



ROLE OF PLATELET RICH PLASMA IN EARLY OSTEOARTHRITIS OF KNEE JOINT

Orthopaedics

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ABSTRACT

Introduction- Osteoarthritis is a chronic disorder of synovial lined joints where there is progressive softening and disintegration of articular cartilage accompanied by new growth of cartilage and bone at the joint margins, cyst formation and sclerosis at subchondral regions of bone, mild synovitis and capsular fibrosis. The pathogenesis involves an imbalance between normal cartilage derivative and repair mechanisms, which results in net cartilage loss, hypertrophy of bone, and osseous outgrowths called osteophytes. Among the elderly, knee Osteoarthritis is the leading cause of chronic disability. Because of the increased lifespan and obesity the prevalence of osteoarthritis is on the rise in Indian population. **Aims and Objectives-** To Evaluate effectiveness of intra articular injections of platelet-rich plasma (PRP) for patients presenting with primary osteoarthritis of knee. To analyse whether it could be a cost effective disease modifying measure, devoid of major side effects and operative costs. **Materials and methods --** The study was conducted at the Department of Orthopaedics, GMC, Kota between the period November 2020- December 2021. Patients were subsequently called at 3 months, 6 months and 12 months and the efficacy of Platelet Rich Plasma in reducing pain, stiffness and physical function were assessed and scored on WOMAC index. **Results-** In our study we chose 100 patients with classic findings of Osteoarthritis. The Global WOMAC had mean value of 74.2 at pre injection period which decreased to 62.46 at 3 months follow up and 47.68 at 6 months and declining to 33.40 at 12 months. The Individual variables such as pain, stiffness and physical function were also assessed. Mean score for pain showed a decrease from 16.58 to 11.32 at 3 months post injection. At the end of 12 months follow up, the mean was 5.34. The mean of Physical function decreased from a pre injection score of 52.12 to 24.62 at 12 months follow up. The mean of stiffness score showed a decline from a pre injection score of 5.5 to 3.4 at 12 months follow up. **Conclusion-** Our study has revealed a significant improvements in pain reduction, improved symptoms and Quality of Life. The walking distance of the patient improved and they were able to perform daily activities with much ease. PRP is an effective choice of treatment modality of Knee Osteoarthritis.

KEYWORDS

INTRODUCTION

Osteoarthritis (OA) is a chronic musculoskeletal condition that commonly affects the knee and/or hip joints. Osteoarthritis causes substantial pain and disability and impacts on quality-of-life. Knee OA has been ranked as the 11th highest contributor to global disability and 38th highest in years lived with disability. There is no cure for OA, and to date, most research has focused on treatments to alleviate pain and prevent functional decline. Recommended drug therapies (such as analgesics and anti-inflammatory agents) and non-drug therapies (such as exercise) have short-term clinical benefits but effect sizes are generally small to moderate. Furthermore, use of these drugs can have serious adverse consequences, while uptake and maintenance of exercise is often poor leading to lack of long-term benefit. The role of glucosamine sulphate and chondroitin sulphate as symptom- and disease-modifying agents is still being debated. Having failed these treatment options, joint arthroplasty is a common procedure for advanced hip or knee OA. While it is an effective definitive treatment, it is expensive and there is a risk of serious medical and post surgical complications. Thus, as OA is typically progressive with symptoms and structural deterioration driving the need for joint replacement, identifying efficacious, safe treatments that address both symptoms and structure is an important objective. However, therapies that affect the underlying biological processes responsible for OA pathogenesis have potential. One such biologic therapy receiving increasing interest is platelet-rich plasma (PRP) injections into the affected joint. There are several possible advantages of PRP as a treatment for OA. First, it is relatively easy to use because its preparation is rapid and technically straightforward, and the administration is minimally invasive requiring a simple intra-articular injection which can be performed in the office. Second, it is likely to be safe because the patient's own proteins are used and bioactive molecules can be appropriately concentrated, thereby avoiding many adverse effects and drug interactions. Indeed, no major adverse events have been reported in the literature with those that have been reported being minor and transient, including bleeding, tenderness, swelling and/or bruising at the injection site. Third, PRP is generally not considered a drug or therapeutic substance and, therefore, in many countries, does not have the regulatory requirements that would be needed for other biologic therapies. Aim of this article will be to evaluate effectiveness of intra articular injections of platelet-rich plasma (PRP) for patients presenting with primary osteoarthritis of knee and to analyse whether it could be a cost effective disease modifying measure, devoid of major side effects and operative costs.

