ARC Journal of Orthopedics
Volume 4, Issue 2, 2019, PP 1-7
ISSN 2456-0588
DOI: http://dx.doi.org/10.20431/2456-0588.0402001
www.arcjournals.org

Platelet-Rich Plasma (PRP) is a New Hope for Patients with Knee Joint Osteoarthritis

Alaa Ali M. Elzohry[1*], Bahaa Gamal Saad[2],

Mohammed Farghaly Abd Elhamed[2], Mohamed Hussien El Gasser[2]

[1]*Lecturer of Anesthesia, Intensive care and Pain management, South Egypt Cancer Institute, Assiut University*

[2]*Assistant Lecturer of Anesthesia, Intensive care and Pain management, South Egypt Cancer Institute, Assiut University*

Corresponding Author:** ***Alaa Ali M. Elzohry, *Lecturer of Anesthesia, Intensive care and Pain management, South Egypt Cancer Institute, Assiut University,* ***E-mail:*** *alaa.zohiry@ hotmail.com*

Abstract

Background: *Autologous Platelet-Rich Plasma (PRP) is the volume of plasma with a high platelet concentration above normal baseline values. Platelets are sources of high concentrations of cytokines and a group of growth factors which regulate healing processes as well as tissue regeneration. Osteoarthritis (OA) of knee is one of the most common debilitating conditions associated with pain and limitation in daily living activities which negatively affect quality-of-life. It is a disease of the entire joint, involving not only the joint lining but also cartilage, ligaments, and bone.*

Aim of the Work: *We aim to illustrate the role of Platelet-Rich Plasma in management of Osteoarthritis (OA) of knee.*

Study Design: *Narrative review article.*

Conclusion: *The current review revealed that Osteoarthritis (OA) of knee joint has multi mechanism and increase the risk of complications bed redden as such, accounts for burden on economics budget.*

Keywords: *Osteoarthritis - PRP – Cytokines-VAS score- Knee joint.*

1. INTRODUCTION

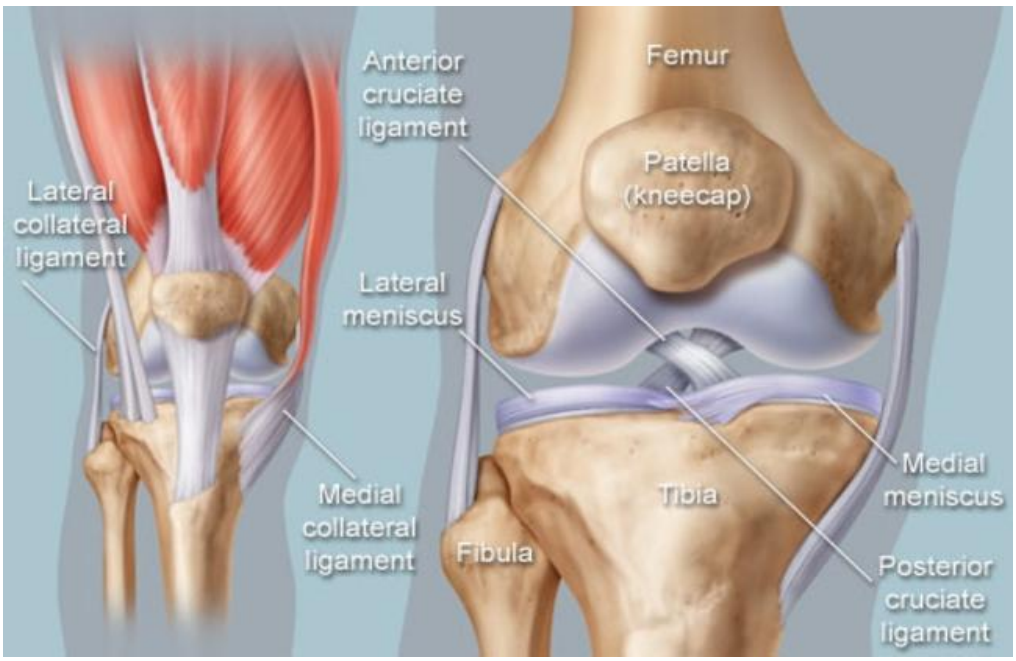


Figure1. *Anatomy of knee joint*

The anatomy of knee joint is very complicated as shown in (figure 1) so it is liable to trauma and OA. Oosteoarthritis (OA) refers to a clinical syndrome of joint pain with multifactorial pathology that is characterized by the gradual loss of articular cartilage, osteophyte formation, sub-chondral bone remodeling, and inflammation of the joint (1).

