A Study of Platelet Rich Plasma Therapy in Osteoarthritis in a Tertiary Care Hospital in North India

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ABSTRACT

Introduction: Platelet-rich plasma (PRP) platelet concentration is more than that in peripheral blood. Presently, review of literature favours PRP use over other intra-articular treatments to improve pain scales in the short and medium term (6–12 months). This was a preliminary study using PRP as an intra-articular treatment for knee osteoarthritis, compared with an intra-articular control (hyaluronic acid), in early osteoarthritis.

Material and methods: One fifty patients of early osteoarthritis were included in the study along with controls PRP was administered intraarticularly to these patients at 3, 6 and 12-weeks intervals hyaluronic acid was administered to 150 controls.

Results: Improvement in symptoms of pain was seen in 95% patients. Remaining five percent patients were lost to follow up.

Conclusion: The present study shows an improvement in 95% of patients which compares well with other studies.

Keywords: Anti-Inflammatory Intra-Articular Therapies, Clinical Evidence, Knee Osteoarthritis, Platelet-Rich Plasma

INTRODUCTION

Platelets are small, anucleate fragments with occasional reddish granules, 2 micrometers in diameter, 8 fl volume with variable size and shape. Reticulated platelets are young platelets with their RNA content, recently released from the bone marrow. The platelet membrane consists of a phospholipid bilayer with glycoproteins and lipids. The platelet membranous systems consist of surface connected canalicular system and dense tubules. The membrane cytoskeleton consists of membrane skeleton and microtubules. Platelets possess secretory granules and mechanism for their release.[1] It includes alpha and dense granules, lysosomes and peroxisomes. Alpha granules and dense bodies are the main secretory granules that release cargo (for example fibrinogen and ADB) upon platelet activation. Platelet alpha granules have beta thromboglobulin, platelet factor 4, thrombospondin and have a role in angiogenesis. The lifespan is 8 to 12 days. Three factors (Factor 5, fibrinogen, and vWF) are found in platelets and granules contribute significantly to coagulation. Platelet fibrinogen contributes up to 10% of platelet protein.

Approximately, 800 proteins and molecules, comprising cytokines, chemokines, membrane proteins, metabolites, messenger molecules are found in platelets. Platelets are involved in various immune response, angiogenesis, and tissue regeneration.[3–5] This study was planned using PRP as an intra-articular treatment for knee osteoarthritis, compared with an intra-articular control (hyaluronic acid), in early osteoarthritis.

MATERIAL AND METHODS

A total 150 patients reported to the Orthopaedic outpatient department of a tertiary care hospital in North India. Patients who complained of pain in the knee were selected for the study.

They were graded as follows:

- **Grade 1:** Stiffness of knee relieved by hot fomentation and rest. Radiological evidence Nil.
- **Grade 2:** Stiffness with pain increased by activity like squatting and climbing stairs relieved by rest and analgesics. Radiological evidence showing mild affusion and increase in patelo femoral distance. Mild may or may not be osteophyte formation. They were given PRP intra-articularly at 3, 6, 12 weeks interval. Patients showed 95% benefit in their symptoms. 3-5% patients did not report for follow-up (figure-1).

Whitman in 1997[6] first described the use of platelet concentrate although blood-derived fibrin glues were used to plug wounds and assist in healing of wounds.[7] Platelet concentrates was called platelet-rich plasma (PRP), in 1998.[8]

Preparation Methods (figure-2,3)

PRGF-System® (BTI Biotechnology Institute, Vitoria, Spain): At least 1 million platelets per microliter are available in PRP. It must have a platelet concentration of

