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Intra articular injection of platelet rich plasma in grade 1 and 2 knee osteoarthritis and assessment of functional outcome: A longitudinal interventional study

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Abstract

Osteoarthritis of knee joint is one of the most important problem which increases disability adjusted life year. Various modalities of treatment are available for the treatment of osteoarthritis of knee. Intra articular injection of platelet rich plasma in knee joint is also one of the treatment options available for osteoarthritis knee. This longitudinal interventional study is to evaluate the efficacy of single intra articular injection of platelet rich plasma in grade 1 and grade 2 osteoarthritis. Consent was received from the patients with knee osteoarthritis and was injected with intra articular injection of autologous platelet rich plasma intra articularly. Pre-injection WOMAC scores were analyzed and post-injection scores were analyzed at 1,3 and 6th month. Results showed statistically significant report with decrease in WOMAC scores after injection. In conclusion, there is improvement in physical function and decrease in pain and stiffness in patients of knee osteoarthritis injected with single intra articular platelet rich plasma injection with effects confirmed by our study till six months post injection.

Keywords: Platelet rich plasma, osteoarthritis knee, intra articular injection

Introduction

Osteoarthritis is a degenerative condition which results in destruction of the articular cartilage and the subchondral bone. The symptoms of osteoarthritis of knee include pain in the knee joint and stiffness. Usually there is asymmetric involvement of the joints. Disability due to osteoarthritis occurs as the subject ages and it affects the daily living of the patient [1]. population with age more than 60 are more prone for the development of osteoarthritis in which 10 percent of males and 18 percent of females are affected [2]. Knee being a huge joint, has bony structures with the cartilages, ligaments and synovial membrane containing synovial fluid. More use for standing and gait make the knee joint a site for OA [3].

The important features of OA knee is found to be pain during maximum days in a month along with confirmation of OA with imaging techniques. The prevalence of the disease is 22% to 39% in our country [4]. The origin is multifactorial being post traumatic, inflammatory and metabolic changes [5].

Stages of Osteoarthritis

Stage 1: Osteophytes deposits in knee joint, but without the lysis of cartilage. Patient has complaints of discomfort and have normal Roentgenogram findings. Not even medical treatment is Needed at this stage [6].

Stage 2: Osteophytes are visualised in Roentgenogram and reduction of cartilage is seen. This causes diminishing the joint motion and leads to stiffness [7].

Stage 3: Vandalization of cartilage causing space reduction between bones. Roentgenogram reveals mislaying of cartilage [7].

Stage 4: Joint space narrowing and chondral destruction present. Radiograph shows joint space narrowing. Deformity requires surgical correction [7]. osteoarthritis is declared by proper history taking, physical examination, blood analysis and endorsed by Joint aspiration, Roentgenogram, MRI (for cartilage damage) [8].

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The treatment for osteoarthritis are: Non- invasive treatments are Physiotherapy and administrating drugs of non-steroidal anti-inflammatory group. Invasive treatments are Intra articular injections and joint replacement surgeries [9-12]. Total knee Arthroplasty is the last resort for the management of severe degenerative changes and deformities [13, 6].

Platelet Rich Plasma (PRP) plasma concentrate of platelets. PRP has bio active molecules and these molecules undergo degranulation and results in releasing cytokines and growth factors. This accelerates the neo vascularization and tissue remodeling. In osteoarthritis, intra articular PRP injection causes multiplication of cartilage forming cells and increase cartilaginous matrix. Platelet Rich Plasma alters the disease process rather than just providing symptomatic relief like other non-surgical treatments [17, 21].

This study is to assess the effectiveness of Intra articular injection of Platelet Rich Plasma (PRP) in pain relief and improvement in functional benefits in patients suffering from OA knee by diagnosing the cases of grade 1 and 2 osteoarthritis using Kellgren Lawrence scale and assessment of the functions of the patients using WOMAC scores and follow up for 1, 3 and 6 months.

