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Original Article

Evaluation of Pain Regression in Patients with Temporomandibular Disc Displacement with Reduction Treated by Intra-Articular Platelet-Rich Plasma Injections versus Arthrocentesis: A prospective double blind Randomized Controlled Clinical Trial

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Abstract:

Objectives: The objective of this study is to examine the benefit of an intra-articular platelet-rich plasma (PRP) injection and to compare this with arthrocentesis in Patients with Temporomandibular Disc Displacement with Reduction.
Subjects and Methods: Twenty four patients who did not respond to conservative treatment of anterior disc displacement with reduction were included in this study. They were randomly allocated to one of two study arms: the 'intervention' group who treated with intra articular PRP injection or the control group who treated with Arthrocentesis.
Results: In this study, both groups showed significant improvement in TMJ pain, maximum mouth opening (MMO) and clicking 2 weeks after treatment that maintained thereafter.
Conclusion: It is possible to conclude that intra-articular PRP injection was equivalent to arthrocentesis regarding reduction of TMJ pain with more beneficial effects of arthrocentesis on MMO and TMJ sound.

Keywords: TMJ anterior disc displacement with reduction; arthrocentesis; intra-articular platelet-rich plasma; PRP

Introduction

Patients with anterior disc displacement with reduction (DDWR) most frequently suffer from pain which is one of the most common orofacial pains with a prevalence of about 6 % worldwide [1]. The continuum of symptoms also includes limited, asymmetric mandibular motion and TMJ sounds.

Current treatments of the DDWR are largely targeted at symptomatic relief of joint pain and improvement of mandibular range of motion. Treatment approaches vary depending on the symptoms and degree of dysfunction[2] .

Treatment regimens can include medication, occlusal appliances, physical therapy modalities, mobilization, exercises, minimally invasive procedures (arthrocentesis and arthroscopic procedures) and open surgical interventions that are only used when all other possible therapeutic options have been exhausted[3,4] .

Opinions about the treatment of DDWR are as controversial as beliefs about its etiology and therefore, the management of this disorder should begin with conservative, reversible measures and escalate slowly to irreversible procedures if necessary. Minimally invasive procedures are recognized increasingly as first line intervention in patients who do not respond to conservative management [5, 6]. Of these procedures, arthrocentesis and intra-articular injectionof platelet rich plasma (PRP) have been applied with varying degrees of success.

Preliminary findings gave encouraging results for the use of PRP in temporomandibular joints (TMJ) with inflammatory/degenerative processes[7]. PRP is a natural concentrate of blood growth factors and is thought to deliver activated platelets which play an important role in coagulation, haemostasis, have analgesic properties by releasing protease activated receptor 4 peptides. When injected, the activated platelets secrete numerous proteins including growth factors, such as (platelet derived growth factor, transforming growth factor ß, vascular endothelial growth factor), endostatins, platelet factor 4 and angiopoietins; all of which are involved in the healing process[8]. Thus PRP may reduce inflammation, provide pain relief, improve function and stimulate possible cartilage regeneration at the site of injury [9, 10].

Subjects and Methods

Patients with clinical findings of pain in the involved joint, difficulty in mouth opening, restriction in movement, and clicking sound were evaluated clinically and with magnetic resonance images (MRI).

Clinical examination

Each patient was asked to point to the site of pain using one finger. Pointing to TMJ denotes articular disorder. The right and left TMJs were palpated bilaterally via preauricular approach during opening and closing of the mouth to determine the presence of joint sound and tenderness. The maximal mouth opening (MMO) was measured by the distance in mm between the incisal edges of the upper and lower incisors using a ruler.

MRI examination

Preoperative T1-weighted and T2-weighted MRIs for right and left joints in closed and maximum mouth opening positions were requested for each patient

PRP Injection Technique

PRP preparation

An even number of the tubes were placed in the rotor of the Hettich Universal 32R Refrigeration Centrifuge and spun at 3200 rpm for15 minutes. This separates the blood into 3 distinct layers: with platelet-poor plasma (PPP) as the top yellow layer; a middle buffy coat layer containing platelets and leukocytes; and a red bottom layer containing red blood cells. Inside a biosafety cabinet, the buffy coat layer and the lower one third of PPP were aspirated from the test tubes using a micropipette and transferred into sterile microcentrifuge tube. Hereafter, the procedure was completely performed inside the biosafety cabinet. The microcentrifuge tube was shaken for 10 seconds to resuspend the platelets. 1 mL of PRP for

each TMJ was supplied for intra articular injection.(fig1)

