International Journal of Medical Science in Clinical Research and Review
Online ISSN: 2581-8945
Available Online at http://www.ijmscrr.in Volume 7|Issue 01 (January-February)|2024 Page: 23-31

Review Paper

Promise of PRP in Hamstring Injury, is it Far Fetched? A Literature Review

Authors:
Anirban Mallick[1], Jahnavi Dande[1], Sandipan Das Sarma[2]
[1]Sports Physician, Sports Authority of India, India
[2]Sports Physician, Army Medical Corps, India
Corresponding Author:
Jahnavi Dande
Dept. of Sports Medicine, National Institute of Sports, Patiala, Punjab, India

Article Received: 25-November-2023, Revised: 15-December-2023, Accepted: 05-January-2024

ABSTRACT:
Hamstring strain injuries (HSI) represent up to 29% of all injuries in the athletic population and up to 50% in sprinters. Variety of modalities have been used by sports physicians in order to expedite healing and reduce time to return to sports (RTS). The potential in restoration of muscle anatomy post-injury and relatively non-invasive mode of application have made platelet rich plasma (PRP) injections gain popularity as a possible treatment option in accelerating healing of hamstring injuries. But studies have utilized diverse methodologies making it inconclusive to find definitive outcome. Electronic databases were used to search the evidence using relevant Medical Subject Headings for the available research studies. Although no adverse effects have been reported so far, robust clinical evidence in support of PRP injections is still lacking. Hence this literature review is aimed at available evidences to find any consensus regarding application of PRP in treatment of hamstring injuries.

Keywords: PRP, Hamstring injury, Athlete, Adjunct therapy, Sports

INTRODUCTION:

Muscle injuries are common in athletes and the mechanisms by which they occur are also varied. Prevalence of muscle strains in athletic population is around 12-16%[1]. Few muscle groups, especially diarthrodial muscles (crossing two joints) and those frequently subjected to eccentric loads such as hamstring, gastrocnemius, quadriceps and hip flexors are more at risk of strain[2]. Hamstring strain injuries represent up to 29% of all injuries in athletic population and up to 50% in sprinters[3]. The risk of re-injury is also very high at about 12-31%[3]. Such a high injury and re-injury rates put the athletes at risk of game time and other financial loss while at the same time it is challenging for medical team to optimize the management plan. This has made newer modalities like platelet-rich plasma (PRP) injections gain popularity as a possible treatment option in accelerating healing of hamstring injuries.

PRP has been used as an adjunctive modality to reduce inflammation, accelerate healing process and facilitate earlier return to play (RTP)[4]. PRP is prepared by centrifuging autologous blood producing separate layers based on density of their contents. Although the preparation methods are variable, to enhance the concentration of individual components to a predetermined therapeutic level, platelets and leucocytes are separated from erythrocytes and are further centrifuged. PRP can either be activated or non-activated. In activated PRP, release of growth factors is facilitated by addition of activating agents such as calcium chloride with or without thrombin whereas for inactivated PRP, growth factors are released upon contact of platelets with intrinsic collagen and thromboplastin. Platelets in PRP play an important role in release of different type of growth factors which are crucial in healing process. Some data point towards the optimal concentrations of platelets being at around four to five times of that found in the serum[5]. Whereas at the same time concentrations more than double can actually be counterproductive and further damage the tissue. In contrast to general belief that leukocyte rich (LR) formulations are superior to leukocyte poor (LP) PRP, recent studies comparing the two formulations in tendinopathy have yielded better healing response with LP[5]. Research seems to be inconclusive about the optimum concentrations of platelet and leukocyte in the treatment of acute muscle injuries. Research has suggested that muscle regeneration and myogenesis is facilitated by various growth factors. These include insulin-like growth factor-1 (IGF- 1), transforming growth factor β1 (TGFβ-1), platelet-derived growth

factor (PDGF), fibroblast growth factor 2 (FGF-2), hepatocyte growth factor (HGF), tumour necrosis factor-α (TNF-α), and prostaglandins (PG) etc. Laboratory studies have shown IGF-1 to stimulate myoblast proliferation and differentiation as well as improve myogenesis in skeletal muscles of mice[6,7]. Whereas in-vivo studies have shown FGF-2 to increase diameter as well as number of newly formed muscle fibres. To prevent fibrosis in skeletal muscles a balance between TGFβ-1 and PGE-2 is essential. Antifibrotic agent like losartan when added to PRP can improve muscle healing process[8]. By increasing protein expressions of PCNA, cyclin A2, cyclin B1, cdk1, and cdk2, PRP helps in proliferation of skeletal muscle cells[9]. As the efficacy of PRP at improving clinical outcomes in sports injuries still remains unclear, this review aims to help sports physicians have a better understanding of PRP and its efficacy for the treatment of hamstring injuries as an adjunct.

