



Effectiveness of The Intra-Articular Injection of Platelet Rich Plasma in The Treatment of Patients With Primary Knee Osteoarthritis

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ABSTRACT

Background:- Knee osteoarthritis is a chronic medical condition of public health importance in this setting. It is mostly diagnosed when preventive measures are no longer practicable due to reliance on the radiological diagnosis. The aim of this work was to evaluate the effect of intra-articular injection of PRP on the functional status of the knee joint as by WOMAC scale and pain on the visual analogue scale for pain (VAS) and on the ultrasonographic finding of the OA knee. **Methods:-** The present study was carried out in people's college of medical sciences and research centre, Bhopal from November 2012 –April 2014. The study consisted of 25 patients out of which 8 patients had bilateral involvement so in total 33 knees were included in our study. It was a prospective study. **Results:-** Of 33 knees of 25 patients (8 with bilateral involvement) were studied in the department of orthopedics. Patients with kellegren II and kellegren III had shown highly statistically significant improvement at the end of follow up .Both with WOMAC and VAS. **Conclusion:-** From the presented results it was found that intra-articular injection of PRP is an effective and safe method for treatment of knee OA. Maximal improvement was seen in younger patients and those with shorter disease duration.

KEYWORDS

Platelet rich plasma; Intra-articular injection; Osteoarthritis; Knee; VAS scale, WOMAC scale.

Introduction

Osteoarthritis is the most common joint disease, and is characterized by progressive loss of articular cartilage, subchondral bone sclerosis, osteophyte formation, synovial membrane changes, and an increase in synovial fluid with decreased viscosity and lubrication properties. Mechanical, biochemical, and genetic factors are all involved in pathogenesis of osteoarthritis.¹⁻² Structurally, synovitis³, progressive articular cartilage loss⁴⁻⁵, osteophyte formation⁶ and subchondral sclerosis⁷, generally in weight bearing joints such as knee and hip, give rise to biomechanically unstable joints that result in loss of function⁸. Clinically, patients with OA experience pain, stiffness, loss of motion, weakness, and joint instability, all leading to functional limitation and disability.⁹ Perhaps the earliest descriptions of OA were provided by Heberden and Haygarth in the 19th century.¹⁰ In the 1930s and 1940s, Stecher¹¹ showed that there were two forms of this disease, idiopathic and post traumatic. The first x-ray grading system was developed in the 1950s by Jonas Kellgren and John Lawrence.¹² The current treatment modalities for OA are largely intervention-based, as they address symptoms only. Therapeutic approaches range from psychosocial, pharmacological, and physical therapy interventions to surgical replacements of degenerated joints. The field of using platelet rich plasma (PRP) in clinical and basic science research is growing. There is experimental evidence for positive effects of PRP in the context of soft tissue healing, ligament and bone regeneration, and inflammation reduction¹³⁻¹⁶. In another study on Egyptian patients with lateral epicondylitis and with plantar fasciitis, PRP was found promising and effective in both¹⁷. The aim of this work was to evaluate the effect of intra-articular injection of PRP on the functional status of the knee joint as by WOMAC scale and pain on the visual analogue scale for pain (VAS) and on the ultrasonographic finding of the OA knee.

Methodology

The present study was carried out in people's college of medical sciences and research centre, Bhopal from November 2012 –April 2014. The study consisted of 25 patients out of which 8 patients had bilateral involvement so in total 33 knees were included in our study. It was a prospective study. The permission from the institutional ethical committee was sought. All patients with knee pain presented in Orthopaedic OPD were screened clinically, Radiologically (AP & lat in standing position) and Pathological investigations was done. Those were found eligible for the study were explained about the study. After obtaining their willingness a written explained consent in the patients own language which he or she can read and write Or in case of an illiterate his left thumb impression in the presence of an attendant who can both read and write was taken. After screening the grade of OA was ascertained according to Kellegren and Lawrence classification of osteoarthritis.¹² The functional assessment will be done by WOMAC scale and pain by VAS. The patients were followed up at 2 weeks, 4 weeks 12 weeks and 24 weeks in OPD. The intra-articular infiltration of one knee was conducted in Operation Theater under aseptic precautions, with the patient in the supine position and the knee to be flexed at 90°, the infiltration was done through the antero-medial or antero-lateral arthroscopy portals; The patient was observed for a period of 15 minutes after injection with the limb in a functionally resting position. During the period of treatment the patients was forbidden to take non-steroid anti-inflammatory drugs 72 hours before and were advised not to carry out heavy physical activity involving the lower limb for at least 2 weeks after the procedure. Paracetmol was used as a rescue drug in a case of pain. For pain in contra-lateral knee the maximum dose upto 2gm per day was used. The contra-lateral knee was infiltrated after 1months of the last injection for which a fresh consent

was obtained.

