The Egyptian Journal of Hospital Medicine (Apr. 2015) Vol. 59, Page 227- 232

Effect of Platelet-Rich Plasma Intra Articular Injection on Patients with Primary Knee Osteoarthritis

Nadia Abdel Salam Elkadery[1], Mohammed Aly Elwy[1], Eman Mahmoud Ghaniema[1], Hossam Moussa Sakr[2], Ahmed Ibrahim Hammad[1].

Departments of Physical medicine, Rheumatology & Rehabilitation[1] and Radiodiagnosis[2]
Faculty of medicine, Ain Shams University
Address for Correspondence: Ahmed Ibrahim Kamal Eddin Afifi Hammad, Mob.:01001315507,
Email:ahmedhammad1981@gmail.com

ABSTRACT

Background: Osteoarthritis (OA) is the most common type of arthritis. It is a degenerative joint disease. OA is usually defined according to radiographic changes. Conventional radiographs (CR) were considered the most relevant outcome measure to assess the progression of OA in clinical trials and epidemiological studies. Many modalities are used in treatment of knee OA. There is a distinct need for new procedures that are cost effective by reducing the need for pharmaceutical and surgical management, while targeting the biochemical process of OA. Platelet-rich plasma (PRP) is one of these new procedures. PRP was found to increase hyaluronic acid (HA) concentration, stabilizing angiogenesis in patients with osteoarthritic knees.

Aim of the study: Was to assess the value of intra articular injection of autologous platelet rich plasma in management of knee osteoarthritis.

Patients and methods: This study was conducted on 40 patients with primary knee osteoarthritis, divided into 2 groups; study group treated with 3 injections of PRP, and control group treated with single dosed high-molecular weight HA. Clinical assessment and visual analogue scale (VAS) scoring were done pretreatment and 3 months post treatment.

Results: Clinical improvement and reduction of VAS in both groups which is significant at the study group. **Conclusion:** PRP injection could be considered as a simple, safe, effective and non-palliative treatment that may promote cartilage healing in knee osteoarthritis as it improve the clinical condition and the function of the joint. Hence, it may represent a useful addition to the available therapeutic options for knee osteoarthritis.

Key words: knee, Osteoarthritis, Platelet-rich plasma.

INTRODUCTION

Osteoarthritis (OA) is a degenerative joint disease that is considered as a chronic disease of the whole joint. [(1)] Pain and other symptoms of OA may have a profound effect on quality of life affecting both physical function and psychological parameters. [(2)] The incidence of knee OA increases by age.[(3)] Prevalence of knee OA in men is lower compared with women. [(4)]

OA has multifactorial etiologies as age, sports participation, injury to the joint, obesity, and genetic susceptibility that predispose adolescent athletes to the development of premature osteoarthritis. Previous knee trauma increases the risk of knee OA 3.86 times. [(5)] Determination of risk factors and their modification may reduce the risk of OA and prevent subsequent pain and disability. [(6)] Also, joint inflammation is a present feature of OA, notably in the early stage. [(7)] It is believed that cytokines and growth factors play an important role in the pathophysiology of OA that are closely associated with functional alterations in synovium, cartilage and subchondral bone.[(8)] Although OA is not a classical inflammatory arthritis, the development and progression of OA may involve inflammation even in the early stages of the disease.[(9)]

The onset of OA is frequently insidious. Symptoms may be continuous or intermittent and. At first, the pain may only be noticed after the joint is used and be relieved by rest**.** However, when OA becomes severe and advanced, pain is experienced at rest and often awakens the person at night. Joint stiffness is also a feature of OA.[(10)]

Patients often note that their knees "give way," a so-called instability symptom. Knee giving way may indicate the presence of an internal derangement such as a meniscal tear or a tear of the anterior cruciate ligament and it may also reflect

DOI: 10.12816/0012180

weakness of the muscles that support the joint.[11] Persistent knee pain, limited morning stiffness, and reduced function are the three symptoms that are recommended for the diagnosis of knee OA by the European League Against Rheumatism (EULAR).[12]