It is a disease of the entire joint, involving not only the joint lining but also cartilage, ligaments, and bone.

It is characterized by breakdown of the cartilage, bony changes of the joints, deterioration of tendons and ligaments, and various degrees of inflammation of the synovium (2).

A recent cohort study concluded that radiologic features of knee osteoarthritis were very common in adults: 13% of women 45 –65 years of age (an incidence of 3% per year). Osteoarthritis commonly affects middle age to elderly population.

Investigators have theorized the increase in osteoarthritis in women during menopause may partially be attributed to the hormonal factors (3) as shown in figure 2.

2. PATHOPHYSIOLOGY

In recent years, an increasing number of patients are being diagnosed with osteoarthritis, which has a notable impact on human health.

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. (4-6)

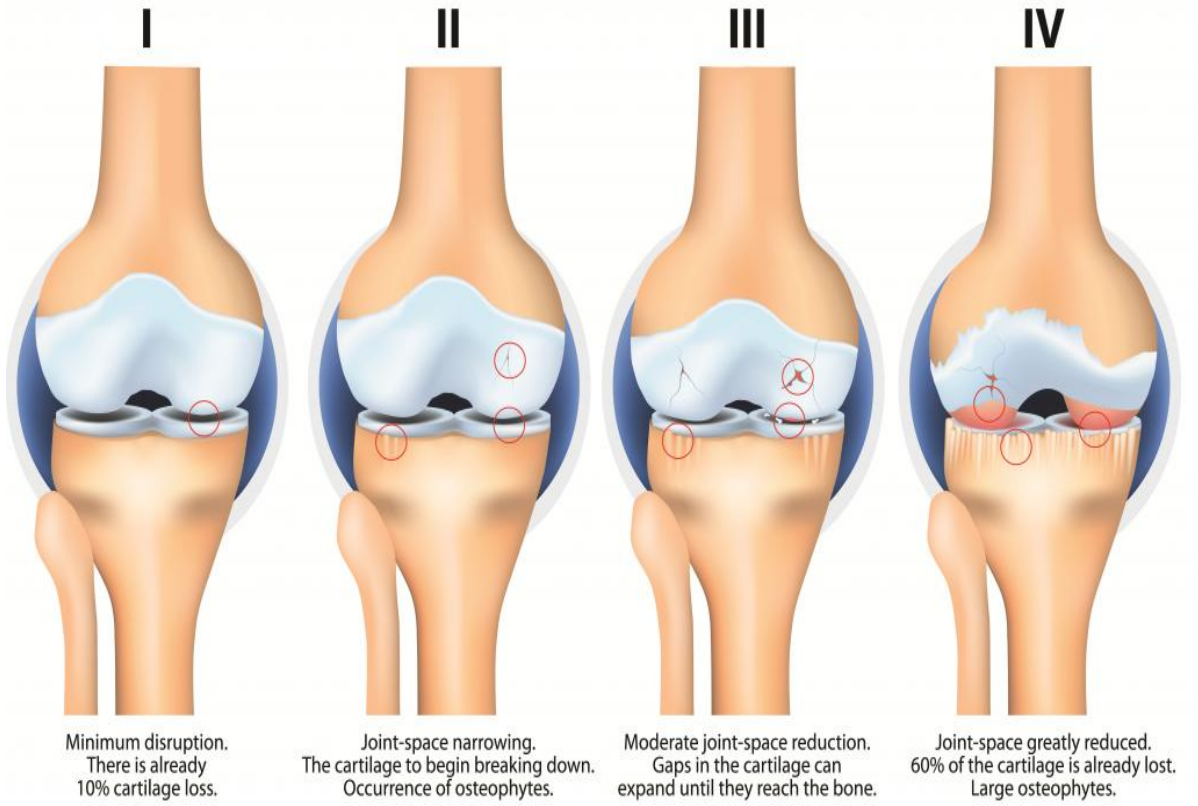


Figure2. *Stages of knee joint OA*

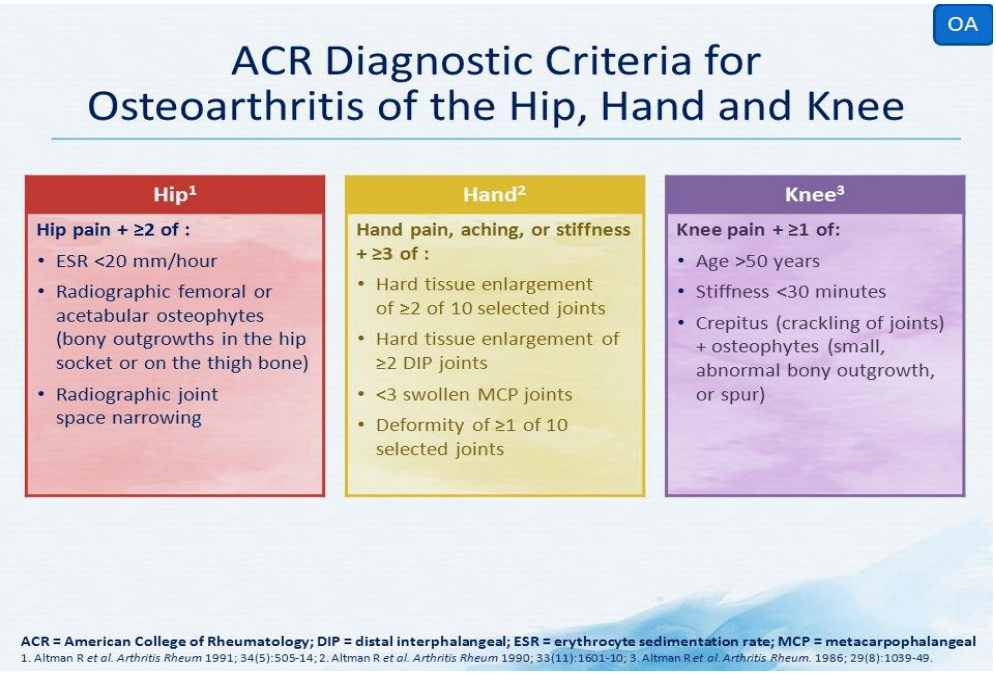
The causes of osteoarthritis are complex, and the pathogenesis related to this disease is not well understood (7). Osteoarthritis is divided into primary and secondary osteoarthritis according to the presence of local and systemic risk factors.

Osteoarthritis is frequently diagnosed as rheumatoid arthritis or ankylosing spondylitis in clinical differential diagnosis .It is the most common disease of arthritis and can occur together with other types of arthritis (8-9).

SO we can finally define osteoarthritis (OA) of knee as one of the most common debilitating conditions associated with pain and limitation in daily living activities which negatively affect quality-of-life. It is the most common form of joint disease and among the top 10 causes of disability worldwide. (10)

Diagnostic criteria for osteoarthritis have been developed by the American College of Rheumatology. These criteria are outlines in table 1.

Table1. *Diagnostic criteria for osteoarthritis*



Another classification of knee osteoarthritis is Kellgren and Lawrence grading scale. It is based on radiological imaging and consists of different grades:

Grade1: doubtful narrowing of joint space and possible osteophyte lipping;

Grade2: definite osteophytes and possible narrowing of joint space;

Grade3: moderate multiple osteophytes, definite narrowing of joint space and some sclerosis and possible deformity of bone ends; and

Grade4: large osteophytes, marked narrowing of joint space, severe sclerosis and definite deformity of bone ends (12-14).

