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Effect of Platelet-Rich Plasma on function and healing of condylar fracture after closed reduction in traumatized patients

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Abstract

Background: Mandibular condyle fracture is one of the most common fractures in the maxillofacial region. No researcher has yet studied the effects of Platelet-Rich Plasma (PRP) on condylar fracture healing. In this study, we aimed to evaluate the effects of PRP injection on function and recovery of the fractured mandibular condyle after closed reduction in traumatized patients.

Methods and Materials: Only patients with stable and repeatable occlusion were included in this randomized clinical trial. Patients who were candidates for open reduction or those with bone or joint disease were excluded from the study. Sixty-four patients were randomly divided into two equal groups: Treatment (PRP injection after closed reduction) and control (only closed reduction). Pain intensity, Maximum Mouth Opening (MMO), and lateral movements were compared between the two groups before and after intervention.

Results: Fifty-one (79.7%) patients were males, and 13 (20.3%) were females. The patients' mean (standard deviation) age was 26.18 (4.61) years. No significant difference was observed among groups considering age and gender. The pain intensity decreased significantly after the removal of MMF in the treatment group, while no significant pain reduction was observed in the control. Considering MMO and lateral movements, there was no statistically significant difference between the two groups before surgery, but they were significantly higher in the treatment group immediately after (maxillomandibular fixation) MMF.

Conclusion: The current study showed that PRP injection after closed reduction can significantly reduce pain intensity in patients with condylar fractures. Also, maximum lateral movements and MMO will be higher than the control group immediately after MMF removal, but the difference between groups reduces after two weeks.

Key Words: mandibular condyle fracture, platelet-rich plasma maximum mouth opening, pain

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INTRODUCTION

Condylar fracture is the most common fracture in the mandible and one of the most common fractures in the maxillofacial region [1, 2]. Mandibular condyle fracture can cause dysfunction, malocclusion, ankylosis, limitation of jaw movements, developmental disturbances in children, and subsequent facial asymmetry. The essential point of condylar reconstruction in patients is to restore the occlusion, esthetic, and function.

Closed and open reduction are the two major techniques for condylar fracture management. Maxillomandibular Fixation (MMF) and immobilization of the jaws for 2 to 6 weeks are the basis of the closed method. In contrast, in the open technique, the fractured bone is fixed by special screws and plates after reduction. There is no need for immobilization [3]. The most prevalent

treatment method for this type of fracture is the closed technique. Compared to open, it leads to fewer complications such as less tissue manipulation, less damage to the sensory and motor nerves, and less probability of complications resulting from surgery and anesthesia, including bleeding and infection [4, 5]. However, due to the long immobilization period, some problems such as hypomobility of the jaw and masticatory muscles, feeding and eating disorders, synovial membrane thickening, and temporomandibular disorders may occur [1, 2].

Platelet-Rich Plasma (PRP) is produced by autologous blood heparinization for 15 minutes and separating platelets from other blood components. Platelets are then diluted with a normal saline solution. PRP injection is an emerging regenerative method for orthopedic injuries with promising anti-inflammatory, analgesic, and antibacterial properties [3]. It is now proven that PRP can repair intra-articular Hyaluronic Acid (HA), increase glycosaminoglycan synthesis by chondrocytes, balance articular angiogenesis, and provide a scaffold for the migration of stem cells [4].

Considering previous studies, compared to HA injection, PRP injection has better analgesic effects. It also improves jaw movements and joint sounds in patients with osteoarthritis or disk displacement more than HA [5,6].

No researcher has yet studied the PRP effects on condylar fracture healing, particularly. In this study, we aimed to evaluate the effects of PRP injection on function and recovery of the fractured mandibular condyle after closed reduction in traumatized patients.

METHODS AND MATERIALS

This randomized clinical trial was conducted after the approval of the ethical committee in Tehran, Iran. Patients with mandibular condyle fractures who visited Valiasr Naja and Imam Hossein Hospitals between November 2022 and July 2023 and were more than 18 years old were studied. Only patients with stable and repeatable occlusion (for the possibility of MMF) were included. Patients who were candidates for open reduction or those with bone or joint disease were excluded from the study. The other exclusion criterion consisted of patients with the bisphosphonate or other bone modifier drug intake, patients who did not have a correct perception of pain such as diabetic patients with neuropathy, pregnant and lactating women, patients with continued jaw growth, patients with a history of maxillofacial surgery, impossibility of MMF due to patient intolerance or underlying diseases such as epilepsy, impossibility of follow up, and displacement of condyle to cranial fossa or outside of the articular capsule. This study protocol was approved by the committee of the medical ethics group of Shahid Beheshti University of Medical Sciences (IR.SBMU.TEB.POLICE.REC.1402.013) and the Iranian Registry of Clinical Trials (IRCT20190429044341N2).

