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Original Research Article

TO DETERMINE THE EFFECTIVENESS OF A SINGLE INTRA-ARTICULAR INJECTION OF AUTOLOGOUS PLATELET-RICH PLASMA IN THE TREATMENT OF EARLY STAGE OSTEOARTHRITIS OF THE KNEE

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Abstract

Background: Platelet-rich plasma (PRP), which contains growth factors derived from the patient's own blood, is one of the least invasive therapies used to treat knee osteoarthritis (OA). The aim is to assess the efficacy of a solitary intra-articular administration of autologous platelet-rich plasma in managing early-stage knee osteoarthritis. **Materials and Methods:** A quasi experimental study was done on 30 Patients with early-stage osteoarthritis of the knee who attended OPD of the in the Department of Orthopaedics, in collaboration with the Department of Transfusion Medicine, Regional institute of Medical Sciences (RIMS), Imphal, Manipur form October 2019 to September 2021 over a period of two years. Age, sex, occupation, weight, height, body mass index (BMI), early stage of osteoarthritis of the knee, pain, knee stiffness and physical functions of the knee were observed. All patients were followed- up after one month and after six month post intra-articular injection. In each follow up, clinical history and examination were performed. The patient was evaluated using the VAS score and WOMAC score and the findings were documented. **Result:** In our study the pre-treatment VAS score was 7.600 ± 1.328 while it was reduced to 6.500 ± 1.279 in 1 month follow up and to 4.533 ± 1.431 at the end of 6 months follow up. In our study, the pre-treatment WOMAC total score was 76.733 ± 7.610 while it was reduced to 68.933 ± 8.333 in 1 month and to 56.100 ± 8.005 at the end of 6 months follow up. The pre-treatment WOMAC pain score was 14.966 ± 2.525 while it was reduced to 12.933 ± 2.545 in 1 month follow up and to 9.166 ± 1.858 at the end of 6 months follow up. The pre-treatment WOMAC stiffness score was 3.266 ± 1.229 while it was reduced to 2.366 ± 0.964 in 1 month follow up and to 1.200 ± 0.714 at the end of 6 months follow up. The pre-treatment WOMAC physical function score was 58.500 ± 4.133 while it was reduced to 53.633 ± 4.999 in 1 month follow up and to 45.733 ± 5.800 at the end of 6 months follow up. **Conclusion:** The result revealed that the autologous single platelet- rich plasma injection is an effective treatment for early osteoarthritis of the knee joint.

INTRODUCTION

Osteoarthritis is the most common disease of joints in adults around the world. It ranks as the fifth highest cause of years lost to disability in the whole population in high-income countries, and the nineth highest cause in low and middle-income countries.[1] Osteoarthritis is a degenerative joint disease, occurring primarily in older persons characterized by erosion of the articular cartilage, hypertrophy of bone at the margins (i.e. osteophytes), subchondral sclerosis, and a range of biochemical and morphologic alterations of the synovial membrane and joint capsule. Typical clinical symptoms are pain and stiffness, particularly after prolonged activity. The major etiologic factors affecting degree of risk for developing osteoarthritis are age, joint location, obesity, genetic predisposition, joint mal-alignment, trauma, and gender.[2]

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The age standardized prevalence of radiographic knee osteoarthritis in adults age $\geq$ 45 was 19.2% among the participants in the Framingham Study and 27.8% in the Johnston County Osteoarthritis Project. In the third National Health and Nutrition Examination Survey (NHANES III), approximately 37% of participants age >60 years or older had radiographic knee Osteoarthritis. Knee osteoarthritis is more common in women, with female-to-male ratios varying between 1.5:1 and 4:1. Prevalence rates for knee osteoarthritis, based on population studies in the USA, are comparable to those in Europe. These studies report that severe radiographic changes affect 1% of people aged 25–34 and this figure increases to nearly 50% in those 75 years and above. Among participants aged over 45 years in the Framingham Study, the prevalence of radiographic knee osteoarthritis was 19.2% and, in those over 80 years, the figure rose to 43.7%. According to data produced by the Dutch Institute for Public Health, the prevalence of knee osteoarthritis in those aged 55 and above was 15.6% in men and 30.5% in women. In India the crude prevalence of clinically diagnosed knee osteoarthritis was higher in the urban (5.5%) than those in the rural community (3.3%).[3] Osteoarthritis is the second most common rheumatologic problem and it is the most frequent joint disease with a prevalence of 22% to 39% in India.[4]

