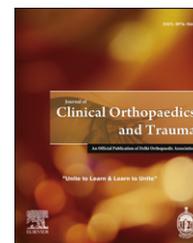


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Original Article

Platelet rich plasma therapy: A comparative effective therapy with promising results in plantar fasciitis

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ABSTRACT

Chronic muscle & tendon injuries are one of the problems which are encountered by human being since last long time. These injuries are generally repetitive strain injuries, commonly found in athletes. There are various treatments which include conservative methods in initial stages to surgery in later stages. On minimal invasive aspect Ultrasound-guided fenestration and tenotomy surgery has been used with good results as an effective treatment of chronic tendinopathies.^{1,2} There are various injectable agents which were also researched including simple solutions such as hyperosmolar dextrose³ (prolotherapy) to complex orthobiologic agents such as bone morphogenic protein,⁴ but none have achieved uniform success. Platelet rich plasma (PRP) injection has emerged as a treatment alternative for many musculoskeletal conditions. We have done this study on sixty patients to evaluate & compare the effects of platelet rich plasma & steroid injection on patients with planter fasciitis. The results at the 1, 3 & 6 months were evaluated, which showed the good results with platelet rich plasma in comparison to steroid injections.

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Chronic muscle & tendon injuries are one of the problems which are encountered by human being since last long time. These injuries are generally repetitive strain injuries, commonly found in athletes. There are various treatments which include conservative methods in initial stages to surgery in later stages. On minimal invasive aspect Ultrasound-guided fenestration and tenotomy surgery has been used with good results as an effective treatment of chronic tendinopathies.^{1,2}

There are various injectable agents which were also researched including simple solutions such as hyperosmolar dextrose³ (prolotherapy) to complex orthobiologic agents such as bone morphogenic protein,⁴ but none have achieved uniform success.

The planter fasciitis is one of the degenerative chronic tendinopathy which is seen in athletes & general population. There is inflammation of thick band of tissue which attaches to the calcaneum. There are microtears at the junction of bone & fascia. These tears can be there due to sudden weight gain, long distance running, flat shoes, improper shoe inserts, tight tendo Achillis, etc. These microtears are the root cause of problem.

Healing of these microtears are associated with relief in problem.

Platelet rich plasma (PRP) injection has emerged as a treatment alternative for many musculoskeletal conditions including planter fasciitis. At present the planter fasciitis is

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treated by weight reduction, changes in shoes, shock wave therapy, NSAID, controlled ankle motion (CAM), local steroid injections, etc. In recent years the PRP has emerged with its implication in various fields including planter fasciitis.

Although concentrated platelet therapy, which includes PRP, has been used for 20 years, it has recently gained popularity due to its effectiveness in treating ailments of American professional football player and their accelerated return to play & glittering victory in the 2009 Super Bowl.⁵ Various authors have done studies over the use of PRP in planter fasciitis but there is no study which shows its comparable effectiveness to other agents. In this study we have tried to represent the comparable efficacy of PRP over steroid (which is a very common agent used to treat planter fasciitis). The autologous PRP do not have side effects (like steroid like tear of the tendon or fibers in long run).

1. PRP

Defined as a platelet concentration higher than the physiologic platelet concentration found in healthy whole blood.^{6,7}

A more objective definition of five times the platelet concentration of whole blood.⁸ The ability to concentrate platelets allows a higher concentration of the bioactive growth factors reported to promote healing.

