Published online 2019 September 2.

Research Article

1	6		
		7	

Does Intra-Articular Platelet Rich Plasma Injection Improve Meniscal Repair Outcomes?

Rehab Abdelaal Elnemr^{1,*}, Hoda Mohamed Abdelnaby¹ and Mohamed Mahmoud Elshafei²

¹Physical Medicine Rheumatology and Rehabilitation Department, Faculty of Medicine, Alexandria University, 01006500715, Alexandria Governorate, Egypt ²Intervention Radiology, Faculty of Medicine, Alexandria University, Alexandria Governorate, Egypt

corresponding author: Physical Medicine Rheumatology and Rehabilitation Department, Faculty of Medicine, Alexandria University, 01006500715, Alexandria Governorate, Egypt. Email: elnemr.rehab@gmail.com

Received 2018 October 14; Revised 2019 January 04; Accepted 2019 January 22.

Abstract

Background: Meniscal tear surgeries have many long term sequelae. Intra-articular platelet rich plasma injection is thought to stimulate repair and increase meniscal function.

Objectives: To assess the effect of 6-monthly intra-articular injection of platelet rich plasma (PRP) on the pain assessment and functional status of knee joint undergone meniscal repair.

Methods: A randomized controlled trial was carried out on thirty patients who had undergone arthroscopic meniscal repair and presented with persistent pain within 4 months after surgery. Half of the patients were randomly intra-articularly injected with 5 mL PRP at 1 month intervals for 6 injections and the other half were not injected and taken as a control group. Clinical examination, visual analogue scale (VAS), knee injury and osteoarthritis outcome score (KOOS) score and Doppler ultrasonography were performed before and after PRP treatment.

Results: After 6 months, in the PRP injected group, there was a significant improvement in VAS score (1(1-3)) and KOOS score (86.2 \pm 4) compared to baseline values (9 (7-10) and 62 \pm 9.8 respectively; P < 0.001) as well as significant decrease in the percentage of degeneration of medial femoral condyle (MFC), lateral femoral condyle (LFC), medial tibial condyle (MTC), lateral tibial condyle (LTC) measured by Doppler Ultrasonography (US), (6.16 \pm 3.33 and 9.07 \pm 3.66, respectively; P = 0.031).

Conclusions: This study showed that intra-articular PRP injection following meniscal repair can be effective in reducing pain, improving knee function, and slowing the rate of cartilage degeneration that accounts for early osteoarthritis.

Keywords: Meniscal Repair, PRP, Regeneration, Ultrasound

1. Background

The menisci play a crucial role in protecting biomechanical operations of the knee. It also provides joint lubrication and cartilage nutrition as well as proprioception (1).

Meniscal injuries result in knee joint instability and hence, it is a strong predictor of later knee osteoarthritis (OA) (1). One of the procedures done to treat the injured menisci is partial or total meniscal excision. Though well-established knowledge found that all meniscectomies knees eventually develop arthritic changes as a long term sequalae (2-4). The severity of these changes is proportional to the amount of meniscus removed. Structural, biochemical, and mechanical articular cartilage changes following partial meniscectomy are thought to be due to increased intra-articular contact stresses and loss of the load distribution that operates to prevent the menisci from extruding out of the joint throughout axial loading and decreased stability of the knee (2, 5, 6). It was proved that articular cartilage loss following partial meniscectomy (6.9% per year) is significantly higher compared to healthy controls (2.3% per year) (7).

Arthroscopic repair of torn menisci has thus become the mainstay treatment methodology if the repair is feasible (8). All repair techniques are the accepted arthroscopic repair techniques (9). Many factors are thought to have effects on the results of meniscal repair; such as tear location, size, and chronicity, repair technique; patient age, body mass index (BMI), level of activity and habits, as well as the presence of associated injuries. Favorable results are observed after treatment of longitudinal acute tears within the peripheral vascular zone of the meniscus and in young people with stable knees (10). However, meniscal repair doesn't consider the underlying biological changes to the microenvironment that is attributable to OA. In addi-

Copyright © 2019, Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License (http://creativecommons.org/licenses/by-nc/4.0/) which permits copy and redistribute the material just in noncommercial usages, provided the original work is properly cited.

tion, repair of avascular meniscal tears is associated with high failure rate because of the limited healing capacity in the inner two-thirds of the meniscus, leading to biomechanical alterations and articular cartilage degeneration (8). Thus, biological therapy as well as tissue engineering may be used alternatively or complementary to repair the avascular zone of the menisci (11).

