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SALVAGING KNEE IN OSTEOARTHRITIS

Orthopaedics

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KEYWORDS

Introduction

The impact of osteoarthritis in elderly population in our society is steadily increasing, because of the continued rise in the mean age of the population. With treatment being variably effective and difficult, it still remains a challenging problem worldwide for all orthopedic surgeons. The regeneration capacity of cartilage is limited because of its isolation from systemic regulation and lack of vessels and nerve supply. Unlike, most tissues none of the inflammatory processes is available for its repair, and chondrocytes cannot migrate from an intact healthy site to the site of osteoarthritis. OA has a major impact on functioning of the knee and independence and ranks among the top ten causes of disability worldwide.

Clinical OA is defined by features in the history and on examination. It invariably requires the presence of joint pain in addition to other features like deformity in knee and restriction of movements. Pain is typically more after prolonged walking or standing and typically gets exacerbated on climbing stairs, squatting and sitting cross legged. The patient may have repeated episodes of acute exacerbations of the condition characterised by increase in pain and swelling due to synovitis with or without effusion. The condition is slow progressive and may lead to various deformities due to involvement of tibio-femoral joint. Symptoms get exacerbated in associated conditions of over-weight, systemic diseases like diabetes mellitus and previous joint disease involving the articular cartilage

AIM

To salvage osteoarthritis knee by non surgical means of intra-articular injection of Platelet Rich Plasma and Depomedrol.

Objectives

1) To find out the efficacy of platelet rich plasma in osteoarthritis knee.
2) To compare the efficacy of platelet rich plasma with Depomedrol in osteoarthritis knee.

MATERIAL AND METHOD

The study titled as "Salvaging Knee in Osteoarthritis" is a prospective study with randomised selection of patients for the assessment of outcome of treatment of Primary Osteoarthritis knee with intra articular injections of platelet rich plasma (PRP) or steroid (Depomedrol). The study was carried out in the department of orthopaedics, AVBRH, JNMC, Sawangi (Meghe).

A total of 121 patients suffering from OA knee were included in the study. These patients were randomly selected for injection in a sequential manner i.e. case number 1,3,5,7 and so on sequentially were given injection Depomedrol. Case number 2,4,6,8 and so on sequentially were given injection PRP

- Of the total 121 patients enrolled for the study 21 patients were lost in follow up. Hence the data was analysed only for 100 patients who had completed the follow up.
- Patients were evaluated prospectively at enrolment and at 1, 3 and 6-months follow-up.

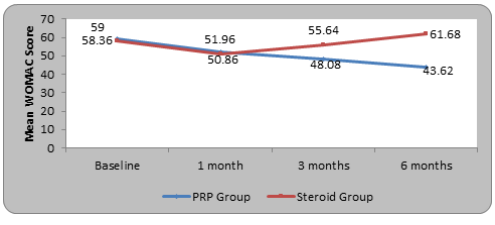
OBSERVATIONS AND RESULTS

1) Grade 1 patients were excluded from the study. A total of 29 patients (15 PRP, 14 steroid) were grade 2 patients, grade 3 comprised of 53 patients (25 in PRP, 28 in steroid) and 18 patients(10 in PRP, 8 in steroid) were included in grade 4 OA knee.
2) Comparison of WOMAC score in PRP and Steroid groups show both the groups to be significantly effective in improving WOMAC scores at 1 month follow up, but there on at 3 and 6 month follow ups PRP was found to be more effective in improving functional outcome in patients suffering from OA knee. While patients in the steroid group showed worsening of mean WOMAC scores at 3 month and 6month follow ups.