Although the diagnosis of knee OA in the most cases can be made by the clinical findings and physical examination ,however identification of joint damages are necessary for both diagnostic confirmation as well as extent of joint involvement.[13] CR is the first diagnostic procedure as usually requested to demonstrate the structure-pain relationship in knee OA. Radiographic assessment of OA relies mainly on the evaluation of both osteophytes and joint space narrowing.[14]

MRI is not necessary for most patients with suggestive symptoms of OA and/or typical plain radiographic features. However, MRI of the knee has a diagnostic role in patients with joint pain and symptoms such as locking, popping, or instability that suggest meniscal or ligamentous damage.[15] However, many individuals with radiographic knee OA are asymptomatic and in contrary in many patients with knee pain suggestive of OA radiologic findings are absent.[16]

In recent years, sonography has been utilized to obtain a better understanding of osteoarthritis. Although the application of sonography to inflammatory diseases has been common and widespread, it has been applied to osteoarthritis less frequently.[17] It facilitates minimally invasive interventional procedures (e.g., intra-articular injections and aspirations).[18]

Treatment of OA consists of a combination of non-pharmacologic and pharmacologic modalities. Recommendations for the management of hip and knee OA was published by ***Altman et al.*** [19]. The goal of OA treatment is to control symptoms, prevent disease progression, minimize disability, and improve quality of life. Treatment of OA includes various techniques and principles of non-pharmacological and pharmacological treatment options.[20] The non-pharmacologic therapy for patients with osteoarthritis included patient education, self-management programs (eg, Arthritis Foundation Self-Management Program), personalized social support through telephone contact, weight loss (if overweight), aerobic exercise programs, physical therapy, range-of-motion exercises, muscle-strengthening exercises, assistive devices for ambulation and for activities of daily living, patellar taping, lateral-wedged insoles (for genu varum), bracing, occupational therapy, joint protection and energy conservation.[21] Only if symptoms persist after the appropriate use of nonsurgical treatment, surgery should be considered. Surgical treatment options are arthroscopic debridement, cartilage repair surgery, osteotomy with axis-correction, and uni-compartmental or total knee arthroplasty (TKA).[22] Recent researches focus on nontraditional treatments as autologous conditioned cell-free serum, stem cells, and platelet-rich plasma.

Patients and Methods:

Study design : This study was a systematically randomized ,double arm clinical trial that was conducted on 40 patients with primary knee osteoarthritis diagnosed according to ***Altman et al.*** [23] classification of OA of the knee. They were divided into two groups matched in age and sex (20 cases per group): the study group was treated with intra-articular PRP injection of the affected knee, while the control group was treated with intra-articular injection of high molecular weight (900 KD) single dosed hyaluronic acid (HA) prefilled syringe (Crespine gel®).

Patients were excluded if they were obese, having secondary OA, not suitable for blood donation, had a history of intra-articular corticosteroid injection within 6 weeks, or knee surgery. Also, presence of effusion or usage of a nonsteroidal anti-inflammatory medication one week before injection excluded the patients.

Patients were subjected to full medical history and thorough physical examination. Clinical assessment was done focusing on presence morning stiffness, tenderness, crepitations, and synovial hypertrophy. Assessment of pain was done using the visual analogue scale (VAS) from 0-10 cm.

CR was used to classify the patients according to Kellgren- Lawrence

(K-L) scale [24] and to exclude patients with grade IV.

PRP is prepared by venesection of 35 ml venous blood from the medial cubital vein was done using a butterfly cannula (19-21 gauges) connected to a 60 ml syringe with gentle suction. The blood is drawn into a sterilized 50 ml falcon tube containing 5 ml of anticoagulation citrate dextrose-A solution (ACD-A).The aspirated blood was gently agitated to thoroughly mix the anticoagulant with the blood. Using the centrifuge device (Centerion 2006®, England), two centrifugations (the first at1, 800 rpm for15 min to separate erythrocytes, and a second at 3,500 rpm for 10 min to concentrate platelets) produced a unit of 5 ml of PRP. A puffy coat (which is the layer between the stagnant red layer of RBCs and the straw colored layer of plasma) is aspirated using a 10 ml syringe. Prior the injection, 0.5ml of 10% of Ca-chloride was added to the PRP unit (1:10) to activate platelets.

For the study group, PRP was injected into the supra patellar bursa guided by sonography to ensure proper needle placement. The injections using fresh PRP was repeated three times with one week interval.

