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Original article

Investigating the effect of intra-articular PRP injection on pain and function improvement in patients with distal radius fracture

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ABSTRACT

Introduction: Distal radius fractures are common injuries that cause pain and disability. There is a clear need for biomedical engineering research to develop novel strategies to improve functional results following intra-articular distal radius fractures. However, no pharmacotherapeutic agent has been investigated to resolve this problem. The aim of this study was to evaluate whether the platelet-rich plasma (PRP) can be considered a novel additional therapy to improve the outcomes of this injury.
Hypothesis: Pain reduction and functional improvement can be noticed after PRP use in distal radius fracture.
Materials and methods: A randomized trial study was designed with 30 patients who had intra-articular distal radius fractures (Frykman type 3, 4, 7, 8). Closed reduction and percutaneous pinning under guide of fluoroscopy were done for them. Fifteen cases received intra-articular autologus PRP. Patients were followed for 3 and 6 months and "patient-rated wrist evaluation" (PRWE) questionnaire was completed and range of motion of the wrist was measured.
Results: The mean of pain score and the score of specific and usual activities at 3 months follow-up in the case group and in the control group were (8.33 versus 19.67), (10.66 versus 26.8), and (6.2 versus 13.4), respectively. The mean of pain score and score of specific and usual activities at 6 months follow-up in the case group and in the control group were (3.6 versus 12), (3 versus 15.7), and (1.2 versus 6.8), respectively. The case group was significantly different from the control group. The mean of loss of flexion and extension of the wrist at 3 months follow-up in the case group was significantly different from the control group as well.
Conclusion: PRP may have significant effect on reduction of pain and amount of difficulty in functions, including specific and usual activities after intra-articular distal radius fractures.
Level of evidence: Level III, Therapeutic trial.

1. Introduction

Distal radius fractures represent about 16% of all fractures, which are treated by surgeons [1]. According to presence of pain and disability in patients with distal radius fracture and accession of this fracture in population, there is a clear need for biomedical engineering research to develop novel strategies to improve functional results of intra-articular distal radius fractures. Therefore, a thorough understanding of the potential treatment options of its associated problems is of paramount importance. Recently, attention is paid to the biology of the healing environment to influence the body's natural process of healing in order to achieve better outcome, one of which is autologous platelet-rich plasma (PRP). PRP, which has been widely used in a variety of clinical applications, is a concentration of platelet in a small volume of plasma [2]. The effectiveness of PRP is based on its high level of growth factors, including platelet-derived growth factor (PDGF), transforming growth factor-b (TGF-b), fibroblastic growth factor (FGF), vascular endothelial growth factor (VEGF), insulin-like growth factor-1 (IGF-1), and epidermal growth factor (EGF) [3].

As a result, we designed this study to assess the effect of PRP on functional results of intra-articular distal radius fractures, including pain and range of motion.

2. Material and methods

This was a case-control study of 30 randomly selected distal radius fractures, which are treated at a referral University Hospital

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from September 2013 to September 2014. Patients were examined by the authors, and randomly inserted in case or control group.

Our treatment protocols were approved by the local Ethical Committee and a written informed consent was obtained from each patient.

In this study patients with intra-articular, distal radius fractures (Frykman type 3, 4, 7, 8) were selected [4].

2.1. Inclusion criteria

The patients were selected in ages between 18 and 50 years old who had simple intra-articular distal radius fracture (Frykman type 3, 4, 7, 8) without comminution, within less than 7 days before reference.

2.2. Exclusion criteria

Exclusion criteria were consisted of the patients who refused to participate in research, the patients with previous joint destruction due to rheumatoid diseases, previous intra-articular distal radius fracture, and limited range of motion of wrist due to malunion of previous fracture in this region, joint collapse and step off in post operation X-ray and the patient with subluxation of distal radiulnar joint in post operation X-ray.

