

# An Analysis of the Efficacy of Platelet-Rich Plasma Injections on the Treatment of Internal Derangement of a temporomandibular Joint

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## ABSTRACT

**Background:** A Temporomandibular joint (TMJ) internal derangement (TMJID) is a disruption within the internal aspects of the TMJ in which the disc is displaced from its normal functional relationship with the mandibular condyle, after which the articular portion of the temporal bone causes joint dysfunction, joint sound, malocclusion, and locking of the mouth. Conservative and invasive techniques can be used for the treatment of TMJID. A platelet-rich plasma (PRP) injection is a simple, less invasive surgical procedure for the treatment of internal derangement. The objective of this study was to evaluate the efficacy of PRP injections in decreasing or eliminating pain, clicking, and limitation of mouth opening in patients with TMJID after they were proven to be unresponsive to conservative treatments. The aim is to also show more predictable clinical results.

**Methods:** The study involved 70 patients between 19 and 46 years-old, 62 of which were female and 8 of which were male (female to male ratio 7:75). There were a total of 140 joints with anterior disc dislocation with reduction, as confirmed by Magnetic Resonance Imaging (MRI). PRP was injected in the TMJ in the superior joint space. Pain intensity, maximal interincisal opening, and TMJ sounds were assessed and compared for evaluation of treatment success.

**Results:** There was a statistically significant reduction in pain intensity and joint sound and an increase in mouth opening.

**Conclusions:** This study shows that intra-articular PRP injection for the treatment of anterior disc displacement with reduction of the TMJ is a more effective method to reduce pain intensity and joint sound as well as increasing the patient's mouth opening range. (*J Bagh Coll Dentistry 2017; 29(3):39-44*)

## INTRODUCTION

Temporomandibular Disorder (TMD) describes a set of musculoskeletal troubles in the masticatory system and is the major cause of non-dental originated pain in the oro-facial area which includes the head, face and associated structures. The etiology of TMD has not been yet determined by occlusion, temporomandibular joint (TMJ) anatomy, functional and psychological factors can be concerned. Internal derangement of the TMJ is one of the most common types of TMD, referring to an unusual position of the articular disk in relation with the mandibular condyle and the articular eminence of the temporal bone. <sup>(1)</sup>

The main goal of the treatment for TMJID is to raise the range of motion and decrease the functional pain of the TMJ. <sup>(2)</sup> a lot of non-operative approaches have been made over the years, including occlusal splint therapy, Self-Care and medication. Conservative management is suggested for internal derangement. Surgical interventions include arthrocentesis, arthroscopy, disc repositioning, or Discectomy for patients with resistant internal derangement. <sup>(3)</sup>

Intra-articular administration of medications is a well-known management method in orthopedic and rheumatic disorders related to pain, effusion, inflammation of cartilage, bone and joint capsules and fibrous adhesions. At this time, agents used for intra-articular injection inside the TMJ area include hyaluronic acid (HA) and steroids. The rationale for the use of HA in the treatment of TMJID is that the direct injection of HA into the joint allows for acquisition of proper concentrations with smaller doses favoring superior permanence in the joint. For that reason, HA preparations have short half-lives. Therefore; the long-term effects cannot be solely attributed to the substitution of the molecule itself. The term "viscosupplementation" indicates the restoration of viscoelastic properties, such as cushioning, lubrication, and elasticity. <sup>(4)</sup>

The term "biosupplementation" is used to indicate the restoration of joint rheology, anti-inflammatory and anti-nociceptive effects, the normalization of endogenous HA synthesis, and chondroprotection. These activities explain why the clinical efficacy is maintained for several months. Orthobiologics is a method for increasing of rate of bone and soft tissue healing through the application of natural materials from biological sources. <sup>(5)</sup>

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Platelet rich plasma (PRP) is a new therapeutic agent that has several prospective advantages over corticosteroids in the treatment of the TMJID; PRP has been shown to exhibit anti-inflammatory, analgesic, and antibacterial properties. PRP also restores intra-articular HA, increases glycosaminoglycan chondrocyte synthesis, balances joint angiogenesis, and provides a scaffold for stem cell migration. Basic science studies have indicated that PRP stimulates cell proliferation and the production of cartilage matrices by chondrocytes and bone marrow-derived mesenchymal stromal cells and increases the production of HA by synoviocytes. The results of using PRP to facilitate the repair of chondral and osteochondral defects have had mixed success, with clinical studies indicating that PRP bone marrow-derived stromal cell constructs aid in the repair of chondral defects. Additionally, PRP has also been shown to be maintained 1 year after intra-articular injection in patients experiencing knee pain. Furthermore, PRP therapy provides the delivery of a highly concentrated cocktail of growth factors to accelerate healing. A transforming growth factor (TGF) is present in PRP and has been associated with chondrogenesis during cartilage repair.<sup>(6)</sup> In this study, we hypothesized that PRP would improve the symptoms and function of TMJID, possibly through the release of growth factors and bioactive molecules.