Statistical analysis

The data was entered in Microsoft office excel 2007. The data was analyzed using Epi-info software. The continuous variable was analyzed as mean and standard deviation while categorical data as percentage and proportion. Statistical analysis was done using Statistical Package of Social Science (SPSS Version 19; Chicago Inc., USA). Data comparison was done by applying specific statistical tests to find out the statistical significance of the comparisons. Quantitative variables were compared using mean values and qualitative variables using proportions. Chi square test, Mann Whitney U test, ANOVA & Tukeys Post Hoc test was used to compare the data. Significance level was fixed at $P < 0.05$.

Results

Of 33 knees of 25 patients (8 with bilateral involvement) were studied in the department of orthopedics. Out of 25 patients there were 6 males and 19 females. There was no statistically significant difference in distribution of subject according to age ($p=0.3271$). Mean age of study subject that is 58.60yrs. while mean age for male and female was 60.0 and 58.16 respectively. There was no statistically significant difference in mean age between male and female ($p=0.692$). According to stage of kellegren, out of 33 knees of 25 subject (8 bilateral), 14 were in stage II and 19 were in stage III, there was no statistically significant difference among male and female in respect to stages of kellegren. ($p=0.341$). In 8 patients both the knees were involved while in 17 patients only unilateral involvement was seen, of these 12 knees were involved on right side and 5 knees were involved on left side. There was highly significant statistical difference ($p=0.001$). **Table 1** reveal mean pain score at different time interval. In respect to stage of kellegren in stage II mean pain score at baseline was 37.71 ± 2.3 which decreased continuously and at the end of 24 week it was 15.64 ± 2.4 while it was 18.11 ± 2.3 for stage III. There was statistically highly significant difference between stage II and III ($p=0.001$). **Table 2** reveals mean stiffness score at different time interval according to stages of kellegren. In stage III it was higher than stage II that is 16.95 ± 1.3 and 14.93 ± 1.4 respectively at baseline and there was statistically highly significant difference ($p=0.001$) at baseline, while at the end of 24 weeks the mean stiffness score for stage II was 4.21 ± 1.8 and for stage III 4.26 ± 0.93 . There was no statistically significant difference ($p=0.865$). **Table 3** reveals mean function score at different time interval according to kellegren stage. Mean function score was higher in stage III than in stage II that is 141.58 ± 5.1 and 128.79 ± 4.2 respectively there was statistically highly significant difference at all time interval between stage II and III ($p=0.004$). It was also decreasing in both the stages. It was 141.58 ± 5.1 for stage III at baseline which was continuously decreasing and at the end of 24 week it was 76.79 ± 5.8 and at the end in stage II it was 70.50 ± 5.6 . **Table 4** reveals mean VAS score at different time interval. Mean VAS score was 6.86 ± 0.66 at baseline while at the end of 24 week it reduced to 2.07 ± 0.73 . Initially there was significant difference between stage II and III. But at 12 and 24 week there was no significant difference ($p=0.234$). Mean pain score (VAS) was calculated at different time interval. At base line mean pain score was 41.09 ± 3.53 and than it was continuously decreasing and at the end of 24 week it was only 17.06 ± 2.5 . There was statistically highly significant difference between baseline and 24 week in mean pain score ($p=0.001$).

Discussion

The present study was conducted in the Department of Orthopedics, People's college of medical sciences and research centre bhanpur Bhopal from 01-11-2012 to 30-04-2014. The purpose of this study was to observe the effectiveness of Intra-articular Injection Of Autologous venous PRP in patients with symptomatic knee OA, in terms of target of diminishing pain, improving function and return to previous activities. This preliminary study was performed to provide potential outcome measures and data to determine whether PRP is safe and effective for knee OA. In improving the targets the data