2.3. PRP preparation

Arthrex double syringe ACP (autologous conditioned plasma) system was used for PRP preparation. Some previous researches approved a system for PRP preparation and product included concentrated growth factor [5–8]. According to these guidelines, approximately 10 cm^3 of venous blood was slowly taken from patient's hand at a rate of 1 cm^3 every two seconds. It was prepared in the operative field with a designed syringe. The sample was centrifuged with speed of 1500 rpm for 5 minutes in operation room under the aseptic condition. About 3–5 mL ACP was extracted from primary sample. Then, ACP was injected in radiocarpal joint from dorsal approach. All injections in the radiocarpal joint were performed in less than 20 minutes after sampling.

2.4. Surgical technique

All of the patients were operated till 2 days after reference. The patients underwent suitable anesthesia by one anesthesiologist. The patient's upper extremity was in operation field from arm for later aseptic sampling.

Under guide of fluoroscopy (C-Arm) closed reduction and percutaneous pinning of fracture was done. Then, the patients, belonging to the case group (15 patients), underwent injection of PRP in radiocarpal joint. Then, short arm cast was applied as routine.

2.5. Follow-up

After 2 weeks, the first visit was done and radiography was taken. After 6 weeks, the second visit was done and X-ray was taken. Cast was removed and motion of the wrist was started under supervision of one physiotherapist. At 3 and 6 months after operation, the patients were visited. Recent studies showed that the "patient-rated wrist evaluation" (PRWE) is a reliable, valid method for assessing pain and function in individuals with distal radius fracture. At each visit, the PRWE questionnaire was completed and range of motion of the wrist including flexion, extension, ulnar deviation, radial deviation, supination and pronation was measured and recorded. The PRWE contains 15 items: a 5-item pain subscale (4 questions on pain intensity and one on frequency), a 6-item specific activities subscale and a 4-item usual activities subscale. Special activities include: door knob using affected hand, cut meat using a knife in affected hand, fasten buttons on shirt, push up from chair using affected hand, carry a 10 Ib object in affected hand, using bathroom tissue in affected hand. Usual activities that were evaluated include: personal care activities (dressing, washing), household work (cleaning, maintenance), work (job or usual everyday work, recreational activities). Patients rate their difficulty in all domains of function. Individual subscales can be totalled [9–11] (Fig. 1).

2.6. Data analysis

We had multiple quantitative data, which were inserted in SPSS software for analysis. Variants were range of motion of the wrist (flexion, extension, ulnar deviation, radial deviation, supination, pronation), pain score, and functional evaluation (specific activities, usual activities). Descriptive data analysis of the items on the PRWE was performed using SPSS v. 11. Comparison of quantitative variables was conducted by Student *t*-test between the two groups. *P*-value less than 0.05 was considered statistically significant.

3. Results

The demographic and clinical features of the patients are presented in Table 1.

No systemic or local complications were found at any time.

Analysis revealed significant improvement in pain, specific and usual activities scores following PRP injection in the case group compared with the control group (Figs. 2 and 3). But, no statistically significant difference in wrist motions including radial deviation, ulnar deviation, supination, pronation, flexion, and extension was found in 6 months follow-up except, some improvement in flexion and extension in 3 months follow-up.

The comparison of the pain, usual and specific activities values and wrist motions between the two groups have been showed in Tables 2 and 3, respectively.

4. Discussion

Among the emerging technologies, PRP has been recently explored in several clinical investigations. PRP modulate inflammation and angiogenesis largely because of their ability to produce high levels of growth factors and chemokines [12].

In orthopaedics, PRP is generally considered a tool for promoting bone repair, especially when combined with bone allografts [13]. PRP seemed to be useful, particularly in clinical situations where the bone repair was compromised, such as in diabetic fractures [14]. In spine fusion surgery, PRP improved the result when added to autologous bone graft [13,15]. Other applications of PRP in orthopaedics concern the use for the repair of cartilage, tendons and ligaments [13,16]. In some orthopaedic applications, PRP are delivered through intra-articular injection for the treatment of knee osteoarthritis or through percutaneous injection for the treatment of delayed unions or non-unions [16–18]. Our study was the first clinical trial research that was performed about effect of PRP on functional results of intra-articular distal radius fractures.