Technique

A line was drawn from middle of the tragus to the outer canthus of the eye. The entrance point is located along the canthotragal line,10 mm from the middle of the tragus and 2mm below the line. Auriculotemporal nerve block anesthesia wa performed using one carpule of Mepicaine L[1]. An 18 gauge needle of 10 ml plastic syringe loaded with normal saline solution was inserted into the superior joint compartment (SJC). The saline solution was then injected. The joint entry was confirmed by the presence of rebound pressure on the piston of the syringe and the flow back of some drops of the solution on removal of the syringe's barrel from the needle after injection. The saline solution was injected in the SJC under manual pressure with the patient in a mouth-open position, in order to expand the joint cavity and then it was withdrawn. The injection-ejection process was repeated 10 times. Then 1ml of PRP is injected into the SJC and the needle was withdrawn. At the end of the procedure, the patient was asked to open and close the mouth several times for a minute to ensure equal distribution of PRP.(fig 2)

Arthrocentesis Technique

Two points were marked on the skin over the articular fossa and eminence along a line drawn from the middle of the tragus to the outer canthus of the eye. The posterior inlet point was located along the canthotragal line 10 mm from the middle of the tragus and 2 mm below that line. The anterior outlet point was located 20 mm from the middle of the tragus and 8 mm below the canthotragal line. Auriculotemporal nerve block anesthesia was performed using one carpule of Mepicaine L. Subcutaneous injection of Mepicaine L at the inlet and outlet points was performed to augment the auriculotemporal nerve block anesthesia.

About 1cm spacer was placed between teeth to increase the intra-articular space and to stabilize and fix the condylar position at the operated side during injection. A 18 gauge needle was inserted into the SJC through the posterior inlet point and 2ml of saline solution was injected to distend the joint space. The joint entry was confirmed by the presence of rebound pressure on the piston of the syringe. At the outlet anterior point another 18 gauge needle was inserted into the distended compartment.Lavage of the SJC with 100 ml of normal saline solution was performed manually to establish free flow of the washing solution. The needles were then removed and the patient was asked to gently manipulate his or her jaw in vertical, protrusive and lateral excursion to remove any excess of intra-articular fluid.(fig 3)

Results

Tables 1, 2 and 3 summarize demographic characteristics of both groups. There is no significant difference in either age or duration of symptoms between both groups.

Clinical results

I. TMJ pain

The assessment of the TMJ pain throughout the study intervals is shown in table 4. There is statistically significant reduction in pain intensity in both groups after 2 and 4 weeks. After 8 weeks pain score is "zero" in both groups.There is no statistically significant difference between both groups preoperatively and after 2 and 4 weeks.

[1]Mepecaine L: Mepevacaine HCl 2% with Levonordefrin 1:20000, Alexandria Co. For Pharmaceuticals, Alexandria, Egypt.