Platelet-rich plasma (PRP) as an autologous biologic therapy is a promising strategy to help induce tissue healing. It is considered as plasma with concentrated platelets above normal values (3 - 8 times the concentration of normal platelet levels) (12). It contains growth factors, chemokines, interleukins and cytokines released from platelets to enhance the natural healing process and tissue regeneration within the treatment site (13). It also contains proteins and bioactive molecules that play a crucial role in the cellular repair cascade (14, 15). Because PRP contains growth factors and plasma proteins, it will regulate pro- and anti-inflammatory signals causing angiogenesis equilibrium (16, 17).

Although PRP has been employed in clinical practice for a few times, to date, few clinical researches support its use in meniscal lesions and in improving meniscal repair outcomes (18). One matter of importance is the paucity of prior published randomized controlled studies assessing the effect of PRP on meniscal healing.

2. Objectives

The aim of this work was to assess the impact of 6monthly intra-articular injection of PRP in patients who had undergone unilateral arthroscopic isolated meniscal repair for complete meniscal tears located at the red-white zone of the meniscus, performed by a single surgeon and presented with knee pain within 4 months after surgery. Our hypothesis was that intra-articular PRP injection may add beneficial effect on post-meniscal repair outcomes regarding pain and functional state of the operated knee.

3. Methods

3.1. Subjects

The study was done on 30 patients undergoing arthroscopic isolated meniscal repairs by single surgeon and presenting with knee pain within 4 months after surgery. Approval from local Ethics Committee was obtained and institutional review board approval was granted. A written informed consent was taken from all participants.

Inclusion criteria were patients aged 18 - 55 years undergoing complete meniscal tear in red-white zone repaired by single surgeon and complaining of pain within 4 months after repair. Exclusion criteria were some systemic disorders, such as diabetes, autoimmune diseases, hematological disorders, cardiovascular diseases, infections, local knee injuries other than meniscal injury as well as patients receiving treatment with anticoagulants-anti-aggregates or use of non-steroidal anti-inflammatory drugs (NSAIDs) within 5 days before blood being taken.

Random, double blinded selection of 15 patients to constitute the PRP-group was injected intra-articularly with about 5 mL of PRP in the operated knee joint, at 1-month intervals, for 6 injections. The other fifteen patients were not injected and constituted the control group.

3.2. Study Design

At the first visit all patients were subjected to (1) thorough general and meniscus repair related history taking focusing on articular cartilage status, zone, type, chronicity of tear, and type of repair (2). General examination and complete knee joint examination. The severity of pain was assessed by visual analogue scale (VAS) (19). The Knee injury and osteoarthritis outcome score (KOOS) questionnaire was applied to all studied patients in order to evaluate the function of the operated knee (20). Patients were instructed to complete the KOOS form by considering their operated knee at first visit, 3 and 6 months following PRP injection for the PRP group and two times (baseline and 6 months later) for the non-PRP group.

High resolution ultrasonographic examination was performed by a single radiologist who was blinded for the studied subject by using Siemens Prima apparatus, utilizing high resolution multi-frequency probe (3.5-7 MHz). Using transverse suprapatellar scans tangential to the upper patellar pole at 90° knee flexion to assess for tibio-femoral cartilage thickness, regularity of the cartilage margins and knee effusion (21). Ultrasonography reports included comment on increased vascularity (Doppler activity), and synovial hypertrophy. The cartilage thickness was measured within the weight-bearing area from four anatomical locations; namely, the medial femoral condyle (MFC), the lateral femoral condyle (LFC), the medial tibial condyle (MTC), and the lateral tibial condyle (LTC). Measurements were done two times at the first visit (baseline) and after six months for the operated knees for both groups.

