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Research Article

TO STUDY AUTOLOGOUS PLATELET RICH PLASMA IN THE TREATMENT OF OSTEOARTHRITIS KNEE IN INDIA

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ABSTRACT

Osteoarthritis represents failure of the joint where all the structures have suffered pathologic changes mainly hyaline cartilage degeneration. It is highly prevalent especially in old age group, and its ill impact on daily activities makes it a leading cause of disability in the older age group. To evaluate the effectiveness of autologous platelet rich plasma in treatment of osteoarthritis knee in reducing pain, stiffness and improving physical function and to find out the efficacy of platelet rich plasma in the treatment of osteoarthritis knee as a disease modifying, cost effective conservative modality. Total 60 patients were selected for the study fulfilling the inclusion criteria and were randomly divided into two groups of control (normal saline) and test (PRP) and were assessed using WOMAC scale and VAS scale for the assessment of pain stiffness and physical function, follow up was done at 6 weeks, 3 months and 6 months. The global WOMAC score (PRP) showed a mean of 73.3 at pre-injection period which decreased to 61.6 at 6 weeks follow up and 46.03 at 3 months follow up which reduced to 32.1 at 6 months. The mean pain score (PRP) reduced from 16.4 to 11.7 at 6 weeks post injection and 7.36 at 3 months post injection. At the end of 6 months follow up , mean pain score was found to be 5.5.The mean pain score in group 2 (control group) showed a marginal decrease from 16.2 to 13.9 at 6 weeks post injection but returned to 15.7 at 6 months follow up. Our study revealed a significant reduction of pain , stiffness and improvement of physical function in patients injected with autologous platelet rich plasma.

Keywords: - Primary Osteoarthritis, Platelet Rich Plasma, Knee Stiffness, Conservative Management of Osteoarthritis.

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INTRODUCTION

Osteoarthritis represents failure of the joint where all the structures have suffered pathologic changes mainly hyaline cartilage degeneration. It is highly prevalent especially in old age group, and its ill impact on daily activities makes it a leading cause of disability in the older age group. Because of ageing and obesity the prevalence of osteoarthritis is increasing. Osteoarthritis involves certain joint and spares others. It commonly affects hip, knee, first metatarsophalangeal (MTP) joint and cervical and lumbosacral spine. In hands, distal and proximal interphalangeal joints and first carpometacarpal (CMC) are involved. Usually the wrist, elbow and ankle joints are not involved.

Diagnosis of osteoarthritis can be made by radiographic findings such as reduction of joint space and osteophytes, however most of the people with x-ray findings of osteoarthritis are asymptomatic What concerns us is symptomatic osteoarthritis which includes joint pain, functional and vocational disability, visits to clinicians and disease cost. Pathological changes in osteoarthritis include hyaline cartilage loss, increase in thickness and sclerosis of subchondral bone, marginal osteophytes, meniscal degeneration.

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Various pathways lead to joint failure but the initial step is often joint injury due to failure of the protective mechanisms.

Osteoarthritis is different from simple wear and tear as its distribution is asymmetrical and is often associated with abnormal loading rather than frictional wear. Osteoarthritis is also associated with previous injury to the joint following any trauma and is called secondary osteoarthritis. Prevalence of primary osteoarthritis is 22-39% in India [1] affecting mainly middle to old age group and is almost always associated with history revealing repetitive joint loading. However metabolic derangements of articular cartilage are seen in a few patients.

The aim of this study is to evaluate the effectiveness of autologous platelet rich plasma in treatment of osteoarthritis knee in reducing pain, stiffness and improving physical function.

Since platelet rich plasma provides a cocktail of growth factors directly into the joint cavity. Platelet rich plasma is postulated to modify the disease process and believed to cause regeneration of the articular cartilage, unlike other conservative methods which provide symptomatic relief and halt the degenerative process.

Autologous platelet rich plasma is a cost effective tool that could obviate the requirement for joint replacement arthroplasty or at least decrease the number of revision surgeries.

Through this study we aim to find out the efficacy of platelet rich plasma in the treatment of osteoarthritis knee as a disease modifying, cost effective conservative modality.

To evaluate the role of autologous platelet rich plasma in the patients diagnosed with primary osteoarthritis and to find out whether it will be a cost effective method for delaying the need for surgery keeping in mind the side effects and its role as a disease modifying modality.

MATERIALS AND METHODS

Study Design

Randomized control trial. Patients were assessed under parameters such as pain, stiffness, physical function using WOMAC scale and assessed for pain using visual analogue scale at pre-injection, 6 weeks post injection, 3 months post injection and 6 months post injection. The patients attending the in-patient as well as the outpatient department of orthopaedics at Rajiv Gandhi Institute of Medical Sciences, Putampalli, Kadapa and with complain of bilateral knee pain were screened and among those who were diagnosed with osteoarthritis knee were chosen for the study.