demonstrated significant and almost linear improvements in WOMAC and VAS scores at 2, 4, 12 and 24 week follow-up supporting the fact that PRP injections could represent a valuable treatment in patients with knee OA. Cartilage assessment was limited because of the small sample size and limited resources. Overall, several patients were satisfied after treatment, in all age groups that had significant OA. The study included a range of patients with varying degree of OA both anatomically and functionally, explains the variation of overall satisfaction. The findings suggest a trend that documents improvement in pain scores and function, with a favorable experience. Osteoarthritis is a major public health problem which causes pain and disability in one third of all affected patients [18](#). It is one of the crucial musculoskeletal disorders characterised by the imbalanced homeostasis and destruction of the articular cartilage, in which pro-inflammatory cytokines are important catabolic regulators during OA cascade [19](#). Platelet-rich plasma (PRP) is a natural concentrate of autologous growth factors from the blood. It allows in a simple, low cost and minimally invasive way to obtain a concentration of many growth factors [20](#). The application of PRP to treat OA of the knee can be considered a relatively new therapeutic indication [21](#). This study has been carried out on 20 patients suffering from mild to moderate OA. They were injected in their knees by PRP for six injections at monthly-intervals. In our patients, a statistically significant improvement was observed regarding most of the clinical aspects, such as, tenderness in joint line, function and range of motion. Actually, the role of PRP in the cartilage repair is a matter of debate. A recent study reported that qualitative MRIs demonstrated no change per compartment in at least 73% after PRP injections [22](#). But a lot of in vitro studies evaluated the effect of PRP on chondrocytes; Gaissmaier et al., reported that addition of human platelet supernatant may accelerate chondrocyte expansion, even though it can also lead to de differentiation [23](#). In another study, an autologous conditioned serum was administered in horses with experimentally induced OA and reported a significant clinical improvement in lameness, decreased synovial membrane hyperplasia, less gross cartilage fibrillation and synovial membrane haemorrhage and increased synovial fluid concentration of interleukin-1 receptor antagonist. They stated that PRP may influence the overall joint homeostasis, reducing synovial membrane hyperplasia and modulating the cytokine level, thus leading to an improvement in the clinical outcome, even if only temporarily and without affecting the cartilage tissue structure and joint degenerative progression [24](#). Wu et al. investigated the feasibility of PRP to support chondrogenesis; they found that gelled PRP provided a 3-dimensional environment for seeded chondrocytes and was successfully used to deliver chondrocytes in cartilage defects in a rabbit model [25](#). Mitsuyama and colleagues reported that PRP promotes human chondrocyte proliferation, cells expanded with 30% PRP can express chondrocyte phenotype, and can serve as scaffold for autologous chondrocyte implantation that has potential availability for repair of osteoarthritis with chondral defects [26](#). Regarding humans, an old case report has been described, where plasma rich in growth factors was used to treat an articular cartilage avulsion in a soccer player. They reported an accelerated and complete articular cartilage healing [27](#). Recently, it has been stated that PRP has an anabolic effect on chondrocytes and bone marrow-derived stem cells with resulting increase in the cell proliferation and matrix production, as well as an anti-inflammatory effect via down regulation of known catabolic signaling pathways [28](#).

Our study showed that this method of treatment is very safe as no complications such as infection or fever occurred among study subjects. Only minor adverse events were detected such as mild pain at injected area and skin bruises. Patel and colleagues reported mild complications such as nausea and dizziness, which were of short duration [29](#) and these complications were not reported in our patients.

Conclusion

In conclusion we can say that platelet rich plasma intra-articu-

lar injections are very helpful in decreasing pain, stiffness and day to day functions. While this modality is very economic as compared to other intervention practiced, with no adverse reactions.

Table 1:- Mean pain score WOMAC (max-50) at different time interval according to Kellegren stage.

Stage	0 days(Baseline) MEAN±S.D	2 week MEAN±S.D	4 week MEAN±S.D	12 week MEAN±S.D	24 week MEAN±S.D
TWO	37.71±2.3	29.36±2.1	22.64±2.4	15.29±2.01	15.64±2.4
THREE	43.58±1.7	33.37±2.4	25.84±2.6	18.63±2.4	18.11±2.2
Mann Whitney U- test value	4.50	26.0	45.0	40.0	58.00
P-Value	0.001(HS)	0.001(HS)	0.001(HS)	0.001(HS)	0.006(S)

Table 2:- Mean stiffness score WOMAC(max-20) at different time interval according to Kellegren stage

Stage	0 week(Baseline) MEAN±S.D	2 week MEAN±S.D	4 week MEAN±S.D	12 week MEAN±S.D	24 week MEAN±S.D
TWO	14.93±1.4	11.0±1.5	7.43±1.15	4.25±1.05	4.21±1.18
THREE	16.95±1.3	11.95±1.2	8.16±1.06	4.95±1.11	4.26±0.93
Mann Whitney U- test value	41.50	95.0	95.0	88.5	128.50
P-Value	0.001(HS)	0.15(NS)	0.148(HS)	0.008(S)	0.865(NS)

Table 3:- Mean function score WOMAC(max-170) at different time interval according to stage

Stage	0 days(Baseline) MEAN±S.D	2 week MEAN±S.D	4 week MEAN±S.D	12 week MEAN±S.D	24 week MEAN±S.D
TWO	128.79±4.2	111.07±0.05	92.79±6.70	73.50±6.08	70.50±5.6
THREE	141.58±5.1	119.95±8.03	98.68±3.4	80.26±5.6	76.79±5.8
Mann Whitney U- test value	4.50	63.50	50.0	50.0	54.00
P-Value	0.001(HS)	0.01(S)	0.002(HS)	0.002(HS)	0.004(HS)

Table 4:- Mean VAS score(max-10) at different time interval according toKellegren stage

Stage	0 week(Baseline) MEAN±S.D	2 week MEAN±S.D	4 week MEAN±S.D	12 week MEAN±S.D	24 week MEAN±S.D
TWO	6.86±0.66	5.79±0.69	3.86±0.77	2.36±0.842	2.07±0.73
THREE	8.26±0.73	6.26±0.73	4.58±0.76	2.68±0.671	2.37±0.597
Mann Whitney U- test value	26.0	86.50	69.5	104.5	103.50
P-Value	0.001(HS)	0.06(S)	0.014(S)	0.259(NS)	0.234

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