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The role of platelet rich plasma in delayed union of long bones

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Abstract

Objective: To assess functional outcome of infiltration of platelet rich plasma (PRP) in delayed union of long bones.

Design: Prospective clinical study with 6 months of follow-up.

Methods: Clinically proven 25 patients of delayed union were included in study according to inclusion and exclusion criteria after getting written and informed consent, treated by autologous PRP infiltration thrice 4 weeks apart, evaluation done clinically as well as radiologically (At baseline and 6 month interval).

Results: Out of twenty five patients, union was achieved in 22 patients (88%) at the end of six months, 2 cases progressed to non-union and one patient was lost for follow-up.

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

Keywords: role, platelet rich, plasma, delayed union, long bones

Introduction

Delayed union, by definition, is present when an adequate period of time has elapsed since the initial injury without achieving bone union. Bone healing, or fracture healing is a proliferative physiological process in which the body facilitates the repair of a bone fracture [1, 2, 3].

For normal fracture healing to occur a number of requirements must be met e.g.: Viability of fragments (i.e. intact blood supply), mechanical rest this can be achieved by not moving and external immobilization, e.g. cast or internal fixation and absence of infection. The process of healing is different depending on the configuration of the fracture fragments and can be divided into three main categories (i) spontaneous (indirect/secondary) healing, (ii) contact (angiogenic/primary) healing (iii) gap healing [1, 3, 4]. Fracture healing is a complex physiological process involving a coordinated interaction of hematopoietic and immune cells within the bone marrow, in conjunction with vascular and skeletal cell precursors [5]. Several different cytokines and growth factors play role in healing of a fracture [6]. Delayed union is a fracture that requires more time than standard to heal but over time it shows progression toward healing [7].

Average healing times of common fractures are as follows Phalanges (3 weeks), metacarpals(4-6 weeks), Distal radius (4-6 weeks), Lower arm(8-10 weeks), Humerus (6-8 weeks), Femoral neck (12 weeks), Femoral shaft (12 weeks), Tibia (10 weeks) [1, 4]. Non-union is defined by the United States Food and Drug Administration as established when a minimum of nine months has elapsed since injury and the fracture shows no visible progressive signs of healing for three months [4, 8]. Non-union is generally classified as hypertrophic, oligotrophic or atrophic according to the radiological appearance [4, 8]. Atrophic non-union is characterized by little or no callus and resorption in the bone ends while in oligotrophic and hypertrophic non-union, blood flow is sufficient and an excessive amount of callus is seen. Insufficient mechanical stability is a reason which leads to non-union [9]. In the treatment of delayed union or non-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 [7].

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Platelet Rich Plasma (PRP) stimulates natural healing process through growth factors contained in the platelets. PRP applied to the wound area accelerates the physiological healing process, provides support for the connection of cells, reduces pain and has an anti-inflammatory and anti-bacterial effect.^[10] Studies in literature have reported the use of PRP in the treatment of nonunion^[11, 12, 13, 14].

Materials and Methods

The study was conducted on 25 patients with Delayed Union of Long bones at the Department of Orthopaedics, Kempegowda Institute of Medical Sciences Hospital and Research Centre, Bengaluru.

It was a prospective study with the duration of the study being 18 months. Patients aged between 18-65 years of either sex were included in the study. The patients who had clinical and radiological signs of delayed union at the end of 5 months after the initial surgery were included in the study.

Patients with pathological fracture and established nonunion were excluded from the study.

The study design was discussed with every selected patient and his/her written consent was taken prior to commencement of the study.

Patients were evaluated with standard AP and lateral views.

Mechanism of PRP

Whenever any damage occurs, healing process takes place. Healing occurs in three phases: Inflammation, proliferation and remodeling^[15]. Alpha granules of platelets contain various growth factors, such as Platelet-derived Growth Factor (PDGF), Transforming Growth Factor Beta (TGF-β), 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^[16]. PRP has an exclusive combination, which helps in healing process through the concentration of inflammatory mediators^[15]. PRP also has an antimicrobial effect, which helps in wound healing process. In spite of its beneficial effects, PRP is less likely used by healthcare professionals because of its high cost^[16].

Preparation of PRP

One unit of autologous blood is collected from the patient in a blood donation bag. The platelets are separated by triple centrifugation technique. This separates whole blood into packed cells (sediment), plasma and platelet concentrate (supernatant). The platelet concentrate is kept in the agitator, to avoid clumping, till it is used. Packed cells are transfused back to the patient. About 25-50ml platelet concentrate is separated per unit of whole blood. The procedure of preparation of platelet concentrate is done in the blood bank. The platelet concentrate thus obtained, should be used within 72 hours after the collection^[17].