Selected patients were classified using the Kellgren Lawrance classification for osteoarthritis knee and were graded between grade 0 to grade 4 depending on the severity and were included in the study after informed written consent.

Total of 60 patients were selected for the study and were randomly divided into two groups of 30 each. Group 1 received intra-articular injection of platelet rich plasma in bilateral knee and was considered as the study group. Group 2 received intra-articular normal saline and was considered as control group.

Randomization was done and both the groups were compared in relation to age, gender, height, Body Mass Index and WOMAC score.

Other parameters such as pain, stiffness and physical function were also compared pre as well as post injection.

Exclusion Criteria

1. Immunosuppresed patients.
2. Patients with secondary osteoarthritis.
3. Patients with connective tissue disorders.
4. Patients with inflammatory disorder of joints.

Inclusion Criteria

1. Patients with primary osteoarthritis.
2. Patients willing to participate in the study.

RESULTS

Osteoarthritis is a clinically heterogenous degenerative condition which is characterized by articular cartilage destruction, due to failure of protective mechanisms and imbalance between cartilage degeneration and regeneration.

In our study we chose random 60 subjects with classical findings of osteoarthritis and randomly divided them into two groups of test subjects and control group respectively. Both these groups were compared on the baseline characteristics of age, height, weight, BMI, pre injection WOMAC score. 30 of these patients were given intra-articular platelet rich plasma and other 30 were given normal saline as control.

The Efficacy of platelet rich plasma in reducing pain, stiffness and physical function were assessed and scored according to WOMAC scoring index for both study as well as control group. The results were analysed using unpaired t test and chi square test.

Age distribution in group 1 (test group) showed mean age of 54.1 while group 2 (control group) mean age was 54.7. The p-value derived using unpaired t test was found to be 0.7798 rendering the age factor insignificant.

Gender distribution was compared in both groups and found to be 56.67 % in males and 43.3 % in females. The p-value using chi square test was found to be 0.7953. Thus the gender factor was insignificant.

Height distribution in group 1 (test group) showed mean height to be 156.9 cm while group 2 (control group) mean height was found to be 157.5 cm.

The p-value using unpaired t test was 0.7369 rendering the height factor insignificant.

Weight distribution in group 1 (test group) showed mean weight to be 66.2 kg while group 2 (control group) mean weight was found to be 66.2 kg. The p-value was found to be 1.0000. The weight factor was insignificant.

BMI distribution in group 1 (test group) showed mean of 26.96 while the group 2 (control group) mean BMI was 26.9. The p-value was found to be 0.9368. The BMI was found to be insignificant.

Thus our study ensured that all the patients were comparable on baseline characters.

The global WOMAC score showed a mean of 73.3 at pre-injection period which decreased to 61.6 at 6 weeks follow up and 46.03 at 3 months follow up which reduced to 32.1 at 6 months.

Our study showed a significant decrease in global WOMAC score, which was also consistent throughout the study period.

The individual variables such as pain, stiffness and physical function were assessed.

The mean pain score reduced from 16.4 to 11.7 at 6 weeks post injection and 7.36 at 3 months post injection. At the end of 6 months follow up, mean pain score was found to be 5.5

The mean pain score in group 2 (control group) showed a marginal decrease from 16.2 to 13.9 at 6 weeks post injection but returned to 15.7 at 6 months follow up.

The p-value using unpaired t test showed significant improvement. Secondary variable stiffness showed significant difference at 3 month follow up and 6 month follow up.

The mean physical function reduced from a pre injection score of 51.3 to s23.2 at 6 months follow up in group (test group).

Group 2 (test group) showed a marginal dip in mean physical function scores from 48.3 to 45.4 and to 43.6 at 3 months post injection. The score levelled to 46.1 at the end of 6 months.

Visual analogue score showed a decrease in mean of 7.3 to 2.9 which denoted a change of patients perception of pain from intense, dreadful, horrible pain to mild, annoying pain in group 1 (test group).

Group 2 (control group) showed a marginal dip from 6.6 to 4.9 thus revealing insignificant changes in pain.

Thus there was significant reduction in pain in patients treated with autologous platelet rich plasma while the test group injected with normal saline initially showed reduction of pain due to placebo effect but ultimately resulted in return of pain and stiffness, thus showing that autologous platelet rich plasma is a superior entity in conservative treatment of osteoarthritis.

