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Comparative study for efficacy of autologous growth factor rich plasma (GFRP) versus combination of low molecular weight hyaluronic acid and autologous growth factor rich plasma (GFRP) in bilateral osteoarthritis knee (Grade 1, Grade 2 according to Kellgren-Lawrence grading system)

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Abstract

Osteoarthritis knee in initial stages can be managed conservatively by various methods, here we did comparative study between intraarticular GFRP injection vs combination of low molecular weight hyaluronic acid & GFRP injection in bilateral osteoarthritis knee, we concluded that when Growth Factor Rich Plasma (GFRP) is combined with low molecular weight hyaluronic acid, it had added effect and the results are much better as compared to the knees when only Growth Factor Rich Plasma (GFRP) injection was injected.

Keywords: Osteoarthritis, low molecular weight hyaluronic acid, GFRP, Kellgren-Lawrence grading system

1. Introduction

Knee osteoarthritis is the most common articular disease. For the knee OA, various conservative treatment modalities are recommended by clinical guidelines. The non-pharmacological modalities are patient education and self-management, exercises, weight reduction, walking supports (crutches), bracing, shoe and insoles modification, local cooling/heating, acupuncture, and electromagnetic therapy. Pharmacologic therapies can be summarized as non-steroidal anti-inflammatory drugs, opioids, and slow-acting drugs (glucosamine and chondroitin sulfate). If orally administered drugs are ineffective, intraarticular injection (corticosteroids, viscosupplements, blood-derived products) is the last nonoperative modality that can be preferred. New studies have focused on modern therapeutic methods that stimulate cartilage healing process and improve the damage, including the use of low molecular weight hyaluronic acid and platelet-rich plasma (PRP) as a complex of growth factors. Due to the high incidence of OA and its consequences, we decided to study the long-term effect of intraarticular injection of GFRP and HA on clinical outcome and quality of life of patients with knee OA grade 1, grade 2 as per Kellgren-Lawrence Grading system of osteoarthritis knee) as regards the pain relief and to evaluate the need for analgesics after the procedure in both the groups at different stages of follow up and compare it with the pre-procedure level [1, 2].

The major contraindication for IA injections is septic arthritis. In addition, in the presence of overlying soft tissue infection, there is risk of iatrogenic seeding to the joint.

When the various potential conservative treatment modalities and the uncertainty in regards to evidence-based recommendations are considered, it is inevitable that some inconsistencies exist between clinical guidelines [3]. However, the consensus occurs in two points: (1) The optimal conservative management of knee OA requires a combination of pharmacological and non-pharmacological treatment modalities customized to individual patient needs; and (2) The

main goals of conservative management are to reduce pain, improve function and quality of life, and limit disease progression [4, 5].

Osteoarthritis (OA) refers to a clinical syndrome of joint pain with multifactorial etiopathogenesis that is characterized by the gradual loss of articular cartilage, osteophyte formation, subchondral bone remodeling, and inflammation of the joint. OA is a major source of disability owing to pain and loss of function. It is the most common form of joint disease, and among the top 10 causes of disability worldwide. With aging of the population and increasing obesity, OA arises as a major public health problem and an important financial burden for the global economy [6].

1.2 Kellgren-Lawrence Grading System for OA, 1957 [7]

(This is radiological assessment in which x-ray of both knees AP view in standing position are taken).

Grade 0: Normal, no features.

Grade 1: Questionable presence of osteophytes/questionable presence of joint space narrowing / both.

Grade 2: Definite presence of osteophytes with possible joint space narrowing or definite mild joint space narrowing

Grade 3: Definite moderate joint space narrowing (at least 50%) Osteophytes usually present, Cysts/sclerosis may be present

Grade 4: Severe joint space narrowing with subchondral bone sclerosis and possible deformity of bone ends.

2. Material and methods

The study was conducted on patients admitted for treatment of osteoarthritis knee. 30 patients of either sex with bilateral osteoarthritis knee (Grade 1 & Grade 2 as per Kellgren-Lawrence grading system of osteoarthritis knee) were selected for this study in the age group of 40 years and above.