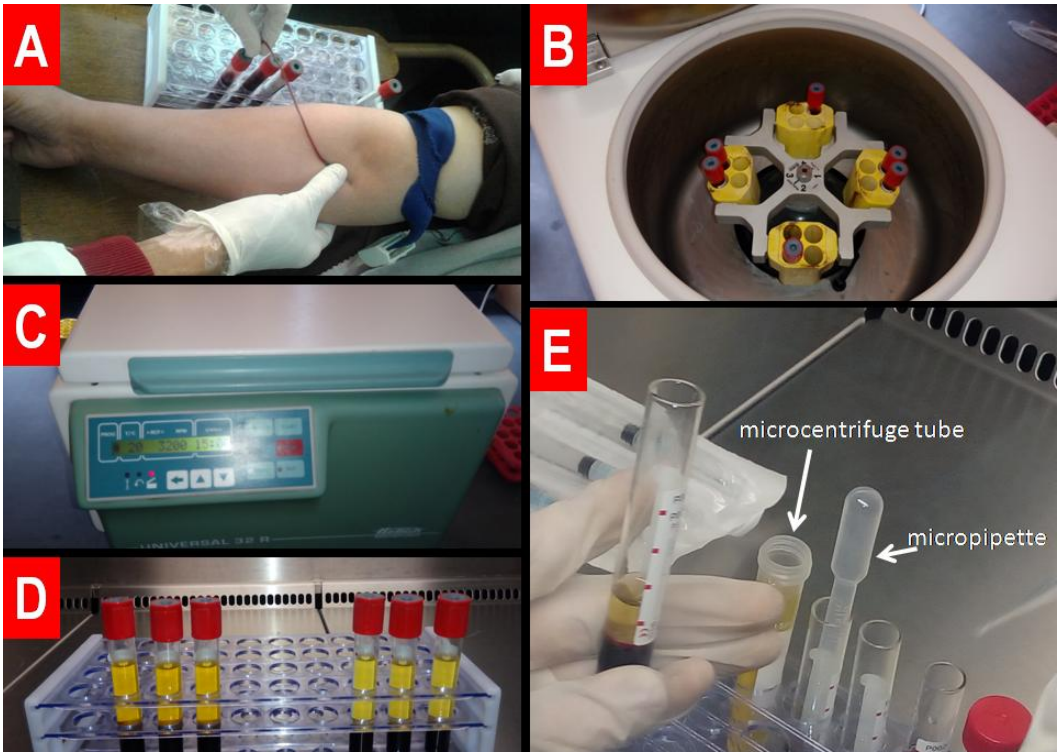

Figure (1): Steps A through E demonstrate the steps required for PRP preparation.

Maximum mouth opening

Table 5 summarize the assessment of MMO at the study intervals. PRP injection group showed significant increase in the MMO immediately postoperative and after 2 weeks followed by insignificant increase after 4 and 8 weeks

In the Arthrocentesis group, there is statistically insignificant increase in the MMO immediately postoperative followed by significant increase after 2 weeks then insignificant increase after 4 and 8 weeks.

II. Clicking

Table 6 illustrate thefrequency of joint clicking in both groups throughout the follow up intervals. There is no statistically significant difference preoperatively. Immediately postoperative the frequency of joint clicking in theArthrocentesis group is statistically significantly lower than in the PRP injection group. This continued till 4 weeks postoperatively. Eight weeks postoperatively, there is no statistically significant difference between both groups

Discussion

Considering the fact that the primary aim of treatment is to relieve pain and to restore complete range of mandibular motion rather than removal of the cause, arthrocentesis has been assessed as a treatment for DDWR which is refractory to conservative therapies and present data suggest that it is likely an effective therapy.

