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Original Research Paper

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PLATELET RICH PLASMA IN DELAYED UNION FRACTURE OF LONG BONE (A PROSPECTIVE STUDY OF 25 CASES)

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ABSTRACT

Background: Functional outcome of infiltration of autologus platelet rich plasma (PRP) in delayed union of long bones. **Designe:** Prospective clinical study with 6 months of follow-up. **Methods:** Clinically proven 25 patients of delayed union were included in this study according to inclusion and exclusion criteria after getting written and informed consent, treated by autologous PRP infiltration thrice 1 weeks apart, evaluation done clinically as well as radiologically. **Results:** Out of twenty five patients, union was achieved in 21 patients (84%) at the end of six months, 4 cases progressed to non-union.The mean time between PRP injection & Union was 12.2 weeks. Final assessment was done according to RUS score at 6 months of follow-up Most of the patients 72% (18 patients) were in Excellent category, 12% (3 patients) were in Fair category and 16% (4 patient) was in poor category.

Conclusion: Autologus Platelet rich plasma infiltration locally is effective method in the treatment of delayed union of long bone fractures.

KEYWORDS : platelet rich plasma, delayed union, long bones.

INTRODUCTION:

Incidence of Delayed union of fractures occurs in 5% to 10% of long-bone.[1] Early recognition of delayed or nonunion improves outcomes and prevents further anxiety and disability for the patient. Delayed union, by definition, is present when an adequate period of time has elapsed since the initial injury without achieving bone union. The fact that a bone is delayed in its union does not mean that it will become a non-union. Non-union is one of the end results of a delayed union, and the differentiation between the two is sometimes difficult to make[2].

Classically the stated reasons for delayed union are problems such as Inadequate reduction, inadequate immobilization, distraction, loss of blood supply, and infection .[3] It has many other causes including bone or soft tissue loss, soft tissue interposition, pathological fracture, poor splintage or fixation, and fracture distraction. Risk factors include NSAIDs, Cigarette Smoking, infection, thyroid imbalance, hyperparathyroidism (primary hyperparathyroidism presenting as delayed fracture union).

PRP is a particularly attractive source of growth factors. It is easily obtained from the patient's own blood. Its factor levels are approx. 8-fold higher than those of peripheral blood, thus facilitating wound and tissue healing.

MATERIALS AND METHODS

The study was conducted on 25 patients with Delayed Union of Long bones at the Department of Orthopaedics, Sardar Patel Medical College, Bikaner. It was a prospective study with the duration of the follow-up being 6 months. Patients aged between 18-50 years of either sex were included in the study. The patients who had clinical and radiological signs of delayed union were included in the study. The study design was discussed with every selected patient and his/her written consent was taken prior to commencement of the study.

Following were selection criteria.

(A) INCLUSION CRITERIA

- Patients with the age group of 15 – 55 years.
- The patients who had clinical and radiological signs of delayed union after 3 months of the initial injury.

(B) EXCLUSION CRITERIA

- Patients with platelet counts of less than 150,000 per micro litter.
- Patients with haemoglobin measures of less than 10g/dl.
- Patients with Active inflammatory disease.
- Patients with any recent febrile or infectious disease.
- Patients with history of any malignancy (including hematologic and non hematologic malignancies), Diabetes Mellitus, Pregnant woman.
- Patients with history of autoimmune and platelet disorders, treatment with anticoagulant and anti platelet medications 10 days before injection, Patients with consistent use of NSAIDs within 48 hours before procedure and use of systemic steroids during past 3 months.
- Patients with infected non union.

Mechanism of PRP

Whenever any damage occurs, healing process takes place. Healing occurs in three phases: Inflammation, proliferation and remodeling. Alpha granules of platelets contain various growth factors, such as Platelet-derived Growth Factor (PDGF), Transforming Growth Factor Beta (TGF-□), vascular endothelial growth factor, Insulin-like Growth Factor-1 (IGF-1), hepatocyte growth factor, and Fibroblast Growth Factor (FGF), which accelerate mitosis, vasculogenesis, and differentiation. PRP has an exclusive combination, which helps in healing process through the concentration of inflammatory mediators. PRP also has an antimicrobial effect, which helps in wound healing process.

PRP preparation

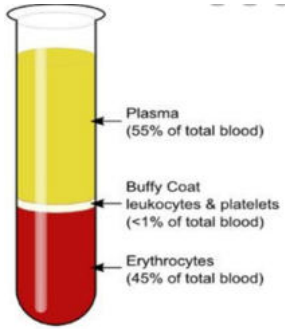
PRP is prepared by a process known as differential centrifugation. In differential centrifugation, acceleration force is adjusted to sediment certain cellular constituents based on different specific gravity. In our institute, The PRP required for injection was prepared by the Multi Disciplinary Research Unit, Sardar Patel Medical College , Bikaner. There are many ways of preparing PRP. It can be prepared by the PRP method or by the buffy-coat method. In my study PRP was prepared with PRP method. In the PRP method- 40 cc of venous blood was collected from anti-cubital vein under aseptic conditions into four, 10 cc ACD (acid citrate dextrose) containing vaccutaner tubes; All tubes were placed in

centrifuge machine in such a way that each of them was counter balanced by another.

