Evaluation Of Platelet-Rich Plasma Effect On Treatment Of Temporomandibular Joint Anterior Disc Displacement

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Abstract: The use of Platelet-Rich-Plasma (PRP) may provide a new and improved treatment option for early and late Temporomandibular Joint (TMJ) disc displacement. However, there are no long-term studies on its use in TMJ arthritis in the literature. The present study evaluate 28 patients with different degrees of disc displacement over a period of time. These patients had experienced no pain reduction following conservative approaches (including splint therapy) and minimally invasive arthrocentesis treatment. All patients had evidence of disc displacement associated with pain and discomfort, and sometimes clicking. The patients were without systemic joint disease, septic arthritis, or autoimmune arthritis. Only patients who had not responded to conservative therapy were included in the present study. Pain intensity was recorded for each patient using a 0-10 VAS scale. Maximum Inter-incisal Opening (MIO) was also recorded. This assessment was performed at the pretreatment stage and then examinations 3, 6, 9, 12 months respectively after administration of two intra-articular injections of autologous PRP. The results after 12 months revealed that intra-articular injection of autologous PRP appeared to be an effective treatment method for patients with disc displacement in this study. At the 12-months follow-up, all patients improved their mouth opening significantly. The majority of the PRP patients showed decreased pain. The average pain score before PRP administration was 7.5, while 3 months after PRP administration the pain score was 4.2. The pain score continued to decrease, reaching nearly 2 after 6 months and 0.5 by the end of 12 months. In conclusion, the use of PRP was found to be an effective and predictable treatment option for disc displacement.

Keywords: Platelet-rich plasma; Temporomandibular joint; disc displacement

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Introduction

Temporomandibular joint (TMJ) disc displacement is defined as an abnormal relationship of the disc to any of the other components[1]. However, the pathogenesis of disc displacement has shifted focus from pathologic causes [2,3] to more complex biochemical causes [4-6]. It is manifested as pain with movement, muscular pain, earache, clicking or popping sounds during opening and/or closing, limited range of motion, headache, tenderness, and muscular spasm [7].

Treatment of disc displacement of the TMJ typically begins with nonsurgical treatment modalities such as bite appliances and diet modification. Surgical intervention, which includes open operations (discopexy, discectomy, pterygoid dysjunction, arthrotomy, and joint replacement) or closed operations (arthroscopy or arthrocentesis), is a controversial issue. It is limited to cases that do not respond to conservative treatment [8,9]. Although arthroscopy is a minimally invasive procedure and preserves the articular tissue [10], it lacks the facility afforded by traditional instrumentation [11,12].

Arthrocentes is was developed by Nitzan et al. [13] and is widely used in the treatment of disc displacement [14,18]. This is a useful method and is a minimally invasive procedure. It has been found to significantly improve clinical outcomes [19,22]. Sodium hyaluronate and corticosteroids have been widely used injectable materials with short-term effect on the patients [23-26]. The application of PRP in vitro proved to enhance human stromal and mesenchymal stem cell proliferation [27] and improved pain and symptom relief in knee injury (in vivo) [28]. PRP provides a high concentration of growth factors and transforming growth factors, which accelerate healing in chondral tissues and increase hyaluronic acid concentration. This also contributes to stabilizing angiogenesis in patients with osteoarthritic knees [29-31].

The present study is a trial to improve the final outcomes of arthrocentesis as a line of treatment by implementing post-procedural PRP injection, aiming to correct the displaced disc and alleviate the pain.

Material and Methods

This study was conducted on a pilot sample comprising 18 patients. The study subjects included 7 males and 11 females with an age range from 20 to 50 years and an average age of 35 years. All patients were selected from those attending the out-patient clinic of Al-SayedGalal University Hospital, Al-Azhar University in Cairo, Egypt.

The patients suffering from temporomandibular joint (TMJ) internal derangement were
planned for PRP injection into the joint space and posterior attachment after failure of conservative treatment.

**Design of the study**

1) One month of conservative treatment (soft diet, analgesics)

2) Another month of conservative treatment (soft diet and occlusion splint)

3) Minimally invasive surgical treatment (arthrocentesis with lavage treatment using 150-mL of Ringer solution and HA injection at the end of the lavage).(Fig.1 A&B)

All patients completed the study throughout the planned observation period.

