

## **Rationale of PRGF intra-articular injection in temporomandibular disorders management**

**Marwa Safwat, MSc, OMFS<sup>1</sup>, Khaled Barakat, PhD, OMFS<sup>2</sup>**

1: Assistant lecturer of Oral and Maxillofacial Surgery Department, Faculty of Dentistry, Minia University, E-mail: marwa.m.safwat@mu.edu.eg

2: Professor and head of Oral and Maxillofacial Surgery Department, Faculty of Dentistry, Minia University, E-mail: send2kbarakat@yahoo.com

Corresponding author: **Marwa Safwat**, E-mail: marwa.m.safwat@mu.edu.eg

### **Abstract**

Management of temporomandibular disorder (TMD) still attains researchers' interest. Recently, platelets rich plasma (PRP) products especially plasma rich in growth factors (PRGF), has gained the focus of researchers in musculoskeletal field for being safe autologous substance with promising outcomes. PRGF is a serum that devoid the white blood cells, RBCs, however, the platelets were concentrated by 2.84-fold. The regenerative effect of the PRGF and its known therapeutic rule on injured tissues renders it research worthy topic. At this article we will review the rationale of PRGF intra-articular injection in TMD patients.

**Keywords:** Temporomandibular joint, plasma rich in growth factors, internal derangement, Osteoarthritis.

### **Introduction**

Temporomandibular disorder (TMD) is a collective term encompasses multiple disorders affecting the temporomandibular joint (TMJ). Among those conditions internal derangements (ID) and osteoarthritis are the most prevalent conditions affecting the joint. ID of the TMJ has been defined as an abnormal functional relationship of the disc with the condyle, fossa, and articular eminence. ID includes all types of intracapsular interferences that impede smooth functional joint movements as disc displacement conditions, disc adhesions, disc dislocations, subluxations, and dislocations of the disc condyle complex.[1-3] Many factors were attributed to cause disc derangement conditions, including joint overloading, micro or macrotrauma to the joint, joint hypermobility, and joint inflammatory conditions or infections.[4] On the other hand, OA of the TMJ is a degenerative condition of the joint arises due to inflammation or joint overloading and is characterized by alteration of the joint components.[5]

Clinical diagnosis consists of detailed history and physical examination. The typical signs and symptoms of TMD are pain in the preauricular region, headache behind and around the eyes, and pain radiating from the joint to the temple, ears, side of neck and upper shoulder. The pain is typically aggravated by wide opening, chewing or other joint activities, such as clenching and bruxism. Palpation of preauricular area usually reveals clicking, popping or crepitus sounds because of disc interference. In cisal opening, protrusion, and contralateral movements distance are decreased and may interfere with mastication and normal functions. The joint, muscles of mastication, sternocleidomastoid muscle and trapezius muscle are often tender to palpation.[6, 7]

Keeping in mind that the aim of TMJ ID& O Amanagement is to reduce pain and discomfort and improve jaw mobility, the management starts from non-surgical techniques passing with lysis and lavage and injecting various drugs and ending with arthroscopic surgical techniques and open arthrotomy. Usually, surgical techniques aim to correct disc position and are used when non-surgical and minimally invasive techniques failed to alleviate the symptoms.[3, 8-10]

Lysis and lavage techniques are minimally invasive effective modality for ID& OA management. Lysis and lavage can be accomplished either under arthroscopic control or blindly using TMJ arthrocentesis. Arthrocentesis comprises lavage of the superior compartment of the TMJ with Ringer's lactate solution after placing two needles into the upper joint compartment.[11] Arthrocentesis is an easy, minimally invasive, and highly efficient procedure to decrease joint pain and increase the range of mouth opening in cases suffering ID and particularly for cases of closed lock.[3]At the end of arthrocentesis, many substances can be injected into the TMJ superior compartment to promote enhancement of the condition.[3] Among those substances, the injection of Platelet Rich Plasma (PRP) products, especially the plasma rich in growth factors (PRGF), has greatly attracted the interest of the researchers in the musculoskeletal field.

