

Does Single Intra-Articular Plasma-Rich Plasma (PRP) Injection for Temporomandibular Joint (TMJ) Internal Derangement Relieve Joint Pain?

Basem T. Jamal

Consultant and Associate Professor Oral & Maxillofacial Surgery, King AbdulAziz University, Jeddah, Saudi Arabia

ABSTRACT

Introduction: The temporomandibular disorder (TMD) is a common pathological entity and is found in 31% of the adult population. Different minimally invasive techniques, such as the injection of diverse substances into the joint, arthrocentesis have exhibited good clinical results and such modalities would be considered either for severe TMDs or after the failure of conservative treatments. Several studies endorsed intra-articular injections of platelet-rich plasma (PRP) as an effective procedure to decrease TMD tenderness. The primary aim of this study is to assess the effectiveness of a single PRP injection in terms of reducing pain, and improving mandibular motion in patients affected by internal derangement of the TMJ.

Materials & Methods: The study consisted of 10 patients who reported to the oral and maxillofacial surgery clinic with painful dysfunction of the temporomandibular joint who received a single injection of PRP in the TMJ. Variables measured including pain score and mouth opening were assessed preoperatively and postoperatively. SPSS 24.0 was used for data management and statistical analysis. The level of significance was set at 0.05 for all statistical tests using chi-square.

Results: The group of 10 patients consisted of 9 women and 1 man. The age of the participants ranged from 27 to 75 years, and a median age of 45.5. Upon the follow up visit within 1-3 months: 7/10 patients showed a significant reduction of the pain intensity (more than 50% reduction of pain intensity), 2/10 patients showed a partial resolution of the symptoms with minimal reduction of pain and one patient showed no improvement in either pain or mouth opening and subsequently underwent arthrocentesis. The PRP injections were successful in decreasing pain intensity scores to below 5 in most cases. A Chi-squared test was performed to test for an association between the PRP injections and pain intensity score and the outcome supports the conclusion that there is a strong correlation between the PRP injection and pain and that it is statistically significant.

Conclusions: TMD symptoms and movement limitations disrupt everyday life and in cases with severe illness, studies showed that the conservative treatment measures lead to insignificant or low improvement in quality of life. For this reason, a fast acting and effective method of reducing pain and movement limitations is essential and our study findings support the role of PRP injections. It exhibited a very strong negative relationship, which indicates that the PRP injection and pain scores are inversely related.

Corresponding Author e-mail: bjamal@kau.edu.sa

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INTRODUCTION

It has been found that 31% of the adult population suffers from temporomandibular disorder (TMD), or dysfunction of the temporomandibular joint (TMJ), on the basis of a meta-analysis published in 2021 by Valesan et al.¹ Disorders of the temporomandibular joint (TMDs) are more prevalent in women and tend to affect people between the ages of 20 and 40.^{2,3} TMDs are progressive painful conditions characterized by limited mandibular movement, deviations or deflections upon opening the mouth, locked jaw, and tenderness, clicking or crepitus in the joint.⁴ TMDs are broadly divided in three groups: muscles disorders, disc displacement disorders and other TMJ disorders such as osteoarthritis and arthrosis.⁵

Internal derangements of TMJ in the form of disc displacements with or without reduction are characterized by pain and discomfort in the TMJ area as well as joint sounds. It is an intracapsular dysfunction that leads to degenerative changes in the disc and articular surface.⁶ The pain, stiffness, and loss of function

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caused by osteoarthritis (OA) of the temporomandibular joint are symptoms of degenerative changes in bone, cartilage, and supportive tissues of the TMJ.⁷ Most of patients with internal derangement of the TMJ improve clinically with non-surgical treatments such as analgesics, non-steroidal anti-inflammatory drugs (NSAIDs), occlusal splints, and physiotherapy.^{8,9} However, the use of minimally invasive procedures, such as the injection of diverse substances into the joints, arthrocentesis, and arthroscopy with lysis and lavage, has demonstrated favorable clinical results, and these procedures may be considered for severe TMDs or when conservative treatments have failed^[10,15,16]. There are several studies that support the effectiveness of PRP intra-articular injections in reducing tenderness associated with TMD.^{17,18}

Platelet-rich plasma (PRP) is defined as a three- to eight-fold concentrated autologous solution of platelets obtained after sequestering and concentrating autologous blood by gradient density centrifugation, and it is associated with many growth factors, such as platelet-derived growth factor, transforming growth factor, vascular endothelial growth factor, epithelial growth factor, insulin-like growth factor, basic fibroblast growth factor, and three blood proteins (fibrin, fibronectin, vitronectin).^{19, 20} PRP represents an emerging regenerative therapy for injuries in the orthopaedic field with promising results showing anti-inflammatory, analgesic and antibacterial effects.²¹⁻²⁴ The rationality of PRP in the treatment of osteoarthritis is that platelets release the growth factors to drive fibroblasts in the synovium to secrete hyaluronic acid (HA)^[25] and maintained levels of HA stabilize cartilage protection and joint lubrication.²⁶

A major advantage of getting PRP from autologous blood is that everyone has access to the raw material for making it and its a free resource. Furthermore, this ensures a significantly low risk of allergic reactions or adverse effects. The primary aim of this study is to assess the effectiveness of a single PRP injection in terms of reducing pain, and improving mandibular motion in patients affected by internal derangement of the TMJ.