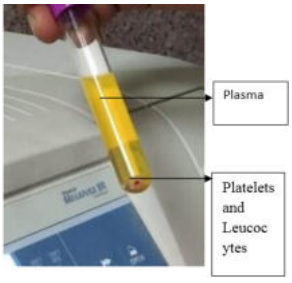
1. FIRST SPIN: After placing the tubes in centrifuge machine they were centrifuged at 1800 rpm for 5 minutes.
2. Blood in the all four tubes was separated into 3 layers after first spin.

A. Upper layer that contains mostly platelets and WBC,
B. Intermediate thin layer that is known as the buffy coat and that is rich in WBC
C. Bottom layer that consists mostly of RBCs.

3. With the help of Micropipette the serum and the buffy coat (leucocytes and platelets) was drawn from the each tubes into another 10 cc tube. Thus, total 20 cc of plasma was obtained, which was divided into two tubes of 10 cc each. These two tubes were modified and capped to fit into the centrifuge machine.
4. **SECOND SPIN:** After placing the tubes in centrifuge machine, centrifuged again at 4500 rpm for 10 minutes.



After first spin



After 2nd spin

After second spin the tubes contains platelet poor plasma on top and platelets and leucocytes at bottom. The supernatant was drawn and discarded leaving about 3.5 cc at the bottom as platelet rich fraction of plasma. Similarly, 3.5 cc of platelet rich plasma was obtained from second tube. In total 7 cc of platelet rich plasma was available, of which 6 cc injected at fracture site under aseptic conditions and 1cc is sent for culture and cell counts.

Procedure Of Infilteration

2 ml lignocain local Anaesthesia was injected at the fracture site (after sensitivity test). The platelet concentrate was transferred to a 10cc syringe, 18G long stainless steel needles was inserted to the delayed union site under C-arm guidance , micro trauma was incited at the site by multiple pricks. The platelet concentrate was infiltrated into the delayed union site. Three injection of PRP was infiltration in all cases at interval of 1 week.

Observation

RUS Scoring, which is based on the visibility of fracture line and presence or absence of callus on plain radiographs after a period of six months from the initial infiltration of PRP was observed.

Male 88% and Female 12%.The age distribution that showed predominant delayed union in our study was found to be 18-25yrs (48%) and the least was found to be in 36-45 and 46-55yrs (12% each). We also noticed that most of cases of delayed union were of fracture Tibia bone that was 64%, 28% cases of femur shaft and only 4% cases of delayed union of fracture Humerus and Ulna each. We also noted occupation of patient in which maximum patient with Delayed union fracture were Farmer (56%) and minimum were student (4%). Other factors of Non union and Delayed union include NSAIDs, Cigarette Smoking, Tobacco chewing, infection, thyroid imbalance, hyperparathyroidism (primary hyperparathyroidism presenting as delayed fracture union). Mean Platelet concentration in blood was 2.45 lac/ml and Mean platelet concentration in PRP was 10.9 lac/ml. Platelet concentration was increased by 4-5 times by centrifugation machine. We didn't use WBC filter.

DISCUSSION

In the treatment of delayed union the biological and mechanical factors should be evaluated first. After achieving mechanical stability with internal or external fixation, an attempt is made to achieve union with grafts, growth factors or with physical means. There are many cause of delayed union. One of them is low concentration of Growth factor. Early attempts at using PRP in the treatment of bone defects were made by oral and maxillofacial surgeons in 1994. Marx et al. achieved greater mandibular density in patients who had received PRP (74%/55.1%).[4,5] Platelet Rich Plasma (PRP) stimulates natural healing process through growth factors contained in the platelets. PRP applied to the fracture site accelerates the physiological healing process, provides support for the connection of cells, reduces pain and has an anti-inflammatory and anti-bacterial effect. Both plasma and its preparation contain growth factors that play a role during the initial phase of healing and bone regeneration. The primary growth factors involved in bone regeneration are platelets (platelet-derived growth factor – PDGF), transforming growth factor beta – TGF-β, insulin-like growth factor-1 – IGF-1, and the epidermal growth factor – EGF[6,7].

25 cases of Delayed union Fracture of Long Bone which were infiltrated with 3 doses of Platelet Rich Plasma (PRP) at weekly interval and followed up to six months post-infiltration. At six month we assessed the cases clinically, radiologically and used RUS score for final outcome. RUS Scoring, which is based on the visibility of fracture line and presence or absence of callus on plain radiographs after a period of six months from the initial infiltration of PRP.