**Fig.1A**-showing lavage of joint space, **B**- showing sublasyn injection.

**Preoperative assessment**

**I- Clinical evaluation**

1) Measurement of maximum mouth opening

   Inter-incisal distance was recorded in millimeters by measuring the vertical distance between the incisal edges of the upper and lower central incisors (maximum pain free mouth opening). Active mouth opening was measured and recorded.

2) Assessment of lateral and protrusive jaw movements

   Lateral movements were recorded in millimeters by measuring distance between midline of upper and lower central incisors. Right and left lateral movements summed and divided by 2 to give
mean lateral movement. Protrusive jaw movement was recorded in millimeter by measuring the horizontal distance between the incisal edge of the labial surface of the upper and lower central incisors.

3) Assessment of TMJ pain

The TMJ was palpated bilaterally by index finger during rest and function. The degree of the pain was recorded at each observation and given score value, 0 - No pain, 1 - Mild pain, 2 - Moderate pain, 3 – Severe pain.

4) Patient mark on a visual analogue scale

Patient was asked to mark their pain level during function (chewing, mandibular movement) and at rest on a visual analogue scale (VAS) (a 100 mm VAS).

5) Assessment of TMJ click

TMJ click was measured by asking the patients to open and closed his or her mouth several times and clicking was recorded as present (early clicking, late clicking) or absent.

II- Radiographic evaluation

Orthopantomogram to show the bone of the TMJ, evaluate the joint space and to exclude any patient with osseous pathology.

Magnetic resonance imaging (MRI) to reveal the status of the TMJ disc, capsular effusion and degenerative changes [Fig 7].

Magnetic resonance image was performed with a 3 Tesla MRI machine (Siemens Magnetom vision). A 7.5cm surface coil was used to examine the TMJ bilaterally at the same time. Images were performed before treatment and 15 months after treatment.

Fig.2A-showing anterior disc displacement in MRI (closed mouth) while,

Fig.2B- confirming the that it is not reducible in open position MRI.

Presurgical treatment

All patients were subjected to conservative treatment as the first line of treatment in all TMJID cases, patients were instructed to do the following:
1) Apply moist heat & cold packs.
2) Eat soft diet only.
3) Take medications.
4) Wear the splint.
5) Undergo corrective dental treatments.
6) Avoid extreme jaw movements.
7) Don’t rest your chin on your hand or hold the telephone between your shoulder and ear. Practice good posture to reduce neck and facial pain. Keep your teeth slightly apart as often as you can to relieve pressure on the jaw. To control clenching or grinding during the day, place your tongue between your teeth.
8) Only the patients who did not respond to the conservative treatment within 45 days were subjected to arthrocentesis & PRP injection.

**Operative procedures**

Consent form was signed by each patient before the procedure.

**1- Premedication**

One hour before surgery, broad spectrum antibiotic (unictam 1000 mg) was administered intravenously.

**2- Anaesthesia**

All patients were operated on under deep sedation.

The sedative agent was administered through induction phase by using a hypnotic agent (Midazolam) (Dormicum**, 1mg) mixed with an Opioid analgesic (Fentanyl**, 2 to 20 mcg/kg).

The surgical field was disinfected using betadine. The patient was draped with sterile towels secured by toweleclips.

**3- Arthrocentesis and injection technique**

A-Before the arthrocentesis was performed 10 ml of autologous venous blood was drawn from the patient and PRP was prepared as the following:

**PRP reparation**

PRP was prepared from the venous blood sample taken from the antecubital vein. The blood was drawn into test tubes containing sodium citrate and then centrifuged for 6 min at 1500 rpm. The blood was separated into 3 layers: a red bottom layer containing red blood cells; a pink middle layer containing PRP; and a yellow top layer containing PPP. The middle plasma layer (PRP) was then drawn from the test.

**B-TMJ arthrocentesis**

The patient was placed in a supine position on the C.T scan machine and the condyle was palpated by the operator’s hand whilst the mandible was moved in a lateral, open and closed direction. An 18 gauge needle (spinal needle) was inserted into the joint space. Sagittal, coronal and axial cuts
were performed done in multi slice mode to confirm that the needle tip was inside the upper joint space, then the second needle (B) was inserted 10 mm away and 1 mm below the first needle in the majority of patients. Accurate placement was confirmed by 3D reconstruction while the two needles were inside the joint. The joint was then flushed with 150ml saline under continuous pressure.