MATERIALS AND METHODS

Hospital based, prospective, interventional study on patients with primary OA of knee. The study was conducted on the patients attending the OPD of Orthopaedics at Government Medical College, Kota, a tertiary teaching center of South Rajasthan, between the period of November 2020 to December 2021. Patients with complaints of bilateral knee pain were screened and those diagnosed as bilateral Knee Osteoarthritis were chosen for the study. The Patients were classified either grade 0 to 4 on the Kellgren-Lawrence grading scale or grade 1 to 4 on the Ahlback scale, were included in the study after prior well informed written consent. Hundred Patients were chosen and randomly divided into two groups of fifty each. Group I received intra articular injection Platelet Rich Plasma in to both knees served as study group. Group II received normal saline and served as control. Randomization ensured that both the groups were comparable with respect to age, sex, height, weight, body mass index and pre injection WOMAC score.

Inclusion Criteria

Patients with bilateral osteoarthritis of knee joint, older than 40 years of age, grade 2 and 3 of Kellgren and Lawrence grading system who are fit for procedure.

Exclusion Criteria

Immunosuppressed patients, secondary osteoarthritis, any deformity around knee joint, inflammatory disorder of joints, who have received steroid injections within past 6 months, any tumour, metabolic disease of bone, coexisting backache and spinal deformity, any fractures/operations around knee joint, use of anticoagulants, liver disease.

Procedure

Subjects were thoroughly explained about the procedure and informed consent form was obtained. Study participants attended a screening visit (visit 1) that included history taking, physical examination, knee radiography (standing Anterior-posterior (AP) and lateral views), laboratory testing if required (complete blood count with differential, erythrocyte sedimentation rate, C-reactive protein, and survey of used medications and supplements. Prior to injections all patients were personally examined and evaluated in detail as per their symptoms and signs and disabilities such as pain, its site, duration, severity, degree of disability, difficult in walking, tenderness at joint line, painful restriction of flexion, crepitation, local warmth, synovial thickening, effusion, fixed flexion deformity etc.

A baseline weight bearing and sitting of X-rays of both the knee joints was done to know the status of OA. Patients were screened for any

fractures/operations around knee joint. All patients were treated with 4 intra-articular injections of autologous PRP (at 2 week interval) in affected knee and the other knee was taken as control.

Technique Of Platelet-rich Plasma Preparation

1.30 ml of venous blood was drawn using 60ml disposable syringe and poured into four 8.5-ml ACD-A containing vacuum sterile glass tube. 2.The blood sample was then centrifuged for 1500 rpm for 7 min at 22 degree Celsius in centrifuge machine (PRP centrifuge, Model –R-8C, REMI Company, WHO guidelines, with ISO9001/2008 certification) resulting in the three following layers: the inferior layer composed of erythrocytes, the intermediate layer composed of leukocytes, and the superior layer made of plasma. 3.Using separate 20cc disposable syringe the buffy coat layer together with the plasma layer was transferred into another sterile tube (without anticoagulant) and centrifuged for another 6 minutes at 3000 rpm.

The lower 1/3rd is PRP and upper 2/3rd is platelet-poor plasma (PPP) is obtained after 2nd centrifugation. 4. Using 20cc disposable syringe remove platelet poor plasma. Remaining platelet rich plasma gently shaken to suspend platelets in the PRP and gently aspirated and used for the intra-articular injection within 30 minutes of preparation. 5. An aliquot of product was sent to the laboratory for analysis of platelet concentration. 6.

All the procedures were performed in the same office setting. No activating agent (calcium chloride and thrombin) was used. Prepared amount of PRP was used for local injection into the patient according to the mentioned technique. By above method we achieved a platelet count ranging from 10.2 to 13.6×10^5 platelet/ μ l.

Injection Procedure

4 ml of PRP injection was given under full aseptic conditions. The part shaved, painted with antiseptic solution, draping was done with sterile plain sheets. Hands washed with povidone scrub solution, sterile gown was worn and sterile gloves were donned after wearing mask and cap. Patients were kept on operating table in the supine position with the knee flexed at 90 degrees. Patients were advised to relax his/her quadriceps muscle and check the movement of patella. The injection syringe was covered to prevent patients from being able to identify the contents of the syringe. In addition, patients were asked to turn their heads away from the direction of the syringe when the surgeon performed the injection procedure.