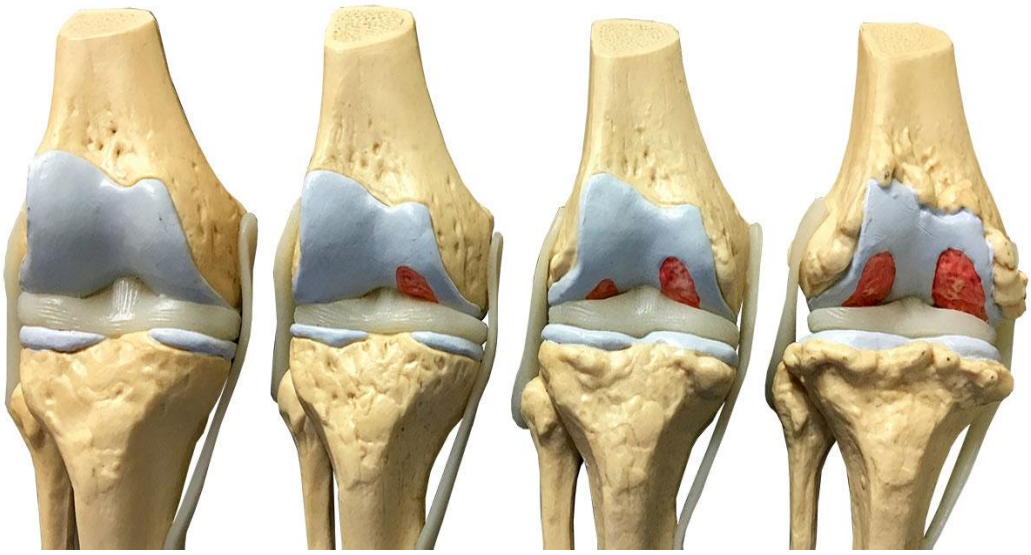


Figure3. *Pathological grads of knee OA*

3. Treatment of knee OA

The non pharmacological modalities include patient education, exercises and self management, lifestyle modifications such as dieting and weight reduction, walking supports (canes/crutches), bracing, shoe and insole modification, local hot/cold applications, acupuncture, and electromagnetic therapy. (15-16) Physical therapy is generally used, with exercises to maintain range of motion and strength. Pharmacologic therapies can be in the form of analgesics (paracetamol), NSAIDs, opioids, and slow-acting so-called nutraceuticals (glucosamine and chondroitin sulfate).

If orally administered drugs are ineffective (17). Intra-articular injections with corticosteroids seem to be safe. (18) More than one clinical guidelines reported high recommendations that these injections reduce pain for short term, especially if accompanied by effusion (19-20)

Glucosamine is one of the building blocks of cartilage, which can be taken as a tablet as a supplement to the diet, or sometimes as an injection (21).

The clinical guidelines of the American Academy of Orthopedic Surgeons) reported strong recommendation of not prescribing glucosamine for symptomatic patients while other three guidelines (22) stated fairly low level strength of recommendation for conditional use or even uncertainty about it.

4. PLATELET RICH PLASMA

Autologous Platelet-Rich Plasma (PRP) is the volume of plasma with a high platelet concentration above normal baseline values (23). Platelets are sources of high concentrations of cytokines and a group of growth factors which regulate healing processes as well as tissue regeneration (24).

4.1. Mechanism of Action of Platelet Rich Plasma

Autologous platelet concentrate suspended in plasma, also known as PRP, can be prepared from samples of centrifuged autologous blood. Exposure to a solution of thrombin and calcium chloride degranulates platelets, results in the formation of platelet gel and this stimulate the release of growth factors and bioactive molecules (25).

Therefore, platelets actively participate in healing processes by delivering a broad spectrum of growth factors (insulin like growth factor, transforming growth factor b- I, platelet derived growth factor, and many others) and other active molecules (e.g., arachidonic acid metabolites, cytokines, chemokines, ascorbic acid, extracellular matrix proteins, and nucleotides) to the injured site (26).

These factors altogether contribute to comprehensive roles of PRP, including anti inflammation, angiogenesis, chondrogenesis, chondrocyte proliferation, bone remodeling, coagulation, and cell differentiation and this, in turn, reduces inflammation , pain & can then be used as an adjunct to surgery with the intent of promoting hemostasis and accelerating healing (27).