PRP is a product of autologous blood which is obtained by sequestering and concentrating the blood by gradient density centrifugation.PRP contains three- to eight-fold the concentration of platelets. The concentrated platelets contain many growth factors and bioactive proteins released by activated platelets, which seem able to help the regeneration of tissues and promote the natural healing process.[12]In addition, PRP application has an inhibitory effect on specific pro-inflammatory cytokines. This dual action of promoting regeneration and decreasing tissue breakdown may permit the acceleration of the tissue healing process with subsequent faster recovery.[13]

PRGF, one of the PRP products, is characterized by the absence of leukocytes and the presence of a specific dose of platelets and growth factors.[3]PRGF provides platelet-derived growth factors and endogenous fibrin scaffolds for regenerative purposes. Many of the autologous growth factors and proteins released from the fibrin scaffold of PRGF may play a pivotal role in the repair or regeneration of the damaged cartilage.[14]In the past few years, the injection of PRGF has been extended to the treatment of TMJ Id following promising results of managing knee osteoarthritis.[12, 14] ID usually involves structural alteration of cartilage and sub chondral bone in response to different mediators that are responsible for altering the content of joint tissue. Regarding TMD, many researchers have reported the outcomes of injecting PRGF in TMJ patients suffering internal derangement and osteoarthritis. They investigated the outcomes of injecting PRGF alone, compared to other substances like hyaluronic acid, compared to arthrocentesis, or as a complement following arthroscopy.[3, 5, 12, 13, 15-18] Generally, the results were encouraging especially regarding improvement of joint pain and jaw movements.

The pain relieving effect of PRGF may be attributed to the release of proteases that bind to nociceptive receptors, as well as to an increase of specific cannabinoid receptors. Platelets participate in healing processes by delivering various types of growth factors, arachidonic acid metabolites, extracellular matrix proteins, nucleotides, and other active molecules, to the injected joint. All these factors in synergy with local cells like fibroblasts, osteoblasts, chondrocytes, and mesenchymal stem cells, might augment tissue healing and enhance the regeneration of bone and cartilage in the TMJ .[3]The regenerative effect of PRGF on the joint cartilages may be

associated with the regulation of certain pathways that act on interleukin-1, inhibiting its inflammatory activity, as well as with the release of numerous cytokines related to the complex processes of the combination and secretion of molecules that induce a positive response in the repair of damage to the joint cartilage.[7, 13, 19, 20]

### **Conclusion**

In conclusion, the clinical results of injecting PRGF in TM joints with ID& OA are encouraging to proceed to more randomized controlled trials to obtain sound evidence considering its role in managing such conditions.