Table 1: Comparison of WOMAC score in PRP and Steroid groups using unpaired t test

	PRP Group		Steroid Group		t-value	p-value
	Mean	SD	Mean	SD		
Baseline	59	13.55	58.36	12.47	0.24	0.80,NS
1 month	51.96	11.67	50.86	11.34	0.47	0.63,NS
3 months	48.08	10.69	55.64	11.56	3.39	0.001,S
6 months	43.62	10.33	61.68	12.48	7.99	0.0001,S

Graph 1: Comparison of WOMAC score in PRP and Steroid groups

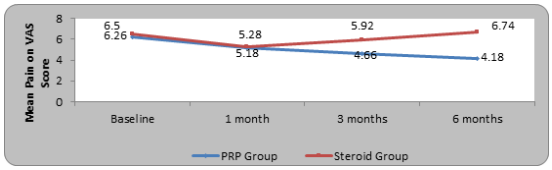


3) Comparison of VAS score in PRP and Steroid groups show both the groups to be significantly effective at 1 month follow up, but there on at 3 and 6 month follow ups PRP was found to be more effective in relieving the pain in patients suffering from OA knee. While patients in the steroid group showed worsening of mean VAS scores at 3 months and 6 months follow ups.

Table 2: Comparison of pain on VAS score in PRP and Steroid groups

	PRP Group		Steroid Group		t-value	p-value
	Mean	SD	Mean	SD		
Baseline	6.26	1.00	6.50	1.07	1.15	0.25,NS
1 month	5.18	0.84	5.28	0.96	0.54	0.58,NS
3 months	4.66	0.74	5.92	1.12	6.61	0.0001,S
6 months	4.18	0.84	6.74	1.12	12.86	0.0001,S

Graph 2: Comparison of pain on VAS score in PRP and Steroid groups



4) USG guided thickness could not be performed for all the patients included in the study, it was only performed on a few patients at pre-treatment and at 6 months follow up.

A 40 year old individual with symptomatic OA knee was considered as control for measurement of cartilage thickness for this study. Baseline value for femoral cartilage thickness in a 40 year old with symptomatic OA knee was found to be 1.35mm.

2 patients of grade II OA knee in the steroid group underwent USG guided measurement of femoral cartilage thickness at the completion of the treatment and their values were 1.15 and 1.27 respectively.

6 patients in grade III and grade IV OA in PRP group underwent USG guided measurement of femoral cartilage thickness at the completion of the treatment and their values were as shown in the following table-

Table 3: 6 months follow up values of USG guided cartilage thickness

USG guided cartilage thickness of patients in mm at 6 months post PRP injection	
Case 1 = 1.35	Case 4=1.32
Case 2=1.0	Case 5=1.25
Case 3= 1.25	Case 6=1.0

These values are in the range expected in advanced osteoarthritis knee keeping in mind the value of cartilage thickness in a 40 year old symptomatic OA knee patient, so there is no indication of any decreased rate of degeneration or regeneration of a damaged cartilage by use of either PRP or depomedrol.

Thus there is no statistically significant improvement in femoral cartilage thickness at 6 month follow up compared to a symptomatic 40 year old patient with OA knee.

DISCUSSION

Osteoarthritis of knee is a degenerative disease affecting the cartilage of knee joint leading to pain, decreased range of motion, hampered functional outcome, difficulty in performing day to day activities like walking, sitting cross legged and squatting etc. Articular cartilage lesions and degeneration are difficult to treat and present a challenge for orthopedic surgeons because of the poor blood supply of hyaline cartilage and its inherent low healing potential(1-4)

Osteoarthritis of knee, as the name suggests is a degenerative inflammatory condition affecting the cartilage of the knee joint. It is known that the patient suffering from OA knee may have recurrent episodes of acute synovitis leading to increase in the intensity of pain, restriction of movement, effusion, etc.

In view of their anti-inflammatory action, intra-articular steroid injections have been indicated for their use in OA knee. With satisfactory early onset of action and symptomatic relief, intra-articular steroids were used vastly in earlier days but later on it was found that they have a short term relief up to 1 month post injection(5) As the steroids do not modify the course of disease and neither halt the process of degeneration of cartilage or repair the already affected cartilage their use has now been surpassed by other more long term acting options like intra-articular hyaluronic acid or intra-articular PRP injections(5)