## MATERIALS AND METHODS

### Patients

A prospective study with a 6 month follow-up period was designed. Patients were educated about the study and provided verbal consent. The study included 70 patients who had anterior disc displacement with reduction causing functional disability, pain, limitation in mouth opening, and clicking. These patients had no prior success in TMJID treatment using conservative treatments. The study took place between November 2014 and October 2015. An MRI was used to evaluate the extent of TMJID.

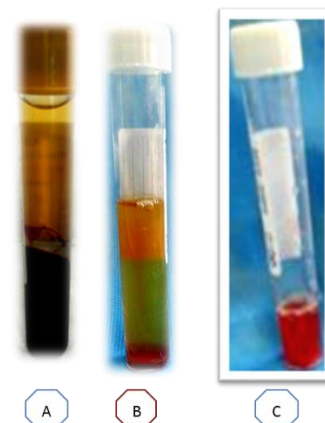
Patients who had central perforation of an articular disc, advanced arthrofibrosis, or ankylosing osteoarthritis, Subjects who had any previous surgery, poor overall health, unwillingness to participate, numerous dental defects. Patients with disc displacement without reduction, diagnosis of inflammatory or a connective tissue disease, contra-indications associated with the use of PRP, (Platelet function disorders, fibrinogen deficiency, and anticoagulation treatment), thrombocytopenia,

malignant disease in the head and neck region, infection of the affected joint, injection of sodium hyaluronate or corticosteroids into the target TMJ during previous 6 months, and pregnant and lactating lady were excluded from this study.

The patient's age, gender, previous treatments, pain, joint sound, and the extent of mouth opening were recorded. PRP injection was applied to the patients' joints. Pain was evaluated on a visual analog scale (VAS) from 0 (no pain) to 10 (worst pain). Induction of a pathologic noise with joint movement was assessed with a stethoscope placed over bilateral TMJs. Maximal mouth opening was recorded (mm). All assessments were repeated by the same physician 1 month, 3 months, and 6 months after the PRP injection.

### Preparation of PRP

PRP was prepared by a sample of 10 mL of blood and is collected from every patient in 10 mL vacuum tubes containing 1ml of 10% sodium citrate for anticoagulation (Figure 1). The tubes are centrifuged at 1200 rpm for 10 min at room temperature, enabling the separation of three components (Figure 1): red cells (bottom of the tube), white cells (thin layer on top of the red cells) and plasma (top layer) then the plasma is decanted into a new sterile 10 mL tube and is centrifuged again in the same machine at the same speed for five minutes. At the stop of this centrifugation (Figure 1), the upper plasma layer that is obtained (accounting for approximately 50%) was discarded because of the small quantity of platelets. The lower portion, which is rich in platelet sand, is the PRP (Figure 1).<sup>(9)</sup>

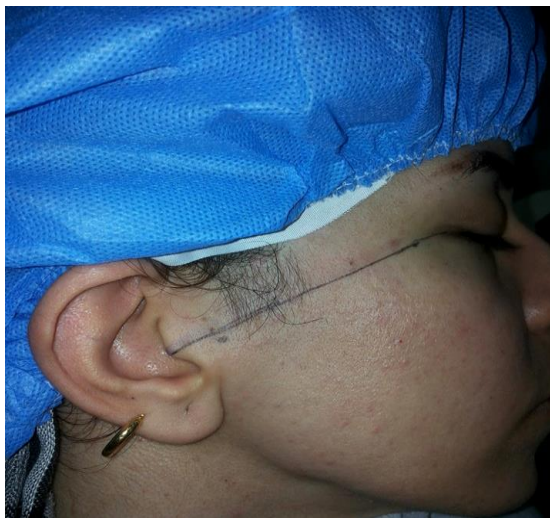


**Figure 1: (A) Illustrates the separation of plasma from erythrocyte. (B) Illustrates PRP and PPP. (C) Illustrates PRP.**