### **References**

1. Wilkes, C.H., *Internal derangements of the temporomandibular joint. Pathological variations.* Arch Otolaryngol Head Neck Surg, 1989. **115**(4): p. 469-77.
2. Holmlund, A.B. and S. Axelsson, *Temporomandibular arthropathy: correlation between clinical signs and symptoms and arthroscopic findings.* Int J Oral Maxillofac Surg, 1996. **25**(3): p. 178-81.
3. Fernandez Sanroman, J., et al., *Does injection of plasma rich in growth factors after temporomandibular joint arthroscopy improve outcomes in patients with Wilkes stage IV internal derangement? A randomized prospective clinical study.* Int J Oral Maxillofac Surg, 2016. **45**(7): p. 828-35.
4. Ogren, M., et al., *Hypermobility and trauma as etiologic factors in patients with disc derangements of the temporomandibular joint.* Int J Oral Maxillofac Surg, 2012. **41**(9): p. 1046-50.
5. Giacomello, M., et al., *PRGF(R) endoret injections for temporomandibular joint osteoarthritis treatment: a one-year follow-up.* J Biol Regul Homeost Agents, 2019. **33**(6 Suppl. 2): p. 215-222 DENTAL SUPPLEMENT.
6. Gauer, R.L. and M.J. Semidey, *Diagnosis and treatment of temporomandibular disorders.* Am Fam Physician, 2015. **91**(6): p. 378-86.
7. Fernandez-Ferro, M., et al., *Comparison of intra-articular injection of plasma rich in growth factors versus hyaluronic acid following arthroscopy in the treatment of temporomandibular dysfunction: A randomised prospective study.* J Craniomaxillofac Surg, 2017. **45**(4): p. 449-454.
8. McCain, J.P. and R.H. Hossameldin, *Advanced arthroscopy of the temporomandibular joint.* Atlas Oral Maxillofac Surg Clin North Am, 2011. **19**(2): p. 145-67.
9. Chen, M.J., et al., *Use of Coblation in arthroscopic surgery of the temporomandibular joint.* J Oral Maxillofac Surg, 2010. **68**(9): p. 2085-91.
10. Zhang, S.Y., et al., *New arthroscopic disc repositioning and suturing technique for treating internal derangement of the temporomandibular joint: part II--magnetic resonance imaging evaluation.* J Oral Maxillofac Surg, 2010. **68**(8): p. 1813-7.
11. Nitzan, D.W., *Arthrocentesis-incentives for using this minimally invasive approach for temporomandibular disorders.* Oral Maxillofac Surg Clin North Am, 2006. **18**(3): p. 311-28.
12. Comert Kilic, S. and M. Gungormus, *Is arthrocentesis plus platelet-rich plasma superior to arthrocentesis plus hyaluronic acid for the treatment of temporomandibular joint*

- osteoarthritis: a randomized clinical trial. Int J Oral Maxillofac Surg, 2016. 45(12): p. 1538-1544.*
13. Hanci, M., et al., *Intra-articular platelet-rich plasma injection for the treatment of temporomandibular disorders and a comparison with arthrocentesis. J Craniomaxillofac Surg, 2015. 43(1): p. 162-6.*
  14. Vaquerizo, V., et al., *Comparison of intra-articular injections of plasma rich in growth factors (PRGF-Endoret) versus Durolane hyaluronic acid in the treatment of patients with symptomatic osteoarthritis: a randomized controlled trial. Arthroscopy, 2013. 29(10): p. 1635-43.*
  15. Pihut, M., et al., *Evaluation of pain regression in patients with temporomandibular dysfunction treated by intra-articular platelet-rich plasma injections: a preliminary report. Biomed Res Int, 2014. 2014: p. 132369.*
  16. Hegab, A.F., et al., *Platelet-Rich Plasma Injection as an Effective Treatment for Temporomandibular Joint Osteoarthritis. J Oral Maxillofac Surg, 2015. 73(9): p. 1706-13.*
  17. Comert Kilic, S., M. Gungormus, and M.A. Sumbullu, *Is Arthrocentesis Plus Platelet-Rich Plasma Superior to Arthrocentesis Alone in the Treatment of Temporomandibular Joint Osteoarthritis? A Randomized Clinical Trial. J Oral Maxillofac Surg, 2015. 73(8): p. 1473-83.*
  18. Haigler, M.C., et al., *Use of platelet-rich plasma, platelet-rich growth factor with arthrocentesis or arthroscopy to treat temporomandibular joint osteoarthritis: Systematic review with meta-analyses. J Am Dent Assoc, 2018. 149(11): p. 940-952 e2.*
  19. Anitua, E., et al., *Platelet-released growth factors enhance the secretion of hyaluronic acid and induce hepatocyte growth factor production by synovial fibroblasts from arthritic patients. Rheumatology (Oxford), 2007. 46(12): p. 1769-72.*
  20. Anitua, E., et al., *Plasma rich in growth factors (PRGF-Endoret) stimulates tendon and synovial fibroblasts migration and improves the biological properties of hyaluronic acid. Knee Surg Sports Traumatol Arthrosc, 2012. 20(9): p. 1657-65.*