

Role of Platelets Rich Plasma Intra-Articular Injections in the Treatment of Knee Osteoarthritis among Elderly

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Abstract

Background: Knee OA is a major public health problem among elderly. It is a debilitating condition associated with increased morbidity and disability. Thus, the development of therapeutic interventions could enhance the quality of life for the elderly

Aim: To evaluate the clinical efficacy of platelets rich plasma intra articular injections in treatment of Knee Osteoarthritis among Elderly.

Methods: one arm clinical trial on 44 elderly participants all of them received a single session of intraarticular PRP injection, they were subjected to physical function and mobility assessment using Western Ontario and McMaster Universities Arthritis Index (WOMAC) questionnaire and pain assessment by the numeric pain rating scale (NRS-11) at 6 and 12 months post injection.

Results: study reported a statistically significant improvement in all functional WOMAC assessment scores and NRS after 6 months and 12 months post injection follow up with the tendency for gradual decline of clinical improvement till the end of follow up after 1 year.

Conclusions: Intraarticular PRP injections are safe, effective and reliable treatment option providing functional improvement and pain control for elderly patients with knee OA

Keywords: osteoarthritis, Western Ontario and McMaster Universities Arthritis Index (WOMAC), platelets rich plasma (PRP), elderly.

Background: Osteoarthritis (OA) is the most prevalent chronic degenerative joint disease in the world and one of the most common sources of pain, disability and worse impact on quality of life and independence in the elderly. Near 50% of the world's population aged 65 and older suffer from

OA, and 80 % of symptomatic OA people have limitations in movement, while 25 % cannot perform their normal daily activities.¹

Although OA was considered a “wear and tear” degenerative condition of articular joints as a result of biochemical and mechanical changes in the

joint, it has been demonstrated an inflammatory component to OA that includes increased activity of a number of tissues Pro-inflammatory cytokines in OA cartilage that accelerate degradation of cartilage matrix.²

The prevalence of symptomatic OA increases with age: it is estimated that 18 % of women and 9.6 % of men over age 60 have knee OA. With increased longevity and obesity in the population the burden and prevalence of OA is expected to grow.³

Globally; approximately 250 million people have osteoarthritis of the knee (3.6% of the population), accounting for 25% of visits to primary care physicians, and half of all NSAID prescriptions. It is estimated that 80% of the population have radiographic evidence of OA by age 65, although only 60% of those will have symptoms.⁴

Limitations in walking, stair climbing, and squatting are common patient complaints that greatly interfere with their activities of daily living and recreation. Also physical manifestations of knee OA have direct impact on other aspects of patient's lives such as social interactions, mental functioning, and sleep quality. The burden of knee OA on individuals, health systems, and social care systems is considered as a public health crisis.⁵

The goals of osteoarthritis treatment include alleviation of pain and improvement of functional status. Lifestyle adaptations; exercise, physical therapy, weight loss and dietary supplements help in improving the functional status, gait, pain, and functional capacity in people with OA of the knee.^{6,7}

Pharmacological agent in the elderly should be tempered with caution regarding increased sensitivity to medications, drug-drug interactions and associated co-morbidities.⁸ They commonly exert a symptomatic relief rather than tissues repair, includes analgesics (acetaminophen, NSAIDs and stronger analgesics (i.e. opioids)), Glucosamine and chondroitin Complementary supplements, Intra-articular injections either Intra articular corticosteroids or hyaluronic acid.^{9,10}

Since some of these treatments have had short- and mid-term effects on improving patients' functions and decreasing the level of disability and cannot change the pathophysiology of the disease, therefore searching for a minimally invasive solution to improve joint surface status and lead to a fast regain of full activity led to the recent development of injective biological treatment

approaches, like platelets rich plasma (PRP).^{11,12}

PRP is a simple, economic and minimally invasive therapy that provides a concentrate pools of growth factors (GFs) stored in platelet granules help in the regulation of articular cartilage, promote cellular recruitment, growth, and morphogenesis, activate and accelerate the physiological processes of healing and modulate inflammation as well.^{13,14}

Although clinical interest in PRP has developed as evidenced by the flurry of scientific research and studies, firm conclusions from the published literature concerning the effect and safety of PRP in the treatment of knee OA in elderly population remain scarce.