2. Materials and Methods

After obtaining the IEC approval, a prospective longitudinal interventional study is conducted for a period from November 2017 to May 2019 in a tertiary care centre in patients of knee osteoarthritis with age: 40 – 70 years diagnosed with Kellgren and Lawrence scale as grade 1 and 2 in roentgenogram of knee anteroposterior (weightbearing stance) and lateral views with symptoms more than two months. Patients with diabetes mellitus, history suggestive of malignancy, inflammatory arthritis, immunodeficiency disorders, bleeding disorders, septic arthritis, post traumatic, previous treatment with systemic corticosteroids and NSAIDs 2 days prior to injection. Sample size is calculated with the following formula, for single proportion $n = 4pq/l^2$ $p = 82\%$ [based on previous study] [22]. 10% of non response error is 6.1, $n = 70$ Data was collected as follows: proper history and examination findings noted, diagnosis of knee osteoarthritis made through roentgenogram of knee anteroposterior view (weight bearing stance) and lateral view and graded with Kellgren Lawrence scale, and after informed and written consent from patients with grade 1 and 2 osteoarthritis, autologous platelet rich plasma was injected intra articularly

under sterile conditions and follow up was done at one, three and six months. Statistical analysis was done with descriptive statistics technique, paired t test, anova test.

Preparation of platelet rich plasma

10ml of venous blood collected with EDTA → centrifuged at 2600rpm for fifteen minutes → platelet rich plasma (5 times more platelets when compared to blood) prepared.

Procedure: under sterile conditions, platelet rich plasma of amount 5 ml is injected in to the suprapatellar pouch of the knee joint which is approached superolaterally and knee mobilization is done for 10 mins. Patients are observed for 30 mins for any adverse reactions.

Western Ontario and McMaster universities arthritis index (WOMAC) scale

The Western Ontario and McMaster Universities Arthritis Index (WOMAC) is used for evaluation of functional outcome in Knee Osteoarthritis. It has 24 questions which is subdivided into 3 subclasses [23, 24].

Statistical analysis: Statistical analysis has descriptive statistics like mean, and inferential statistics like paired t test, ANOVA test.

3. Results

The mean (SD) age of the population was 50.21 (6.68) years. The above figure shows that 36 (51.4%) of the subjects were males. Also 34 (48.6%) were females. The mean (SD) BMI (Kg/m^2) of the population was 25.29 (2.39)

Table 1: WOMAC scores injection among study population

Characteristics	Preinjection	1 ST Month	3 RD Month	6 TH Month
Mean	73.94	66.6	56.77	44.77
Standard deviation (SD)	9.387	6.813	8.991	11.609
Median	74	66	56	42
Mode	76	64	54	42
Minimum	8	52	38	24
Maximum	86	80	72	66

Inferential statistics

The paired t-test, also referred to as the paired-samples t-test or dependent t-test, is used to determine whether the mean of a dependent variable (WOMAC Score) is the same in two related groups

Table 2: Paired T Test of Two Related Samples

Scores		Mean	Std. Deviation	t value	p value
Pair 1	Preinjection Score–WOMAC Score 1 st Month	7.343	9.926	6.189	.000*
Pair 2	Preinjection Score–WOMAC Score 3 rd Month	17.171	10.640	13.502	.000*
Pair 3	Preinjection Score–WOMAC Score 6 th Month	29.171	12.113	20.149	.000*

*p value<0.001 highly significant

The above table showed that there was a significant reduction in WOMAC Scores pre-injection of PRP and post injection and the difference was statistically significant with increase in difference between scores.

Repeated ANOVA Test: Tests within the subjects

Table 3: Green house Geisser correction

	Degree of freedom	F value	Standard error	p value
Green house Geisser	1.452	314.038	100.208	<0.001*

*p value<0.001 highly significant

The inferential statistics using ANOVA with repeated measures with a Greenhouse-Geisser correction, the mean scores for WOMAC Scores were significantly different ($F(1.452, 100.2018) = 314.038, p < 0.001$).