Recent systematic review of the measurement properties of the PRWE showed that this test is a valid, reliable assessment test. Also, the study of Changulani et al. showed that the PRWE score is the most responsive instrument for evaluating the outcome in patients with distal radius fractures, while the "Disabilities of the Arm, Shoulder and Hand" (DASH) score is the best instrument for evaluating patients with multiple joint involvement [10,11].

Name: _____ Date: _____

PATIENT RATED WRIST EVALUATION

The questions below will help us understand how much difficulty you have had with your wrist in the past week. You will be describing your average wrist symptoms over the past week on a scale of 0-10. Please provide an answer for **ALL** questions. If you did not perform an activity, please **ESTIMATE** the pain or difficulty you would expect. If you have never performed the activity, you may leave it blank.

1. PAIN

Rate the **average** amount of pain in your wrist over the past week by circling the number that best describes your pain on a scale from 0-10. A zero (0) means that you **did not** have any pain and a **ten (10)** means that you had the **worst pain you have ever experienced** or that **you could not do the activity because of pain.**

RATE YOUR PAIN: Sample Scale ☞	0 No Pain	1	2	3	4	5	6	7	8	9	10 Worst Ever
At rest	0	1	2	3	4	5	6	7	8	9	10
When doing a task with a repeated wrist movement	0	1	2	3	4	5	6	7	8	9	10
When lifting a heavy object	0	1	2	3	4	5	6	7	8	9	10
When it is at its worst	0	1	2	3	4	5	6	7	8	9	10
How often do you have pain?	0 Never	1	2	3	4	5	6	7	8	9	10 Always

2. FUNCTION

A. SPECIFIC ACTIVITIES

*Rate the **amount of difficulty** you experienced performing each of the items listed below - over the past week, by circling the number that describes your difficulty on a scale of 0-10. A **zero** (0) means you did not experience any difficulty and a **ten** (10) means it was so difficult you were unable to do it at all.*

Sample scale →	0 No Difficulty	1	2	3	4	5	6	7	8	9	10 Unable To Do
Turn a door knob using my affected hand	0	1	2	3	4	5	6	7	8	9	10
Cut meat using a knife in my affected hand	0	1	2	3	4	5	6	7	8	9	10
Fasten buttons on my shirt	0	1	2	3	4	5	6	7	8	9	10
Use my affected hand to push up from a chair	0	1	2	3	4	5	6	7	8	9	10
Carry a 10lb object in my affected hand	0	1	2	3	4	5	6	7	8	9	10
Use bathroom tissue with my affected hand	0	1	2	3	4	5	6	7	8	9	10

B. USUAL ACTIVITIES

*Rate the **amount of difficulty** you experienced performing your **usual** activities in each of the areas listed below, over the past week, by circling the number that best describes your difficulty on a scale of 0-10. By "usual activities", we mean the activities you performed **before** you started having a problem with your wrist. A **zero** (0) means that you did not experience any difficulty and a **ten** (10) means it was so difficult you were unable to do any of your usual activities.*

Personal care activities (dressing, washing)	0	1	2	3	4	5	6	7	8	9	10
Household work (cleaning, maintenance)	0	1	2	3	4	5	6	7	8	9	10
Work (your job or usual everyday work)	0	1	2	3	4	5	6	7	8	9	10
Recreational activities	0	1	2	3	4	5	6	7	8	9	10

Fig. 1. Patient-rated wrist evaluation test.

Table 1
The demographic and clinical features of the patients.

	Age (mean)	Sex (M/F)	Side (R/L)	Frykman classification
Case ($n = 15$)	32.33	12/3	3/12	Type 3: 11 Type 4: 3 Type 7: 1
Control ($n = 15$)	33.4	13/2	7/8	Type 3: 10 Type 4: 4 Type 7: 1
P-value	0.776	1	1	1