The current study was conducted to evaluate the clinical efficacy of platelets rich plasma intra articular injections in treating knee Osteoarthritis among elderly.

Methods

One arm clinical trial conducted on 44 elderly patients aging 60 years old or more recruited from Ain Shams University hospitals clinics and inpatient wards.

Ethical consideration:

The study methodology was reviewed and approved by the Research Ethical Committee; Faculty of Medicine Ain Shams University (REC-FMASU) and the Research Review Board of the Geriatrics and Gerontology Department, Faculty of Medicine, Ain Shams University. Informed consent was taken from every subject participating in this study

Patients selection included radiographic findings of minimal to moderate OA (grade 1,2 and 3) of the knee joint, according to Kellgren-Lawrence scale.¹⁵

Exclusion criteria were uncontrolled diabetes, severe cardiovascular diseases, infections, immunosuppression, patients on therapy with anticoagulants, antiplatelet or use of NSAIDs within 10 days before injection, body mass index \geq 35 and Patients with severe knee osteoarthritis (grade 4)

Clinical and functional assessment

At the first visit all patients were subjected to full history taking, general examination and complete knee joint examination. The severity of pain was assessed by Numeric rating scale (NRS) which is a unidimensional measure of pain intensity in adults including those with chronic pain due to rheumatic

diseases. Patients were asked to complete the Western Ontario and McMaster Universities Arthritis Index (WOMAC) questionnaire in order to evaluate the function of the affected knee.¹⁶ It is a validated scale designed to assess functional difficulties associated with lower limb OA. Patients rate their difficulty with 17 different tasks using a scale from 0 to 4, with higher scores indicating more difficulty. The total response to these 17 tasks was calculated as an overall disability score.

Bilateral Plain X-ray of the affected knee, anteroposterior and lateral views were done for grading of knee OA which was done according to the Kellgren–Lawrence grading system.¹⁵

All patients were injected intra-articularly with about 2-3 ml of PRP for each affected joint in single session. Injection was performed with the patient in the supine position using classic lateral or ventral approaches. After injection, patients were instructed to perform mild effort for 24 hours post injection and to use ice packs over the injected joint and not to use NSAIDs during this period

Platelet rich plasma preparation

The procedure consisted of 30 ml of venous blood samples taken from every patient and collected in sterile sodium citrated tubes. Platelet concentrates were obtained by the following technique: The tubes with citrated blood were centrifuged at 1800 rpm for 15 min to separate erythrocytes, and at 3500 rpm for 10 min to concentrate platelets.¹⁷ By this method, 3 ml of PRP were obtained and injected immediately

Follow up assessment

After 6 and 12 months, all patients were re-evaluated by physical examination, assessment of NRS for pain and WOMAC for functional status.

Statistical Analysis

The collected data were coded, tabulated and statistically analyzed using IBW SPSS statistics (Statistical Package for social Sciences) software version 22.0, IBW Corp., Chicago, USA, 2013.

Results

This study was carried out on 44 patients who were suffering from mild to moderate knee OA. Mean age was 64 years and mean BMI was 29.3 [Table

(1)]. Mean scores for NRS and WOMAC subscales were shown in (figure 1)

Table1: descriptive data of the study sample:

	Mean± SD
Age	64.091± 4.074
Height	167.841± 6.765
Weight	82.500± 7.795
BMI	29.343± 2.628
OA grade:	
Grade I	8 (18.18%)
Grade II	17 (38.64%)
Grade III	19 (43.18%)

Results showed significant improvement in NRS scores at 6 months and 12 months follow up with high statistically significant difference ($P = < 0.001$) over baseline score. The improvement in scores was better after 6 months than 12 months with high statistically significant difference ($P = < 0.001$) [Table (2)].

Table 2: Comparison of NRS scores pre & post injection among the studied cases

	Time	Paired Differences		Paired Samples Test	
		Mean	SD	T	P-value
NRS	B/6M	4.795	0.878	36.223	<0.001*
	B/12M	1.114	0.813	9.085	<0.001*
	6M/12M	-3.682	0.883	-27.651	<0.001*

B: baseline, M: month NRS: numeric pain rating scale

There was a highly statistical significant difference in clinical response as regard WOMAC pain, stiffness and physical function subscales scores at 6 and 12 months of follow up. This clinical improvement was the best after 6 months of PRP injections with gradual decline in clinical response till the 12th month of follow up [Table (3)].