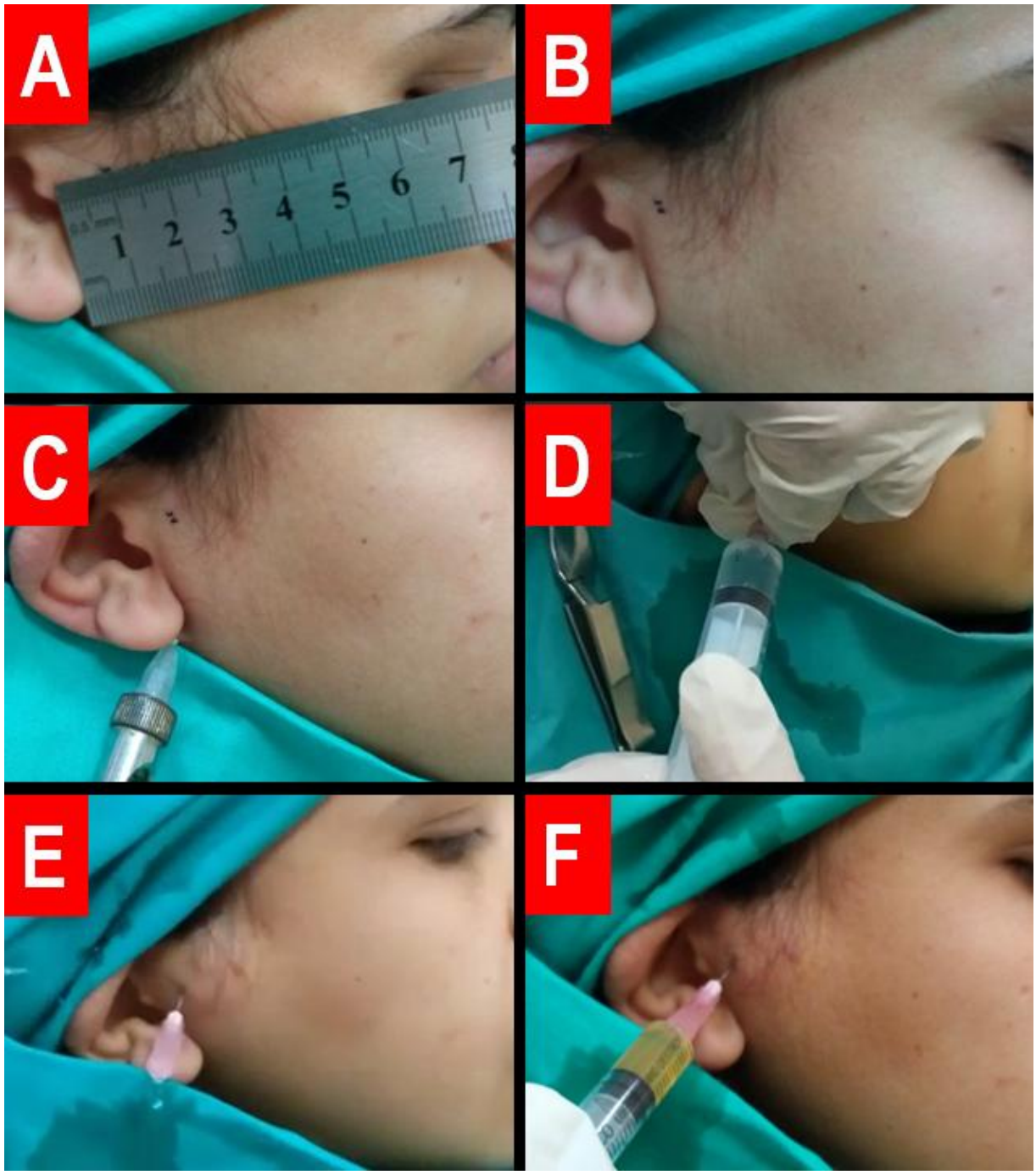

Figure (2): Steps A through F demonstrate the steps for the PRP injection Technique