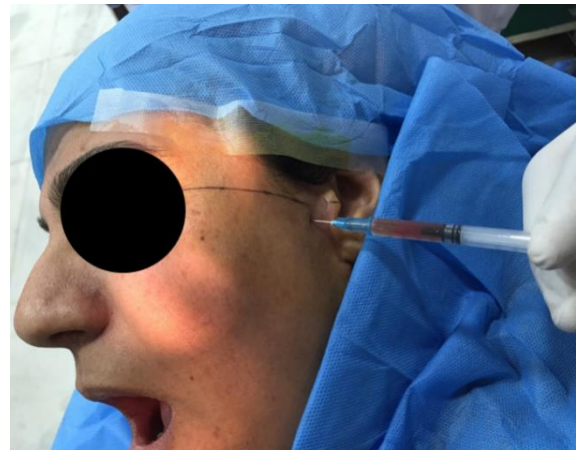
### Operative technique

Intra-articular injections of PRP were preceded by collection of peripheral blood from the ulnar vein of the patient using a double centrifuge, using vacuums tubes with sodium citrate as an

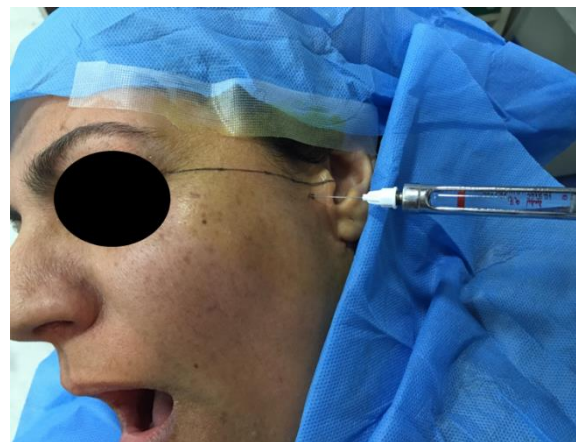
anticoagulant. The patient was seated at a 45° incline with their head turned contralaterally to provide a simple approach for the joint to be managed. The procedure was carried in aseptic conditions, the ear and pre-auricular skin above the TMJ was prepared and draped with topical antiseptic solution, a line was drawn from the lateral canthus to the most posterior and central point on the tragus (Holmlund–Hellsing Line) (Figure 2).<sup>(7)</sup> The posterior point of entry is located along the canthotragal line 10 mm from the middle of the tragus and 2 mm below the canthotragal line. This is the approximate area of the maximum concavity of the glenoid fossa. The distance is about 25 mm from skin to the center of the joint space,<sup>(10)</sup> the point of entry is placed 10 mm further along the canthotragal line and 2 mm below it. The auriculotemporal nerve was blocked with about 2 ml of local anesthetic, which was first injected into the joint cavity to relax this virtual space. Subsequently, the needle was gently withdrawn to the skin surface to also anesthetize the soft tissues over the joint (Figure 4) and a 21-gauge needle was used for introduction into the superior joint space at the glenoid fossa. Approximately 0.5 ml of PRP was injected to distend the superior joint space (Figure 3). The skin was disinfected once again after the injection.



**Figure 2: Illustrates the preparation of patient and points on the canthotragal line.**



**Figure 3: Illustrates the procedure for PRP injection.**



**Figure 4: Illustrates injection of local anesthesia in TMJ**

The PRP was injected into the joint without activating calcium chloride and thrombin because it has been shown that non-activated PRP can enhance mesenchymal stem cell proliferation, chondrogenic differentiation, and osteoinductivity.<sup>(8)</sup>

#### **Statistical analysis**

Data collected from a clinical follow-up was analyzed using a statistical package for social sciences (SPSS) software and Excel (Vers. 21) for tables and figures involving descriptive statistics, inferential statistics (paired sample T test to assess the reliability of data. A *p*-value of <0.05 was considered significant; if the *p*-value was <0.01, then it was considered highly significant. A *p*-value of >0.05 was considered insignificant.

## **RESULTS**

No important complications were reported. Patients experienced short-term swelling and soreness above the TMJ for the first day following procedures. A total of 140 joints in 70 patients (62 females, 8 males) were included in the study group. Mean age of the patients was 31.5 years.