Discussion

This study assessed the clinical response to PRP intra-articular injections on functional and pain outcomes in knee OA patients. It included 44 elderly subjects with knee OA.

Table (3): Western Ontario and McMaster Universities Arthritis Index (WOMAC) and subscales scores pre and post PRP injection

	Time	Paired Differences		Paired Samples Test	
		Mean	SD	T	P-value
WOMAC P	B/6M	5.489	1.430	35.997	<0.001*
	B/12M	1.818	1.466	11.631	<0.001*
	6M/12M	-3.670	1.624	-21.202	<0.001*
WOMAC S	B/6M	2.364	0.833	26.619	<0.001*
	B/12M	0.898	0.695	12.109	<0.001*
	6M/12M	-1.466	0.787	-17.471	<0.001*
WOMAC PF	B/6M	17.727	5.807	28.639	<0.001*
	B/12M	5.625	3.785	13.940	<0.001*
	6M/12M	-12.102	4.431	-25.622	<0.001*
WOMAC Total	B/6M	25.045	7.482	31.403	<0.001*
	B/12M	7.455	6.556	10.666	<0.001*
	6M/12M	-17.591	5.682	-29.040	<0.001*

WOMAC: Western Ontario and McMaster Universities Arthritis Index, P: pain, S: stiffness, PF: physical function, B: before.

On studying the effect of PRP injection on WOMAC functional assessment tool total and subscales (pain, stiffness and physical function) scores and the Numerical Rating Scale (NRS) for subjective measurement of pain symptoms, significant clinical improvement in all scores post injection after 6 months of follow up was observed.

Also there was a significant clinical improvement achieved after 12 months of follow up when compared with baseline assessment scores, however this clinical response was much more less than scores achieved after 6 months of injection denoting gradual decline in clinical efficacy of PRP injections over time.

Findings agreed with results shown by Duymus et al., 2017 study included a total of 33 patients and stated a significant improvement after 6 and 12 months follow up, however the estimated clinical efficacy and benefits of PRP injections were limited by time, and the estimated duration of effectiveness was at 1 year.¹⁸

Also Vaquerizo et al., 2013 study on ninety-six patients with mean age of 63.6 years, found significant improvement in WOMAC scores when compared with baseline scores. Although this improvement remained statistically significant until study completion but reduction in the clinical efficacy after 12 months had occurred.¹⁹

Using Osteoarthritis Outcome Scores (KOOS) and Subjective International Knee Documentation Committee (IKDC) subjective functional assessment tools; Filardo et al. 2012 found that the scores improved markedly from the basal evaluation to the end of therapy and the follow-up at 6 and 12 months with tendency of the scores to

fall at the 12-month follow-up even though it remained significantly better than the basal level.²⁰

On the other hand Gobbi et al., 2012 found that the best clinical improvement after 2 intra-articular injections of autologous PRP was achieved after 1-year follow-up.²¹

The study of Sampson et al., 2010 demonstrated significant and almost linear improvements in functional assessment with no adverse events reported. The majority of the patients expressed a significant improvement and favorable outcome after 12 months of treatment.²²

On contrary Kon et al., 2010 study enrolled 100 patients with mean age of 47 years, significant clinical improvement achieved after 6 months of follow up, then functional scores became significantly worse at the 12th month of follow-up (P = 0.02).²³

Filardo and his colleagues, 2011 studied the long term effect of PRP injections in knee OA patients and reported that all of the evaluated functional parameters among subjects showed a marked worsening over time, with a significantly lower score at end point follow-up.²⁴

The controversy in results of the clinical efficacy and duration of PRP injections may be as a result of differences in PRP products preparation techniques and centrifugation, platelets concentrations, presence of leukocytes and erythrocytes and difference in number of injections and their intervals as well as patient criteria and selection which could be a reason for the different results in various clinical applications.

An objective limitation of this study is the lack of control group. In addition to relatively the small sample size included. Another limitation was the lack of imaging assessment to evaluate OA progression either MRI or ultrasonography which provide more objective data as regard the benefit of treatments.

Conclusion:

PRP is a minimally invasive injection procedure appears to be safe, effective and reliable treatment, provides quantifiable benefits for pain relief and functional improvement among elderly with knee OA. Further studies are required with larger sample sizes with longer follow-ups and objective outcome measures.

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