For the control group, the HA was injected into the knee joint using either the anterolateral or anteromedial approaches.

Reassessment was done 3 months post treatment, using the clinical assessment and pain assessment using VAS.

Ethics

The study methodology was reviewed and approved by the Research Review Board of the Physical Medicine, Rheumatology, and Rehabilitation Department and Ethical Committee of Faculty of Medicine, Ain Shams University.

Statistical methods

The collected data were coded, tabulated, revised and statistically analyzed using SPSS program (version 18). Quantitative variables were presented in the form of means and standard deviation (SD). Qualitative variables were presented in form of frequency tables (number and percent). Comparison between quantitative variables was done done using independent and paired t-test. Comparison between qualitative variables was done using Chi square test. P-values <0.05 were considered significant for all tests.

RESULTS

Both groups were matched in age, sex, BMI, and K-L scale. As regard the clinical assessment, no significant difference between both groups before treatment. After treatment clinical picture was significantly better among PRP group. All clinical findings was improved in both groups except synovial hypertrophy, the differences were significant only in cases of crepitation (PRP group only) and tenderness (both groups).

Also, there was no significant difference between study groups regarding disease duration, clinical picture and radiographic grading before trial. As regards the VAS, there were significant reduction in VAS scores in both groups, but VAS score was significantly lower among PRP group than in HA group 3 months after treatment.

DISCUSSION

As regards the clinical improvement, it is near to the results of **Hassan *et al*. [25],** which reported improvement in the clinical picture of the study group 6 months post PRP injection. Also, the results of VAS reduction are supported by the results of **Sanchez *et al*. [26]** that reflected a significant improvement in joint pain, stiffness, and physical function in the PRP group after 5 weeks post final injection. Also, **Wang-Saegusa *et al*. [27]** reported improvement of EQ Visual analogue scale (EQ_VAS) and Western Ontario and McMaster Universities (WOMAC) scores at the 6-month follow-up in 261 patients with OA symptoms more than 3 months who had 3 intra-articular injection of autologous PRP at 2-week intervals. This data favors the benefit of PRP injection in knee OA. However, these results are not enough, but can be can a first step in a road to larger studies, with longer follow-up period, and with objective methods of assessment in order to get more conclusive results about PRP.

CONCLUSION

The study found an improvement of pain and clinical symptoms in patients with knee OA, after PRP intra-articular injection,

that was more significant than after HA injection.

Acknowledgments: Thanks to the grant office, faculty of medicine, Ain Shams University, which offered 5000 EGB for this research.

REFERENCES

1- Grazio S and Balen D (2009): Obesity: Risk factor and predictors of osteoarthritis. Lijec Vjesn.,131:22–6.

2- Bliddal H and Christensen R (2009): The treatment and prevention of knee osteoarthritis: a tool for clinical decision-making. Expert Opin Pharmacother., 10(11): 1793-80.

3- Altman R (2010): Early management of osteoarthritis. Am J Manag Care; 16: S 41-7.

4- Srikanth V, Fryer J, Zhai G, Winzenberg T, Hosmer D, and Jones G (2005): A meta-analysis of sex differences prevalence, incidence and severity of osteoarthritis. Osteoarthritis and Cartilage, 13(9):769-81.

5- Blagojevich M, Jinks C, Jeffery A, and Jordan K (2010): Risk factors for onset of osteoarthritis of the knee in older adults: a systematic review and meta-analysis. Osteoarthritis and Cartilage, 18: 24-33.

6- Zhang Y and Jordan J (2010): Epidemiology of osteoarthritis. Clin Geriatr Med., 26(3):355-69.

7- Sellam J and Berenbaum F (2010): The role of synovitis in pathophysiology and clinical symptoms of osteoarthritis. Nature Reviews Rheumatology, 6:625-635.

8- Fernandes J, Martel-Pelletier J, and Pelletier J (2002): The role of cytokines in osteoarthritis pathophysiology. Biorheology, 39: 237–246.

9- Andresa MC, Imagawa K, Hashimoto K, Gonzalez A et al. (2011): Suppressors of cytokine signaling (SOCS) are reduced in osteoarthritis. Biochemical and Biophysical Research Communications,407: 54-59.