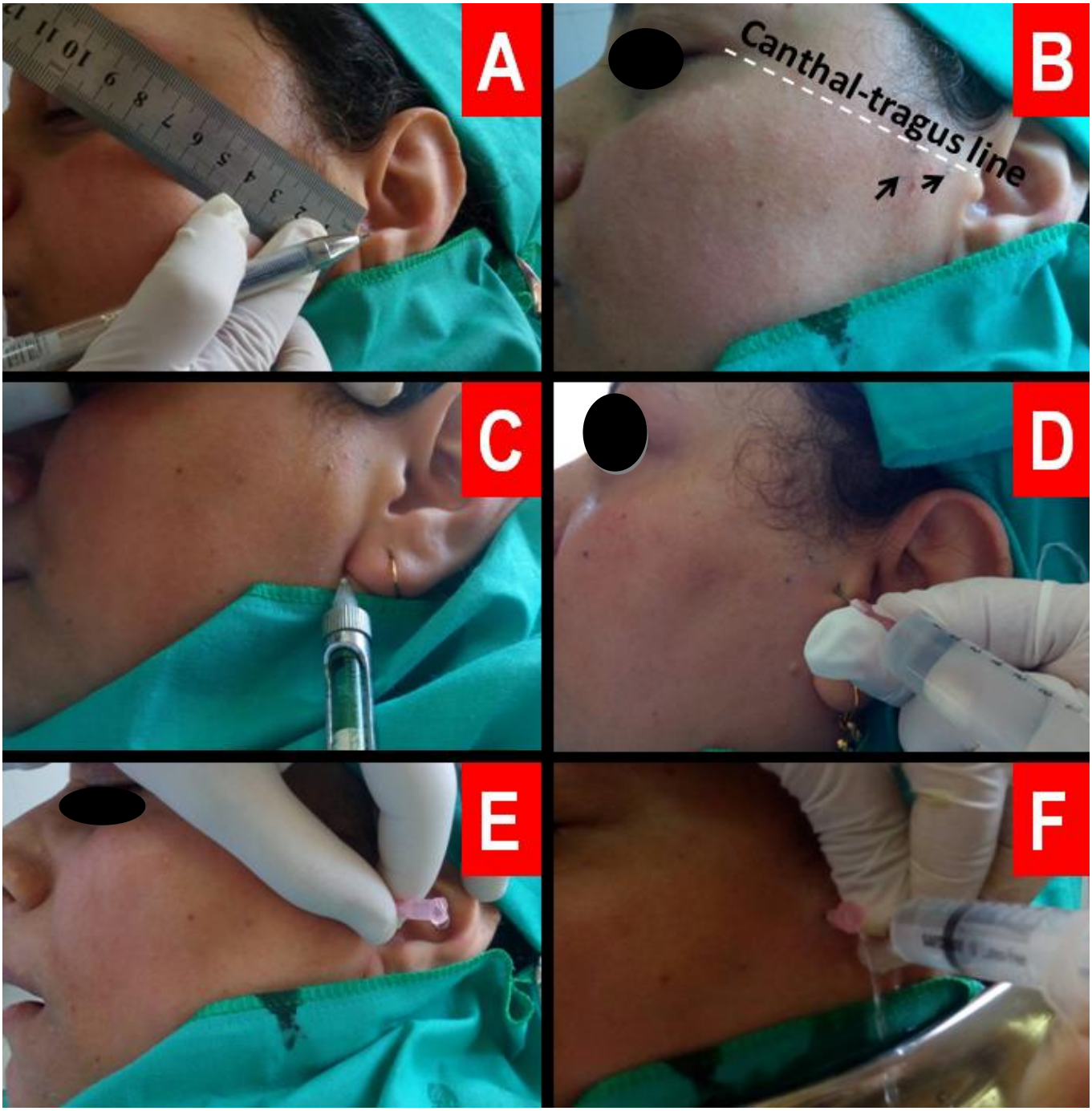

Figure (3): Steps A through F demonstrate the steps for the Arthrocentesis technique

Table 1: Descriptive statistics and independent student "t" test comparing age (years) in both groups.

	PRP injection		Arthrocentesis		"t"	Probability
	Mean	St Dev	Mean	St Dev		
Age (Years)	29.00	6.93	30.67	8.71	0.519	0.305 NS
Duration (months)	20.25	12.73	14.17	7.30	1.436	0.082 NS

Table 2: Frequency distribution of sex in both groups

	Males	Females	"z" values	Probability
PRP injection	2	10	3.266	0.001*
Arthrocentesis	3	9	2.449	0.01*
"z" values	0.503 NS	0.503		
Probability	0.308 NS	0.308		

Table 3: Frequency distribution of affected side in both groups

	Bilateral	Unilateral	"z" values	Probability
PRP injection	10	2	3.226	0.001
Arthrocentesis	8	4	1.633	0.05
"z" values	0.943	0.943		
Probability	0.173 NS	0.173 NS		

Table 4: Descriptive statistics, one-way ANOVA showing effect of time on pain score in each group and independent student "t" test comparing both groups in each follow up interval

Pain	PRP injection		Arthrocentesis		T	Probability
	Mean	St Dev	Mean	St Dev		
Preoperative	8.33	1.155	8.17	1.030	0.373	0.356
2 weeks	3.83	1.528	5.08	2.065	1.686	0.053
4 weeks	0.83	1.528	1.67	1.775	1.233	0.115
F ratio	85.500		44.895			
Probability	0.0000		0.0000			
LSD	1.175		1.397			

Table 5: Descriptive statistics, one-way ANOVA showing effect of time on mouth opening in each group and independent student "t" test comparing both groups in each follow up interval

MMO	PRP injection		Arthrocentesis		T	Probability
	Mean	St Dev	Mean	St Dev		
Preoperative	25.75	2.77	25.58	3.18	0.137	0.446 NS
Immediate	36.75	1.91	36.50	6.40	0.130	0.449 NS
2 weeks	39.25	2.09	44.08	4.17	3.591	0.001*
4 weeks	39.58	2.39	45.08	3.53	4.470	0.0001*
8 weeks	39.83	2.17	45.50	3.90	4.403	0.0001*
F ratio	82.376		45.396			
Probability	0.0000*		0.0000*			
LSD	1.870		2.005			

Table (6): Frequency of joint clicking in both groups throughout the follow up intervals.