The most common form of treatment for knee OA includes a combination of non-pharmacological interventions and various pharmacologic interventions like topical agents, systemic agents and intra-articular agents like corticosteroids and hyaluronic acid derivatives. Unfortunately, to date, no drug has been conclusively proven to be structure or disease modifying.[5] Because of limitations in the effectiveness of conventional management options, alternative options such as biological and regenerative methods are coming into vogue. Autologous platelet-rich plasma (PRP), which contains a pool of growth factors, appears to offer an easy solution for delivering multiple growth factors needed for tissue repair. PRP therapy provides delivery of a highly concentrated of growth factors to accelerate healing. However, at present, there are limited studies documenting the effectiveness of a non-surgical PRP injectable for intra-articular use in knee osteoarthritis.[6]

Platelet-rich plasma (PRP) is defined as a volume of autologous plasma containing a higher platelet count than peripheral blood (150,000–350,000 platelets/μl). PRP has at least three growth factors like platelet derived growth factors (PDGF), transforming growth factor beta1 (TGF-b1) and transforming growth factor beta2(TGF-b1).[7,8] Although there are sporadic studies from a few institutes in India, yet there is no study conducted in Manipur or North East India. Therefore, the purpose of this study is to observed over a period of time and document the effectiveness of PRP in the treatment of early stage of osteoarthritis of the knee joint in patients attending RIMS Hospital, Imphal seeking treatment in the Department of Orthopaedics, RIMS, Imphal.

MATERIALS AND METHODS

A quasi experimental study was done on 30 Patients with early stage osteoarthritis of the knee who attended OPD of the in the Department of Orthopaedics, in collaboration with the Department of Transfusion Medicine, Regional institute of Medical Sciences(RIMS), Imphal, Manipur form October 2019 to September 2021 over a period of two years. Ethical approval was taken from the Institutional Research Ethics Board, before starting the study and informed consent was taken from all the participants. Age, sex, occupation, weight, height, body mass index (BMI), early stage of osteoarthritis of the knee, pain, knee stiffness and physical functions of the knee were observed.

Inclusion Criteria
The study included sample of both the sexes under the age group 35-75 years.
Diagnosis was mainly based on clinical presentation of osteoarthritis.

Exclusion Criteria
Secondary Osteoarthritis for e.g., trauma, congenital, metabolic, endocrine, calcium deposition disease and other joint disease.
Cases with advanced pathological conditions and which needs surgical intervention were also excluded.

Methodology
After obtaining institutional ethics committee approval from RIMS, Imphal, and written informed consent of patients who fulfill the inclusion criteria and do not have any exclusion criteria were explained about the purpose and procedure of the study. Pre-injection VAS and WOMAC scores of the patients were documented. In the OPD of the Department of Orthopaedics, 30 ml of venous blood sample was taken from the patients and collected in sterile acid citrate dextrose A tubes. In the Department of Transfusion Medicine, the tubes were centrifuged at 1800 rpm for 15 minutes to separate erythrocytes , and at 3500rpm for 10 minutes to concentrate platelets. By this method, 3-5 ml of autologous platelet-rich plasma was obtained.9 Once the PRP was prepared, it was injected in the affected knee within 2 hours . The injection was done in an operating room .The patient was placed in supine position with the knee in 90-degree flexion. The skin of the affected knee was painted with iodine-based antiseptic solution and draped in the standard manner. The intra-articular injection of PRP in the affected knee was made very slowly through the anterolateral approach using a 22 guage needle. At the end of the procedure, the patient was instructed to passively flex and extend the knee a few times to allow the PRP to distribute itself throughout the knee before becoming gel form. After the injection, the patient were monitored for 30 minutes before

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discharge. The patient was advised not to take any NSAIDS nor to apply local ice for a week after injection to avoid reduction efficacy on PRP. All affected knees received a single intra-articular PRP injection.