MATERIALS AND METHODS

The study consisted of 10 patients, 9 females and 1 male, and age ranged from 27 to 75 years, who reported to the oral and maxillofacial surgery clinic with painful dysfunction of the temporomandibular Joint. Only patients whose diagnosis were under groups II and III of RDC were included in study while patients in RDC/TMJ group I were excluded.

Patients' history was reordered including the chief complaint, intensity of the pain, associated symptoms of limited mouth opening or locked jaw, previous treatment modalities of the TMD, social data, and past medical history. Pain was assessed preoperatively and recorded on a 0-10 scale based on the visual analogue scale (VAS) with 0: no pain and 10: the worst imaginable pain. Clinical examination was performed evaluating masticatory muscles tenderness, presence of joint sounds, mandibular range of motion, deviation on mouth opening and dental evaluation. Panoramic x-ray was done to exclude to exclude any TMJ pathology and dental-related pain.

All patients had occlusal splints constructed in the form of hard, clear, full vacuum splints, 2 ml in thickness and each

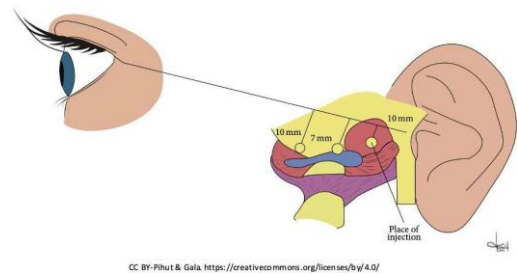


Fig. 1: Illustration of the Holmlund-Helsing line and the placement of the injection point within the temporomandibular joint By Pihut & Gala.

patient was instructed to wear the occlusal splint at night during sleep and during day time at times when patient notice frequent clenching e.g. desk work, watching tv..... Written consent was obtained from the patients prior to procedure.

Under aseptic protocol, Holmlund-Helsing line (HH) was drawn from the middle of the tragus of the ear to the lateral canthus of the eye and PRP was injected into the upper joint space; the point of injection was marked 10 mm from the middle tragus on HH line and 2 mm below this point. It corresponded with the upper compartment and retrodiscal zone as illustrated in figure-1. (CC. creative commons licenses/by/4.0/ BY-Pihut & Gala).²⁷ The patient was instructed to open his/her mouth halfway and the PRP injection was administered to the affected joint both in the periarticular and intraarticular area with a volume of approximately 1.5 to 2 mL. After injection, the skin was disinfected once again. Patients were given information that experiencing an unpleasant and transient sensation of fullness or compression in the joint regions was possible.

Variables measured preoperatively were reassessed at 1-3 months postoperatively. Patient information summarized in table-1. SPSS 24.0 was used for data management and statistical analysis. The level of significance was set at 0.05 for all statistical tests using chi-square.

RESULTS

A total of 10 patients were involved in the study, 9 women and 1 man. The age of the participants ranged from 27 to 75 years. The median age was 45.5 with interquartile ration IQR of 33.75-62. Three patients (30%) were diagnosed in stages II (early-intermediate), three patients (30%) diagnosed in stage III (intermediate), and four patients (40%) diagnosed in stage IV (Intermediate-late) on the Wilkes classification scale. There was a wide range of duration of the TMD symptoms (2 months to 12 years), with a median of 15 months with IQR of 5-57 months.

7 of the 10 patients exhausted different conservative modalities prior to considering PRP injections with no response to the conservative therapy and only 3 patients had the PRP injection parallel with the conservative therapy measures including the splint therapy due to the severity of the symptoms.