Use of platelet-rich plasma is considered experimental / investigational for all orthopedic indications. This includes, but is not limited to, use in the following situations:

A. Primary use (injection) for the following conditions (28-30):

-Achilles tendinopathy, -Lateral epicondylitis, -Osteochondral lesions, -Osteoarthritis, -Plantar fasciitis

B. Adjunctive use in the following surgical procedures:

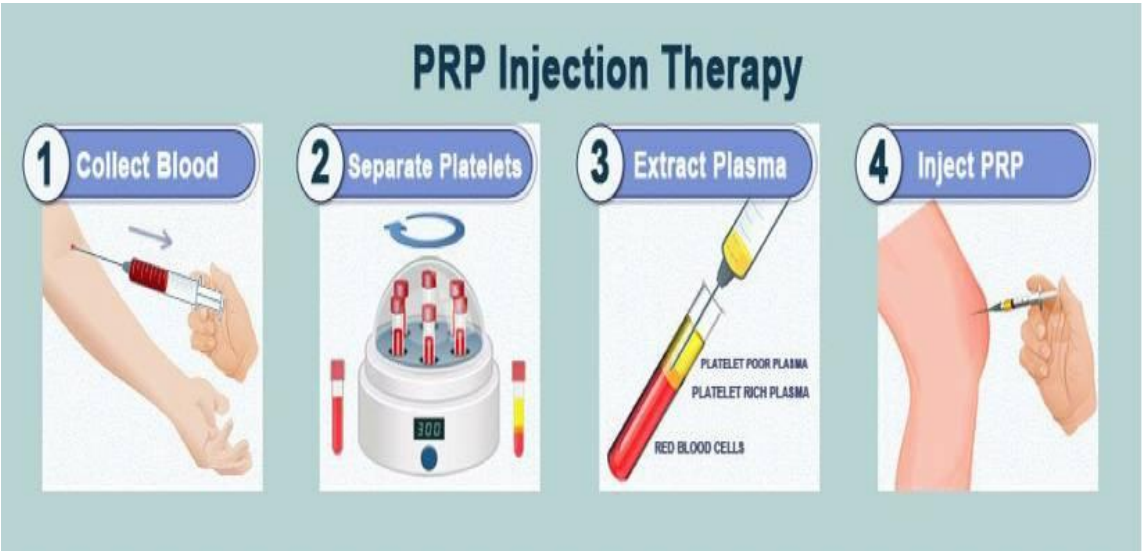
-Anterior cruciate ligament reconstruction, -Hip fracture, -Long-bone nonunion

-Patellar tendon repair, -Rotator cuff repair, -Spinal fusion

4.2. Preparation of PRP

The steps of preparation as shown

in next figure; (4)



5. Discussion

A number of RCTs and several systematic reviews of RCTs evaluating the use of PRP for knee osteoarthritis (OA) have been published. Protocols used in PRP interventions for knee OA varied widely (31). For example, in the studies identified in the Laudy et al (2015) systematic review, PRP was prepared using single, double, or triple spinning techniques and interventions included between 1 and 3 injections delivered 1 to 3 weeks apart. (32)

Xu et al (2017) conducted a systematic review and meta-analysis of RCTs comparing PRP with hyaluronic acid (8 trials), or placebo (2 trials), for the treatment of knee OA (see Table 1).21 Risk of bias was assessed using Cochrane criteria. Four studies were assessed as having low quality, three as moderate quality, and three as high quality. Meta-analyses including 7 of the trials comparing PRP with hyaluronic acid showed that PRP significantly improved Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) or International Knee Documentation Committee (IKDC) scores compared with HA at 6-month follow-up; however, when meta-analyses included only the 2 high-quality RCTs, there was not a significant difference between PRP and hyaluronic. (33-34) (Note that WOMAC evaluates 3 domains: pain, scored from 0-20; stiffness, scored from 0-8; and physical function, scored from 0-68. Higher scores represent greater pain and stiffness as well as worsened physical capability. The IKDC is a patient-reported, knee-specific outcome measure that measures pain and functional activity.) (35)

In the meta-analysis comparing PRP with placebo, a third trial was included, which had four treatment groups, two of which were PRP and placebo. This analysis showed that PRP significantly improved WOMAC or IKDC scores compared with placebo; however, only one of the trials was considered high quality and that trial only enrolled 30 patients. All meta-analyses showed high heterogeneity among trials (I2≥90%). (36)