All patients in this study were treated with one dose PRP (0.5 ml) intra-articularly. The differences in pain scores (VAS) between pre- and post-injection were statistically significant ( $p < 0.05$ ) (Table 1). The most intense distinction was between pre-injection and 6 months after injection (6.528,  $P < 0.01$ , HS). The mean of maximum mouth opening pre-injection 32 and 6 months

post-injection 39.27 MMO (Table 2). The difference in MMO between pre- and post-injection at 6 months was statistically significant. Seventy joints had pathologic sounds at first examination; 6 months after treatment, only two joints had a pathologic sound ( $p < 0.05$ ) (Table 3).

**Table 1: VAS Results**

	Pre-operative	Post-operative 1 month	Post-operative 3 month	Post-operative 6 month
	VAS	VAS	VAS	VAS
Mean	8.142	3.157	1.942	1.614
SD	1.195	1.519	0.866	1.561
ANOVA	F=3.69.9 P<0.01 HS			
*High significant				

**Table 2: MAXIMUM MOUTH OPENING Results**

	Pre-operative	Post-operative 1 month	Post-operative 3 month	Post-operative 6 month
	MIO	MIO	MIO	MIO
Mean	32	37.21	38.21	39.27
SD	1.922	2.369	1.971	1.647
ANOVA	F=59.133 P<0.01 HS			
*High significant				

**Table 3: Joint Clicking Results.**

Bilateral	Pre-operative	Post-operative 1 month	Post-operative 3 months	Post-operative 6 month
	CLICKING	CLICKING	CLICKING	CLICKING
Yes	70	6	4	2
NO	0	64	66	68
Chi-square	156.8			
P-value	P<0.01			
Sig	HS			
* High significant	r=0.906			

**DISCUSSION**

**Age distribution**

In this study, the mean age was 31.5 years old and the range was between 19 and 46 years-old with maximum age group ranging from (30-39) years. This could be explaining why certain age groups have a greater risk for developing TMJ than others. These results are in agreement with Edmond et al<sup>(11)</sup> and Blasberg and Greenberg et al<sup>(12)</sup>. The increase could also be due to social tensions among this age group.

**Sex distribution**

In this study, there is an evidence of a high predilection of TMJ among females, with a female to male ratio of 7:75. This can be supported by studies suggesting that females suffer higher levels of pain and dysfunction, and have a greater

persistence of symptoms over a longer time, such as the results in Steven et al, which showed functional estrogen receptors have been identified in the female TMJ but not in the male TMJ. Estrogen may also promote degenerative changes in the TMJ by increasing the synthesis of specific cytokines, whereas testosterone may inhibit these cytokines.<sup>(13)</sup> All patients had improvement in symptoms related to the intra-articular derangement and increased mandibular movements. Results are in agreement with studies done by M Hancı et al and Lippross et al.<sup>(14)</sup> Females suffering more problems than male due to divorce and marital status may indirectly lead to TMJID.

### **Parameters and Data**

The efficacy of PRP injections in TMJID in this study was based on 3 clinical parameters: reduction in pain, absence of clicking during function, and an increase in maximum mandibular movements. Many researchers and clinicians have reported similarly positive results from PRP treatment.

### **Pain**

At the first follow-up visit, the mean pain score reduced from 8.1 to 3.1 for all patients. At the second follow-up visit, the mean pain score reduced to 1.9 for all patients. At the third follow-up visit, the mean pain score reduced to 1.6 for all patients. The data elicited from (AVS) showed an overall significant reduction in pain from 8.1 to 1.6 ( $P < 0.01$ HS). These results are in agreement with the M. Hancı et al study, wherein the researchers described a decrease in pain in TMJID in 10 cases of patients treated with PRP. <sup>(15)</sup> It is known that TMJ dysfunction is related to alterations in joint intra-articular pressure and biochemical components of the synovial fluid rather than to the change in cases disc position in the case of disc displacement of TMJID. <sup>(13)</sup> The analgesic effect of PRP has been highlighted in Lee et al, where results pointed to an augmentation of the cannabinoid receptors CB1 and CB2; this might be related to the analgesic effects of PRP. <sup>(16)</sup> Our results were also in agreement with other studies. <sup>(8) (11)</sup>

### **Maximum mouth opening**

The study data elicited significant improvement in the MMO of patients ( $P$  value  $< 0.01$ , with success rate 100%). These results are in agreement with previous studies <sup>(17) (8)</sup> like Lippross et al., where researchers found that PRP reduced the levels of all markers related to the inflammation of TMJ; intra-articular injection of PRP helped to maintain the integrity of the chondral surface and thereby facilitated joint movement. <sup>(18)</sup>