Recent studies are focusing on possibility of preserving normal homeostasis or reversing structural damage as a target to delay the need for more invasive surgical procedure. Till date no proven disease modifying therapy is available which can completely halt the process of degeneration and thus affect the course of arthritis so as to avoid early osteoarthritis to land up into advanced OA knee. However, current pharmacologic intervention may only reduce pain temporarily, thus making it sustainable for the patient to perform his day to day activities within the range of pain limit(6)

Recently, there is an increase in the use of autologous blood products that might provide cellular and humoral mediators to favour tissue healing in a variety of conditions(7-13)

The rationale is based on the activity of Growth Factors (GF) carried in blood. The fact that platelets secrete GFs and active metabolites means that their applied use can have a positive influence in clinical situations involving tissues with a low healing potential such as cartilage.

Blood-derived GFs have already been studied for their potential in helping cartilagerepair(13, 7, 8, 9, 14-17). Gaissmaier et al.(15) investigated the effect of human platelet supernatant on chondrocytes in human articular biopsy specimens and observed an acceleration of chondrocyte expansion. Mishra et al(17) described how PRP enhanced mesenchymal stem cell proliferation and chondrogenic differentiation in vitro which might justify its use in osteoarthritis knee in view of cartilage repair and thus may be a promising solution in the treatment of OA knee. However, the evidence base for use of PRP is still in its early stages, and it needs to be studied thoroughly so as to clarify its specific indications in case of OA knee.

Few studies have evaluated the effectiveness of PRP in OA. The results of Kon et. al(12) were comparable with those obtained in this study, showing sustained efficacy of PRP. Recently, there has been an increasing prevalence of the use of autologous blood products (PRP) that might provide cellular and humoral mediators to favour tissue healing in a variety of conditions(7, 8, 9-12).

Herein the findings of the present study are discussed in relation to other similar studies:-

1) Total number of patients

Out of the total 121 patients who were enrolled under the study, there were a total of 70 (57.85%) females and 51(42.15%) males, showing female predominance of OA knee in this study. Eventually 21 patients were lost in follow up and the study was completed with 100 patients .Data analysis was done keeping these 100 patients in consideration.

2) Male/female ratio

In this study 100 knees were included, out of which 46 were male and 54 were female showing female preponderance. Male : female ratio in the followed up patients was 0.85:1. This was comparable with data produced by the Dutch Institute for Public Health, according to them the prevalence of knee OA in those aged 55 years and above was 15.6% in men and 30.5% in women(18).

3) Age wise distribution

Mean age of the patients enrolled under this study was 62, with age range from 40 to 85 years. Majority of patients (34 knees) were of age group 60 to 69 years.

Mean age of patients included in the study in PRP group was 59, with range being from 40 to 76 years.

Mean age of patients in steroid group was 61, with range being from 40 to 85 years

Our results were comparable to the study performed by García-Escudero JB et al.(6) who noted female predominance of OA knee with female/male ratio of 75/43. Mean age in their study was 59 years with age range of 34 to 81 years in their study.

4) Side involved

49 were right sided and 51 were left sided knees. This was found statistically to be non significant

5) Grade wise distribution in PRPand steroid groups as per Kellgren-Lawrence grading system Patients with grade II, grade III and grade IV OA knee as per Kellgren-Lawrence grading system were included n this study, out of which 29 knees (15 PRP+14 steroid) were grade II OA and 53 knees(25 PRP + 28 steroid) were III OA and 18 knees were grade IV (10 PRP + 8 steroid). Grade III osteoarthritis was the commonest (53%) followed by grade II and grade IV in our study Similar results were seen in studies performed by Nayana Joshi Jubert

et al.(19) and García-Escudero JB et al.(6) who noted 67.7% patients having grade III OA followed by 11.01 % of grade I OA and grade II OA each and 10.16% patients of grade IV OA knee as per Kellgren-Lawrence grading system.

6) Effect of treatment at 1month, 3 months and 6months follow up using WOMAC Score

a) PRP group

50 knees received intra-articular PRP injection out of which 15 knees were grade II OA, 25 knees grade III OA and 10 knee grade IV OA.