**PRP injection**

1-First injection

The second needle (B) was removed while the needle at point (A) was used for injection of PRP. 2cm$^3$ of PRP was injected into the upper joint space, then the needle was removed and inserted at the end of the disc to inject a further 1 cc of PRP into the posterior attachment.(Fig.3)

After that the site of injection was covered by a gauze dressing.

2-second injection

The second injection of prp was done after 3 months by the same protocol without lavage.

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Clinical follow up criteria measured

1- Measurement of maximum nonassisted pain-free mouth opening

2- Measurement of lateral and protrusive jaw movements.

3-Assessment of TMJ pain by palpation.

4-Patient pain assessment on a visual analogue scale.

Fig. 3 showing PRP injection after lavage
5-Assessment of TMJ click.

The patients were recalled for follow up after one week then every 4 weeks. Data was collected at the first week after surgery then at the intervals of 3, 6 and 9 and 12 months post-operatively.

Radiographic follow up

Orthopantomogram and MRI were taken pre-operatively and 12 months post-operatively. (Fig. 4 A&B)

![Fig. 4 showing MRI for the patients postoperative showing disc recapturing in open as well as closed positions.](image)

Statistical analysis of the data

Statistics were done by computer using Epi-info Software, version 6.04. A word processing, data base and statistics program. A significant result is considered if \( p < 0.05 \). Highly significant result is considered if \( p < 0.01 \).

All efforts have been made to eliminate potential sources of bias. The study has been designed and reported in accordance with the STROBE statement.

Results

On the level of Pain evaluation:

Twelve months after application, patients had decrease of pain intensity (Figure 5). Of the 18 patients who underwent PRP therapy, 14 patients experienced a reduction in pain at their 1-month
follow-up examination with different degrees, mean VAS decrease from 7.46 (SD 1.10 to 7.10) with SD 1.22 was 3.38 in paired test and it was not highly significant (p=0.02). After treatment, pain relief was significantly more pronounced after 3-months with a mean VAS decrease from 7.46 preoperative to 4.22 (22.28 in paired test (p=0.01). The differences in pain at various times following the second injection were evaluated with paired Student’s T-test. The mean VAS decreased from 7.46 preoperative to 1.67 after six months (SD of .77), corresponding to mean decrease of 5.79 of original value and 41.47 in paired test. This difference was highly significant (p=0.01).

After 9 months the mean VAS decrease from 7.46 preoperative and .71 at 9 months was statistically of high significant value (p=0.01).

At the end of follow up period (12 months) there was high difference between preoperative mean readings (7.46) and at 12 month mean readings (0.50) which was highly statistically significant (p=0.01).

Range of opening

The mean interincisal mouth opening before treatment was 33.5mm (SD of 3.1, range from 16–39 mm). At the 3-month follow-up, patients mouth opening improved from average 33.5mm to
36.8mm with average improvement of 3.3 mm. The mean difference in mouth opening after 6 months was 4.8 mm and there was which was high statistically (p=0.01)

After 12 months the mouth opening increased by 8mm ±1.5mm high statistically significant (p= 0.01)

**On The Level Of Disc Position**

Analysis of the MRI after 12 months clarified that there were marked changes toward the normal disc position.(Fig.6) the differences between the patients suffering from disc displacement with early reduction (DDWER) preoperative and postoperative were 9 to 13 while (DDWLR) was 10 to 7 and (DDWOR) was 9 to 4 and the normal was 0 to 4 which considered as highly significant changes toward the normal position after 12 months follow up period. The 14 patients who experienced improvement post-operatively were included, and we have used “case” to refer to each of the 28 temporomandibular joints (with each patient having two temporomandibular joints).