The number of patients was calculated considering the results of a similar study (6) and through the formula: $N=(r+1)\ \sigma^2/rd^2$. Confidence interval of 95%, study power of 80%, and standard deviation of 1 were assumed. Finally, 64 patients were included (32 in each group). Random distribution in two groups was done using Random Allocation software [7]. Patients were blinded relative to their group. The Maximum Mouth Opening (MMO) was recorded before surgery (T_0) based on the distance between the incisal edges of the upper and lower incisors in millimeters. The lateral movement was also recorded before surgery by measuring the maximum change in the distance between the upper and lower jaw midlines in millimeters (average of the right and left directions).

In both groups, MMF was achieved using the conventional arch bar and 26-gauge stainless steel wire under general anesthesia. Twenty ml of venous blood was drawn and poured into special PRP tubes in the treatment group. The blood was mixed with 5 ml of citrate-phosphate-dextrose solution and centrifuged at 800 rpm for 5 minutes. The supernatant was then removed, and the bottom layer was considered PRP. About 1 to 1.5 ml of PRP was then injected into the fractured joint space. To determine the approximate location of the injection, the surgeon tried to touch the condyle with the needle after the patient's mouth opened as much as possible. The other criterion for determination of the injection area was to draw a connecting line between the tragus and the external canthus and place the needle about 1 cm anterior to the tragus and 2 cm below the line.

The day after surgery, MMF was performed in both groups using a 28-gauge wire and remained between 2 and 4 weeks, depending on the fracture severity. A high-protein high-calorie liquid diet was prescribed for the patients. One gram of intravenous cefazolin was administered every 6 hours during hospitalization, and after discharge, ten ml of 250 mg/5ml cefalexin oral suspension was prescribed every 6 hours for five days.

The pain intensity after surgery was recorded using a 10 mm Visual Analog Scale (VAS). Intravenous paracetamol and acetaminophen syrup were used to control pain. When patients were trying to open their mouths after arch bar removal, the pain intensity was again recorded. MMO and lateral movements were also recorded immediately after removing MMF (T_1) and two weeks later (T_2). Patients were trained to actively open their mouths in these two weeks (active physiotherapy).

Statistical analysis

Statistical analysis was performed using SPSS version 21.0 (SPSS Inc., Chicago, IL, USA). Independent samples T and chi-square tests were used to compare the means of quantitative variables between two study subgroups. The U-Mann Whitney test was used in non-parametric conditions. The ANOVA was also used to compare the means of quantitative variables in several independent groups. Bivariate analysis and Pearson correlation coefficient were utilized to determine the relationship between quantitative variables. Crosstab (Wilcoxon in nonparametric condition) was also used to relate qualitative variables of the study

RESULTS

Descriptive statistics

Sixty-four patients were randomly divided into two equal groups in our study. Of those, 51 (79.7%) were males and 13 (20.3%) were females. No significant difference was observed among groups considering gender (p=0.830). The mean (standard deviation (SD)) age of patients was 26.18 (4.61) years with a rang of 17 to 35. The mean age did not differ between two groups significantly (p=0.408) (Table 1).

Tab. 1. Descriptive statistics of the included patients

Gender	Total number (percentage)	Treatment group	Control group
Male	51 (79.7%)	26 (81.2%)	25 (78.1)
Female	13 (20.3%)	6 (18.8%)	7 (21.9%)
Mean age ± SD	26.18 ± 4.61	26.38 ± 4.11	25.97 ± 5.14

Pain

Immediately after surgery, pain intensity was significantly higher in the treatment group than control. The intensity decreased significantly after recovery period and removal of MMF in the treatment group, while no significant pain reduction was observed in the control. Results revealed that there was a statistically significant difference between the two groups considering the pain score changes over time (Table 2).

Tab. 2. Pain intensity after surgery in two study groups

Time	Treatment group	Control group	p-value
	Mean ± SD		
Immediately after surgery	7.5 ± 0.8	6.87 ± 1.0	0.008
After MMF removal	3.28 ± 1.42	6.17 ± 0.83	<0.0001
p-value	0.001	0.145	<0.0001

Maximum mouth opening

There was no statistically significant difference between two groups at T0, but MMO was significantly higher in the treatment group at T_1. Furthermore, MMO did not significantly differ between two groups at T_2.

