Volume 04, Issue 04 (July-August 2021), PP 57-64 **www.ijmsdr.org**
ISSN: 2581-902X

International Journal of Medical Science and Dental Research

Intra-Articular Injection of Platelet-Rich Plasma (Prp) In The Treatment of Temporomandibular Joint osteoarthritis

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Summaray: Temporomandibular joint Osteoarthritis is a chronic painful degenerative pathology.First-line therapies such as mechanical rehabilitation and oral medication have failed. In view of this, researchers have studied new conservative treatments to delay recourse to arthroplastic surgery.
If intra-articular injection of the platelet-Rich Plasma (PRP) in arthritic pathology has shown satisfactory results in humans, can this treatment, which has been studied mainly in gonarthrosis, be applied to the management of temporomandibular joint osteoarthritis? What would be the interest and place of intra-articular injection of PRP among the various therapies for this pathology?

Keywords: Temporomandibular joint- osteoarthritis - intra-articular injection – platelet-Rich Plasma (PRP)

I. Introduction

The temporomandibular joint (TMJ), which is used daily for mastication, swallowing and phonation, can suffer from osteoarthritis like other synovial joints. The management of temporomandibular joint osteoarthritis(TMJO) follows a therapeutic gradient. However, in view of the numerous first-line therapeutic failures, another conservative technique has developed strongly: intra-articular injection of platelet-rich plasma (PRP).

Indeed, following the studies demonstrating the benefits of these injections in aesthetic medicine, implantology and gonarthrosis, we wondered what the place of intra-articular injection of PRP could be in the treatment of TMJO?

II. Therapeutic modalities for treatment of temporomandibular joint osteoarthritis:

Pain management is the primary therapeutic goal, but the intensity and time course of the osteoarthritis must also be assessed.

The management of osteoarthritis follows a therapeutic gradient and can be classified in the following diagram: (1)

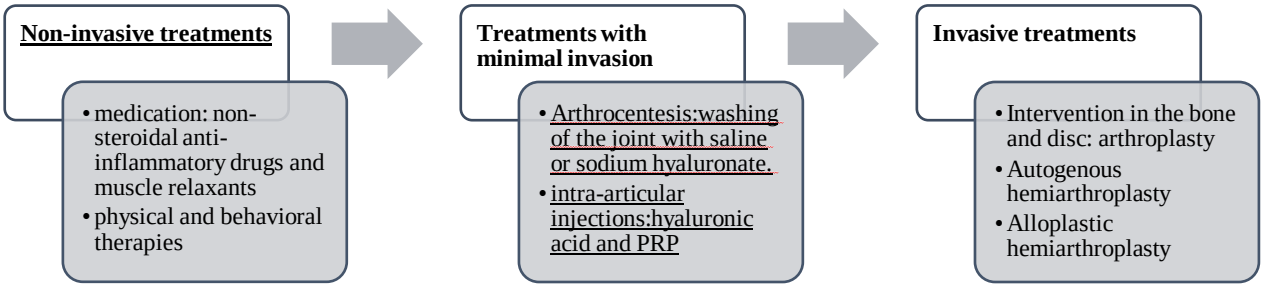


Diagram 1: Therapeutic modalities for temporomandibular joint osteoarthritis

Platelet-Rich Plasma Injection:

Platelet-Rich Plasma is a volume of autologous plasma with a platelet concentration above the reference level in a human. The reference concentration in blood is between 150,000 platelets/µL and 350,000 platelets/µL. (2)

The ideal PRP composition should contain a minimal amount of red and white blood cells and a platelet concentration of approximately 1,000,000/µL. Through its numerous growth factors, PRP stimulates the differentiation as well as the growth of numerous cells (chondrocytes, fibroblasts, osteoblasts), controls inflammation and improves cartilage and bone regeneration. (3)

***Therapeutic effects**

In an osteoarthritic environment, PRP has a dual action: (Diagram 2)

* Stimulation of cell proliferation, secretion of hyaluronic acid by synoviocytes, secretion of collagen, and cartilage and bone regeneration;

* the reduction of the secretion of inflammatory mediators and consequently the reduction of pain and the improvement of healing. (Anti-inflammatory potential) (4, 5)