The PRP-group (15 patients) were injected at one-month intervals, for 6 injections. Pre-injection guidelines were given to all patients in the form of stopping steroidal and non-steroidal anti-inflammatory drugs for at least one week before the procedure, as well as stopping any anticoagulant drugs 5 days before the procedure, increasing intake of fluids within the 24 hours prior to the procedure and anti-anxiety medication were required for anxious patients. Injection, under complete aseptic technique, was performed while the patient was in supine position, and the knee was fully extended, using the lateral approach. Patients were instructed after injection to avoid using the injected leg for 24 hours, to use ice packs over the injected joint and not to use NSAIDs for another one week (22).

3.3. Platelet-Rich Plasma Preparation

Thirty milliliters of venous blood was taken from every patient and collected in sodium citrated sterile tubes. Platelet concentrates were obtained by adjusting centrifuge at 1800 rpm for 15 minutes to separate erythrocytes, then at 3500 rpm for 10 minutes to concentrate the platelets (23). Thus 5 mL of PRP was obtained, 0.2 mL of 10% calcium chloride was added to the final product to activate the platelets and injected immediately without storage. It is believed that freshly-harvested PRP would possibly preserve the platelet functions better (22).

Follow up was done following six PRP monthly injections; all patients were re-evaluated again by VAS, KOOS score as well as by musculoskeletal high-resolution ultrasonography. After 3 PRP injections, both groups were reevaluated by VAS and KOOS only.

3.4. Statistical Analysis

Data of the patients were entered on the applied math package for Science (SPSS version 17, Chicago, IL, USA). Quantitative data were demonstrated as mean and standard deviation, whereas the qualitative data were demonstrated as number and percentage. Paired *t*-test and chi square test were used to study differences between quantitative and qualitative data at baseline and after 6 PRP injections. Spearman's correlation coefficient analysis was performed to identify factors associated with better functional outcomes. A statistically significant cutoff value was set at P < 0.05.

4. Results

4.1. Participants' Characteristics

Demographic data and clinical findings of our studied patients (PRP and non-PRP groups) are shown in Table 1. There was no statistically significant difference between both groups, (P < 0.05).

4.2. Clinical Outcomes Comparison Analysis

Comparison between pre-PRP injection (baseline), 3 months and 6 months post-PRP injection within the studied PRP-patient group regarding VAS and KOOS findings are reported in Table 2. There was a statistically significant decrease in VAS assessment at 3 months and more at 6 months post-PRP injection. Moreover, KOOS assessment was significantly increased at 3 months and more at 6 months following PRP injection.

Comparison between both groups according to the VAS and KOOS findings at pre-injection, 3 months and 6 months post-injection are demonstrated in Table 3. There was statistically significant difference between both groups regarding both parameters at 3- and 6-months post-injection. The PRP-injected group showed more decrease in VAS assessment as well as more increase in KOOS assessment than non-injected group along the follow up periods (3 and 6 months post-injection).

4.3. Ultrasonographic Imaging Outcomes Comparison Analysis

Ultrasound findings of both groups and comparison between different parameters pre-injection (baseline) and 6 months post-injection are demonstrated in Table 4. There was significant decrease in the percent of degeneration of all US measurements between pre-injection and 6 months post-injection in both groups. Moreover, there was statistically significant difference between both groups according to the total change in the US findings after 6 months.

4.4. Complications

No complications were noted among patients who enrolled in our study.

5. Discussion

In the current study, a statistically significant improvement was observed regarding pain (as assessed by VAS), knee function (as assessed by KOOS) as well as total ultrasound cartilage thickness (calculated as % of change) between both groups (PRP and non-PRP injected patients) at 6 months after PRP injection. In addition, there was statistically significant decrease in pain (by VAS) and increase in knee function (by KOOS) within the studied PRP-patient group between baseline, 3 months and 6 months after injection.