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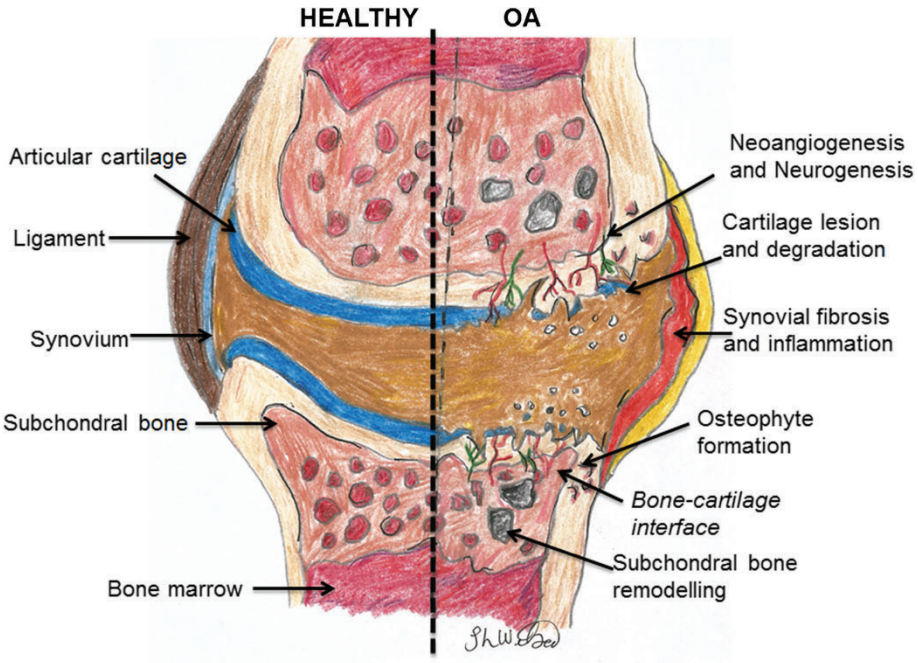

Figure-1: Comparison of a healthy (left) and OA knee joint (right)