In the treatment group, the amounts of MMO were significantly higher at T_1 relative to T_0, and at T_2 relative to the T1. In the control group, there was not any significant difference between T_1 and T_0 whereas a significant improvement was observed at T_2. (Table 3).

Tab. 3. Maximum mouth opening in two study groups at different times

Time	Treatment group	Control group	P value
	Mean ± SD		
T_0	14.69 ± 2.48	14.37 ± 2.85	0.638
T_1	26.97 ± 2.52	17.50 ± 3.51	<0.0001

T_2	31.78 ± 2.23	31.13 ± 2.31	0.267
T_1– T_0 (p-value)	<0.0001	0.165	-
T_2 – T_1 (p-value)	<0.0001	<0.0001	-
T_2 – T_0 (p-value)	<0.0001	<0.0001	<0.0001

Lateral movements

There was no statistically significant difference between two groups at T_0, but MMO was significantly higher in the treatment group at T_1. After two weeks, lateral movements increased in both groups but the amounts in the treatment groups remained higher than the control group, significantly.

The results indicate that the improvement in the lateral movements over time (before surgery to 2 weeks after removal of MMF) was significant in both groups. In the treatment group, the amounts of lateral movement were significantly higher at T_1 relative to T_0, and at T_2 relative to the T_1. In the control group, there was not any significant difference between T_1 and T_0 while a significant improvement was observed at T_2. (Table 4).

Tab. 4. Maximum mouth opening in two study groups at different times

Time	Treatment group	Control group	p-value
	Mean ± SD		
T_0	3.66 ± 0.90	3.43 ± 0.72	0.29
T_1	7.47 ± 0.91	3.70 ± 0.83	<0.0001
T_2	8.44 ± 1.62	7.17 ± 1.05	0.001
T_1–T_0 (p-value)	<0.0001	0.304	-
T_2–T_1 (p-value)	<0.0001	<0.0001	-
T_2–T_0 (p-value)	<0.0001	<0.0001	<0.0001

Effects of age and gender

Effects of age and gender on the main outcome of the study are demonstrated in (Table 5). Age and gender did not have any significant effect on any of the variables of the study in both groups.

Tab.5. Effects of age and gender on the main outcome of the study

Group	Variable		F	p-value
Treatment	Pain	Age	3.47	0.073
		Gender	0.045	0.834
	Maximum mouth opening	Age	2.539	0.088
		Gender	0.55	0.526
	Lateral movements	Age	2.317	0.139
		Gender	0.104	0.75
Control	Pain	Age	3.066	0.068
		Gender	0.038	0.849
	Maximum mouth opening	Age	3.03	0.087
		Gender	0.14	0.709
	Lateral movements	Age	3.629	0.062
		Gender	0.309	0.712

DISCUSSION

Mandibular condyle fracture is a prevalent fracture in the maxillofacial region that is predominantly treated by closed technique. In this clinical trial, 64 patients with condylar fractures were randomly divided into two treatment and control groups. In the treatment group, PRP was injected into the fracture site one day before MMF. The pain intensity was evaluated immediately after surgery and after MMF removal. MMO and maximum lateral movement were also measured before surgery (T_0), immediately after MMF removal (T_1), and two weeks later (T_2).

In the present study, about 80% of the patients were males, which is consistent with previous research in this field. Men usually experience a busier social life, so there is a greater risk for fractures such as condylar fracture [8, 9]. In our study, there was no difference between the two groups considering gender. Also, age and gender did not have any significant effect on any of the variables of the study in both groups. The patients' mean age in our study was 26.18 years, which was not much different from other similar studies. In a retrospective study in China with 22 years of follow-up, which was conducted to evaluate the etiology, pattern, and treatment options of condylar fracture, the mean age of 549 patients was about 30 years [9]. In another study in Greece in 2006, 138 out of 368 patients were between 21-30 years old [9]. In contrast, in a systematic review by Jamal et al. in 2022, the mean age of patients was more than 43 years. They had examined the

fractures in the long bones, which may be the reason for this difference [10].