The average platelet concentration of whole blood is 200,000 per μl (normal range 150,000–350,000 per μl).⁷ Platelets are small anucleated cytoplasmic fragments of megakaryocytes that are commonly thought of as the responsible agents for hemostasis. Although the platelet is central to the coagulation cascade, it is also essential to tissue healing. The first step of the healing process is clot formation and platelet activation.⁷ Many growth and differentiation factors are released from the α -granules, which are the storage units found in platelets.⁹ 95% of the existing factors are released within 10 min of clot formation, whereas the rest of the growth factors are released as they are formed over several days.¹⁰ In vivo and in vitro researches also suggest that PRP induces over expression of additional endogenous growth factors beyond what is contained within the platelet concentrate.^{11,12}

1.1. Mode of action

The potential benefits of PRP are thought to rely on intrinsic properties and interplay between the concentrated growth factors.^{6–8,13} Some of these important growth factors include platelet derived endothelium growth factors, transforming growth factors- β , vascular endothelium growth factors, fibroblast growth factors, epidermal growth factor and insulin like growth factor-1. Complex interaction of this growth and differentiation factors, along with adhesive protein factors such as fibronectin and vitronectin are what is responsible for the healing response, promoting the long regenerative process of chemotaxis, cell proliferation, removal of tissue debris, angiogenesis, extracellular matrix formation, osteoid production and collagen synthesis.^{7,8,14,15}

The needle induced bleeding during injection provide the clotting factor thrombin needed to activate platelets. Needle

penetration of tendon may also be considered before the PRP injection. Exposure to within the tissue further activates platelets. Bovine thrombin, calcium or soluble type-1 collagen has also been used to activate platelets but usually in the intraoperative settings.¹⁶

Four categories of platelet concentrate preparation are recognized:

1. leukocyte-poor or pure platelet rich plasma
2. leukocyte platelet rich plasma
3. pure platelet-rich fibrin clot
4. leukocyte platelet-rich fibrin clot.¹³

Factors such as centrifugation force and duration of centrifugation can yield different platelet concentration levels and composition. However, each has different biological effects and potential uses. To our knowledge, no evidence, no evidence-based classification scheme or guidelines specifying optimal use has been reported.

1.2. Clinical applications

Bone healing in oral maxillofacial surgery, Post operative wound healing, Post operative rotator cuff repair integrity in orthopedic surgery. The positive effects in these intraoperative applications have stimulated the use of PRP in the sports medicine outpatient clinic setting, mostly for chronic tendinopathies and often in a collaborative setting involving a musculoskeletal radiologist who assists in diagnosis, imaging-guided injection of PRP and follow up.

1.3. Wound healing process

Involves an intricate process that is often categorized into three overlapping phases: inflammation, proliferation and remodeling. Once tissue injury occurs, a hematoma forms at the site of tissue damage, platelets adhere to expose collagen creating a clot and inflammatory phase begins with activation of platelets resulting in release of growth bioactive and hemostatic factors.¹⁷ Each factor plays a unique but codependent role in the early stages of intrinsic and extrinsic pathways of clotting cascade. Access to the wound site by neutrophils and macrophages occurs within hours of injury and likely serves to provide phagocytosis of tissue debris.¹⁸ Within a few days of injury the proliferative phase begins that is characterized by angiogenesis, collagen deposition, granulation tissue formation, epithelialization and wound contraction. Finally spanning from several weeks to months after an injury, the remodeling phase involves collagen maturation and apoptosis of excess cells.^{19–21}

1.4. Results of various studies

The first published in vitro study showed that PRP stimulated the proliferation of cells such as osteoblasts, fibroblasts, tenocytes, chondrocytes and mesenchymal stem cells.^{4,13,16,22,23}

Lucarelli and colleagues²⁴ showed that PRP had a positive effect on human stem cell proliferation and markedly increased cell numbers with increasing PRP concentration

from 1% to 10%. Another in vitro study of cultured human tenocytes showed that PRP promoted tendon regeneration by inducing proliferation and total collagen production.²⁵ However, other in vitro studies have reported contrasting results.²⁶ The ability of PRP to differentiate cell lines is also controversial. One study showed that PRP can stimulate stem cell differentiation into osteoblast, but others had mixed results.²⁷

Several animal studies using PRP have produced promising results. Bone healing was enhanced with respect to stronger callus formation in rabbit calvaria defects and in mandibular reconstruction in goats.^{28,29} The mechanism, according to Tomoyasu and colleagues,²⁷ may be from a positive effects of PRP on osteoblastic differentiation.