Visual Analogue Scale(VAS)
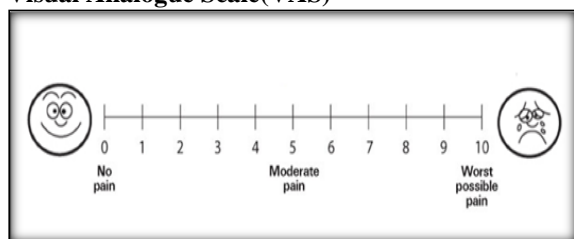
All patients was followed- up after one month and after six month post intra-articular injection. In each follow up, clinical history and examination were performed. The patient was evaluated using the VAS score and WOMAC score and the findings were documented.

Statistical Analysis

Data were checked for completeness and consistency. Descriptive data were summarised in the form of mean, standard deviation, proportions, percentage. The data obtained were recorded and analysed statistically using repeated measures ANOVA wherever applicable.

Statistical analysis were made using the software IBM SPSS version 21.0.

RESULTS

The mean age for all patients was 53.566 ± 10.877. The mean age for female was 53.909 ± 11.216. The mean age for male was 52.625 ± 10.555. There were 22 females and 8 males. The osteoarthritis of the knee mainly affected the housewife's (46.6%), followed by farmers (20.0%) and shopkeepers (20.0%). Majority of the patient in our study were overweight (63.4%) and obese (23.3%). In our study the pre-treatment VAS score was 7.600 ± 1.328 while it was reduced to 6.500 ± 1.279 in 1 month follow up and to 4.533 ± 1.431 at the end of 6 months follow up. In our study, the pre-treatment WOMAC total score was 76.733 ± 7.610 while it was reduced to 68.933 ± 8.333 in 1 month and to 56.100 ± 8.005 at the end of 6 months follow up. The pre-treatment WOMAC pain score was 14.966 ± 2.525 while it was reduced to 12.933 ± 2.545 in 1 month follow up and to 9.166 ± 1.858 at the end of 6 months follow up. The pre-treatment WOMAC stiffness score was 3.266 ± 1.229 while it was reduced to 2.366 ± 0.964 in 1 month follow up and to 1.200 ± 0.714 at the end of 6 months follow up. The pre-treatment WOMAC physical function score was 58.500 ± 4.133 while it was reduced to 53.633 ± 4.999 in 1 month follow up and to 45.733 ± 5.800 at the end of 6 months follow up.

Table 1: Basic profile of the patients

	No. of patients(n)	Percentage(%)
Sex		
Female	22	73.3
Male	8	26.7
Side involved		
Right	24	80
Left	6	20
Occupation		
Housewife	14	46.6
Shopkeeper	6	20.0
Business person	2	6.7
Farmer	6	20
Carpenter	2	6.7
BMI		
Under weight(>18.5)	0	0
Normal(18.5 - 24.99)	4	13.3
Over weight(25 - 29.99)	19	63.4
Obese(>30)	7	23.3

Table 2: Means of Visual Analogue Scale (VAS) Scores for single intra-articular injection of autologous PRP in the treatment of early osteoarthritis of the knee

Time	Mean	p value
Pre-treatment	7.600 ± 1.328	0.000
Post-treatment 1 month follow up	6.500 ± 1.279	
Post-treatment 6 month follow up	4.533 ± 1.431	

Table 3: Means of WOMAC pain sub-score for single intra-articular injection of autologous PRP in the treatment of early osteoarthritis of the knee

Time	Mean	p value
Pre-treatment	14.966 ± 2.525	
Post-treatment 1 month follow up	12.933 ± 2.545	0.000
Post-treatment 6 month follow up	9.166 ± 1.858	

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Table 4: Means of WOMAC stiffness sub-score for single intra-articular injection of autologous PRP in the treatment of early osteoarthritis of the knee

Time	Mean	p value
Pre-treatment	3.266± 1.229	
Post-treatment 1 month follow up	2.366± 0.964	0.000
Post-treatment 6 month follow up	1.200± 0.714	

Table 5: Means of WOMAC physical function sub-score for single intra-articular injection of autologous PRP in the treatment of early osteoarthritis of the knee