5.1. Previous Studies and Interpretation of the Results

In agreement with our findings, Pujol et al. (24) reported that PRP can slightly improve clinical outcomes, following open repair for horizontal cleavage. More recently, Kaminski et al. (25) found that PRP augmentation in meniscus repair results in a significant improvement in the rate of meniscus healing and improves the chances of meniscus healing by over six times with low adverse events related to it. They used MRI in follow up assessment but we favor the use of US as it's an easy, rapid, as well as cost efficient method. On the other hand, Griffin et al. (26) found

	PRP Group (N = 15)	Non-PRP Group (N = 15)	P Value
Gender			1.000
Male	14 (93.3)	13 (86.7)	
Female	1(6.7)	2 (13.3)	
Age, y	27.7 ± 2.9	30.1 ± 4	0.068
Height, cm	173.1 ± 5.8	173.5 ± 8	0.876
Weight, kg	81.7 ± 14.4	77.1 ± 13.6	0.376
BMI, kg/m ²	27.2 ± 4.3	25.5 ± 3.3	0.230
Operated side			0.464
Right	7 (46.7)	9 (60)	
Left	8 (53.3)	6(40)	
Mechanism of injury			0.273
Significant trauma	9 (60)	6(40)	
Repeated micro traumata	6 (40)	9 (60)	
Site of tear (zone of injury all were within the peripheral 10% to 30% of the meniscus)			
Middle and posterior third of the medial meniscus	8 (53.3)	6 (40)	0.414
Middle and posterior third of the lateral meniscus	7 (46.7)	9 (60)	0.464
Tear pattern			1.000
Vertical longitudinal	11 (73.3)	11 (73.3)	
Transverse radial	4 (26.7)	4 (26.7)	
Chondral lesion at time of arthroscopy	2 (13.3)	3 (20)	1.000
Technique of meniscal repair			1.000
Inside out	11 (73.3)	12 (80)	
All-inside	4 (26.7)	3 (20)	
Local tenderness	15 (100)	13 (86.7)	0.483
Effusion	9 (60)	8 (53.3)	0.713
Instability	2 (13.3)	5 (33.3)	0.390
Alignment			0.705
Mild varus	6 (40)	5 (33.3)	
Normal	9 (60)	10 (66.7)	
Muscle wasting	6 (40)	5 (33.5)	0.705
ROM			1.000
Full	10 (66.7)	10 (66.7)	
LLD	5 (33.3)	5 (33.3)	
VAS	9 (7-10)	8 (5 -8)	0.09
KOOS scale	62 ± 9.8	66.3 ± 8.7	0.217

Abbreviations: KOOS, knee injury and osteoarthritis outcome score; PRP, platelet rich plasma; VAS, visual analogue scale. ^aValues are expressed as mean ± SD or No. (%). ^bQualitative data were described using number and percent and was compared using Chi square test or Fisher Exact test, abnormally distributed data were expressed in median (min. - max.) and were compared using Mann Whitney test*, while normally distributed quantitative data were expressed in mean ± SD and were compared using student *t*-test Statistically significant at P \leq 0.05.

that outcomes, specifically International knee documenta-

tion scale and Tegner Lysholm knee scale scores, as well as

Table 2. Comparison Between Pre and Post Injection Evaluation Parameters in the Studied PRP-Patient Group ^a				
	Pre-Injection	3 Months Post-Injection	6 Months Post-Injection	
VAS	9 (7-10)	4 ^b (1-7)	1 ^{b,c} (1-3)	
P value		0.001 ^d	0.001 ^d	
KOOS	62 ± 9.8	$83.5^{\rm b}\pm4.4$	$86.2^{\text{b,c}}\pm4$	
P value		0.001 ^d	0.014 ^d	

Abbreviations: KOOS, knee injury and osteoarthritis outcome score: VAS, visual analogue scale,

^aNormally quantitative data was expressed in mean \pm SD and was compared using student *t*-test

^bSignificant between pre and other periods.

^cSignificant between 3 and 6 months.

^dStatistically significant at P \leq 0.05.