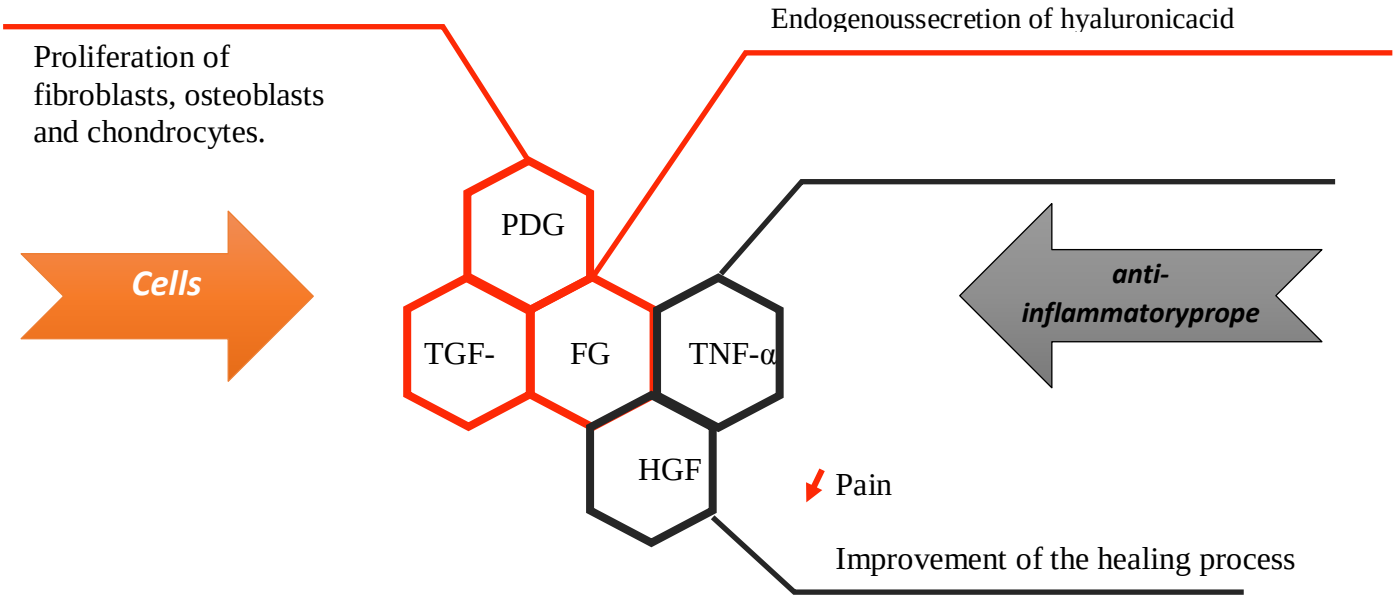


Figure 2: Therapeutic effects of PRP in osteoarthritis according to the authors (4, 5)

However, it has been pointed out that this therapeutic effect of PRP may be modified in the presence of leukocytes. These cells will be responsible for the reactivation of inflammatory processes, which implies rigor in the protocols (6).

***Protocol:**

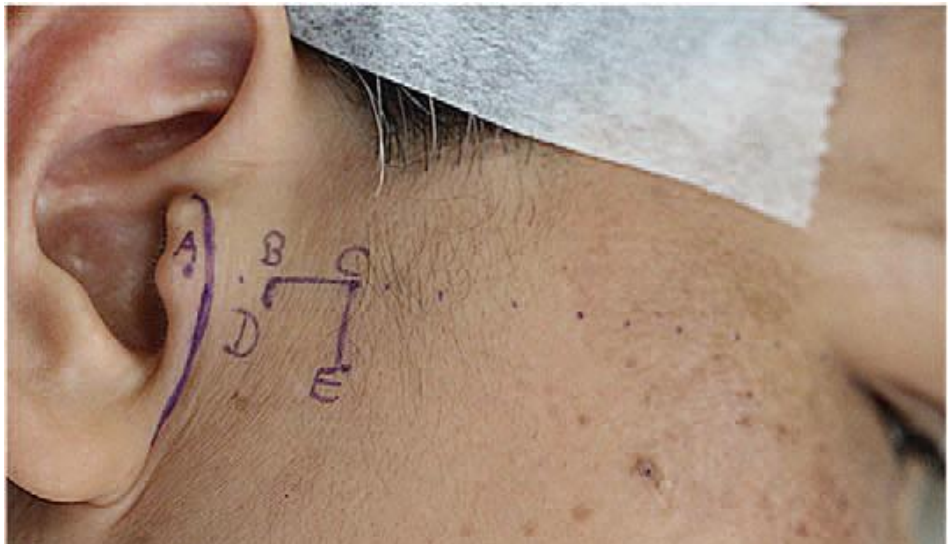
PRP is obtained using gravitational separation techniques of blood elements allowing the collection of growth factors contained in platelets.