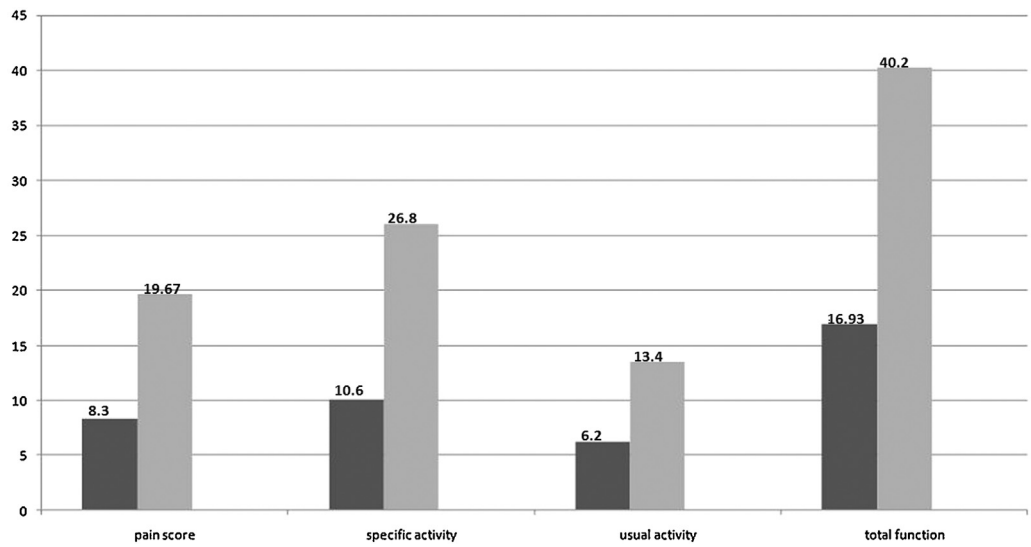

Fig. 2. Scores of pain, usual and specific activities in 3 months follow-up in the two groups. Black: the case group; gray: the control group.

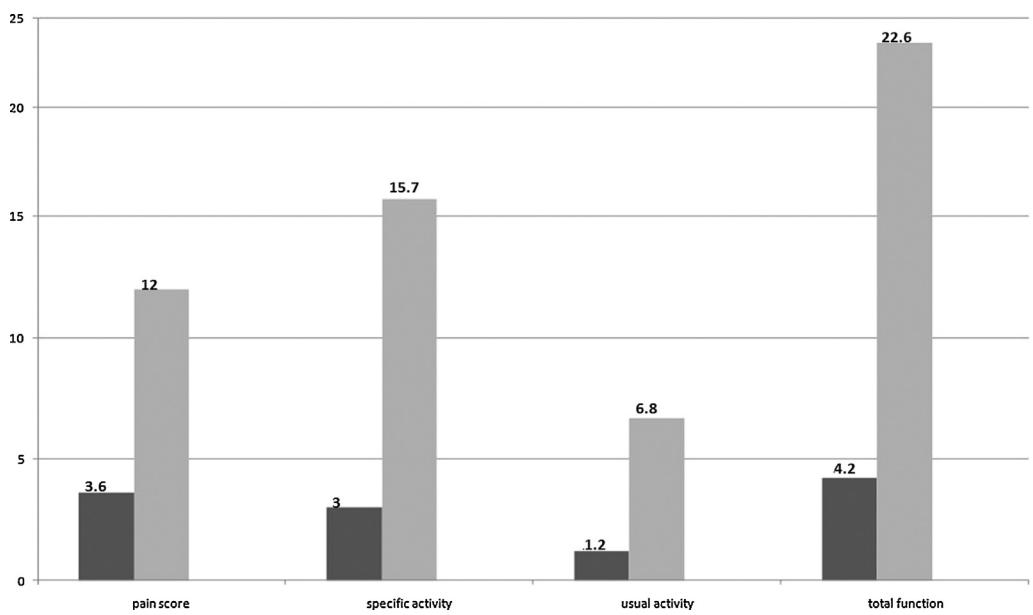

Fig. 3. Scores of pain, usual and specific activities in 6 months follow-up in the two groups. Black: the case group; gray: the control group.

The present study had two principal objectives:

- to investigate if PRP intervention can reduce pain and improve function by using the patient self-reported PRWE questionnaire;
- to identify the potential increase of range of motion after PRP treatment.

The pain is the main disabling factor following distal radius fracture [19].