Infiltration Method

All infiltrations are done either under sedation or short anaesthesia in the operating room under strict aseptic conditions. The platelet concentrate is transferred to a 50cc syringe. 18G or 20G long stainless steel needles are used for the infiltration (Fig. 1). Needle is inserted to the delayed union site under C-arm guidance (Fig. 2), micro trauma is incited at the site by multiple pricks. The platelet concentrate is infiltrated into the delayed union site^[17].



Fig 1: The centrifugation machine used in the study

In our study we prepared PRP on the day of surgery and infiltration was done under local anaesthesia under the guidance of C-ARM in the operation theatre.



Fig 2: Infiltration under C-Arm Guidance

Discussion

In our study we used Modified 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.

There was a male predominance with 23 patients being male accounting for 92% and 2 patients were female accounting for 8%, which is in correlation with other studies. The injured side in our study was right side in 13 patients (56%) and left side in 12 patients (44%).

Table 1: Sex Incidence

	Sex	
	Males	Females
Our Study	23 (92%)	2 (8%)
Justynagolos <i>et al.</i> ^[18]	79 (59.85%)	53 (40.15%)
Deepak Chaudhary <i>et al.</i> ^[19]	5 (83%)	1 (17%)

The age distribution that showed predominant delayed union in our study was found to be 35-44yrs (40%) age and the least was found to be in 45-54 and 55-64yrs (8%) age groups, which was in close correlation with the studies of Justynagolos *et al.* (41 years), Deepak chaudhary *et al.* (32 years) and Hladki *et al.* (39 years).

Table 2: Age Incidence

	Mean age of the patients	Range
Our Study	35.4 years	18-65 years
Justynagolos <i>et al.</i> ^[18]	41 years	16-85 years
Deepak Chaudhary <i>et al.</i> ^[19]	32 years	19-57 years
Hladki <i>et al.</i> ^[20]	39 years	-

In our study the duration between the primary surgery and diagnosis of delayed union and PRP infiltration was a mean of 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.*, Deepak Chaudhary *et al.*, Stanton *et al.* and Say *et al.* where mean duration 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. Our study deviates from Bielecki *et al.* studies where mean duration after primary surgery was <11 months and efficacy was 100%.

Table 3: Union Rate

	Mean time interval between primary surgical treatment and diagnosis of delayed union	The efficacy of PRP infiltration
Our study	4.2 months	88% union
Justynagolos <i>et al.</i> [18]	4.05 months	81.8% union
Deepak chaudhary <i>et al.</i> [19]	4.8 months	83.3% union
Stanton <i>et al.</i> [21]	4 months	91.7% union
Bielecki <i>et al.</i> [22]	<11 months	100% union
Say <i>et al.</i> [23]	7.2 months	30% union

In our study we found that 22 patients out of 25 who had PRP infiltration for three times, four weeks apart and followed up with X-Rays after six months showed excellent results of union according to the Modified Rus Score which is 88% and is in correlation with other studies.

In our study we have two patients who went in for Nonunion and one case was lost for follow up after two infiltrations.

First case which went in for Non Union was a 32 year/Female patient with Delayed Union of Fracture shaft of Femur middle 1/3rd treated with closed reduction and IMIL nail and was infiltrated with PRP 5 months following primary surgery and had no Co-morbidities and no addictions which would hinder the union. The patient was walking without pain and was hesitant for further management. The reason for Nonunion could not be established.

Second case which went in for Non Union was patient a 25 year/Male patient with Delayed Union of Fracture shaft of Femur middle 1/3rd treated with closed reduction and IMIL nail and was infiltrated with PRP 4 months following primary surgery. The patient was a chronic smoker and alcoholic which might hinder the union rate significantly. This patient was treated with Exchange Nailing and union was achieved eventually.

The other case which was lost in follow up was a 54 year/Male patient with Delayed Union of fracture shaft of Tibia distal 1/3rd treated with closed reduction and IMIL nail and was infiltrated for two times and lost in further follow up.

Conclusion

- Platelet rich plasma growth factors infiltrated locally are effective in the treatment of delayed union of long bone fractures.
- The highest incidence of delayed bone union was seen after surgical treatment of femur shaft middle 1/3rd fractures and distal tibial fractures by closed reduction and intramedullary nail fixation
- Infiltration of PRP into the fracture cleft was most effective in the patients with bone union disturbances after middle 1/3rd femur shaft fractures.
- Platelet rich plasma infiltrated locally is effective in the treatment of delayed union of long bone fractures.

Illustrations: Case No.1

**Fig 3:** Case 1

Case No. 2

**Fig 4:** Case 2

Case No. 3

**Fig 5:** Case 3

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