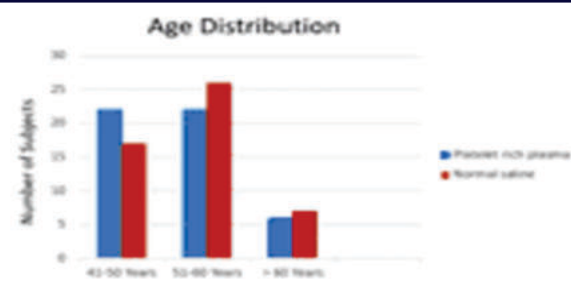
A syringe of 16 gauge size was inserted from superolateral side into the intra-articular joint space of the knee 1 cm above the tibial plateau and 1 cm lateral to the patellar tendon toward the femoral notch. This has been demonstrated to be the most accurate injection site for ensuring intra-articular penetration of the drug (93% accuracy rate). The needle is freely mobile when the joint space is entered. Any excess fluid aspirated. Injection of PRP meets almost no resistance if the needle tip was free in the synovial space followed by application of a small aseptic band aid at the injection site.

The patient was then asked to bend and extend the knee 3-4 times to allow the PRP to spread throughout the joint followed by 10 min of resting supine. Sterile compression bandage was applied after the injection procedure. In the control group, 4 ml of normal saline was injected into the joint space of the patients using similar injection protocol. Patients were given acetaminophen for pain and instructed to limit the use of their affected knee for 24 hours post injection. Patients were advised bed rest for 1 day after which normal activities could resume.

The patients were subjected to a standardized injection protocol and were assessed on variables such as pain, stiffness and physical function using WOMAC scale and for pain using visual analog scale at pre injection, 3 months, 6 months and 12 months for follow up. Outcome analysis for the efficacy was done for reduction in pain, reduction in stiffness and improvement in physical function using WOMAC scale.

The WOMAC (Western Ontario and McMaster Universities) index is used to assess patients with osteoarthritis of the hip or knee using 24 parameters. It can be used to monitor the course of the disease or to determine the effectiveness of therapy. The Patients were also assessed for reduction in pain using Visual analog scale both at pre injection and at 12 months post injection.

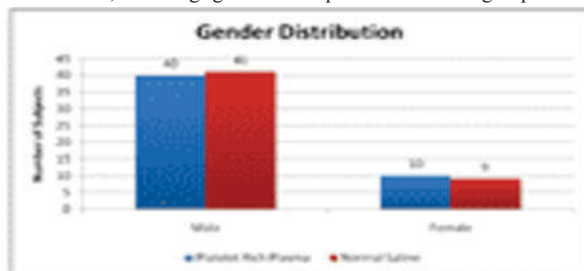
RESULTS



Age Distribution	Platelet Rich Plasma	%	Normal saline	%
41-50 years	22	44.00	17	34.00
51-60 years	22	44.00	26	52.00
>60 years	6	12.00	7	14.00
Total	50	100	50	100

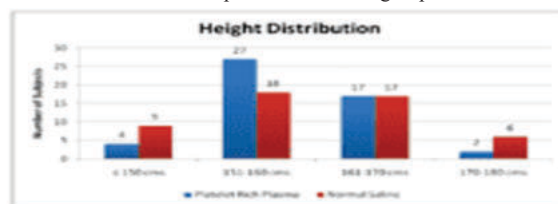
Age Distribution	Platelet Rich Plasma	Normal Saline
N	50	50
Mean	49.92	54.26
SD	7.72	5.36

Age distribution revealed mean age in group I (PRP) to be 49.92 and the mean age in Group II (Normal saline) was 54.16 (youngest age- 41 years & oldest age – 63 years). The p-value derived using unpaired t-test is 0.0112, rendering age factor comparable in both the groups.