Table 1: Comparison of WOMAC score for patients treated with autologous platelet rich plasma and patients treated with normal saline over the period of 6 months

WOMAC score		Pre-injection	6 weeks	3 months	6 month
Platelet rich plasma	N	30	30	30	30
	Mean	73.3	61.6	46.03	32.1
	SD	4.6	6.6	7.6	7.2
Normal saline	N	30	30	30	30
	Mean	69.2	63.7	61.4	66
	SD	5.3	5.9	5.5	5.6
P value Unpaired t test		0.0022	0.1990	0.0001	0.0001

Table 2: Comparison of PAIN score in patients treated with autologous platelet rich plasma and patients treated with normal saline as control over the period of 6 months

Pain score		Pre-injection	6 weeks	3 months	6 month
Platelet rich plasma	N	30	30	30	30
	Mean	16.4	11.7	7.36	5.5
	SD	3.15	3.02	2.07	1.62
Normal saline	N	30	30	30	30
	Mean	16.2	13.9	13.7	15.7
	SD	2.38	2.29	2.45	2.17
P value Unpaired t test		0.7824	0.0024	0.0001	0.0001

Table 3: Comparison of physical function score in patients treated with autologous platelet rich plasma and patients treated with normal saline as control over the period of 6 months

Physical function score		Pre-injection	6 weeks	3 months	6 month
Platelet rich	N	30	30	30	30

plasma	**Mean**	51.3	45.7	34.7	23.2
	SD	3.9	4.4	5.9	5.9
Normal saline	**N**	30	30	30	30
	Mean	48.3	45.4	43.6	46.1
	SD	2.9	4.01	3.9	3.6
P value Unpaired t test		0.0013	0.7835	0.0001	0.0001

Table 4: Comparison of VISUAL ANALOGUE SCORE in patients treated with autologous platelet rich plasma and patients treated with normal saline as control over the period of 6 months.

Visual analogue score		**Pre-injection**	**Post-injection**
Platelet rich plasma	**N**	30	30
	Mean	7.3	2.9
	SD	0.9	1.1
Normal saline	**N**	30	30
	Mean	6.6	4.9
	SD	0.8	0.7
P value Unpaired t test		0.0023	0.0001

DISCUSSION

Over the past few decades there has been a lot of research work to find out the efficacy of various modalities of conservative management of osteoarthritis knee. Management of osteoarthritis knee includes improvement in function, reduction in disability, pain relief and thus improved quality of life [2, 3]. However currently there are no pharmacological agents which could halt the osteoarthritis progression or reverse the existing damage. Existing approach emphasises on preventing or delaying the progression by developing less invasive procedures or application of interventions earlier in the disease process [5] Non-operative therapeutic interventions such as intra-articular injections including glucocorticoids, hyaluronic acid injections, platelet rich plasma (PRP) , non-steroidal anti-inflammatory (NSAIDs) medications, physical therapy and unloaded bracing play a major role in the management of osteoarthritis knee [6]

Autologous PRP is a highly concentrated mixture of platelets, containing growth factors and other bioactive components produced by centrifugal separation of whole blood and is widely used in orthopaedics and sports medicine for the treatment of bone, ligament and tendon injury [7]. The growth factors in PRP have revealed to promote cell recruitment, proliferation and angiogenesis causing reduction in critical regulators of the inflammatory process and reduce the expression of inflammatory enzymes [8] PRP may induce a regenerative response, by improving the metabolic functions of the damaged joint structures [9], and has been shown to have a positive effect on chondrogenesis and mesenchymal cell proliferation [10]

In osteoarthritis of joints PRP has shown to affect the local and infiltrating cells , mainly the synovial cells, endothelial cells, those involved in innate immunity (like macrophages), cartilage and bone cellular components [11]. PRP can have an effect on inflammation and angiogenic process, anabolism and catabolism equilibrium in formation of articular cartilage, and change the existing micro-environment, throughout the disease progression. [13] In knee osteoarthritis, PRP intra-articular injections - primarily aim to encourage repair of articular cartilage, and relieve associated symptoms, potentially delaying the need for joint replacement surgery. PRP injections have shown to have an impact on the entire joint environment, leading to a short term clinical improvement [14]. Comparison between intra-articular injection of PRP versus placebo therapy and injection of hyaluronic acid in mild and moderate osteoarthritis knee, higher clinical outcome scores were seen with PRP use [19]. Using meta-analysis to compare the efficacy of PRP injections versus placebo or other therapeutic methods for treatment of osteoarthritis knee [15] have reported greater pain reductio and functional improvement with the use of PRP [16].