All the patients except one have had some degree of improvement of the symptomatology within 7 days from the injection with a good reduction in articular pain. Upon the follow up visit within 1-3 months: 7/10 patients showed

Table 1: Summary of the patients TMJ disorder classification, duration of symptoms, preoperative and postoperative pain and minimal interocclusal opening (MIO)

Patient	Age	Diagnosis (Wilkes)	Duration of symptoms	Pre-injection pain	Post-injection pain	Preoperative MIO	Postoperative MIO
1	75	III	120 months	7	3	WNL	WNL
2	32	III	4 months	8	6	Limited	Improved
3	45	III	2 months	7	7	Limited	Limited
4	27	II	12 months	6	1	WNL	WNL
5	36	II	2 months	8	4	WNL	WNL
6	59	IV	120 months	6	3	Limited	Improved
7	33	IV	48 months	9	5	Limited	Improved
8	69	II	18 months	7	5	Limited	Limited
9	46	IV	60 months	7	1	Limited	Improved
10	63	IV	8 months	8	4	Limited	Limited

a significant reduction of the pain intensity (more than 50% reduction of pain intensity), 2/10 patients showed a partial resolution of the symptoms with minimal reduction of pain and one patient showed no improvement in either pain or mouth opening and subsequently underwent arthrocentesis.

The average preoperative pain score was 7.3 and postoperatively the average pain score decreased to 3.9. The PRP injections were successful in decreasing pain intensity scores to below 5 in most cases as subjectively assessed by the patients. A Chi-squared test of independence with Yates continuity correction was performed to test for an association between the PRP injections and pain intensity score. The outcome supports the conclusion that there is a strong correlation between the PRP injection and pain and that it is statistically significant ($X^2 = 16.912$, $df=1$, $p < 0.001$). The Phi Coefficient was calculated to determine effect size. It exhibited a very strong negative relationship between the factors ($r = -0.816$), which indicates the PRP injection and pain scores are inversely related.

5/10 patients had limited maximum interincisal opening preoperatively <25mm and 4/5 had immediate improvement of mouth opening to 35mm or more at the follow up visit. Neither the treatment nor the follow-up period was associated with any adverse events.

DISCUSSION

Treatment for TMDs is controversial, and can be classified into one of three categories: nonsurgical, minimally invasive, and surgical. Approximately 70% of TMDs can be treated without surgery, and these methods include soft food diets, behavior modification, pharmacotherapy, physical therapy, inter-occlusal splints, and transcutaneous electrical nerve stimulation^[28]. Nevertheless, these approaches are palliative and do not permanently alter the biochemical environment in the TMJ. Arthrocentesis, arthroscopic lysis and lavage, and intra-articular injections are among the minimally invasive therapies. Intra-articular injections could be with steroids, hyaluronic acid (HA) or material with regenerative properties such as platelet-rich plasma (PRP) and clinical studies have shown that these modalities are effective in relieving pain and improving functional outcomes^[10-14].

Blood plasma containing highly concentrated platelets is known as platelet-rich plasma (PRP)^[29]. There are 2 million platelets per mL in PRP, which far exceeds the normal concentration of 200,000/mL in blood^[30]. A number of knee degenerative pathologies have been successfully treated with PRP in recent years, since it is both safe and capable of reducing pain and improving function^[31,32]. PRP is an injection agent that is not manufactured, but prepared from a patient's own blood sample and its advantage is that the raw material for its production is available to every patient and it is a free resource. In addition, this minimizes the risk of adverse reactions or allergic reactions. Studies have demonstrated that biological therapies, including PRP, are effective and safe methods for treating knee OA-associated pain and joint dysfunction^[33-36].

While PRP has been studied extensively for the treatment of TMDs and temporomandibular disorders (TMDs), there are no unified standards for the concomitant use of arthrocentesis and the dosage or frequency of PRP injections. Because intracapsular injections do not have a standardized protocol, comparing the research available is difficult. We will therefore review the literature regarding three different domains in this discussion, including studies on the effectiveness of PRP in treating TMD and TMJ OA, studies comparing PRP with arthrocentesis, and a comparison of PRP effectiveness with other drugs such as HA and steroids.

It was reported by Hegab et al. that PRP injections alone in the treatment of TMJ osteoarthritis were able to reduce pain and increase mobility of the mandible^[37]. Al-Delayme et al. obtained similar results, showing that in patients with disc displacement without reduction, PRP injections reduced pain and increased mouth opening^[38]. Similarly, Kömert Kiliç et al. reported significant improvements in joint sounds, interincisal opening, and lateral motion after multiple injections of PRP^[39]. Results obtained in this study are in line with the recent literature showing significant reduction in pain intensity in patients with TMJ internal derangement following PRP injections. PRP exerts these effects via an anti-inflammatory and analgesic properties. It was found that PRP reduced the level of inflammatory mediators, which supported the preservation of cartilage integrity^[40]. In addition, treatment with PRP leads to an inhibition of the proinflammatory cytokines that interfere with the tissue healing process, through the suppression of interleukin-1 release^[41]. Moreover, PRP may also

have analgesic effects, possibly through its ability to promote a greater number of cannabinoid receptors CB1 and CB2.⁴²

