين، كلية طب الأسنان، جامعة الازهربنين، أسيوط، مصر

* البريد الإلكتروني: DR.HATEM.MATTAR@HOTMAIL.COM

الملخص :

الهدف: سعت هذه الدراسة إلى تقييم مدى فعالية استخدام الحقن المركزة لنخاع العظم لعلاج الاضطراب الداخلي المتقدم للمفصل الصدغي الفكي (TMJ).

المواد والاساليب : تم تضمين عشرة مرضى تم تشخيص إصابتهم باضطراب داخلي متقدم في المفصل الفكي الصدغي في هذا التحليل بأثر رجعي. خضع جميع المرضى العشرة للعلاج بحقن مركزة لنخاع العظم. تم تقييم فعالية ما بعد العلاج من خلال مراقبة المرضى لمدة ستة أشهر. بالإضافة إلى ذلك، تم استخدام فحوصات التصوير بالرنين المغناطيسي لتقييم النتيجة في نهاية فترة المتابعة.

النتائج: أدى استخدام حقن مركز نخاع العظم لعلاج الاضطراب الداخلي المتقدم في المفصل الفكي الصدغي إلى انخفاض كبير في الألم وتحسينات ملحوظة في الحد الأقصى للفتحة بين التداخلات بعد فترة المراقبة البالغة ستة أشهر

الخلاصه : أثبت حقن مركز نخاع العظم في المفصل الفكي الصدغي أنه فعال نهج يمكن الاعتماد عليه ويمكن تقنيًا لإدارة الخلل الداخلي المتقدم في المفصل الصدغي الفكي.

الكلمات المفتاحية : لحقن المركز لنخاع العظم، المفصل الصدغي الفكي، الاختلال الداخلي المتقدم