The protocol by simple centrifugation, consists of a sampling under anticoagulant and then centrifugation, the PRP settles on the surface of the tube. (7). A new protocol has recently been described: blood is collected without anticoagulant, at a temperature of 4°C and centrifuged twice. The milliliter of surface plasma is collected and incubated at 37 degrees to activate platelets. (8)

According to a systematic review on the therapeutic effect of PRP in TMJO, studies have shown no superiority of one protocol over the other. However, prior to injection, whatever the recommended protocol, it seems advisable to mix the PRP with an activator (thrombin + calcium chloride), in order to allow massive activation of the platelets. (4)

Nevertheless, for the clinical protocol of PRP injection, no consensus has been established: one study proposed a simplified technique (figure 2) which consists in making a vertical line of skin fold of the tragus, a point A in the middle between this line and the tip of the tragus (A), then a horizontal line connecting this point A to the homolateral canthus. On this line two other points are marked point B and C, the distance AB is equal to the distance CB, which is 1cm. On a perpendicular line passing from point B, another point D is determined, this one is distant from point B by 2mm, finally a point E distant from point C by 1cm. The injection of PRP is done at point D. (9)

Concerning the volume of PRP to be injected, in the case of TMJ osteoarthritis, the authors recommend a volume of 2ml (in one to three injections) (6, 4, 9)



SCHEMA : Clinical protocol for PRP injection (9)

III. Current data on the therapeutic efficacy of PRP in TMJ osteoarthritis:

The benefits of PRP on gonarthrosis have prompted researchers to study this procedure on the TMJ. However, the number of studies currently performed is significantly lower because several difficulties are added for the TMJ: its size, its anatomical structure, with a double cavity that make its access very meticulous as well as the proximity of anatomical elements such as the facial nerve.

In September 2018, Chung et al (6) published a meta-analysis of five randomized studies and concluded that PRP is more effective than placebo in relieving pain but not on improving long-term mouth opening. In addition, subgroup analysis showed that PRP significantly reduced pain compared to hyaluronic acid, saline or no injection. Thus, four studies report significant benefits of PRP injection after arthrocentesis or arthroscopy. (6)

In 2015, Cömert et al compared the efficacy of arthrocentesis + PRP to that of arthrocentesis alone and concluded that arthrocentesis+PRP is more effective. Pain decreased in both study groups, but they noted significant improvement in masticatory abilities and cartilage regeneration for the PRP group. Their CBCT evaluations showed bone remodeling in 87.5% of the joints that received arthrocentesis+PRP versus 46.5% for arthrocentesis alone. (10)

In 2018, Lin et al (11) supplemented these results comparing arthrocentesis+PRP and PRP injection alone. The two methods showed no significant difference. Arthrocentesis is the washing of the joint in order to eliminate inflammatory markers, but we have seen that PRP acts directly on the inflammatory process, calling into question the need for prior arthrocentesis (11). (11) It would therefore be interesting to carry out a study distinguishing between PRP injection and arthrocentesis in order to compare them and to analyze whether PRP injection alone would be sufficient.