In the PRP group the mean pre treatment WOMAC score was 59.00. At 1 month, 3 months and 6 months follow up the mean WOMAC scores were 51.96, 48.08 and 43.62 respectively. The change in WOMAC score shows that there is sustained functional improvement at 1 month, 3 month and 6 months follow up.

b) Steroid group

50 knees received intra-articular steroid injection out of which 14 were grade II OA, 28 were grade III OA and 8 were grade IV OA as per the Kellgren-Lawrence grading system In our study in both groups of patients showed statistically significant (p value- 0.0001 in both groups) improvement at 1 month follow-up.

In the steroid group the mean pre treatment WOMAC score was 58.36. WOMAC scores at1 month, 3 months and 6 months were 50.86, 55.64 and 61.68 respectively. The change in WOMAC score shows that there is functional improvement at 1 month followed by gradual worsening at 3 and 6 months

7) Effect of treatment at 1month, 3 months and 6months follow up using VAS Score

a) PRP group

In the PRP group the mean pre treatment VAS score was 6.26 At 1 month, 3 months and 6 months follow up the mean VAS scores were 5.18, 4.66 and 4.18 respectively. The change in VAS score shows that there is sustained improvement in pain at 1 month, 3 month and 6 months follow up.

b) Steroid group

In the steroid group the mean pre treatment VAS score was 6.50. VAS scores at1 month, 3 months and 6 months were 5.28, 5.92 and 6.74 respectively. The change in VAS score shows that there is improvement in pain at 1 month followed by gradual worsening at 3 months and 6 months.

Forogh B et al.(20) conducted a study to determine the clinical utility of intra-articular injection of PRP in the treatment of late-stage knee OA for subjective pain relief 1 month after the infiltration compared with intra-articular corticosteroid injection infiltration, as determined by VAS scale.

Since corticosteroid effects are known to be short, the VAS for the control group worsened at 3 months onwards while it improved in the PRP group.

The above findings of the study indicate PRP group patients have shown sustained and progressive relief in their pain and functional disability as evidenced by VAS and WOMAC scores with single injection. This indicates its effect on the disease pathology and arrest of cartilage degeneration and probably a beginning towards cartilage regeneration. Thus PRP has been found to be effective agent for salvaging moderate to severe OA knee. However the cartilage measurement done in a few patients 6 months post treatment in the present study in comparison to the cartilage thickness of a symptomatic 40 year old patient do no indicate that there is decrease in the rate of cartilage degeneration or regeneration of damaged cartilage in osteoarthritis by use of PRP or steroid, though long term and bigger sample size studies are needed for knowing effect of PRP on cartilage regeneration/degeneration in OA knee USG guided thickness could not be performed for all the patients included in the study, it was only performed on a few patients at pre-treatment and at 6 months follow up. In this study we did not find any significant increase/decrease in femoral cartilage thickness either in PRP group or in steroid group at 6 months follow up.

Normal range of femoral cartilage thickness for an adult is from1.60 to 1.90 mm(21)

A 40 year old individual with symptomatic OA knee was considered as control for measurement of cartilage thickness for this study. Baseline value for femoral cartilage thickness in a 40 year old with symptomatic OA knee was found to be 1.35mm

USG guided cartilage thickness of patients in mm	
Case 1= 1.25	Case 5=1.15
Case 2= 1.27	Case 6=1.0
Case 3 = 1.35	Case 7=1.32
Case 4=1.0	Case 8=1.25

Comparing the results of PRP and steroid, PRP has been noted to be a superior agent in salvaging knee in OA knee based on follow up WOMAC and VAS scores. But we could not produce an objective evidence in the form USG guided cartilage thickness measurement to show cartilage regeneration following single intra-articular injection of autologous PRP.

The results show that use of steroid in osteoarthritis knee is having a short term effect followed by deterioration in pain and function of the knee. This is supported by various authors mentioned above. Thus steroid injection cannot work as a salvage agent in moderate to advanced stages of OA knee. On the other hand PRP was found to be more efficient agent in salvaging knee in OA. Halpern et. al(22) conduced a similar study, they applied a single dose of PRP in 22 patients. They studied the effect of PRP on cartilage repair using Magnetic Resonance Imaging. In their study they concluded that Qualitative magnetic resonance imaging demonstrated no change in cartilage thickness per compartment in at least 73% of patients at one year.