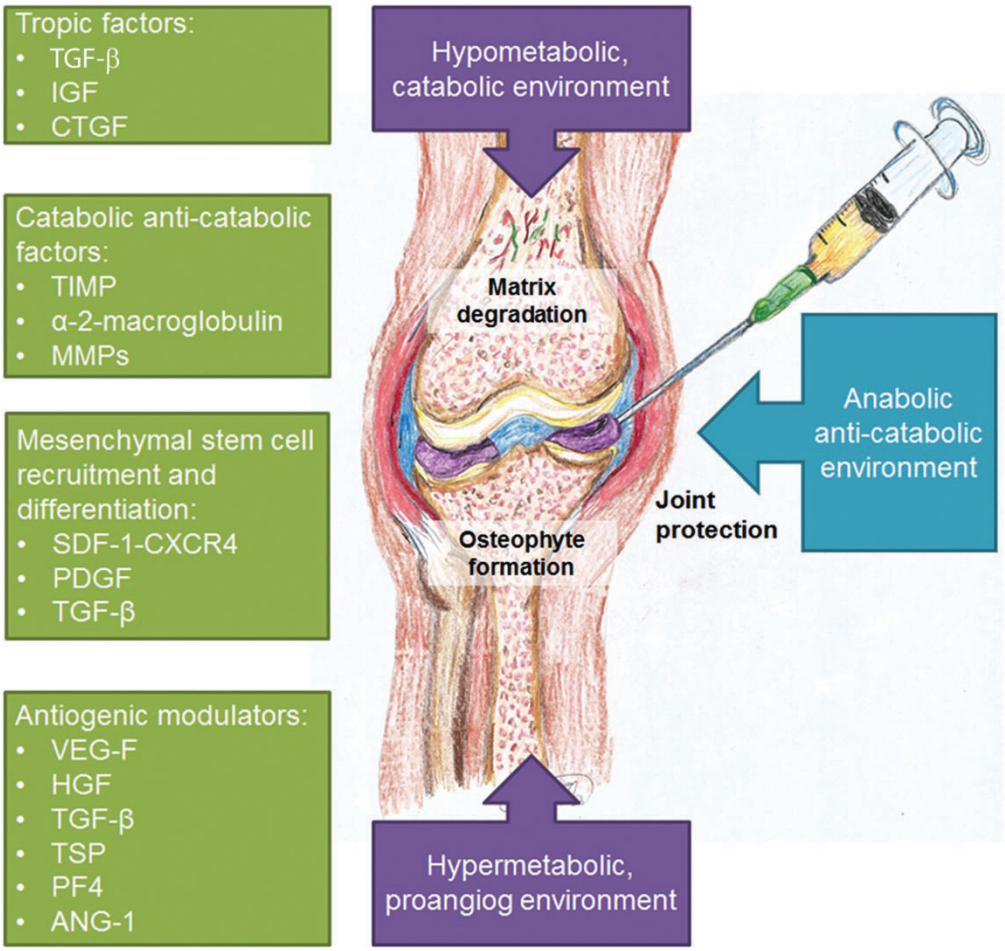

Figure-2: Clinical applications of PRP

approximately 1.5 times the concentration in whole blood. Anitua et al (2004) It has bacteriostatic effect and is used therapeutically having no side effects. One centrifugation at 460× g during 8 min, is used for preparation of PRP.[11]

Platelet Concentrate Collection System (PCCS®Kit) (3i–Implant Innovations, Palm Beach Gardens, FL, USA): Two centrifugations are used the first at3000rpm for 3 minutes and 45 seconds and second 13 minutes at 3000. With a platelet concentration of 1,100,000 and 2,200,000

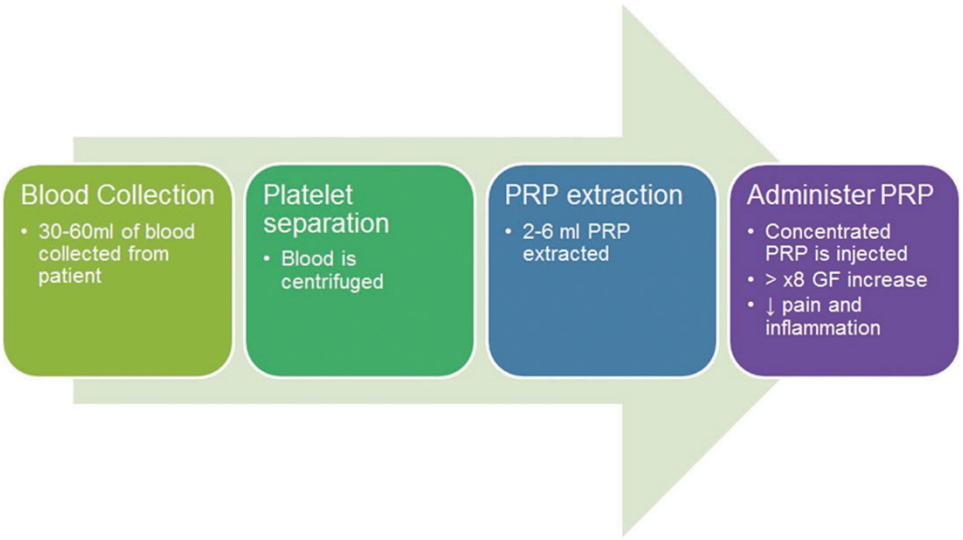

Figure-3: PRP preparation process

and includes leucocytes in a concentration of 5,5000 and 14,800/microlitre.

Gravitational Platelet Separation (GPS® System) (Biomet Merck Biomaterials, Darmstadt, Germany): Platelet concentration of 1,600,000/µL and leukocyte levels of 31,100/µL are available.

Smart PReP® System (Harvest Technologies Corporation, Munich, Germany)[14]: PRP with platelet concentration of 1,250,000/µL and a leukocyte concentration of 19,261/µL is obtained by double centrifugation for 12 minutes.