Laudy et al (2015) conducted a systematic review of RCTs and nonrandomized clinical trials to evaluate the effect of PRP on patients with knee OA (see Table 1).14 Ten trials (total N=1110 patients) were selected. Cochrane criteria for risk of bias were used to assess study quality, with 1 trial rated as having a moderate risk of bias and the remaining 9 trials as high risk of bias. While meta-analyses showed that PRP was more effective than placebo or hyaluronic acid in reducing pain and improving function, larger randomized studies with lower risk of bias are needed to confirm these results. (37) Chang et al (2014) published a systematic review that included 5 RCTs, 3 quasi-randomized controlled studies, and 8 single-arm prospective series (total N=1543 patients) (see Table 1). (38) The Jadad scale was used to assess RCTs, and the Newcastle-Ottawa Scale was used to assess the other studies; however, results of the quality assessments were not reported. Meta-analysis of functional outcomes at 6 months found that the effectiveness of PRP (effect size, 1.5; 95% CI, 1.0 to 2.1) was greater than that of hyaluronic acid (effect size, 0.7; 95% CI, 0.6 to 0.9; when only RCTs were included). (39)

However, there was no significant difference at 12-month follow-up between PRP (effect size, 0.9; 95% CI, 0.5 to 1.3) and hyaluronic acid (effect size, 0.9; 95% CI, 0.5 to 1.2; when only RCTs were included). Fewer than 3 injections, single spinning, and lack of additional activators led to greater uncertainty in the treatment effects. PRP also had lower efficacy in patients with higher degrees of cartilage degeneration. Results were consistent when analyzing only RCTs, but asymmetry in funnel plots suggested significant publication bias. (40)

6. Conclusion

OA of knee joint is multi-factorial pathology and patients with OA of knee are really suffering.

IA injections of PRP and corticosteroids given together for knee OA are an effective non-operative modality of treatment. In combination, they seem to have better efficacy than any of them given alone. These injections are clinically safe and have promising and very positive effects for patient satisfaction.

References

[1] Ma YW, Jiang DL, Zhang D, Wang XB and Yu XT: Radial extracorporeal shock wave therapy in a person with advanced osteonecrosis of the femoral head. Am J Phys Med Rehabil 95: e133-e139, 2016.

[2] Meheux CJ, McCulloch PC, Lintner DM, Varner KE and Harris JD: Efficacy of intra-articular platelet-rich plasma injections in knee osteoarthritis: A systematic review. Arthroscopy 32: 495-505, 2016.

[3] Lee GW, Park KS, Kim DY, Lee YM, Eshnazarov KE and Yoon TR: Results of total hip arthroplasty after core decompression with

tantalum rod for osteonecrosis of the femoral head. Clin Orthop Surg 8: 38-44, 2016.

[4] Roemer FW, Kwoh CK, Hannon MJ, Hunter DJ, Eckstein F, Grago J, Boudreau RM, Englund M and Guermazi A: Partial meniscectomy is associated with increased risk of incident radiographic osteoarthritis and worsening cartilage damage in the following year. Eur Radiol 27: 404-413, 2017.

[5] Tang H, He S, Zhang X, Luo S, Zhang B, Duan X, Zhang Z, Wang W, Wang Y and Sun Y: A network pharmacology approach to uncover the pharmacological mechanism of XuanHuSuo powder on osteoarthritis. Evid Based Comple ment Alternat Med 2016: 3246946, 2016.

[6] Poquet N, Williams M and Bennell KL: Exercise for Osteoarthritis of the Hip. Phys Ther 96: 1689-1694, 2016.

[7] Zhang W, Doherty M, Peat G, Bierma-Zeinstra MA, Arden NK, Bresnihan B, et al. EULAR evidence-based recommendations for the diagnosis of knee osteoarthritis. Ann Rheum Dis. 2010;69:483 9.

[8] Vicenzino B, Souvlis T, Wright A. Musculoskeletal pain. In: Strong J, Unruh AM, Wright A, Baxter GD, editors.Pain: a textboot for therapists. Edinburgh. Churchill Livingstone; 2002.23.Cleland JA, Koppenhaver S. Netter's orthopaedic clinical examination. 2nd ed. Philadelphia: Saunders; 2011

[9] Altman R, Asch E, Bloch D, Bole G, Borenstein D, Brandt K, et al. 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. 1986;29:1039-49

[10] Ringdahl E, Pandit S. Treatment of knee osteoarthritis. Am Fam Physician. 2011;83:1287 -92.25. Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. Ann Rheum Dis. 1957;16:494-502.