The age distribution showed predominant delayed union in 26-35yrs (40%) age group and the least was found to be in 36-45 and 46-55yrs each (12%) age groups, which was in close correlation with the studies of Justynagolos *et al*.[8] (41 years), Deepak chaudhary *et al*.[9] (32 years) and Hladki *et al*.[10] (39 years)

Table no. 2: Age Incidence

Study	**Mean age of the patients**	**Range**
Our study	29.8 years	15-55 years
Justynagolos *et al*.[8]	41 years	16-85 years
Deepak Chaudhary *et al*[9]	32 years	19-57 years
Hladki et al.[10]	39 years	15-65 years

There was a male predominance with 22 patients being male accounting for 88% and 3 patients were female accounting for 12%, which is in correlation with other studies.

We examined the case clinically for Tenderness and we observed that almost all cases had mild to moderate tenderness over fracture site.We also examined for mobility at fracture site in two plane. There was negligible mobility at fracture site.

After clinical and Radiological assessment we infiltrated autologous PRP. We had given 3 consecutive doses at weekly interval. After that followed up at 4th, 8th, 16th and 24th week. At final followed up at 6th month.

In our study the mean duration between the primary surgery and diagnosis of delayed union and PRP infiltration was 4.2 months, and the efficacy of PRP infiltration after a six month follow up was found to be 88% union, which is in correlation with the studies of Justynagolos *et al*[8], Deepak Chaudhary *et al*[9], Stanton *et al*[11] and Say *et al*[13]. where mean duration of delayed union after primary surgery was about 4.05 months, 4.8 months, 4 months and 7.2 months respectively and union was seen in 81.8%, 88.3%, 90% and 30% cases respectively.

Table no. 3 : Union rate

Study	**Mean time interval between primary surgical treatment and diagnosis of delayed union**	**The efficacy of PRP infiltration**
Our study	4.8 months	88% union
Justynagolos *et al*.[8]	4.05 months	81.8% union
Deepak chaudhay *et al*[9]	4.8 months	83.3% union
Stanton *et al*.[11]	4 months	91.7% union
Bielecki *et al*.[12]	<11 months	100% union
Say et al.[13]	7.2 months	30% union

We found that 22 patients out of 25 who had PRP infiltration for three times, 1 weeks apart and followed up with X-Rays after six months showed excellent results of union according to the RUS Score which is 88% and is in correlation with other studies i.e. Justynagolos *et al*[8] Deepak chaudhay *et al*[9], Stanton *et al*.[11]

We examined patient for Tenderness and mobility at fracture site in our follow up. It was decreasing with time. At 4th week tenderness present in 21 patients and at 6 months none case had tenderness. None patient had mobility at fracture site.

According to radiological assessment we noticed that all cases had scanty callus formation at 4th week. It was in increasing manner. At 24th week , 21 patients had good callus formation at fracture site.Mean duration of union after PRP infiltration 3.12 months.We didn't get effect of PRP in 4 patients (12%). They had to go further operative management.

Before PRP

After PRP at 24 week

First case was a 30 year/Male patient with Delayed Union of Fracture Tibia middle 1/3rd treated with closed reduction and IM nail and was infiltrated with PRP 3.5 months following primary surgery and had no Co-morbidities and no addictions which would hinder the union. The IM nail had only static screw, dynamic screw was not inserted during surgery because patient earlier had ACL Reconstruction & the Interference screw of ACL Reconstruction hindered the site of dynamic screw due to which dynamization was not possible at fracture site.

Second case was patient a 25 year/Male patient with Delayed Union of severely comminuted # Supracondylar Humerus operated with open reduction & reconstruction plate fixation and was infiltrated with PRP 3.25 months following primary surgery. There was severe comminution at # site with intra-articular extension which might hinder the union rate significantly.

Third case was a patient 55 year/Male with Delayed Union of Fracture Tibia middle 1/3rd treated with closed reduction and Intramedullary interlocking nail and was infiltrated with PRP 3.5 months following primary surgery. The patient was a chronic smoker and alcoholic which might hinder the union rate significantly.

Fourth case was a 25 year/Male patient with Delayed Union of Fracture Tibia upper 1/3rd treated with open reduction and Upper Tibia lateral locking plate fixation and was infiltrated with PRP 3.5 months following primary surgery and had no Co-morbidities and no addictions which would hinder the union. The reason for Nonunion could not be established.

CONCLUSION

Platelet rich plasma infiltrated locally are effective in the treatment of delayed union of long bone fractures.

Platelet rich plasma is simple method. It can easily prepared by withdrawing blood. It is easy procedure by which we can infiltrated PRP abstract at fracture site without any specific instrumentation and without general anaesthesia. Results of PRP in is effective in delayed union fracture of long bone. It can be used as a therapeutic option for bone union.

It is cost effective treatment option for bone union.

Limitations Of Study

- During preparation of PRP, we did not used WBC filter. It could be better results if we used WBC filter.
- The study did not have any control group.
- This study had small numbers of patients where future studies are required to find out conclusion.

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