There are drawbacks of local injection of steroids at heel: mainly rupture of the plantar fascia and atrophy of the fat pad.^{1,17} In an observational study, Acevedo and Beskin³⁰ reported a plantar fascial rupture rate of 10% in patients after steroid injection for heel pain. Another drawback in the extreme pain experienced by some patients during an infiltration of the tissues surrounding the calcaneum.

2. Methods

Our study was done at the Orthopaedic Department of NIMS Medical College, Jaipur (Rajasthan). This study was conducted between Dec. 2010 and Oct. 2011. After approval from ethical committee total sixty patients were included in study after screening & exclusion from diagnosed planter fasciitis patients. These sixty patients were randomly divided in two groups, each was having thirty patients. Out of this, thirty patients were given PRP therapy while the rest thirty were given local steroid injection. The patients included in our study were more than the eighteen years old, have pain and tenderness centered on the medial tubercle of the calcaneum on weight bearing after rest which resolved, either partly or fully, after activity. Patient using orthoses, insoles, pads were also included in our study.

The patients who were excluded from PRP study were those who received local steroid injection within 6 months, non-steroidal anti inflammatory therapy within one week prior to therapy. Patients who were having significant cardiovascular disease, renal or hepatic disease, pregnancy, any local malignancy, anemia (Hb < 5 gm%), previous surgery for planter fasciitis, diabetes, hypothyroidism, diagnosis of vascular insufficiency or neuropathy were also not included in this study. All patients were gone thorough clinical examination followed by basic investigations (to exclude anemia, diabetes, active infections, liver disorders) & thyroid function tests. Patients were explained about the procedure and there written consent was obtained. In one group about 30-50 ml of venous blood is obtained from the antecubital vein with aseptic technique. An eighteen or nineteen gauze needle was used. In this blood appropriate amount of anticoagulant (about 7 ml of ACD-A) is mixed.

There are variety of systems used to prepare the PRP. In our study we used the PRP FAST SYSTEM (BIO). This system consists of disposable PRP tubes that were used together with a bench top centrifuge. The collected blood is injected into the PRP fast disposable units & then centrifuged for 15 min at

3200 rpm. Afterward the blood is separated into platelet poor plasma and platelet rich plasma. The platelet poor plasma is discarded. The PRP is checked for no. of platelets by Neubauer's chamber. All samples do have platelet count more than 1,000,000/microl in 5 ml volume. Only 50 micro ml of platelet sample was taken from this. After this the PRP is shaken by just turning the tube 2-3 times to mix the platelets. Depending on the initial amount of blood taken the amount of PRP was about 5 ml.

Depending upon the clinical examination the injection is given to the patient at the pre marked area at the medial aspect of heel, which was previously confirmed with radiograph.

All patients were scored by visual analog score before the procedure and after the procedure. They were followed up at the interval of one, three and six month interval.

The other group received injection methyl prednisolone acetate 40 mg/1 ml at the site of maximum tenderness on the medial side of heel. Patients were completely explained about the procedure & a written consent was taken. The part was cleaned & prepared with sprit & povidone iodine. Now the maximum tender point was selected. The injection was given after local anesthesia at this site with 2% xylocaine preparation. The 22G needle was used for this whole procedure. In both group a povidone iodine dressing was done at the injection site after the procedure. Patient was watched for

Table 1 – VAS pain score in patients with PRP therapy.

VAS score before PRP therapy	VAS score at one month	VAS score at three months	VAS score at six months
7	3	3	3
6	2	2	2
7	2	2	2
6	2	2	2
6	2	2	2
7	2	2	2
5	2	2	2
6	2	2	2
7	2	2	2
5	1	1	1
6	2	2	2
6	2	2	2
5	1	1	1
5	1	1	1
5	2	2	2
6	2	2	2
5	2	2	2
7	3	3	3
6	2	2	2
5	2	2	2
6	2	2	2
7	2	2	2
5	2	2	2
6	2	2	2
5	2	2	2
6	2	2	2
7	2	2	2
6	2	2	2
5	3	3	3
6	2	2	2

Table 2 – VAS pain score in patients with steroid injections.