As for hyaluronic acid, in 2020 Al-Moraissi and his colleagues, in a meta-analysis, showed that the latter acts as a lubricator, whereas PRP is a tissue healer. (12)

An important criticism of the efficacy of PRP is that it is closely linked to its composition. The benefits will depend on the concentration of platelets, leukocytes, growth factors and hematopoietic stem cells. A study conducted by Riboh et al in 2016 compared the benefits of PRP by varying its leukocyte concentration in gonarthrosis. They conclude that leukocyte-poor PRP would be more effective than leukocyte-rich PRP. The

two groups studied showed similar local reactions allowing them to state that the adverse effects of PRP do not seem to be related to the leukocyte concentration. (13)

Article	Objective	Material and method	Comparison	Resultsand discussion
Effectiveness of Platelet-Rich Plasma Injection in Patients with Temporomandibular Joint Osteoarthritis: A Systematic Review and Meta-analysis of Randomized Controlled Trials. Chung et al, 2019.	To study the effectiveness of PRP injection after arthrocentesis in patients with TMJ osteoarthritis	Studies included: Randomized controlled studies (n=5). Diagnosis of OA: Based on RDC/TMD. Follow-up: 3, 6, 12 months	Arthrocentesis + PRP vs. Arthrocentesis +HA (n=2) Arthrocentesis + PRP vs.	The addition of PRP to arthrocentesis treatment increases the effectiveness in long-term pain management. PRP significantly reduces pain compared to HA, placebo or no injection.
Effect of arthrocentesis plus platelet-rich plasma and platelet-rich plasma alone in the treatment of temporomandibular joint osteoarthritis. Lin et al, 2018.	To compare the effectiveness of arthrocentesis+ PRP/ PRP alone.	Inclusion: 90 patients. Injection of 2mL of PRP. Diagnosis of osteoarthritis: CBCT based on DRC/TMD. 12-month follow-up	Arthrocentesis+PRP (n=30) vs PRP alone (n=60)	A+PRP is more effective/ PRP alone in improving associated migraine, facial and masticatory pain, and better cartilage repair on CBCT. Statistically significant difference (P=0.019) Recommendation: injection of 2mL of concentrated and purified PRP in TMJ OA.
Temporomandibular Joint Disorders Treated With Articular Injection: The Effectiveness of Plasma Rich in Growth Factors-Endoret. Giacomello et al, 2015	To evaluate the efficacy of intra-articular injection of PRP in the treatment of TMJO.	Inclusions: 13 patients. 2 injections of 2mL of PRP 1 month apart. Diagnosis of osteoarthritis: MRI. Follow-up: 1, 6 and 12 months.	2 injections of 2ml of PRP at 1month intervals.	**After the 1st injection**: Improvement of pain at 7 days. 5 patients were symptom free at 30 days and 8 had partial resolution. **After the 2nd injection:** Joint pain completely disappeared in 11 patients. At 1 year: Effectiveness of the treatment confirmed by the absence of joint pain.
Is arthrocentesis plus platelet-rich plasma superior to	To compare the therapeutic efficacy of arthrocentesis plus	31 patients were randomized into two groups according to the	Compare the therapeutic effectiveness of arthrocentesis	Decrease in symptoms and improvement in mouth opening amplitude, with no

arthrocentesis plus hyaluronic acid for the treatment of temporomandibular joint osteoarthritis: a randomized clinical trial. ***S CömertKiliç 2016***	PRP/ arthrocentesis plus hyaluronic acid in TMJO	treatment technique applied: G1: arthrocentesis+ PRP injection; G2: arthrocentesis plus HA injection. Mouth opening measurements were recorded preoperatively and at 12 months postoperatively	+ PRP/ arthrocentesis +AH	significant difference between the 2 groups.
The Hierarchy of Different Treatments for Arthrogenous Temporomandibular Disorders: A Network Meta-Analysis of Randomized Clinical Trials. Al-Moraissi EA 2020	Therapeutic efficacy: PRP/HA in patients with TMJO	Studies included: Randomized controlled studies (n=36). Diagnosis of osteoarthritis: reduction of pain + improvement of mouth opening Follow-up: 4 years	Compare the therapeutic efficacy: of PRP/ HA	Hyaluronic acid acts as a lubricator while PRP is a tissue healer.

Conclusion

The studies that have appeared on the subject have positive conclusions in terms of the efficacy of PRP in the management of pain associated with Temporomandibular joint Osteoarthritis, but do not demonstrate significant long-term improvement in the functional management and slowing of the arthritic process.

However, more randomized controlled clinical trials including systematic imaging controls are needed to demonstrate probable regeneration and to define a standardized protocol for PRP preparation, volume injected, and frequency of injections.

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