Gender Distribution	Platelet Rich Plasma	%	Normal Saline	%
Male	40	80.00	41	82.00
Female	10	20.00	9	18.00
Total	50	100	50	100

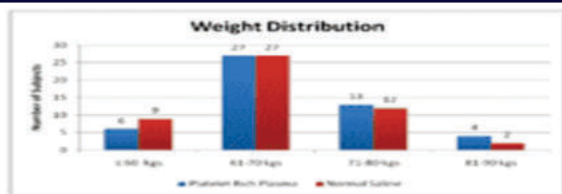
Gender distributions were comparable on both groups with 80% being male 20% being female. The p-value using chi square test is 0.0433. The Gender factor was comparable in both the groups.



Height Distribution	Platelet Rich Plasma	%	Normal Saline	%
< 150 cms	4	8.00	9	18.00
151-160 cms	27	54.00	18	36.00
161-170 cms	17	34.00	17	34.00
170-180 cms	2	4.00	6	12.00
Total	50	100	50	100

Height Distribution	Platelet Rich Plasma	Normal Saline
N	50	50
Mean	159.66	159.68
SD	6.63	8.39

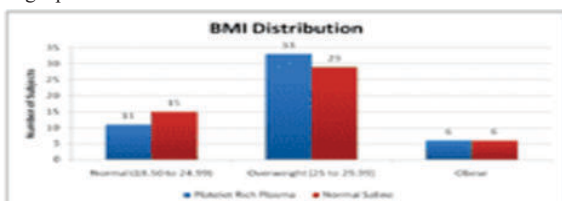
The mean height in group I was 159.66 and the mean height in Group II was 159.68. The p-value using unpaired t test turned out to be 0.0389 which shows that it was comparable in both the groups.



Weight Distribution	Platelet Rich Plasma	%	Normal Saline	%
< 60 kgs	6	12.00	9	18.00
61-70 kgs	27	54.00	27	54.00
71-80 kgs	13	26.00	12	24.00
81-90 kgs	4	8.00	2	4.00
Total	50	100	50	100

Weight Distribution	Platelet Rich Plasma	Rich	Normal Saline
N	50		50
Mean	68.62		67.66
SD	6.84		6.63
P value Unpaired t Test			0.4777

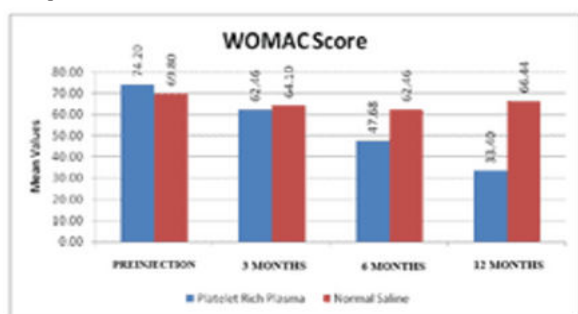
The mean weight, in group I was 68.62 and group II was 67.66 with p-value of 0.0377. This shows that both the groups were comparable for weight parameter.



BMI Distribution	Platelet Rich Plasma	%	Normal Saline	%
Underweight (< 18.49)	0	0.00	0	0.00
Normal (18.50 to 24.99)	11	22.00	15	30.00
Overweight (25 to 29.99)	33	66.00	29	58.00
Obese	6	12.00	6	12.00
Total	50	100	50	100

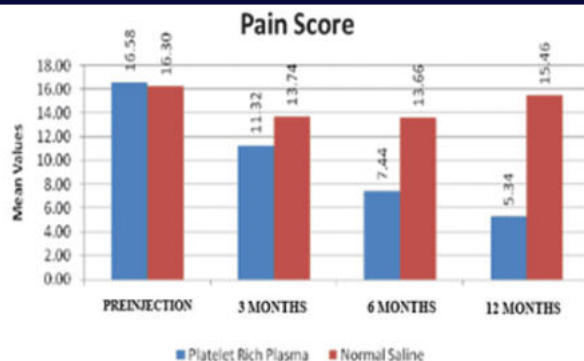
BMI Distribution	Platelet Rich Plasma	Rich	Normal Saline
N	50		50
Mean	26.97		26.64
SD	2.70		2.92

The mean BMI was 26.97 in group I and 26.64 in Group II. The unpaired p value of 0.0243 shows that both groups are comparable in BMI parameter.