10- Dawson J, Fitzpatrick R, Fletcher J and Wilson R (2004): Osteoarthritis Affecting the Hip and Knee. **In:** Stevens A, Raftery J, Mant J, and Simpson S (eds.), Health Care Needs Assessment – the epidemiologically based needs assessment review: Vol. 1, Ch.8. 2nd edition. Radcliffe Publishing Ltd, Abingdon, United Kingdom.

11- Felson D (2004): An update on the pathogenesis and epidemiology of osteoarthritis. Radiologic Clinics of North America,42:1-9.

12- Zhang W, Nuki G, Moskowitz R, Abramson S *et al.* (2010): OARSI recommendations for the management of hip and knee osteoarthritis: Part III: Changes in evidence following systematic cumulative update of research published through January 2009. Osteoarthritis and Cartilage, 18:476-499.

13- Braun H and Gold G (2011): Advanced MRI of articular cartilage. Imaging Med.,3(5):541-555.

14- Roemer F, Crema M, Trattnig S, and Guermazi A (2011): Advances in Imaging of Osteoarthritis and Cartilage. Radiology, 260 (2): 332-354.

15- Wenham C and Conaghan P (2009): Imaging the painful osteoarthritic knee joint: what have we learned? Nature Clinical Practice Rheumatology, 5 (3): 149-58.

16- Muraki S, Oka H, Akune T, Mabuchi A, En-yo Y, Yoshida M, Saika A, Suzuki T, Yoshida H, and Ishibashi H, *et al.* (2009): Prevalence of radiographic knee osteoarthritis and its association with knee pain in the elderly of Japanese population-based cohorts: The ROAD study. Osteoarthritis Cartilage, 17:1137-1143.

17- Martinoli C and Bianchi S (2007): Knee. In: Bianchi S and Martinoli C (eds.), Ultrasound of the Musculoskeletal System. Springer-Verlag Berlin Heidelberg, Germany. pp 637-744.

18- Pinzon E and Moore R (2012): Musculoskeletal Ultrasound: A Primer for Primary Care. In: Tennant F (editor in-chief).Practical Pain Management. PPM Communications, Inc., Glen Mills, Philadelphia. pp 54-61.

19- Altman R, Hochberg M, Moskowitz R, Schnitzer T *et al.* (2000): Recommendations for the medical management of osteoarthritis of the hip and knee. Arthritis and Rheumatism, 43: 1905-1915.

20- Seed S, Dunican K, and Lynch A (2009): Osteoarthritis:A review of treatment options. Geriatrics, 64(10):20-29.

21- Katz W (2007): Non-pharmacologic approaches to osteoarthritis. American Journal of Lifestyle Medicine, 1(4): 2249-255.

22- Rönn K, Reischl N, Gautier E, and Jacobi M (2011): Current Surgical Treatment of Knee Osteoarthritis. Arthritis Article ID 454873, doi:10.1155/2011/454873.

23- Altman R, Asch E, and Bloch D, *et al.* (1986): Development of criteria for the classification and reporting of osteoarthritis. Classification of osteoarthritis of the knee. Diagnostic and Therapeutic Criteria Committee of the American Rheumatism Association. Arthritis Rheum. , 29:1039–1049**.**

24- Kellgren J and Lawrence J (1957): Radiological assessment of osteo-arthrosis. Ann Rheum Dis., 16: 494–502.

25- Hassan A, El-Shafey A, Ahmed H, Hamed M (2014): Effectiveness of the intra-articular injection of platelet rich plasma in the treatment of patients with primary knee osteoarthritis. The

Egyptian Rheumatologist, http://dx.doi.org/10.1016/j.ejr.2014.11.004.

26- Sanchez A, Anitua E, and Azofra J *et al.* (2008): Intra-articular injection of an autologous preparation rich in growth factors for the treatment of knee OA: a retrospective cohort study. Clinical and Experimental Rheumatology, 26 (5): 910-913.

27- Wang-Saegusa A, Cugat R, Ares O, Seijas R, Cusco X, and Garcia- Balletbo M (2011): Infiltration of plasma rich in growth factors for osteoarthritis of the knee short-term effects on function and quality of life. Arch Orthop Trauma Surg., 131:311-7.