Time	Mean	p value
Pre-treatment	58.500± 4.133	
Post-treatment 1 month follow up	53.633± 4.999	0.000
Post-treatment 6 month follow up	45.733± 5.800	

Table 6: Means of WOMAC total score for single intra-articular injection of autologous PRP in the treatment of early osteoarthritis of the knee

Time	Mean	p value
Pre-treatment	76.733± 7.610	
Post-treatment 1 month follow up	68.933± 8.333	0.000
Post-treatment 6 month follow up	56.100± 8.005	

DISCUSSION

In our present study, the mean average age incidence was 53.566 ± 10.877 years which was comparable to the study conducted by Yadav A et al,[10] (mean average age was 53.54 years). The mean average age for female and male were 53.909 ± 11.216 years and 52.625 ± 10.555 years respectively. In our study, 73.33% were female and 26.7 % were male. Therefore, females were more affected than male. In the study conducted by Vamshi R et al6, there were 77% female patients and 23% male patients. The osteoarthritis of the knee mainly affected the housewifes (46.6%), followed by farmers (20.0%) and shopkeepers (20.0%). Majority of the patient in our study were overweight (63.4%) and obese (23.3%). In the study conducted by Narasimha BC. et al,[11] 21.6% of the patients were over weight and 69.2% of the patients were obese. Hence, BMI of more than 25 kg/m2 is an important risk factor for osteoarthritis. In our study the pre-treatment VAS score was 7.600 ± 1.328 while it was reduced to 6.500 ± 1.279 in 1 month follow up and to 4.533 ± 1.431 at the end of 6 months follow up. In the study conducted by Subhash Y et al,[12] the pre-injection VAS score was 8.09±1.45 which decreased to 6.12±1.21 at 1 month, and 4.96±1.49 at 6 months. In our study, the pre-treatment WOMAC total score was 76.733± 7.610 while it was reduced to 68.933± 8.333 in 1 month and to 56.100± 8.005 at the end of 6 months follow up. In the study conducted by Raman SV et al,[13] there was definite decrease in the mean WOMAC scores from 0 day (56.58) to 1st month (30.16), 1st month (30.16) to 6th month (15.16). In the study conducted by Subhash Y et al,[12] the pre-injection WOMAC score was 81±3.6, which decreased to 71±3.8 at 1 month and to 54±4.7 at 6 months. The pre-treatment WOMAC pain score was 14.966± 2.525 while it was reduced to 12.933± 2.545 in 1 month follow up and to 9.166± 1.858 at the end of 6 months follow up. The pre-treatment WOMAC stiffness score was 3.266± 1.229 while it was reduced to 2.366± 0.964 in 1 month follow up and to 1.200± 0.714 at the end of 6 months follow up. The pre-treatment WOMAC physical function score was 58.500± 4.133 while it was reduced to 53.633± 4.999 in 1 month follow up and to 45.733± 5.800 at the end of 6 months follow up. Intra-articular injection of autologous platelet rich plasma into the knee joint is safe and with mild adverse effects like immediate pain over the injection site, which subsided within few minutes without the need for any analgesic. Since the platelets rich plasma was processed in an aseptic condition and the technique was done under strict aseptic precaution in the operation theatre, there were no intra-articular infection and no antibiotic medication was given to the patients after the procedure. There were no complications of active bleeding after the procedures, and only a sterile adhesive bandage with a small gauze pad in the centre were used. There was no allergic reaction since the platelet rich plasma is an autologous product. Hence, intra-articular injection of autologous platelet rich plasma into the knee joint is both safe and effective. There are few limitations in our study such as sample size was small, follow up was for short term and only single injection was given. Long term follow up with large number of patients and multiple consecutive times injections will be required for complete understanding and for accurate correlation of factors affecting outcome after treatment of knee osteoarthritis.[13]

CONCLUSION

The result revealed that the autologous single platelet- rich plasma injection is an effective treatment for early osteoarthritis of the knee joint. However, keeping in mind the limited period of the follow up in the present study and the single setting of injection, we recommend longer follow up studies in multiple settings in larger number of patients to further consolidates our findings and establish the

long-term effectiveness of platelet-rich plasma treatment in cases of osteoarthritis of the knee joint.

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