The release of growth factors from PRP occurs immediately with prolonged and sustained release of growth factors from the platelets possibly resulting in better biological healing and sustained clinical effects [12]. Symptomatic relief of up to 12 months with better improvements in patients with early knee degenerative osteoarthritis changes has been found[18] with significant improvement in function and reduction of pain with three injections per month, showing significantly better results in short term [17] Previous studies in their comparative study used normal saline as control (placebo therapy) against PRP (test group) intra-articular injection and concluded that PRP was much superior over placebo therapy through improved WOMAC score at 6 months, with the patients showing improved results as early as

eighteen days. In a follow up study hypothesised that the anti-inflammatory effect and chondral remodelling induced by PRP could be the reason for improved clinical effect [17]. Previous studies in their study on Leukocyte-poor PRP application for the treatment of knee osteoarthritis concluded that A single dose of WBC-filtered PRP in concentrations of 10 times the normal amount is as effective as 2 injections to alleviate symptoms in early knee OA. The results, however, deteriorate after 6 months. Both groups treated with PRP had better results than did the group injected with saline only [19]. Previous studies studied the effect of PRP in experimentally induced OA in rabbits knee joint concluded that PRP group had near normal joint structure at 16 week post op interval and hence PR could potentially be used for the treatment of osteoarthritis.

Previous studies in their study on Effectiveness of intra-articular injections of sodium bicarbonate and calcium gluconate in the treatment of osteoarthritis of the knee: a randomized double-blind clinical trial concluded that the symptoms of osteoarthritis reduced symptomatically with the use of solution containing sodium bicarbonate and calcium gluconate. The benefits of this combination is maintained for one year of continuous monthly injection protocol and at least for six months after the discontinuation of injection. Prevention of further joint space narrowing was observed with increase in the dose of calcium gluconate. Previous studies in his study "Effectiveness of platelet-rich plasma (PRP) on pain, function and quality of life in knee osteoarthritis patients: a before-and-after study and review of the literature" on a non randomized control trial on 27 patients with osteoarthritis kellegren lawrance grade 2 or more, to find out the effect of pain relief, improvement of physical function and quality of life using WOMAC scoring system in osteoarthritis knee patients by using a protocol of 3 doses of autologous PRP injected weekly. Pre-injection score measured by Visual analogue scale (VAS) was 8.14 which significantly reduced to 2,95 after treatment. WOMAC pain subscale decreased from 14.88 (pre-injection) to 5.55. WOMAC stiffness subscale reduced from 2.44 (pre-injection) to 0.4. WOMAC functional subscale ameliorated from 44.48 (pre-injection) to 15.25. Study concluded that PRP infiltrated in a three dose protocol is effective in the treatment of osteoarthritis knee symptoms such as pain, stiffness while improving function and quality of life, also PRP alleviate knee osteoarthritis symptoms in all radiological knee osteoarthritis grades even the most severe ones with statistical difference [20].

Pharmacological management of osteoarthritis with NSAIDs is associated with risk of gastrointestinal complications with an alarming rise in NSAIDs induced multisystem complications. Joint replacement arthroplasty is a definitive treatment but is reserved for advanced cases with failed conservative management, moreover the post operative morbidity, cost issues, need for technical expertise and revision prevents arthroplasty from being the most frequent form of treatment. Autologous chondrocyte transplantation and attempts at cartilage repair using mesenchymal stem cells and autologous osteochondral plugs are currently under experimental stage. Autologous Platelet rich plasma serves as an entity to provide articular cartilage regeneration thus acting as a disease modifying method for osteoarthritis unlike other modalities of treatment which aim at halting the disease process. Platelet rich plasma offers beneficial effect of various growth factors in platelet to cause regeneration of the articular cartilage in a synovial joint.

CONCLUSION

Osteoarthritis is a degenerative process lead to joint failure of a diarthrodial joint leading to destruction of articular cartilage due to failure of various protective mechanisms. The management of osteoarthritis varies from conservative methods like lifestyle modification, physiotherapy and surgical methods such as joint replacement arthroplasty depending on the stage of the disease. The treatment of osteoarthritis ranges from conservative management with physiotherapy, non steroidal anti inflammatory medications, intra articular glucocorticoid injection, intra articular hyaluronic acid etc to arthroscopic management like debridement. Advanced cases of osteoarthritis where conservative management has failed to provide satisfactory results joint replacement arthroplasty is performed. In our study we injected a concentrated mixture of platelets in the joint cavity and observed the patients for reduction of pain, reduction of stiffness and improvement of physical function. Our study revealed a significant reduction of pain, stiffness and improvement of physical function in patients injected with autologous platelet rich plasma. Though the patients injected with normal saline as control group showed initial improvement with reduction of pain due to placebo effect, their symptoms reappeared after some time during the follow up.Thus we can conclude that autologous platelet rich plasma is an interesting modality for conservative treatment of osteoarthritis knee and has proved to be efficacious and cost effective measure in the observation period of six months.

COMPLICATIONS

There were no complications as such or any incidence of infections in our study group as well as control groups.

LIMITATIONS

Long term follow up needed with MRI to assess the regeneration of articular cartilage.

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