Although many studies have examined the effect of PRP on the healing of long bone fractures, no study has yet examined the effect of PRP injection on improving the conditions of patients with condylar fractures. In a review by Van Lieshout et al. in 2021, just in two studies where PRP was only used in the treatment group, no difference was found compared to the control group. In the other six studies (three only PRP and three PRP along with other substances), positive effects were observed in the treatment group in terms of fracture healing and functional recovery [11]. Furthermore, Jamal et al. investigated the effects of PRP with or without other orthobiological factors on the healing of long bone fractures. 18 studies out of 27 indicated the positive clinical effect of PRP on bone fracture healing, and in only one study unfavorable effects were observed in the PRP group compared to the control group [10].

Many studies have also evaluated the effects of blood products, including PRP, on Temporomandibular Joint (TMJ) problems improvement such as osteoarthritis. Most of these studies have investigated the effect of intra-articular injection of PRP on pain reduction as a factor influencing the patients' quality of life. Gokce Kutuk et al. compared the influences of intra-articular injection of HA, corticosteroid, and PRP in patients with TMJ pain in 2019. They observed a significant reduction in pain during palpation in the HA and PRP groups compared to corticosteroids. All three groups showed significant improvement in the follow-up sessions compared to the amount of pain before the injection. They concluded that PRP injection is more effective than the other groups in TMJ pain reduction [12]. In a review in the same year, researchers admitted that although there is a small number of studies in this field, PRP injection into the joint or using the arthrocentesis method along with PRP injection can be effective in reducing the patient's pain [13]. In the present study, although the pain intensity in the treatment group was higher than the control group immediately after surgery, it was significantly lower after MMF removal. Also, patients in the control group did not experience significant pain reduction, unlike the treatment.

Arthrocentesis is a simple, minimally invasive procedure in which joint fluid and inflammatory mediators are removed from the upper articular space. Researchers have found that this method is effective in reducing intra-articular pain [14]. Abbadi et al. in 2022 have compared the effects of arthrocentesis, PRP injection, and the combination of these two methods in improving the symptoms of patients with TMJ osteoarthritis. Considering the limitation of the study, they acknowledged that although the combination of PRP and arthrocentesis significantly reduced pain intensity more than each procedure alone, all three treatment methods can be effective in the improvement of patients' pain and MMO [15].

Considering MMO, there was no significant difference between the two groups before surgery in the current study, however, the patients in the treatment group could open their mouths almost 10 cm more than the patients in the control group at T_1, which was significant. This difference between the two groups disappeared two weeks after opening MMF. The results revealed that PRP decreases the recovery period, but there is no difference between groups after several weeks considering MMO. The results of previous studies on the effect of PRP on the MMO in patients with TMJ problems have been contradictory. Some researchers have stated that PRP injection with or without arthrocentesis can improve the patients' ability to open their mouths (13, 16). Liapaki et al. have evaluated the effects of HA, corticosteroids, and blood products in patients with TMJ osteoarthritis in a systematic review in 2021. They found none of the groups better than normal saline injection in improving MMO. In contrast, arthrocentesis+ PRP significantly improved the MMO compared to arthrocentesis^{+} HA [16,17].

Protrusive and lateral movements and chewing efficacy after PRP injection in patients with TMJ diseases have also attracted researchers in recent years. Harba et al. (2021) compared the intermittent injection of PRP and HA with the injection of HA alone. After six months of follow-up, they concluded that chewing pain, chewing efficacy, MMO, and mandibular function were significantly better in the PRP+HA group [18]. In another study in 2021, researchers found that PRP and HA injections (alone or in combination) after

arthrocentesis can improve lateral and protrusive movements in patients who have not experienced a successful non-surgical treatment [19]. Their results were compatible with the findings of our study, in which, although there was an increase in lateral movements over time in both groups, the PRP group showed significantly better results at T_1 and T_2.

Despite all the positive findings regarding the effect of PRP on the improvement of bone and joint signs and symptoms, it would be difficult to conclude due to the different methods of preparation and usage (The concentration of platelets and the presence or absence of white blood cells in each study were different, probably). Furthermore, many studies have performed PRP injection in combination with other methods, such as HA injection or arthrocentesis. In addition, there are very few studies, if any, on the effect of PRP injection on mandibular condyle fracture healing. Considering all the above-mentioned facts, the need for more controlled trials with more patients and the use of a standard protocol for the PRP preparation is felt to accurately determine the effects of this orthobiological substance on the improvement of symptoms in patients with condylar fractures.

CONCLUSION

The current study showed that PRP injection after closed reduction can significantly reduce pain intensity in patients with condylar fractures. Also, maximum lateral movements and MMO will be higher than the control group immediately after MMF removal, but the difference between groups reduces after two weeks.

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