[11] Ringdahl E, Pandit S. Treatment of knee osteoarthritis. Am Fam Physician. 2011;83:128 7-92.25.Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. Ann Rheum Dis. 1957;16:494-502.26.

[12] Schiphof D, Boers M, Bierma-Zeinstra SM. Differences in descriptions of Kellgren and Lawrence grades of knee osteoarthritis. Ann Rheum Dis. 2008;67:1034-6.27.

[13] Altman R, Asch E, Bloch D, Bole G, Borenstein D, Brandt K, et al. 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. 1986;29:1039-49

[14] Maricar N, Callaghan MJ, Parkes MJ, Felson DT and O'Neill TW: Clinical assessment of effusion in knee osteoarthritis-A systematic review. Semin Arthritis Rheum 45: 556-563, 2016.

[15] Beumer L, Wong J, Warden SJ, Kemp JL, Foster P and Crossley KM: Effects of exercise and manual therapy on pain associated with hip osteoarthritis: A systematic review and meta analysis. Br J Sports Med 50: 458-463, 2016.

[16] Cuadros MEF, Moro OSP, Florin MJA, et al. Ozone improves pain relief function and quality of life in patients with knee osteoarthritis: A prospective quasi-experimental before-after study. Middle East Journal of Rehabilitation and Health. 2017;4(1):e41821.

[17] Jang SJ, Kim JD and Cha SS: Platelet-rich plasma (PRP) injections as an effective treatment for early osteoarthritis. Eur J Orthop Surg Traumatol 23: 573-580, 2013

[18] Jevsevar DS, Brown GA, Jones DL, Matzkin EG, Manner PA, Mooar P, Schousboe JT, Stovitz S, Sanders JO, Bozic KJ, et al. The American Academy of Orthopaedic Surgeons evidence-based guideline on: treatment of osteoarthritis of the knee, 2nd edition. J Bone Joint Surg Am. 2013;95:1885–1886.

[19] Handl M, Amler E, Bräun K, Holzheu J, Trc T, Imhoff A B, et al. Positive effect of oral supplementation with glycosaminoglycans and antioxidants on the regeneration of osteochondral defects in the knee joint. Physiol Res 2007; 56:243Y9.

[20] Zhang W, Nuki G, Moskowitz RW, Abramson S, Altman RD, Arden NK, Bierma-Zeinstra S, Brandt KD, Croft P, Doherty M, et al. 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 Cartilage. 2010;18:476–499.

[21] Reid MC, Shengelia R, Parker SJ. Pharmacologic management of osteoarthritis-related pain in older adults. Am J Nurs. 2012;112:S38-S43

[22] Zhang W, Moskowitz RW, Nuki G, Abramson S, Altman RD, Arden N, et al. OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. Osteoarthr Cartil. 2008;16:137-62

[23] Towheed T, Maxwell L, P. AT, Shea B, Houpt JB, Welch V, et al. Glucosamine therapy for treating osteoarthritis (review). Cochrane Database Syst Rev [Internet]. 2009. Available from: http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD002946/frame. html. doi: 10. 1002/ 14651858.CD002946.pub2

[24] Zhang W, Moskowitz RW, Nuki G, Abramson S, Altman RD, Arden N, et al. OARSI

recommendationns for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. Osteoarthr Cartil. 2008;16:137-62.

[25] Hochberg MC, Altman RD, April KT, Benkhalti M, Guyatt G, McGowan J, et al. American Coll ege of Rheumatology 2012 recommendations for the use of non pharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. Arthritis Care Res (Hoboken). 2012; 64:4 55-74.

[26] Pierce TP, Jauregui JJ, Elmallah RK, Lavernia CJ, Mont MA and Nace J: A current review of core decompression in the treatment of osteonecrosis of the femoral head. Curr Rev Musculoskelet Med 8: 228-232, 2015.

[27] Ulrich-Vinther M, Maloney MD, Schwarz EM, Rosier R, O'Keefe RJ. Articular cartilage biolo gy. J Am Acd Orthop Surg 2003; 11:421Y30.

[28] Pietrzak WS, Eppley BL. Platelet rich plasma: Biology and new technology. J Craniofac Surg 2005;16:1043–54.