METHODOLOGY:

Identification and Selection of Studies:

A systematic search of the literature available in English language was carried out, from 2010 to 2022 in different databases such as PubMed, Cochrane Library, CINAHL, SPORT Discuss, Direct, and Sage Pub using keywords PRP, injection, hamstring, and hamstring injury. In case of limited information on specific topics, additional resources were obtained from reference list cited in the aforementioned literature. A total of 1089 articles were selected out of which duplicates were removed. Then from remaining 504 articles, total of 25 articles were selected after applying inclusion criteria. Finally 14 studies were selected for this review based on exclusion criteria, which are summarized in table 1 as per PICOS principle.

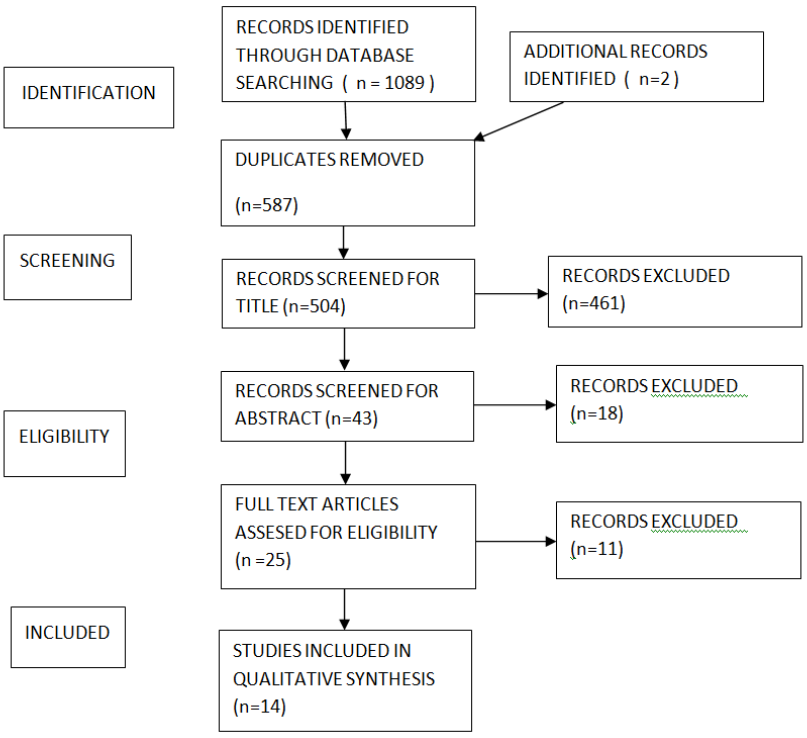

Figure 1 Flow diagram of the selection steps of the identified articles

Eligibility Criteria:

Inclusion Criteria:

- Acute or chronic hamstring injury involving PRP as a treatment modality
- Meta analysis or systematic reviews, Randomized Controlled Trial (RCT), case reports, case series, prospective cohort studies, case control studies, retrospective reviews, pilot studies
- limited to human studies
- limited to English language
- limited to full text available

Exclusion Criteria:

- Muscle injury not specific to hamstring
- Surgical treatment of hamstring injury
- Modalities used other than PRP

RESULTS:

PRP as an Adjunct in Decreasing Recovery Time of Hamstring Injury as Compared to Rehabilitation Alone:

Seow et al.[10] in their systematic review and meta-analysis couldn't find any significant difference in their short-term follow-up about physical therapy (PT)+PRP injection being superior to PT alone in reducing both mean time to RTP and re-injury rates. 10 RCTs which were part of the systematic review and meta-analysis conducted by Haiko IMFL Pas et al.[11] showed rehabilitation exercises to be more effective in acute hamstring injuries as compared to PRP injection. No significant benefit of PRP in comparison to non-injected control group was observed with a Hazard ratio of RTP calculated using a fixed effects model (HR of 1.03; 95% CI 0.87 to 1.22, Z=0.35, p=0.73). PRP studies included in this meta-analysis showed heterogeneity of data and blinding pattern. In their RCT by Hamid et al.[12] the authors concluded the PRP group (mean RTP 26.7 ± 7.0 days) attained complete recovery significantly earlier than control group (mean RTP 42.5 ± 20.6 days) with significantly lower pain severity scores in the study group in comparison to the control group. A smaller sample size with 80% power and 5% type I error were the major limitations. Double blinded RCT by Hamilton et al.[13] involving athletes with acute hamstring injuries showed single PRP injection to be of no superior benefit when compared to intensive rehabilitation alone. In patients with acute hamstring injuries as part of a placebo controlled double blinded RCT by Reurink G et al.[14], no benefit of PRP was observed over placebo injections with respect to time to RTP, re-injury rate and changes in either of patient-reported, clinical measures and MRI findings. In their pilot RCT by E. Bezuglov, et al.[15], authors found significantly shorter RTP in PRP group (11.4 ±1.2 days) when compared to controls (21.3 ±2.7 days) without any episodes of re-injuries in either group during 6 months follow-up; limitations being smaller sample size and no MRI done at the follow-up. Krauss, et al.[16] found that the use of PRP injections showed promising results in treating chronic high hamstring tendinopathy. In a case series by Fader et al.[17], although not statistically significant, 80% or more improvement was observed in pain scores following PRP in 10 out of 18 patients of chronic proximal hamstring injuries. Retrospective review by Wetzel et al.[18] suggested that all patients who received PRP not only had a significant reduction in pain and disability even after failing traditional conservative treatment but also were able to return to pre-injury level of sports.

Effect of PRP on Hamstring Injury Acute vs Chronic:

Hamid et al.[12] in their study on acute hamstring injuries less than 7 days old found PRP to be beneficial in decreasing pain severity scores and at the same time providing significantly shorter time to RTP. E. Bezuglov et al.[15] suggested beneficial effect of PRP in players sustaining 2a and 2b acute hamstring lesions classified on the basis of The British Athletics Muscle Injury Classification and verified by high-resolution real-time ultrasonography (US). Hamilton et al.[13] suggested acute Grade I or II hamstring injuries as confirmed on MRI and less than 5 days old were not an indication for PRP treatment in athletes. Similar findings were observed by Reurink G et al.[14] where there was no benefit of PRP injections in acute setting in which first injection was given within 5 days of injury and a second injection 5–7 days later when followed up to 1 year. The effect of PRP injections on different grades of hamstring injuries is unclear due to lack of similarity in inclusion of various grades of injury; whereby two studies[13,14] grouped grade I and II strains together and one study[12] included grade II strains only. Players with acute hamstring injuries diagnosed clinically and by US and MR imaging as a part of case series by G. Zanon et al.[19] when given PRP between 48 and 72 hours post-injury could not have a faster recovery; although PRP was able to form a stable scar. In a case control study[20], when PRP injection was administered at the site of the injury under ultrasound guidance within 24 to 48 hours of injury, no significant benefit was found. Authors of a cohort study[21] including patients who received PRP injection within 8 days after the injury, found that a single PRP injection did not shorten the time to RTP in sports with severe acute hamstring injuries. As is evident from the research, not all types of hamstring injuries are similar as the types differ depending upon the muscle involved, mode of injury and the type of muscle damage and accordingly the duration of rehabilitation and recovery can vary[22].

Some short studies which were primarily focused on chronic hamstring injuries, found some benefit of PRP therapy. Out of these studies, Krauss et al.[16] suggested that PRP injections were found beneficial in treating chronic proximal hamstring injuries (duration of symptoms = 4.1 years). In a case report[23] of proximal hamstring injury, promising result was found by application of PRP injection along with rehabilitation. Wetzel et al.[18] in their retrospective review found benefits of giving PRP in injuries having mean duration of 289 days. Similarly, in a retrospective case series[17], it was found that there was beneficial effect of PRP when given in chronic proximal hamstring injuries having mean duration of 32.6 months. However, one prospective cohort study[24] conducted on patients with

chronic proximal hamstring injuries did not show any improvement in clinical outcomes on 8 weeks follow-up. Given the dissimilarities in the findings among the given studies, the evidence regarding the effect of PRP injections in the management of both acute as well as chronic hamstring injuries is still inconclusive.