Plateltex® (Plateltex, Bratislava, Slovakia): Platelet concentration is approximately 1,600,000/µL and a double centrifugation is done.[14]

The most critical issues about PRP are:

1. The variety of preparation methods (concentrations and centrifugation) and platelet activation techniques;
2. The choice of autologous plasma against homologous or allogeneic: the choice to use autologous plasma is strongly recommended in order to avoid problem of contagious disease and immune response;
3. The presence of leucocytes: is hasn't been proved if they add an immune response;
4. The timing and cost of preparation;
5. The long-term safety assessment;

The healing process depends not only on growth factors but also on appropriate wound care, infection control and nutrition (global takeover)

PRP may be prepared by, single centrifugation, double centrifugation, or blood selective filtration procedures, and on manual or automatic systems operated in open or closed circuits. Ex vivo, platelet activation can be triggered mechanically with freeze–thawing cycles, chemically with thrombin or calcium chloride, or endogenously.[9,12]

Mishra and colleagues proposed to classify PRPs with two parameters:

Firstly, 'type' of PRP:

1. Increased WBCs and no activation;
2. Increased WBCs and activated;
3. Minimal/no WBCs and no activation;
4. Minimal/no WBCs and activated;

And secondly, its platelet enrichment factor, A if the PRP contains a platelet concentration at or above five times the baseline, or B if platelet concentration is less than five times the baseline.[14]

On the other hand, the PAW (Platelets, Activation, White cells) classification system includes at least three variables:

1. The absolute platelet concentration (P);
2. The method of activation (A);
3. The presence or absence of WBCs and neutrophils (W) relative to the baseline.

Current regulatory framework

PRP is regulated under Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001, in the European Union.[18]

PRP products are regulated according to the Food and Drug Administration (FDA)'s in the US.[21]

RESULTS

One hundred and fifty patients of mild to moderate grade of OA were given PRP intra particularly at 3, 6- and 12-weeks interval. Control group was treated with hyaluronic acid.

Follow up of patients was done in Orthopaedic Department at monthly intervals.

Patients given injection of PRP showed improvement of pain and swelling of the knee.

Three to five percent of patients were lost to follow up. Patients who were obese were asked to reduce weight and they reported that they had good improvement in symptoms along with loss of weight.

DISCUSSION

Increased interest has been seen in the efficacy of PRP injected intra-articularly for managing osteo-arthritis (OA) without surgery. Shen et al[17] did a meta-analysis of 14 randomized clinical trials totalling 423 patients where they compared PRP to various methodologies including hyaluronic acid,

injection of stocicosteroid and oral medications. Using the Western Ontario and McMaster University osteo-arthritis index, scores at 3, 6, 12 months follow up (=0.02, 0.04, <0.001 respectively). PRP efficacy has been shown to be more effective with patients with mild to moderate OA. Various workers have suggested that intra-articular PRP injections have a greater advantage in relief of pain than other alternative injections. Injection of PRP increases IL-4 and IL-10 which are anti-inflammatory mediators.

Evidence of clinical efficacy of PRP-derived products in musculoskeletal injuries/ diseases

Preclinical and clinical trials for PRP products namely, direct injection of PRP, gel, clot, either from own blood bank or commercial products. In oral and maxillofacial surgery, treatment of chronic ulcers, ophthalmology, dermatology, and injuries and pathologies associated to tendon, muscle, cartilage and bone.[16-24]

Proposal for a new approach

A single injection, two monthly injections,[29] three injections at 15-day intervals or 21-day intervals; however, the most frequent treatment strategy is to apply 3-weekly PRP injections.

The Kellgren-Lawrence (K–L) grading system, the Ahlbäck classification or cartilage degeneration by magnetic resonance imaging. PRP, compared with HA, showed better performance in younger patients affected by cartilage lesions or early OA than in older patients.

Various approaches have been used including lateral, supero-lateral,[10] para-patellar,[30] and lateral mid-patellar,[29] among others. After-injection recommendations also vary, including rest (10 or 20 min of immobilization[18,20,26]).

CONCLUSIONS

PRP is useful as it delivers a supraphysiological amount of growth factors and cytokines contained within platelets. It is a promising therapeutic modality with clear evidence of safety.

PRP has been found to be more efficient than other IA treatments such as HA injections, to improve pain scales in the short and medium term, 6–12 months as shown by various clinical trials. Further studies are needed to elucidate use of PRP in mild to moderate OA. Multicentric studies in large hospitals with orthopaedic departments will unravel the benefits of PRP in OA further. If PRP is recommended after these trials it will be a panacea for optimal care in needy patients.

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