Radiological assessment was done as per Kellgren-Lawrence Grading System for OA. In all the 30 patients randomly selected one knee was comprised Group A in which combination of low molecular weight hyaluronic acid and autologous growth factor rich plasma (GFRP) injection was given in one knee. The other knee receiving only autologous growth factor rich plasma (GFRP) injection comprised group B. Following discharge from the hospital, the participants were followed up on a regular basis with clinical examinations and functional evaluations for pain relief as per VAS scale. Patients were followed up at 1 months, 6 months and 12 months starting from the day of procedure. All the patients were evaluated as per the proforma attached and were followed up at 1 months, 6 months and 12 months for pain relief as per VAS scale. Quantitative variables were described using mean \pm standard deviation (SD) and categorical data by frequency and percentage. Student's t-test was used to compare quantitative variables between groups of patients. Levene's test for equality of variances and t-test for equality of means were used to examine the changes of VAS score at follow-up after treatment. In all tests, p value <0.05 was considered to be statistically significant. Following observations were made at different follow ups:

Patients having uncontrolled diabetes mellitus, having active infection in the body or local skin infection were not included.



Anterolateral Site Marked



10 CC 2% Lignocaine Being Injected



Low Molecular Weight Hyaluronic Acid Gfpr Injection Procedure



12 ML Gfpr (Platelet Concentrate) Extract After 2nd Centrifuge



Gfpr for Injection



GFRP Injected In Knee Joint

2.1 Preparation of growth factor rich plasma

On the day of the surgery, the patient was sent to the Blood Bank. A three chambered blood bag was taken, and 48 ml of CPD (citrate phosphate dextrose) was removed and discarded, leaving just 15 ml of CPD in the bag. 100 ml of patient's whole blood was drawn by a clean, single venipuncture, into the 1st chamber of the blood bag. The bag was kept in the bucket of refrigerated centrifuge (Heraeus Cryofuge 6000i) and balanced accurately, and centrifuged at 2000 rpm at 22 degrees C for 10 minutes. This separated the whole blood into red blood cell concentrate at the bottom and plasma above. 4/5th of the plasma will be separated into the 2nd satellite bag, double sealing the tubing between the primary bag and the satellite bag. The primary bag with RBC concentrate was separated and kept aside. The remaining 2 satellite bags were again centrifuged at 4000 rpm at 22 degrees C for 10 minutes after balancing accurately. The plasma separated into an upper layer of platelet poor plasma (PPP) and platelet concentrate (GFRP) below. The PPP layer was expressed into the 2nd satellite bag, double sealed, separated and kept aside.

The GFRP (platelet concentrate) extract in the 1st satellite bag was approximately 12-18 ml. This bag was sent to the OT immediately, where it was kept at room temperature before use.

2.2 Procedure for intraarticular injection of GFRP and low molecular hyaluronic acid:

GFRP was removed from the blood bag using aseptic technique, and was put in a sterile container. Both knees were exposed and after proper cleaning & draping knee joint was approached through anterolateral site using 18 G disposable steel spinal needle. GFRP and low molecular weight hyaluronic acid injected in one knee joint and other knee injected with only GFRP with 20cc syringe. Needle was removed & aseptic dressing done. Patient was instructed to bend and extend the knee to allow equal distribution of GFRP and low molecular weight hyaluronic acid throughout the joint. Bandage applied. Patient was discharged immediately with instructions to gradual resumption of normal activities.

2.3 Kellgren-Lawrence Grading For Osteoarthritis

K.L. Grading	Group A		Group B		Total
	No. of knees	%age	No. of knees	%age	
Grade 1	15	50	14	46.66	29
Grade 2	15	50	16	53.33	31
Total	30	100	30	100	60

2.4 Vas Score at 1 Months

VAS Score	VAS Scale Improvement (%)	Group A		Group B		Total
		No. of knees	% age	No. of knees	% age	
Excellent	>80	18	60	16	53.33	34
Good	60-80	12	40	14	46.66	26
Fair	40-60	-	-	-	-	-
Poor	<40	-	-	-	-	-
Total		30	100	30	100	60

Results were compared between both groups as per vas score comparison. In group A i.e. the group in which both low molecular weight hyaluronic acid and GFRP injection was given in same knee it was found that, out of 30 cases 18 (60%) patient had excellent results while 12 (40%) patients had good results while none of the patients had fair or poor result. Similarly in group B i.e. the group in which only GFRP injection was given in the opposite knee of the same patient, it was found that 16 (53.33%) patients had excellent results while 14 (46.66%) patients had good result. The mean VAS score in group A was 15.1 mm while in group B it was 23.5 mm and the difference between 2 groups was found to be highly statistically significant ($p<0.01$).

2.5 Vas Score at 6 Months

VAS Score	VAS Scale Improvement (%)	Group A		Group B		Total
		No. of cases	%age	No. of cases	%age	
Excellent	>80	16	53.33	12	40	28
Good	60-80	14	46.66	18	60	32
Fair	40-60	-	-	-	-	-
Poor	<40	-	-	-	-	-
Total		30	100	30	100	60

In group A, it was found that, out of 30 knees 16 (53.33%) patient had excellent results while 14 (46.66%) patients had good results while none of the patients had fair or poor result. Similarly in group B, it was found that 12 (40%) patients had excellent results, 18 (60%) patients had good results and none of the patient had fair or poor results. The mean vas score in group A was 22.0 mm while in group B it was 32.66 mm and the difference between 2 groups was found to be statistically significant ($p<0.05$).