VAS score before treatment with local steroid	VAS score after 1 month	VAS score after 3 months	VAS score after 6 months
7	3	3	4
5	2	2	2
6	4	4	3
5	3	3	3
6	2	3	3
7	3	3	3
5	2	3	3
7	3	3	3
5	2	2	2
6	3	3	3
6	2	2	2
6	2	2	2
6	3	3	3
6	3	2	2
7	4	5	5
7	3	3	3
7	3	3	3
7	2	2	2
7	4	4	4
7	4	4	4
5	3	3	3
5	1	2	2
5	3	3	3
5	3	3	3
7	3	3	3
7	2	2	2
5	2	2	2
5	2	2	2
6	3	3	3
6	2	2	2

15 min then they were send home with advice to take the rest for next 24 h. They were also advised to not to take an anti inflammatory analgesic preparation for it .The paracetamol was the only analgesic which was prescribed. These patients were evaluated with VAS score before the procedure & then after one, three & six months interval.

3. Results

The results were evaluated on the basis of VAS score. The patients were asked to rate their results depending on the scoring system of VAS (Tables 1 and 2).

The follow up of patient done at one month, three months & at six months. Patients were asked about their pain by VAS score. They were also examined for presence of any

complication like soft tissue infection, osteomyelitis, loss of function and presence of stiffness. In our study none of patient develop complication like mentioned above.

There is no significant difference in VAS score in both groups of the patients before the treatment. After one month of treatment VAS score significantly falls in both the groups ($p < 0.001$), but fall in VAS score is higher in PRP therapy (Table 3). At the completion of 3rd month of treatment VAS score increased in steroid therapy, however it is insignificant and remains constant till six months of treatment. Those who are at PRP therapy VAS score falls at three months and remains constant till six months. At one, three and six months those who are on PRP therapy VAS score remains significantly lower from their counter parts.

4. Discussion

In our patient group the age range varies between 30 yr and 85 yr of age. The range of heel pain duration varies from 1 to 120 months, the median duration was 6 months (± 20.6).

The range of participants age's reflects that there is little doubt that planter fasciitis pain affects the adults specially in middle to later age of life.

The results of this trial matches with the findings in other trials that steroid injection is not the only way to have relief in planter fasciitis, PRP therapy should be used in comparison to other therapies for relief. In other patient who continues to seek help for their resistant heel pain due to planter fasciitis, the PRP therapy should be adapted as a choice of therapy for relief. Although this should be advised only after other type of conservative therapy has been failed because there is less involvement of instruments/machines & less exposure to blood products in other type of therapies. Other therapies do also need less expertise in comparison to this therapy. The staff should be trained to form PRP from blood while it is not needed with steroid injections or others. By this trial we are able to keep PRP therapy more superior then the steroid therapy for long term benefit in planter fasciitis patients. There is need of long term trials to establish PRP as a choice of therapy for long term permanent relief from planter fasciitis due to mechanical causes.

Barrett and Erredge³¹ reported complete resolution of symptoms at 1 year in approximately 78% of subjects with plantar fasciitis treated with PRP. However, the study was limited by a small sample size and lack of a control group. Larger-scale randomized controlled studies are needed to help elucidate PRP as a viable treatment of this common musculoskeletal injury.

Table 3 – VAS score before and after treatment among steroid group and PRP group.

	Before treatment Mean (SD)	1 Month after treatment Mean (SD)	3 Months after treatment Mean (SD)	6 Months after treatment Mean (SD)
Steroid (n = 30)	6.03 (0.85)	2.7 (0.75)	2.8 (0.76)	2.8 (0.76)
PRP therapy (n = 30)	5.9 (0.76)	2.1 (1.0)	2.0 (0.45)	2.0 (0.45)
	$p > 0.05$	$p < 0.05$	$p < 0.001$	$p < 0.001$

Conflicts of interest

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

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