Table 3. Compa	arison Between Both Gr	oups Regarding Clinical	l Evaluation Parameters ^a

	PRP Group	Non-PRP Group	P Value
VAS			
3 months	4 ^b (1 - 7)	5 ^b (1-8)	0.474
6 months	1 ^{b,c} (1-3)	5 ^{b,c} (1-7)	0.003 ^d
% Change	\downarrow 84.9 \pm 6.9	\downarrow 38.4 \pm 37.4	< 0.001 ^d
KOOS			
3 months	$83.5^{\mathrm{b}}\pm4.4$	$77.1^{\rm b}\pm 6.3$	0.003 ^d
6 months	$86.2^{\text{b,c}}\pm4$	$81.1^{\text{b,c}}\pm6.1$	0.012 ^d
% Change	$\uparrow 42.2 \pm 22.5$	\uparrow 24.3 \pm 18.8	0.014 ^d

Abbreviations: KOOS, knee injury and osteoarthritis outcome score: PRP, platelet rich plasma: VAS, visual analogue scale,

Normally quantitative data was expressed in mean \pm SD and was compared using student *t*-test

^bSignificant between pre and other periods. ^cSignificant between 3 and 6 months.

^dStatistically significant at P \leq 0.05.

clinical and patient-reported outcomes, as postoperative ROM, return to work, and return to sports/baseline activity after meniscus repair with and without PRP appear similar with no favor for PRP injection and there was no difference in any of these outcome measures between those patients who had PRP and those who did not. This disagreement may be due to several factors; firstly, they had done only one intra-surgical PRP injection not followed by repeated post-operative injections, secondly, lack of objective follow up measures as US or MRI findings, thirdly, no specific surgeon had done the arthroscopic meniscal tear so they have a confounding factor in their results, and finally, lack of power and nature of the study they reported in their work.

Interestingly, we found decrease in the percent of degeneration for each parameter measured in ultrasound before and 6 months after injection in both groups (injected and non-injected) but of no statistically significant level. This may be due to the small sample of our studied patients and short time of follow up. As noted by Cole et al. the value of PRP use in meniscal repair is the possibility of delivering a local concentration of growth factors and other cytokines directly to the repair site (18). The appeal of this is to enhance meniscal vascularity.

5.2. Clinical Implementation

The meniscus is critical for the knee's health and function, but is often injured especially in young athletes in whom unnecessary intervention with secondary cartilage destruction and joint failure may be unfavorable to a competitive future. Recently, greater efforts have been made to determine a more durable alternative to meniscectomy, as the procedure results in increased contact stresses on the articular surface of the knee (27, 28). Meniscal repairs have been studied extensively but are still failing for a number of reasons. The lack of vasculature that provides intrinsic nutrition is believed to be a reason for poor cure (29). The use of PRP was demonstrated to increase healing by introducing a higher concentration of multiple growth factors in the area of meniscal repair (30). The experimental studies' results support the hypothesis that PRP could improve meniscus healing by activating fibro-chondrocytes in the avascular regions of the meniscus (31). The growth factors released from platelets are thought to be associated with the healing cascade initiation, with an increase in the

Fable 4. Comparison of Ultrasound Findings Between Both Groups at Pre and 6 Months Post-Injection ^a					
US Fi	indings	PRP Group	Non-PRP Group	P Value	
MFC					
	Pre-injection	2.5 ± 0.5	2.4 ± 0.5	0.725	
	6 months post-injection	$2.2^{\rm b}{\pm}~0.5$	$2.1^{b} \pm 0.4$	0.366	
	% of degeneration	\downarrow 9.7 \pm 4.6	\downarrow 13.4 \pm 5.6	0.059	
LFC					
	Pre-injection	2.1 ± 0.4	2.2 ± 0.4	0.489	
	6 months post-injection	$2^{\rm b}{\pm}~0.4$	$2.1^{\rm b} {\pm}~0.4$	0.562	
	% of degeneration	$\downarrow 1.7 \pm 2.5$	\downarrow 2.2 \pm 2.5	0.623	
МТС					
	Pre-injection	2.6 ± 0.5	2.6 ± 0.4	0.782	
	6 months post-injection	$2.4^{\rm b}{\pm}~0.5$	$2.2^{\rm b} {\pm}~0.5$	0.338	
	% of degeneration	\downarrow 9.7 \pm 7.6	\downarrow 14.7 \pm 7.9	0.089	
LTC					
	Pre-injection	3 ± 0.5	2.7 ± 0.5	0.202	
	6 months post-injection	$2.9^{\rm b}{\pm}~0.5$	$2.6^{\rm b}{\pm}~0.5$	0.122	
	% of degeneration	$\downarrow 3.3 \pm 4.1$	\downarrow 5.3 \pm 4.7	0.209	
Total US findings					
	Pre-injection	10.12 ± 1.76	9.87 ± 1.62	0.693	
	6 months post-injection	9.51 ± 1.80	8.99 ± 1.56	0.398	
	% of degeneration	\downarrow 6.16 \pm 3.33	\downarrow 9.07 \pm 3.66	0.031 ^c	