Table (1): Comparison between study groups regarding clinical picture before and after trial

Clinical picture	Time	PRP group (N=20)	HA group (N=20)	$P_{PRP/HA}$
Morning stiffness	**Before**	5 (25.0%)	5 (25.0%)	1.000
	After	2 (10.0%)	3 (15.0%)	1.000
	$P_{Bf/Af}$	0.987	0.346	
Crepitations	**Before**	12 (60.0%)	12 (60.0%)	1.000
	After	7 (35.0%)	8 (40.0%)	0.744
	$P_{Bf/Af}$	**0.043***	**0.062**	
Tenderness	**Before**	20 (100.0%)	20 (100.0%)	1.000
	After	9 (45.0%)	12 (60.0%)	0.342
	$P_{Bf/Af}$	**<0.001***	**<0.001***	
Synovial hypertrophy	**Before**	3 (15.0%)	4 (20.0%)	1.000
	After	3 (15.0%)	4 (20.0%)	1.000
	$P_{Bf/Af}$	1.000	1.000	

*Significant

Table (2): Comparison between study groups regarding VAS score before and after trial

Time	Measure	PRP group (N=20)	HA group (N=20)	#P
Basal	**Mean ±SD**	5.8±1.2	6.3±1.5	0.214
	Range	4.0–8.0	3.0–9.0	
Month 3	**Mean ±SD**	3.6±1.2	5.5±1.5	**<0.001***
	Range	2.0–6.0	3.0–7.0	
Change (Month 3 – Basal)	**Mean ±SD**	-2.2±0.6	-0.9±0.9	**<0.001***
	Range	-3.0–-1.0	-3.0–0.0	
	^P	**<0.001***	**<0.001***	

Negative values indicate reduction, #Independent t-test, ^Paired t-test, *Significant

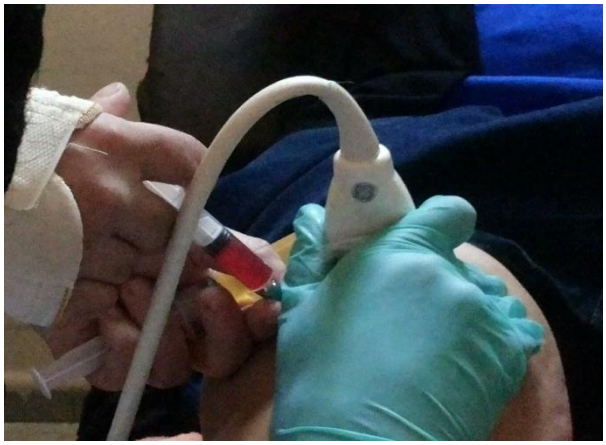

Figure (1): Ultrasound guided knee injection

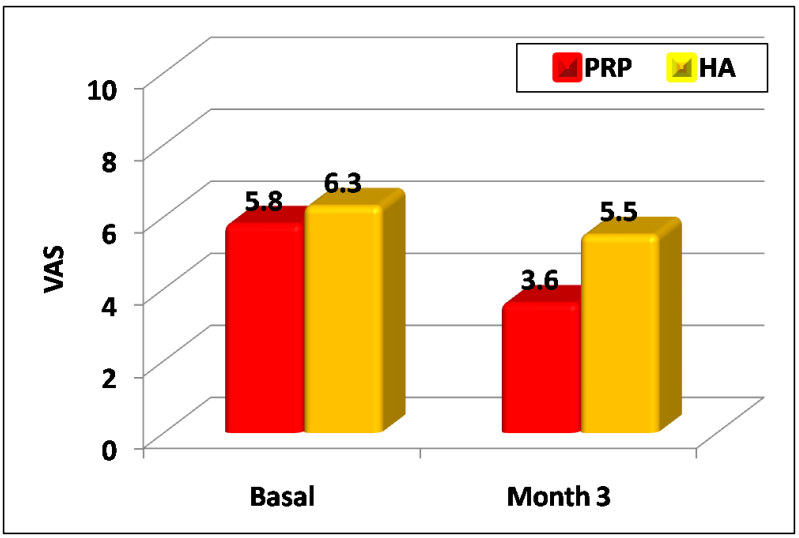

Figure (2): Comparison between study groups regarding VAS score before and after trial