Arthrocentesis has long been considered as the first line of minimally invasive modalities to be applied if conservative therapy fails. The effectiveness of arthrocentesis in reducing pain and decreasing mouth opening has been reported to be 91% and 96%, respectively.^{43,44} However, other studies indicate that arthrocentesis is only temporary and does not rehabilitate TMJ microarchitecture⁴⁵ and hence other modalities have been investigated in the literature either separately or with incorporation with arthrocentesis. Chung et al. study findings in 2018 indicated a beneficial effect of adjuvant PRP to arthrocentesis or arthroscopy for patients with TMJ OA^[46]. However, many studies compared PRP alone to arthrocentesis. Hegab et al. showed pain to improve when PRP is used, whether by injections alone or when combined with arthrocentesis^[37]. In comparing PRP and arthrocentesis for TMJ pain, Hassan and Lin et al. found no significant differences.^{47, 58} Akash et al. in 2020 observed similar findings that both arthrocentesis and PRP alone had a high success rate in eliminating pain, >75%, with no significant difference between the 2 modalities in effectiveness^[49]. In a study by Lin et al.⁴⁸ to compare the efficacy of 2 TMJ-OA treatment approaches, arthrocentesis plus PRP (A+PRP) and PRP alone found that the 2 treatment groups did not show statistically significant differences in the symptom improvement rates of joint crepitus sounds, reparative remodeling, and TMJ arthralgia. However, compared with PRP alone, the A+PRP treatment demonstrated superior performance in improving TMD-associated headache, jaw range of motion <6mm, myofascial pain with referral, and pain when chewing most foods and hence the authors recommended considering arthrocentesis in addition to the PRP in these indications. Also, the authors recommended to use a single injection of 2 mL of high-concentration, high-purity PRP. This is supported by the current study showing improvement with a single PRP injection.

This represents another controversial topic in the intracapsular injection of PRP which warrants further studies to standardize the recommendations concerning the number of PRP injections, its intervals and volume. There is a wide range of parameters in the literature regarding this matter, ranging from 1-4 injections, with intervals ranging from 1-4 weeks and an injection volume ranging from 0.4-5ml.^{4,7,37,39,50,51}

It has also been proposed that other drugs may be used as intra-joint injection therapy in the treatment of TMDs, since the injection of certain biological or abiotic agents into the superior cavity of the TMJ may encourage the regeneration process. Corticosteroids (CS) and hyaluronic acid (HA) have been administered intraarticularly in patients who have failed to respond to conservative treatment methods^[52]. Despite the fact that injections of these drugs can provide pain relief, there have been concerns regarding their effects on joint structures^[53-54]. Although intraarticular CS injections have been widely used, steroids have been reported to provide only anti-inflammatory property and are prone to cause irreversible damage to articular cartilage^[55,56]. Hyaluronic acid, which accounts for the majority of synovial fluid in joints, plays a crucial role in joint lubrication and cartilage protection. HA's therapeutic effect is linked to its ability to reduce adhesion formation and form granulation tissue^[57]. Comert Kiliç et al.

showed that while PRP therapy effects were satisfactory, Its use does not appear to be superior to that of HA according to the results^[7]. However, compared to HA, PRP injections significantly reduced pain and maximum mouth opening in the study by Hegab et al.^[37]. This is consistent with the findings of Fernández- Ferro et al. and Toameh et al. regarding pain control^[51,58]. A similar study by Gokçe Kutuk et al. concluded that PRP is superior to HA and CS for treating TMJ pain^[59]. Subgroup analysis in a study by Chung et al. demonstrated that PRP injection significantly reduced pain compared to HA injection, saline injection, or no injection^[46]. The superiority of PRP over HA has also been fully established in the orthopedic field, with several studies demonstrating that PRP injections were more effective in reducing pain and symptoms and restoring articular function than HA injections^[35, 60-63].

CONCLUSION

TMD symptoms and movement limitations disrupt everyday life. Studies have shown that conservative treatment measures result in insignificant or low improvements in quality of life in severe cases, with prolonged illnesses possibly leading to mental disorders affecting an individual's employment and interpersonal relationships. Therefore, pain reduction and movement limitations must be addressed quickly and effectively. It is possible to use intraarticular injections, such as PRP, as both a preventative measure against deteriorating quality of life and as an emergency treatment for TMJ dysfunction^[63]. And our study findings support this role for PRP injections. Even though the sample size of this study is limited, the results indicate an improved quality of life after treatment, and further studies with a larger sample size will be required to confirm these findings.

Ethics statement:

An informed consent was obtained for all procedures performed and all procedures performed were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the ethical research committee at King Abdulaziz University Faculty of Dentistry, Jeddah, Saudi Arabia

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