### **Joint clicking**

In this study, all patients were suffering from TMJ clicking. At the first follow-up visit, 64 patients (91.4%) showed a significant disappearance of TMJ clicking; at the second and third follow-up visits, 4 more patients (5.7%) showed a significant disappearance of TMJ clicking, meaning that by the final follow-up session, there was significant TMJ clicking sound disappearance in 68 patients (97.14%,  $P < 0.01$ ). From a total of 70 patients, only 2 patients (2.8%) showed no improvement in joint clicking. PRP can support the maintenance of a hyaline-like phenotype, chondrocyte proliferation, and proteoglycan production and it can promote many other bioactive molecules concerned in regeneration. In

this study the success rate of RPR injection for joint clicking was in line with study that was performed by Songeul et al. <sup>(8)</sup>

### **Conclusion**

1-Intra-articular PRP injection is a therapeutic approach that may be an excellent substitute for the management of unmanageable TMJD in the future. The technique is safe, simple and patients approval. After PRP injections, if successful, the patients can resume normal behavior and an improved quality of life; the advantageous effects persist at least for a period of 6 months after injection, with no incidence of distinct side effects. The results herein suggest that for the management of TMJ, PRP injection is a technique bearing plenty of potential advantages, including superior functional outcomes and earlier recovery, reduced pain in TMJ, reduced clicking and an increase in maximum mandibular mobility.

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### الخلاصة

**خلفية مشتركة:** الخلل الداخلي للمفصل الصدغي هو الظروف المولمة التقدمية وتسبب اختلال وظيفي في مفصل الفك ينتج عنه ألم في المفصل وصوت وقفل الفم هناك عدة طرق لمعالجة هذه الحالة منها تحفظية وأخرى جراحية لمعالجة الاضطراب الداخلي للمفصل الصدغي. حقن الصفائح الدموية الغنية بالبلازما هو علاج بسيط وقليل التدخل الجراحي لعلاج الاضطراب الداخلي للمفصل الصدغي من علاج غسل مفصل الفك وناظور المفصل وكذلك العلاجات التحفظية الأخرى مثل الأدوية والعلاجات الطبيعية

الهدف من الدراسة تقييم فعالية الصفائح الدموية الغنية بالبلازما وتأثيرها في خفض أو القضاء على الألم، والنقر والحد من فتحة الفم في المرضى الذين يعانون من اضطراب مشترك في مفصل الفك أن منهم من لا تستجيب للعلاجات المحافظة وإظهار النتيجة أكثر قابلية للتنبؤ سريريا .

**المواد والطرق:** تم إجراء هذه الدراسة في مستشفى البرموك التعليمي ، قسم جراحة الفم والوجه والفكين، من نوفمبر 2014 إلى أكتوبر 2015، وشملت 70 مريضاً (62 أنثى و8 رجال) الذين تتراوح أعمارهم بين 19-46 عاماً يعانون من أعراض آلام المفاصل الصدغي، وفتح الفم محدود والنقر خلال الوظيفة. تم تقييم اضطراب المفصل الصدغي الداخلي مع الفحص السريري وأكد مع صورة الرنين المغناطيسي. وقد تم حقن 5،0 مل من الصفائح الدموية الغنية بالبلازما بإبر عيار 21 في الجزء العلوي للمفصل. وجرى تقييم شدة آلام المفصل الصدغي باستخدام مقياس التناظرية البصرية، وجرى تقييم أقصى فتحة الفم مع مقياس المسطرة المترية وجرى تقييم النقر سريريا بواسطة سماعة الطبيب. تم قياس جميع المعلومات قبل الإجراء ثم بعد 1 شهر، 3 أشهر و 6 أشهر.

**النتائج:** خلال 6 أشهر من المتابعة والفحص السريري ومقارنة النتائج لوحظ انخفاض في الألم مع نسبة نجاح 95.6٪، وتحسين في فتحة الفم والنقر تختفي في 90.3٪ من المرضى .

**الاستنتاج:** أظهر تقنية حقن الصفائح الدموية الغنية بالبلازما في علاج المرضى الذين قدموا مع اضطراب داخلي للمفصل الصدغي، الفوائد العلاجية والبساطة والسلامة وقبول المرضى للتقنية وعدم وجود آثار جانبية كبيرة.