[29] Drengk A, Zapf A, Stürmer EK, Stürmer KM, Frosch KH. Influence of platelet‐rich plasma on chondrogenic differentiation and proliferation of chondrocytes and mesenchymal stem cells. Cells Tissues Organs 2009; 189:317‐26.

[30] Castillo TN, Pouliot MA, Kim HJ, et al. Comparison of growth factor and platelet concentration from commercial platelet-rich plasma separation systems. Am J Sports Med. Feb 2011;39(2):266- 271. PMID 21051428

[31] Hsu WK, Mishra A, Rodeo SR, et al. Platelet-rich plasma in orthopaedic applications: eviden ce- based recommendations for treatment. J Am Acad Orthop Surg. Dec 2013;21(12):739-748. PMID 24292930.

[32] Sampson S, Gerhardt M, Mandelaum B. Platelet rich plasma injection grafts for musculoskeletal injuries:A review. Curr Rev Musculoskelet Med 2008; 1:165–74.

[33] Hunziker EB, Driesang IM, Morris EA. Chondrogenesis in cartilage repair is induced by members of the transforming growth factor-beta superfamily. Clin Orthop Relat Res 2001;391 (suppl):S171–81.

[34] Werner S, Grose R. Regulation of wound healing by growth factors and cytokines. Physiol Rev 2003; 83:835–70.

[35] Sampson S, Gerhardt M, Mandelaum B. Platelet rich plasma injection grafts for musculoskeletal injuries: A review. Curr Rev Musculoskelet Med2008; 1:165–74.

[36] Hunziker EB, Driesang IM, Morris EA. Chondrogenesis in cartilage repair is induced by members of the transforming growth factor-beta superfamily. Clin Orthop Relat Res 2001;391 (suppl): S171–81.

[37] Barrett S, Erredge S. Growth factors for chronic plantar fasciitis. Podiatry Today 2004;17:37–42.

[38] Meheux CJ, McCulloch PC, Lintner DM, Varner KE and Harris JD: Efficacy of intra-articular platelet-rich plasma injections in knee osteoarthritis: A systematic review. Arthroscopy 32: 495-505, 2016.

[39] Laudy AB, Bakker EW, Rekers M and Moen MH: Efficacy of platelet-rich plasma injections in osteoarthritis of the knee: A systematic review and meta-analysis. Br J Sports Med 49: 657-672, 2015.

[40] Xu Z, Luo J, Huang X, et al. Efficacy of platelet-rich plasma in pain and self-report function in knee osteoarthritis: a best-evidence synthesis. Am J Phys Med Rehabil. Nov 2017;96(11):793-800. PMID 28398969.

[41] Hunziker EB, Driesang IM, Morris EA. Chondrogenesis in cartilage repair is induced by members of the transforming growth factor-beta superfamily. Clin Orthop Relat Res 2001;391(suppl):S171–81.

[42] 37. Anitua E, Sánchez M, Nurden AT, Zalduendo MM, de la Fuente M, Azofra J, et al. Platelet released growth factors enhance the secretion of hyaluronic acid and induce hepatocyte growth factor production by synovial fibroblasts from arthritic patients. Rheumatology 2007; 46:1769–72.

[43] 38. Anitua E, Andia I, Ardanza B, Nurden P, Nurden AT. Autologous platelets as a source of proteins for healing and tissue regeneration. Thromb Haemost 2004;91:4‐15.

[44] 39. Pietrzak WS, Eppley BL. Platelet rich plasma: Biology and new technology. J Craniofac Surg 2005;16:1043‐54.

[45] 40-Jordan KM, Arden NK, Doherty M, Bannwarth B, Bijlsma JW, Dieppe P, et al. EULAR Recommendations 2003: an evidence based approach to the management of knee osteoarthritis: report of a task force of the standing committee for international clinical studies including trials (ESCISIT). Ann Rheum Dis. 2003;62:1145-55.

Citation: *Alaa Ali M. Elzohry. Platelet-Rich Plasma (PRP) is a New Hope for Patients with Knee Joint Osteoarthritis. ARC Journal of Orthopedics. 2019; 4(2):1-7. doi:dx.doi.org/ 10.20431/2456-0588.0402001.*