Table 4: Mean difference between WOMAC scores

Scores	Mean	Std. Deviation
Preinjection Score	73.94	9.387
WOMAC Score 1 Month	66.60	6.813
WOMAC Score 3 Month	56.77	8.991
WOMAC Score 6 Month	44.77	11.609

The inferential statistics using ANOVA with repeated measures with a Greenhouse-Geisser correction, the mean scores for WOMAC Scores were significantly different ($F(1.452, 100.2018) = 314.038, p < 0.001$). Post hoc tests using the Bonferroni correction revealed that PRP injection elicited a reduction in WOMAC Scores from pre-injection to 1st month post injection (73.94 ± 9.387 vs 66.60 ± 6.813 , respectively), which was statistically significant ($p < 0.001$). It was also revealed that PRP injection elicited a reduction in WOMAC Scores from pre-injection to 3rd month post injection (73.94 ± 9.387 vs 56.77 ± 8.991 , respectively), which was statistically significant ($p < 0.001$) and a reduction between pre injection and 6th month post injection (73.94 ± 9.387 vs 44.77 ± 11.609 , respectively), which was also statistically significant ($p < 0.001$). Thus we can conclude that a intraarticular PRP injection elicits a statistically significant reduction in WOMAC Score starting from 1 month post treatment.

Selvi 53 Yrs Old Female with Right Osteoarthritis Knee



Fig 1: X-ray R Knee AP and LAT Views



Fig 2: PRP Injection and LAT Views

4. Discussion

The study was done to detect the outcome of physical functions of intra articular injection of platelet rich plasma in individuals suffering from early osteoarthritis knee in tertiary care centre. The study was performed in seventy patients with Osteoarthritis knee Symptoms exceeding the duration of 2 months and diagnosed with the help of Roentgenogram.

The results of this study suggest that intra articular injection of platelet rich plasma provides betterment of pain and improvement in physical functions of subjects with Osteoarthritis Knee. WOMAC scores has reduced in subjects, which was obtained in the pre injection period to the scores obtained in the post injection follow up period (Table 1). There is a significant reduction in the WOMAC scores over time. The lower limit was 40 years and the upper limit was 65 years which was similar to study performed to assess effectiveness of intra articular PRP (Platelet Rich Plasma) [25, 26].

A placebo-controlled study was performed in which one group had single dose of intra articular PRP and the co group had two dose of intra articular PRP and concluded that single dose of intra articular PRP was adequate [27]. In our study the use of single dose PRP injection was found. A study compared Hyaluronic Acid or platelet rich plasma injected intra articularly in subjects with knee osteoarthritis. Hundred and twenty subjects were involved in this study in which it was concluded that platelet rich plasma group got significant results compared to the other group of hyaluronic acid on follow up of six months. This result was same as that of our study on follow up [28].

There were significant deteriorations in WOMAC Scores pre-injection of intra articular PRP and post injection. There was an appreciable difference statistically showing p value < 0.001 which is higher than a different study (Table 2, 3, 4) [29].

WOMAC Score showed a directly proportional relationship between age and Osteoarthritis. It was found that old age patients has more physical functional restrictions and pain. This contradicts to another trial in which age was not considered to be a statistically significant factor in view of outcomes in their clinical trials [27, 30, 25]. The limitations of this study are no comparative group was included in this study for comparison of results, cartilage mapping was not done because of its cost and Sample size was low.

5. Conclusion

Our study relied on single intra articular injection of a highly concentrated mix of platelets into joint cavity and observing the patients for reduction in symptoms of pain, stiffness and improvement in physical function. Our study has revealed a consistent reduction in pain and stiffness and a clear improvement in lifestyle of the patients injected with single intra articular injection of platelet rich plasma with effects confirmed by our study till six months post injection. We further recommend future studies to analyze the results based on radiologic and biological measures, also studies can follow evaluation by cartilage mapping.

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