Abbreviations: LFC, lateral femoral condyle; LTC, lateral tibial condyle; MFC, medial femoral condyle; MTC, medial tibial condyle; PRP, platelet rich plasma; US, ultrasonography.

 $^{a}_{,}$ Normally quantitative data was expressed in mean \pm SD and was compared using student *t*-test.

^bSignificant between pre and other periods.

 $^{c}Statistically significant at P <math display="inline">\leq$ 0.05.

deoxyribonucleic acid and extracellular matrix synthesis (32). To our knowledge, the previous research works considering this scope had done only one intra-operative PRP injection at the time of meniscal repair, not followed by other repeated PRP injections to study the maximal effect of it on augmenting the meniscal healing process.

The strengths of our study are its prospective, randomized, and blinded nature and the use of standard repair techniques by a single surgeon. In addition to objective measuring assessment tools by a single radiologist using US.

Limitations of our study are small number of the studied patients as well as short period of follow up.

5.3. Conclusions

At the end of our work we can conclude that intra articular PRP knee injection after arthroscopic meniscal repair may be effective in reduction of pain, improvement of knee function, and decreasing the percentage of cartilage degeneration following meniscal repair.

Footnotes

Conflict of Interests: It is not declared by the authors.

Ethical Approval: Compliance with Ethics Requirements all procedures followed were in accordance with the ethical standards of the Responsible Committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008 (5).

Funding/Support: No funding support.

Patient Consent: Informed consent was obtained from all patients for being included in the study (serial number: 0303544).

References

- Bhatia S, LaPrade CM, Ellman MB, LaPrade RF. Meniscal root tears: Significance, diagnosis, and treatment. *Am J Sports Med*. 2014;**42**(12):3016– 30. doi: 10.1177/0363546514524162. [PubMed: 24623276].
- Hutchinson ID, Moran CJ, Potter HG, Warren RF, Rodeo SA. Restoration of the meniscus: Form and function. *Am J Sports Med*. 2014;**42**(4):987– 98. doi: 10.1177/0363546513498503. [PubMed: 23940202].