Recommendations for Administration of PRP in Hamstring Injury - Dosing/Frequency of Dosing:

There is inconsistency in various parameters of PRP treatment such as injection procedure, amount of PRP per injection and total number of injections used in different studies selected in this review.

Regarding method of administration, studies utilized either ultrasound guided injections[12,14,15,16,20,21,19,17,24] or injections by direct palpation[18,13,23]. Similarly, varied amount of PRP have been administered ranging from (2.5-3ml)[19], (2.5-4 ml)[17], 3ml[12,13,14,21], 4ml[16], 6ml[18,20,24], 7ml[23], 8ml[15]. In majority of the studies, single injection had been administered except two studies, one by Reurink et al.[14] in which second injection was given 5-7 days later and another by Wetzel et al.[18] in which one of the patient received a second injection into the same site 6.5 months after the initial injection. As amount of PRP, method of administration and number of injections differ in all studies, no clear inference could be drawn. As suggested by meta-analysis[10], no protocol so far has been standardized regarding timing of PRP injections as well as number of injections required. Variability in different PRP treatment protocols needs to be minimized and addressed in future research. Similarly, meta-analysis by Haiko et al.[11] also found heterogeneity among various studies regarding dosing and frequency of PRP injections utilized in acute hamstring injury and could not draw meaningful conclusions in favour of PRP.

DISCUSSION:

Age and severity of injury seem to be the two factors that may be influencing the outcome of PRP on hamstring injury as suggested by various studies in this review. One RCT[12] included patients ranging from 17 to 49 yrs whereas another study[15] included patients ranging from 22 to 31yrs as compared to the two other RCTs[13,14] where subjects ranged from 18 to 50 yrs. All the RCTs included in this review had patients with acute injury only. These wide ranges of participant population made it very difficult to draw any conclusive remark to which age group PRP injections are best suited for. Since majority of athletic population lies within 2nd and 3rd decade age groups and only one small pilot RCT study[15]showed its beneficial effect in younger population, PRP therapy fails to be the primary modality of choice in athletic population and can only be used as an adjunct to PT and not as an independent modality. Apart from the limited availability of extensive research on the topic, lack of standard definitions of rehabilitation protocols and recovery time, and variability among rehabilitation or conservative treatments used as control groups had also been the shortcomings of various studies included in this review. Author definitions of recovery time described in the studies were not consistent; one study[14] stated it as duration (in days) till return to sports whereas two studies[12,13] stated it as time taken (in days) by the patient from injury till clearing RTP criteria. Similar inconsistencies were observed in the different studies while describing RTP criteria. Hamid et al.[12] outlined them as no pain on contraction and palpation of hamstring, active ROM for knee extension to be symmetrical bilaterally, and strength difference of hamstring to be within 10% when compared bilaterally. Whereas another study[13] described RTP as successfully completing criteria based progression of rehabilitation, clinical assessment and isokinetic strength testing without provocation of any symptoms. Bezuglov et al.[15] mentioned the criterion as pain during high intensity football specific exercises at a level of 2 or less (as monitored on pain assessment scale used in the study). Due to limited and inconclusive nature of available evidence, it still remains uncertain as to how effective were PRP injections in the treatment of hamstring injuries when compared to rehabilitation alone.

FUTURE RESEARCH:

Future research should be directed at meaningful and consistent conclusions with respect to the efficacy of PRP treatment in patients with hamstring injuries. As age and severity of injury appear to influence the outcome, further research should aim at addressing the specific age groups of injured athletes and also determine the effects of PRP on various grades of injury. As to the various types of hamstring injuries, the beneficial effects of PRP need to be established in acute, chronic as well as recurrent injuries. Since the natural history of hamstring injury may vary according to the site of lesion, future studies should also take into account whether there exists any variability in response of the effects of PRP in different sites of hamstring injuries. Additionally, it should also aim at formulating a systematic protocol of various parameters for PRP treatment such as total number of injections required, amount of PRP for each injection, injection site, time of injection with respect to initiation of rehabilitation and duration since injury. Given the dissimilarities among the various studies regarding definitions of recovery time and RTP criteria, future studies should aim at establishing standardized definitions of recovery time and outline appropriate RTP criteria. In addition, long term efficacy of PRP injections needs to be investigated along with re-injury rates.