![Fig.(6):Relation between pre operative and postoperative disc position results](image)

**Discussion**

Minimally invasive modalities are typically utilized in the management disc displacement, Minimally invasive treatment includes intra-articular administration of HA and corticosteroids, and arthrocentesis [5]. Bjornland et al. compared the effect of 2 injections of sodium hyaluronate (HA) with that of corticosteroids in 40 patients with TMJ ID. The HA patients had significantly better pain relief
Moystad et al. found no significant difference with 2 intra-articular injections of HA and corticosteroids [33]. Similarly, Kopp found no significant difference between the efficacies of HA and corticosteroids. Intra-articular administration of anti-inflammatory drugs into joints can improve lubrication. In contrast, arthrocentesis provides joint lavage, the irrigation of inflammatory mediators and loose particles of cartilage, thus loosening adhesions [5,13]. Nevertheless, many physicians prefer to use HA at the end of arthrocentesis for its positive effect on inflammatory degenerative disorders as well as the disc displacement [34]. Manfredini et al. compared several arthrocentesis injection options and obtained better results with HA compared to corticosteroids. Noticeable improvement was achieved with repeated arthrocentesis combined with HA application [4,34]. Guarda-Nardini et al. reported improvement after only 2 arthrocentesis combined with HA instillation [34]. In the Guarda-Nardini study, the effect of the application of sodium hyaluronate was significantly lower-only 20%, but it is important to understand that the study dealt only with patients unresponsive to conventional treatment methods (conservative treatment, 2 arthrocentesis therapies combined with HA administration and arthroscopic lavage, but always with no effects) [34]. In the present study, the patients obtained a higher therapeutic effect from intra-articular administration of PRP-90% of patients reported reduced pain and improved mouth opening. PRP therapy is based on the effects of GFs that promote changes in cell proliferation and regulate cellular metabolism. GFs have a vital role in modulating chondrogenic expression [35]. PRP promotes healing through regeneration of degenerative changes in cartilage, bone, and synovial tissue [36]. PRP is widely used in orthopedic surgery, as it promotes healing of wounded tendons and ligaments (medial collateral ligament rupture of the knee, lateral collateral ligament rupture of the ankle and tendon defects) and regenerates OA damage to cartilage and subchondral bone [37-39]. While articular cartilage has limited regenerative capacity due to its avascularity and low mitotic activity, some GFs especially TGF beta, basic fibroblast growth factor, and bone morphogenic protein show a positive effect on cartilage tissue regeneration [31]. The effect of PRP on inflammatory degenerative changes has been described in many studies. In a study of porcine knee arthritis, Lippross et al. reported that PRP reduced inflammatory mediator synthesis in the synovial membrane [40]. These results were confirmed by Liu et al. in a study of rabbit knee synovitis [41]. Sun et al. reported improved healing of osteochondral defects in rabbits, and Ying et al. reported a positive effect of TGF in OA of rabbit TMJs [42,43]. Several clinical trials have shown that PRP therapy is effective for pain reduction and subsequent improvement in joint function. Sánchez et al. treated 40 patients with OA of the hip utilizing intra-articular PRP and found that 57.5% of patients achieved pain reduction on a 6-month follow-up and 16 patients had excellent results [31]. Significant pain reduction was also reported by Filardo et al., who evaluated the use of PRP in 91 patients in a 12-month follow-up study of chronic degeneration of the knee [44]. Sampson et al. noted a reduction in pain and disease improvement in 14 patients with OA of the knee [29]. Similar results were reported by Napolitano et al. in 27 patients with OA of the knee and by Kon et al. in 150 patients with OA of the knee [45,46]. In the present study, PRP was used in patients with OA of the TMJ. Pain reduction and improvement in jaw mobility occurred in 90% of the participants. In this study, PRP was injected into the affected TMJs 2 times in succession with a 3 months interval. However, many orthopedic studies have reported a greater number of repeated applications, mostly 3 at an interval of 3-5 weeks or 9 weeks [31,44-46]. As in other studies, there were no complications related to the administration of PRP [38,44-46]. Contraindications for the use of PRP include platelet dysfunction syndrome, critical thrombocytopenia, hypofibrinogenemia, and hemodynamic instability [47].

**Conclusion**
The results demonstrate the early and late efficacy of double injection of PRP simultaneously with arthrocentesis in patients with disc displacement of the TMJ as an effective and predictable alternative treatment of injectable material. In patients who did not respond to standard treatment, PRP administration showed a significantly higher effect on pain reduction, pain free mouth opening, clicking (If it is injected twice). However further studies are required to evaluate whether the benefits of a single injection persist and whether the PRP is dose dependent or not.

Conflicts of interest

All the authors declared that there was no conflict of interest scientifically and/or financially.

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