- Lyman S, Hidaka C, Valdez AS, Hetsroni I, Pan TJ, Do H, et al. Risk factors for meniscectomy after meniscal repair. *Am J Sports Med.* 2013;41(12):2772–8. doi: 10.1177/0363546513503444. [PubMed: 24036573].
- Muriuki MG, Tuason DA, Tucker BG, Harner CD. Changes in tibiofemoral contact mechanics following radial split and vertical tears of the medial meniscus an in vitro investigation of the efficacy of arthroscopic repair. J Bone Joint Surg Am. 2011;93(12):1089–95. doi: 10.2106/JBJS.I.01241. [PubMed: 21571989].
- Imade S, Kumahashi N, Kuwata S, Kadowaki M, Ito S, Uchio Y. Clinical outcomes of revision meniscal repair: A case series. *Am J Sports Med.* 2014;42(2):350–7. doi: 10.1177/0363546513508261. [PubMed: 24220015].
- Johnson D, Weiss B. Meniscal repair using the inside-out suture technique. Sports Med Arthrosc Rev. 2012;20(2):68-76. doi: 10.1097/JSA.0b013e318252ea26. [PubMed: 22555203].
- Kurzweil PR, Lynch NM, Coleman S, Kearney B. Repair of horizontal meniscus tears: A systematic review. *Arthroscopy*. 2014;**30**(11):1513–9. doi: 10.1016/j.arthro.2014.05.038. [PubMed: 25108905].
- Kwak HS, Nam J, Lee JH, Kim HJ, Yoo JJ. Meniscal repair in vivo using human chondrocyte-seeded PLGA mesh scaffold pretreated with platelet-rich plasma. J Tissue Eng Regen Med. 2017;11(2):471–80. doi: 10.1002/term.1938. [PubMed: 24945790].
- Laible C, Stein DA, Kiridly DN. Meniscal repair. J Am Acad Orthop Surg. 2013;21(4):204–13. doi: 10.5435/JAAOS-21-04-204. [PubMed: 23545726].
- Kaleka CC, Debieux P, da Costa Astur D, Arliani GG, Cohen M. Updates in biological therapies for knee injuries: menisci. *Curr Rev Musculoskelet Med*. 2014;7(3):247–55. doi: 10.1007/s12178-014-9227-x. [PubMed: 25064210]. [PubMed Central: PMC4596159].
- Taylor SA, Rodeo SA. Augmentation techniques for isolated meniscal tears. *Curr Rev Musculoskelet Med*. 2013;6(2):95–101. doi: 10.1007/s12178-013-9165-z. [PubMed: 23512636]. [PubMed Central: PMC3702772].
- Smyth NA, Murawski CD, Fortier LA, Cole BJ, Kennedy JG. Plateletrich plasma in the pathologic processes of cartilage: Review of basic science evidence. *Arthroscopy*. 2013;29(8):1399–409. doi: 10.1016/j.arthro.2013.03.004. [PubMed: 23669235].
- McArthur BA, Dy CJ, Fabricant PD, Valle AG. Long term safety, efficacy, and patient acceptability of hyaluronic acid injection in patients with painful osteoarthritis of the knee. *Patient Prefer Adherence*. 2012;6:905-10. doi: 10.2147/PPA.S27783. [PubMed: 23271899]. [PubMed Central: PMC3526887].
- Metcalf KB, Mandelbaum BR, McIlwraith CW. Application of plateletrich plasma to disorders of the knee joint. *Cartilage*. 2013;4(4):295-312. doi: 10.1177/1947603513487553. [PubMed: 26069674]. [PubMed Central: PMC4297162].
- DeLong JM, Russell RP, Mazzocca AD. Platelet-rich plasma: The PAW classification system. *Arthroscopy*. 2012;28(7):998-1009. doi: 10.1016/j.arthro.2012.04.148. [PubMed: 22738751].
- Raeissadat SA, Rayegani SM, Hassanabadi H, Rahimi R, Sedighipour L, Rostami K. Is Platelet-rich plasma superior to whole blood in the management of chronic tennis elbow: One year randomized clinical trial. *BMC Sports Sci Med Rehabil.* 2014;**6**:12. doi: 10.1186/2052-1847-6-12. [PubMed: 24635909]. [PubMed Central: PMC4006635].
- Raeissadat SA, Sedighipour L, Rayegani SM, Bahrami MH, Bayat M, Rahimi R. Effect of platelet-rich plasma (PRP) versus autologous whole blood on pain and function improvement in tennis elbow: a randomized clinical trial. *Pain Res Treat*. 2014;2014:191525. doi: 10.1155/2014/191525. [PubMed: 24579044]. [PubMed Central: PMC3918359].
- Cole BJ, Seroyer ST, Filardo G, Bajaj S, Fortier LA. Platelet-rich plasma: Where are we now and where are we going? *Sports Health*. 2010;2(3):203-10. doi: 10.1177/1941738110366385. [PubMed: 23015939]. [PubMed Central: PMC3445108].
- 19. McCormack HM, Horne DJ, Sheather S. Clinical applications of visual

analogue scales: A critical review. *Psychol Med*. 1988;18(4):1007-19. doi: 10.1017/s0033291700009934. [PubMed: 3078045].
20. Roos EM, Roos HP, Lohmander LS, Ekdahl C, Beynnon BD. Knee