WOMAC Score	PRE-INJECTION	3 MONTHS	6 MONTHS	12 MONTHS
Platelet Rich Plasma	N: 50	50	50	50
	Mean: 74.20	62.46	47.68	33.40
	SD: 4.85	6.60	8.15	7.59
Normal Saline	N: 50	50	50	50
	Mean: 69.80	64.10	62.46	66.44
	SD: 4.68	5.50	5.44	5.01

The Global WOMAC showed a mean of 74.2 at pre injection period which decreased to 62.46 at 3 months follow up and 47.68 at 6 months and declining to 33.40 at 12 months. The unpaired p value of 0.013 shows significance of the study.



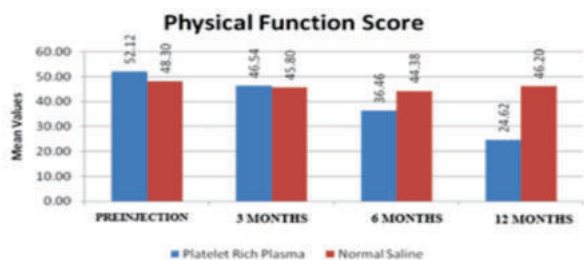
Pain Score	PRE-INJECTION	3 MONTHS	6 MONTHS	12 MONTHS
Platelet Rich Plasma	N: 50	50	50	50
	Mean: 16.58	11.32	7.44	5.34
	SD: 3.08	2.76	1.93	1.42
Normal Saline	N: 50	50	50	50
	Mean: 16.30	13.74	13.66	15.46
	SD: 2.39	2.28	2.35	1.94

Mean score for pain showed a decrease from 16.58 to 11.32 at 3 months post injection. At the end of 12 months follow up, the mean was 5.34. The mean score for pain in group II showed a marginal decrease from 16.30 to 13.74 at 3 months but increased to 15.46 at 12 months follow up. The unpaired p value of 0.0019 shows that the study is significant.



Stiffness Score	PRE-INJECTION	3 MONTHS	6 MONTHS	12 MONTHS
Platelet Rich Plasma	N: 50	50	50	50
	Mean: 5.50	4.60	3.78	3.40
	SD: 1.22	1.20	1.09	1.14
Normal Saline	N: 50	50	50	50
	Mean: 5.16	4.56	4.46	4.78
	SD: 0.93	0.81	0.73	0.84

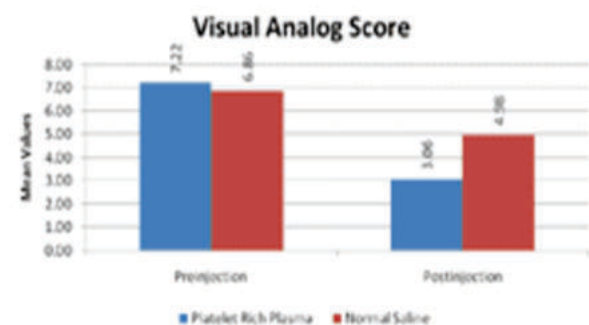
Mean stiffness score decreased from a pre injection score of 5.50 to 3.40 at 12 months follow up in study group and from 5.16 to 4.78 after 12 months in control group showing a significant reduction in our study cases. The unpaired p value of 0.0032 shows the significance of study.



Physical Function Score	PRE-INJECTION	3 MONTHS	6 MONTHS	12 MONTHS
Platelet Rich Plasma	N: 50	50	50	50
	Mean: 52.12	46.54	36.46	24.62
	SD: 3.77	4.53	6.49	6.33
Normal Saline	N: 50	50	50	50
	Mean: 48.30	45.80	44.38	46.20
	SD: 3.17	3.91	3.88	3.67

The mean of Physical function score decreased from a pre injection score of 52.12 to 24.62 at 12 months follow up in Group I (study

group). Group II showed a marginal dip in mean scores from 48.30 to 45.80 after 3 months and to 44.38 at 6 months. The scores leveled at 46.20 at the end of 12 months. The unpaired p value of 0.0041 shows significance of the study.



Visual Analog Score		Preinjection	Postinjection
Platelet Rich Plasma	N	50	50
	Mean	7.22	3.06
	SD	0.97	1.24
Normal Saline	N	50	50
	Mean	6.86	4.98
	SD	0.81	0.89

Visual analog score showed a decrease in mean of 7.22 to 3.06 which denoted a change of patient's perception of pain from intense, dreadful, horrible pain to mild annoying pain in Group I. Group II showed a marginal dip from 6.86 to 4.98 on mean, showing insignificant change in pain. The unpaired p value of 0.0472 shows that the study is significant.