	No of patients with clicking		Z	Probability
	PRP injection	Arthrocentesis		
Preoperative	12	12	0.000	1.000
Immediate	9	4	2.048	0.0204
2 Weeks	9	3	3.795	0.0000
4 Weeks	8	2	2.484	0.0007
8 Weeks	2	1	0.617	0.268

Nevertheless, there is a need for evidence based treatment and a search for less invasive procedures with adequate results. Therefore, this prospective, randomized trial was designed with an aim to evaluate the efficacy of intra-articular injection of PRP for treatment of DDWR in comparison to conventional arthocentesis.

In the present study, there were no significance differences between the two groups in age, gender, duration of symptoms and evaluation of the investigated parameters in baseline. This is important as part of the statistical protocol. Also, the establishment of specific inclusion criteria is important when judging results.

In the current study, both groups showed significant improvement in TMJ pain, MMO and clicking 2 weeks after treatment that maintained thereafter. Considering that increased concentrations of inflammatory mediators have been identified in the synovial fluid of patients with internal derangement, suggesting an underlying degenerative or inflammatory process[12].The excellent patient response to Arthrocentesis could be attributed to the disruption of adhesions, and washing out of inflammatory mediators resulting in decreased pain and increased range of motion [13,14,15]. On the other hand, efficacy of PRP may be

related to its anti-inflammatory effect as evident by the observations of Lippross et al.[16]In their experimental study in a pig model of rheumatoid arthritis of the knee joint, interleukin-1, interleukin-6, tumor necrosis factor, vascular endothelial growth factor, and insulin-like growth factor 1 protein content was measured by immunoassay before and 2 weeks after the second intraarticular injection of normal saline or PRP. They found that the tissue concentrations of the tested inflammatory markers returned to control levels when PRP was injected, and that the reduction of each protein was significant compared to levels in the saline injected specimens.

The results of the current study emphasizes once again the efficacy of arthrocentesis for treatment of patients with DDWR and complement the results of other studies [13-14,15-17] Also, our results are in general agreement with other studies that proved the efficacy of intra-artiular injection of PRP as a treatment for a wide variety of painful TMJ conditions [11,18-19].Nevertheless, studies into its clinical efficiency are not conclusive and one of the main reasons for this is that different PRP preparations are used, eliciting different responses that cannot be compared.Of these different responses is the effect of intra-articular injection of PRP on TMJ clicking. Four weeks after PRP injections, the number of patients with clicking decreased from 12 to 8 in the present study. Contrary, Moon et al [20] found no improvement in 4 patients with TMJ clicking at the same interval. This in part may be due to their small sample size.

Comparing the two groups in the present study revealed more beneficial effects of Arthrocentesis than PRP injection on MMO and joint sound. The improvement in MMO at 2, 4 and 8 weeks after treatment as well as in TMJ sounds immediately postoperative and at 2 and 4 weeks after treatment is significantly higher in the Arthrocentesis group than in the PRP injection group. The difference in pain intensity between two groups was not statistically significant. These findings contradict those of Hanc et al [11] who found that pain intensity and joint sound was statistically significant improved in the PRP group more than in the arthrocentesis group and that the difference in MMO between the two groups was not statistically significant. Therefore, they concluded that intra-articular PRP injection for the treatment of reducible disc displacement of the TMJ is a more effective method than arthrocentesis. The differences in PRP preparations and study intervals; 2, 4 and 8 weeks after the injection of PRP or arthrocentesis in the present study and 1 week, 3 months, and 6 months in the study of Hanc et al [11] could attribute to the differences of the results of the two studies.

The results of this study show the beneficial effects of both arthrocentesis and PRP injection therapies in patients with reducible disc displacement of the TMJ, with improvements in both pain and function. However, the short term evaluation of this study is a considerable shortcoming. Further studies are needed to answer a vital question regarding the use of PRP and how to predict and reproduce the effects of a singular and autologous preparation whose composition can vary greatly among different donors and different acquisition methods.

Conclusion

Within the limitations of this study, it is possible to conclude that intra-articular PRP injection was equivalent to arthrocentesis regarding reduction of TMJ pain with more beneficial effects of arthrocentesis on MMO and TMJ sound. Further studies are needed with larger sample and longer follow-up.

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