Sampson et al.(23)applied three PRP injections at one month intervals to 14 patients with primary or secondary knee OA. They demonstrated improvement, although not statistically significant, in the cartilage thickness on sonography at lateral condyle and intercondylar notch during the first six months follow-up. They attributed the insignificant statistical results to the limited number of patients

The limitations of our study are lack of placebo control group, less number of patients in individual groups, short term of follow up of patients limited only upto 6 months and the doses and frequency of intra-articular injections of PRP need to be standardized.

Objective evidence in support of effect of intra-articular PRP injections at 6 months could not be generated in a scientific way as most of the patients did not agree to undergo ultrasound for cartilage measurement prior to treatment and at follow up.

During the entire time duration of the study, we did not come across any complication of the treatment that may arise as a result of intra-articular injection of either PRP or steroid.

EgemenAyhan et al.(5)in their study of intra-articular injections of corticosteroid, hyaluronic acid or platelet rich plasma for the knee osteoarthritis also mentioned PRP to be safe and a promising option with no serious complications in treatment of OA knee.

SUMMARY

- A total of 121 patients were enrolled under the study out of which 21 were defaulters or who didn't show up for follow up. With final study results and observations finalized for 100 patients.
- Patients above 40 years of age with Kellgren-Lawrence grade 2, 3 or 4 primary OA knee were included in the study.
- Out of the 100 patients, 54 were female and 46 were male.
- Majority of patients (34 knees) were of age group 60 to 69 years. Mean age of patients included in the study in PRP group was 59, with range being from 40 to 76 years.
- 49 were right sided and 51 were left sided knees.
- 29 knees (15 PRP+14 steroid) were grade II OA and 53 knees(25 PRP + 28 steroid) were III OA and 18 knees(10 PRP + 8 steroid).
- 50 knees received intra-articular PRP injection out which 15 knees were grade II OA, 25 knees were grade III OA and 10knees were grade IV OA. Similarly 50 knees received intra-articular steroid injection out of which 14 were grade II OA, 28 were grade III OA and 8 were grade IV OA as per the Kellgren-Lawrence grading

system

- Mean WOMAC and VAS scores significantly reduced at 1month follow up in both PRP as well as steroid groups. However, steroid group showed significant worsening of mean WOMAC and VAS scores at 3 months and 6 months follow up. The mean WOMAC and VAS scores in PRP group showed sustained improvement even at 3 month and 6 month follow up.
- Thus PRP seems to more efficient in improving WOMAC and VAS scores when compared to steroid in salvaging knee in osteoarthritis.
- Thus it is concluded that PRP injection can work as a salvaging agent in moderate to advanced osteoarthritis of knee.
- Steroid injection has been found to be ineffective as a salvaging agent in osteoarthritis knee in comparison to PRP injections.

CONCLUSION

The clinical results of this study show that both these non-surgical modalities (intra-articular injections of PRP or steroid) are useful for the treatment of osteoarthritis of knee. Though steroid might have a short term effect but is still helpful in salvaging knee in osteoarthritis.

Treatment with PRP show significantly better outcome compared wih steroid group; patients achieved lower WOMAC and VAS scores which were subsequently maintained even at 6 months follow up in the PRP group.

Thus intra-articular injection of PRP is a efficient treatment modality for salvaging knee in moderate to advanced OA.

Despite the relatively low number of patients in each sub-group, statistical analysis confirms better results of PRP than the steroid group. Thus concluding that intra-articular injections of PRP is a more efficient and a better non surgical treatment modality for treating OA knee when compared to intra-articular injections of steroid

RECOMMENDATION

Blinded randomized control trials should be performed over a larger sample size of patients to further confirm these findings and understand the mechanism of action, determining whether there is only short-term symptomatic relief or whether PRP also plays a more important role in salvaging knee in osteoarthritis through its disease-modifying properties.

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