DISCUSSION

Osteoarthritis is a chronic disorder of synovial lined joints where there is progressive softening and disintegration of articular cartilage accompanied by new growth of cartilage and bone at the joint margins, cyst formation and sclerosis at subchondral regions of bone, mild synovitis and capsular fibrosis. Osteoarthritis differs from simple wear and tear in that it is asymmetrically distributed, often associated with abnormal loading rather than frictional wear. It is not an inflammatory disorder although at times there are local signs of inflammation. In its most common form osteoarthritis is unaccompanied by any systemic illness. We in our study had randomly chosen 100 patients with classic findings of bilateral Osteoarthritis and divided them in to two groups. Both the groups were comparable on baseline characteristics of age, height, weight, BMI, pre injection WOMAC score etc. Fifty of these patients were administered an intra articular injection of Platelet Rich Plasma and other fifty received Normal Saline. The Efficacy of Platelet Rich Plasma in reducing pain, stiffness and physical function were assessed and scored on WOMAC index for both study and control group. The Results were analyzed using unpaired t-test and chi-square test. Age distribution revealed mean age in group I to be 49.92 and the mean age in Group II was 54.16. The p-value derived using unpaired t-test is 0.0112, rendering age factor insignificant which was in concordance to the studies done earlier by Filardo Get al and Saltzman B M et which demonstrated PRP therapy to be efficacious in all population regardless of age. However Shen L. et al. in their study concluded PRP therapy to be more effective in patients aged 50 years and younger. Gender distributions were comparable on both groups with 80% being male 20% being female. The p-value using chi square test is 0.0433. The Gender factor was insignificant which was also reported in meta analysis studies conducted by Laudy AB et al and Campbell K which reported that PRP therapy is effective in study group irrespective of gender. The mean height in group I was 159.66 and the mean height in Group II was 159.68.

The mean weight, in group I was 68.62 and group II was 67.66 with p-value of 0.0377 (significant). The results obtained were different from the results reported in a study by David J Hunter et al which reported that increased height was associated with an increasing prevalence of both radiographic and symptomatic OA and had a poorer post injection recovery but this was not observed in our study. The mean BMI was 26.97 in group I and 26.64 in Group II. The p-value is 0.0243 which were in concordance to studies conducted by Patel S et al and Jevsevar DS et al. which demonstrated PRP therapy to be effective in all the patients irrespective of their BMI status. Thus, the study ensured that all patients were comparable on baseline characters. The Global

WOMAC showed a mean of 74.2 at pre injection period which decreased to 62.46 at 3 months follow up and 47.68 at 6 months and declining to 33.40 at 12 months. The study showed a significant decrease in global WOMAC score, which was also consistent throughout the study period which further established the role of PRP in OA knee as reported in other studies as well. The Individual variables such as pain, stiffness and physical function were assessed. Mean score for pain showed a decrease from 16.58 to 11.32 at 3 months post injection. At the end of 12 months follow up, the mean was 5.34. The mean score for pain in group II showed a marginal decreased from 16.30 to 13.74 at 3 months but returned to 15.46 at 12 months follow up. The p-value using unpaired t-test showed significant improvement. Secondary variable stiffness showed significant difference at 6 months follow up and 12 months follow up. The mean of Physical function score decreased from a pre injection score of 52.12 to 24.62 at 12 months follow up in Group I (study group). Group II showed a marginal dip in mean scores from 48.30 to 45.80 after 3 months and to 44.38 at 6 months. The scores leveled at 46.20 at the end of 12 months. Visual analog score showed a decrease in mean of 7.22 to 3.06 which denoted a change of patient's perception of pain from intense, dreadful, horrible pain to mild annoying pain in Group I. Group II showed a marginal dip from 6.86 to 4.98 on mean, showing insignificant change in pain. All the scores obtained were in concordance to various studies done earlier by Kanchanatawan W et al which also included the scoring systems involved in our study and showed a decline in all the scores in a follow-up of 2 years. Similarly, Görmeli G et al also reported a global decline in all the scores over a period of 5 year study interval. Overall pain of the patients post injection therapy was reduced significantly and the patients were able to do their day to day activities with much ease.

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