- Roos EM, Roos HP, Lohmander LS, Ekdahl C, Beynnon BD. Knee injury and osteoarthritis outcome score (KOOS)-development of a self-administered outcome measure. *J Orthop Sports Phys Ther.* 1998;28(2):88–96. doi: 10.2519/jospt.1998.28.2.88. [PubMed: 9699158].
- Lee CL, Huang MH, Chai CY, Chen CH, Su JY, Tien YC. The validity of in vivo ultrasonographic grading of osteoarthritic femoral condylar cartilage: A comparison with in vitro ultrasonographic and histologic gradings. *Osteoarthritis Cartilage*. 2008;16(3):352–8. doi: 10.1016/j.joca.2007.07.013. [PubMed: 17920940].
- Filardo G, Kon E, Di Martino A, Di Matteo B, Merli ML, Cenacchi A, et al. Platelet-rich plasma vs hyaluronic acid to treat knee degenerative pathology: Study design and preliminary results of a randomized controlled trial. *BMC Musculoskelet Disord*. 2012;**13**:229. doi: 10.1186/1471-2474-13-229. [PubMed: 23176112]. [PubMed Central: PMC3532098].
- Arora NS, Ramanayake T, Ren YF, Romanos GE. Platelet-rich plasma: A literature review. *Implant Dent.* 2009;18(4):303-10. doi: 10.1097/ID.0b013e31819e8ec6. [PubMed: 19667818].
- Pujol N, Salle De Chou E, Boisrenoult P, Beaufils P. Platelet-rich plasma for open meniscal repair in young patients: Any benefit? *Knee Surg Sports Traumatol Arthrosc.* 2015;23(1):51–8. doi: 10.1007/s00167-014-3417-3. [PubMed: 25377191].
- Kaminski R, Kulinski K, Kozar-Kaminska K, Wielgus M, Langner M, Wasko MK, et al. A Prospective, randomized, double-blind, parallelgroup, placebo-controlled study evaluating meniscal healing, clinical outcomes, and safety in patients undergoing meniscal repair of unstable, complete vertical meniscal tears (bucket handle) augmented with platelet-rich plasma. *Biomed Res Int.* 2018;2018:9315815. doi: 10.1155/2018/9315815. [PubMed: 29713647]. [PubMed Central: PMC5866900].
- Griffin JW, Hadeed MM, Werner BC, Diduch DR, Carson EW, Miller MD. Platelet-rich plasma in meniscal repair: Does augmentation improve surgical outcomes? *Clin Orthop Relat Res.* 2015;**473**(5):1665-72. doi:10.1007/s11999-015-4170-8. [PubMed: 25663423]. [PubMed Central: PMC4385345].
- Arno S, Hadley S, Campbell KA, Bell CP, Hall M, Beltran LS, et al. The effect of arthroscopic partial medial meniscectomy on tibiofemoral stability. *Am J Sports Med.* 2013;41(1):73–9. doi: 10.1177/0363546512464482. [PubMed: 23149019].
- Jang SH, Ha JK, Lee DW, Kim JG. Fibrin clot delivery system for meniscal repair. *Knee Surg Relat Res.* 2011;23(3):180–3. doi: 10.5792/ksrr.2011.23.3.180. [PubMed: 22570832]. [PubMed Central: PMC3341829].
- 29. de Girolamo L, Galliera E, Volpi P, Denti M, Dogliotti G, Quaglia A, et al. Why menisci show higher healing rate when repaired during ACL reconstruction? Growth factors release can be the explanation. *Knee Surg Sports Traumatol Arthrosc.* 2015;**23**(1):90–6. doi: 10.1007/s00167-013-2712-8. [PubMed: 24146050].
- Hutchinson ID, Rodeo SA, Perrone GS, Murray MM. Can platelet-rich plasma enhance anterior cruciate ligament and meniscal repair? *J Knee Surg.* 2015;28(1):19–28. doi: 10.1055/s-0034-1387166. [PubMed: 25101873].
- Tumia NS, Johnstone AJ. Platelet derived growth factor-AB enhances knee meniscal cell activity in vitro. *Knee*. 2009;**16**(1):73–6. doi: 10.1016/j.knee.2008.08.008. [PubMed: 18976925].
- Ishida K, Kuroda R, Miwa M, Tabata Y, Hokugo A, Kawamoto T, et al. The regenerative effects of platelet-rich plasma on meniscal cells in vitro and its in vivo application with biodegradable gelatin hydrogel. *Tissue Eng.* 2007;13(5):1103–12. doi: 10.1089/ten.2006.0193. [PubMed: 17348798].