2.6 VAS Score at 12 Months

VAS Score	VAS Scale Improvement (%)	Group A		Group B		Total
		No. of cases	% age	No. of cases	% age	
Excellent	>80	8	26.66	8	26.66	16
Good	60-80	18	60	12	40	30
Fair	40-60	3	10	8	26.66	11
Poor	<40	1	3.33	2	6.66	3
Total		30	100	30	100	60

In group A, it was found that, out of 30 knees 8(26.66%) patients had excellent results while 18 (60%) patients had good results and 3 (10%) had fair results and 1 (3.33%) had poor results. In group B, it was found that, out of 30 knees 8(26.66%) patients had excellent results while 12 (40%) patients had good results and 8(26.66%) had fair results and 2 (6.66%) had poor results.

The mean vas score in group A was 46.0 mm while in group B it was 47.0 mm and the difference between 2 groups was found to be statistically non-significant ($p>0.05$).

2.7 Complications

Complication	Group A		Group B	
	No. of cases	% age	No. of cases	% age
Superficial Infection	1	3.33%	-	-
Deep Infection	-	-	-	-
Leakage of Synovial Fluid	1	3.33%	-	-
Increased Pain for 24 hours	-	-	2	6.66%

Among group A, one (3.33%) case had a superficial infection at the point of entry which was cured with short course of appropriate antibiotics for 5 days. Another 1(3.33%) cases in group A had leakage of synovial fluid for about 5 days after the opening of the bandage. The problem was resolved with compression bandage for further 1 week. No complication of any form was noted in group B except aggravation of pain for about 24 hours in 2(6.66%) cases.

2.8 Evaluation of Results

Results were evaluated according to visual *analogue* scale (VAS).

0
No pain

100
Very severe pain

Before the surgical procedure the pain is considered at 100 mm in all patients and at every follow up; patient is asked to mark a point on the line to explain how much of pain relief he/she is having and then the distance from the 0 point was measured.

Results evaluation as per VAS Scale improvement

Excellent	> 70%	Improvement
Good	50- 70%	Improvement
Fair	30- 50%	Improvement
Poor	< 30%	Improvement

The comparative evaluation of the results of clinical outcome as regards the pain relief was done for both the knees where one knee had been treated low molecular weight hyaluronic acid plus autologous growth factor rich plasma (GFRP) whereas the other knee of the same patient had been treated with autologous growth factor rich plasma (GFRP) injection only.

We evaluated the need for analgesics after the procedures at all the follow ups in both the groups and compare it with the analgesic requirements before the procedure.

3. Discussion

It is inferred from the above observations that majority of the patients seek medical intervention for their pain relief for osteoarthritis knee in the 6th decade of their life and when the problem is slightly advanced. Females suffer more than the males. The observations being attributed to the post menopausal hormonal changes in the female. Mostly Grade I patient keep on trying the home made remedies for pain relief GFRP injections results in the release of the growth factors and attract the Mesenchymal Stem cells so as to start the chondro protective and chondro regenerative potential in knee joint cartilage and hence result in pain relief in the longer run.

Initially this accounts for improved viscosupplementation. Knee lavage results in immediate pain relief and pain starts appearing back only when new crop of debris starts forming with continued degenerative process whereas GFRP injection takes some time to induce the action and hence the onset of pain relief is slow but long lasting which is clearly shown in the results at different follow up in both the groups. The poor result patients in both the groups at one year were from grade III and as the time passes the efficacy of both the procedures starts decreasing, though the group A (combination group) had marginally better results at one year follow up.

4. Conclusion

Growth Factor Rich Plasma (GFRP) and low molecular weight hyaluronic acid have different modes of action and have proven efficacy in osteoarthritis knees when injected separately too. Though the effect of low molecular weight hyaluronic acid lasts for lesser period than Growth Factor Rich Plasma (GFRP) injection.

In our study we have concluded that when Growth Factor Rich Plasma (GFRP) is combined with low molecular weight hyaluronic acid, it had added effect and the results are much better as compared to the knees when only Growth Factor Rich Plasma (GFRP) injection was injected.

We highly recommend the use of combination of Growth Factor Rich Plasma (GFRP) injection & low molecular weight hyaluronic acid in cases of early osteoarthritis knees to achieve pain relief for longer duration.

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