Results of our study showed that PRP injection provide significant improvement in PRWE for pain. The pain after PRP injection has significantly decreased but was still not pain free. Although the entire control group was satisfied with this result, it remains a point

Table 2
Scores of pain, usual and specific activities in 3 and 6 months follow-up in the two groups.

	Pain (3 m)	Pain (6 m)	Specific activity (3 m)	Specific activity (6 m)	Usual activity (3 m)	Usual activity (6 m)	Total function (3 m)	Total function (6 m)
Case ($n = 15$)								
Mean	8.33	3.6	10.66	3	6.2	1.2	16.93	4.2
Max	13	5	22	5	13	3	35	7
Min	7	3	5	1	1	0	10	2
Control ($n = 15$)								
Mean	19.67	12	26.8	15.7	13.4	6.8	40.27	22.66
Max	31	25	40	32	24	20	64	52
Min	16	8	24	9	12	4	36	14
P-value	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001

Table 3
Loss of range of motion in 3 and 6 months follow-up in the two groups.

	Flexion loss (3 m)	Flexion loss (6 m)	Extension loss (3 m)	Extension loss (6 m)	Radial deviation loss (3 m)	Radial deviation loss (6 m)	Ulnar deviation loss (3 m)	Ulnar deviation loss (6 m)	Supination loss (3 m)	Supination loss (6 m)	Pronation loss (3 m)	Pronation loss (6 m)
Case ($n = 15$)												
Mean	3.3	2	3	1.3	1	0	1.6	0.6	6.6	4.3	1.3	0.3
Max	20	10	20	10	10	0	10	5	40	30	10	5
Min	0	0	0	0	0	0	0	0	0	0	0	0
Control ($n = 15$)												
Mean	12	6.6	8	3.3	0.6	0.3	2	2	15.3	10.6	7.3	3.3
Max	30	20	20	20	5	5	10	10	40	30	30	20
Min	0	0	0	0	0	0	0	0	0	0	0	0
P-value	0.011	0.106	0.045	0.624	0.967	0.775	0.967	0.683	0.217	0.305	0.161	0.325

of interest. Repeated PRP injections might be beneficial for patients who had suboptimal results. This confirms reports by other authors that suggest an improved pain following local administration of growth factors through PRP injections [20,21].

The possible explanation of the novel effect of PRP in decreasing pain and disability following distal radius fracture may be attributed to its immunomodulatory effect. The disabling pain may be related to increased production of the local inflammatory mediators [22]. Interleukin-1beta (IL-1b) mediates the development of the CRPS through activation of cyclooxygenase-1 (Cox-1) and cyclooxygenase-2 (Cox-2). This upregulation of Cox-1 and Cox-2, which converts arachidonic acid into prostaglandin, leads to increased production of prostaglandin E2 (PGE2). PGE2 not only causes vasodilation and hyperalgesia, but also increases the amount of substance P, which is a major pain transmitter. PRP, which contains high levels of IL-1receptor antagonist, effectively inhibits IL-1. In addition, PRP contains high levels of hepatocyte growth factor (HGF), which is also decreases production of Cox-1, Cox-2, PGE2 through disruption of transcription factor NF-kb signalling [23–25].

This study has some limitations. Our sample size is low. So, it is better that the result of our study examed by another larger study. Also, it is better that the follow-up have continued until at least 1 year post-injury, since it is known that some measured parameters of wrist fracture outcome may continue to change up to and beyond 1 year post-injury.

The strength of this study is that there are no similar studies that have examined the use of PRP in the management of distal radius fractures.

According to this study, intra-articular PRP injection is a valid additional treatment in distal radius fracture. PRP may have significant effect on reduction of pain after intra-articular distal radius fractures and reduction of amount of difficulty in functions, including specific and usual activities in 3 months and 6 months follow-up.

It is believed that this attempt will provide a new insight into the effect of PRP and stimulate a multiplicity of later clinical investigations on the utility of this agent in distal radius fracture, leading to provision of better treatment to patients suffering from this conundrum.

All patients gave the informed consent prior to being included into the study. All procedures performed in studies involving human participants 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.

Disclosure of interest

The authors declare that they have no competing interest.

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