CONCLUSION:

In conclusion, since the existing evidence is inconclusive regarding the efficacy of PRP injections in hamstring injuries further large scale high-quality research is needed in order to have impactful confidence in the effect estimates. Although no disadvantages have been reported so far, PRP can not be advised as a primary modality of treating hamstring injuries when compared to rehabilitation management. Guiding clinical research in order to investigate merits and demerits of PRP injections and formulating valid clinical recommendations is important for establishing PRP as a potential tool in the management of hamstring injuries.

References	Study	Participants	Intervention	Outcome measures	Main finding/Conclusion
Pas HIMFL, et al. 2015	SYSTEMATIC REVIEW AND META ANALYSIS	526 participants. Mean ages reported across the studies ranged between 20 and 32 years.	I: PRP +standard rehabilitation program. C: Saline injection with rehabilitation program or rehabilitation program alone.	1)Time to RTP 2) Re-injury rate 3) Subjective patient satisfaction and perceived recovery, Flexibility Isokinetic strength 4) Alteration of MRI (T2 intensity)	Meta-analysis of platelet-rich plasma injections in acute hamstring injuries shows no effect.
Seow, et al. 2020	SYSTEMATIC REVIEW AND META ANALYSIS	207 hamstrings injuries were in the PRP group and 149 in the control group.	I: PRP + PT C: PT or whole blood injection +PT	1) Visual analog scale for pain ; Nirschl pain rating scale; Sports assessment hamstring score 2) RTP 3) Re-injury rates	Non significant evidence to suggest that PRP injection + PT reduced time to RTP or re-injury rates compared to no treatment or PT alone for hamstring injuries in a short-term follow-up.
Hamid, et al. 2014	SINGLE BLINDED RCT	28 participants (median age 21) , 53.6% national level athletes	I: PRP + PATS (Rehabilitation program) C: PATS (Rehabilitation program)	1) Time to RTP: time (days) from data of measure(s) injury onset until patient fulfilled criteria to RTP 2) Subjective pain severity scores (BPI- SF) 3) Subjective pain interference scores (BPI-SF)	A single injection of autologous PRP combined with a rehabilitation program was significantly more effective than a control in reducing the severity of pain and allowing a significantly shorter time to RTP after an acute hamstring injury.
Reurink, et al. 2015	DOUBLE BLINDED RCT	80 competitive and recreational athletes (18–50 y)	I: PRP + Rehabilitation program. C: saline placebo injection +Rehabilitation	1) Time to RTP 2) Re-injury rate at 1-y follow-up 3) Alteration in clinical and MRI parameters 4) Subjective patient satisfaction and perceived	Intramuscular PRP injections showed no benefit compared with placebo injections in patients with acute hamstring injuries in the time to RTP nor in the subjective, clinical, and MRI measures

			program	recovery, NPRS 5) Flexibility: active knee extension, passive SLR 6) Isometric knee-flexion dynamometry 7) Hamstring outcome score	
Hamilton, et al. 2015	TRIPLE BLINDED RCT	90 male professional athletes (18 –50 y)	I:PRP + Rehabilitation program C: Rehabilitation program	1) Time to RTS 2) Re-injury rate 3) Isokinetic strength 4) Alteration of MRI (T2 intensity)	There is no benefit of a single injection over an intensive rehabilitation program in professional athletes who have sustained acute, MRI positive hamstring injuries
E Bezuglov, et al. 2019	PILOT RCT	Forty male professional football players (mean 27 ± 3.3 years)	I:PRP + Rehabilitation program C: Rehabilitation program	1) Time to RTP 2) Re-injury rates.	The use of PRP exerts a beneficial effect on pain relief and allows earlier return to sport.
Wetzel, et al. 2013	RETRO-SPECTIVE REVIEW	15 patients (17 hamstrings) with failed traditional conservative treatment.	I:PRP + Rehabilitation program C: Rehabilitation program	1) Pre- and post treatment visual analog scale (VAS) scores, 2) Return to pre injury sport status. 3) Nirschl Phase Rating Scale (NPRS) scores	This study shows that all patients who received PRP had a significant reduction in pain and disability when comparing VAS and NPRS scores, even after failing traditional conservative treatment.
D C Karli, et al. 2010	CASE REPORT	48-year-old female with severe left proximal hamstring tear MRI confirmed a full-thickness tear of the proximal semi-membranosus tendon near the myotendinous junction.	I:PRP + Rehabilitation program	The improvements noted by the patient coincided with significant tissue healing as reported by the evaluating radiologist on follow-up MRI.	Subjective and functional improvements with near-complete repair on MRI with a single application of platelet-rich plasma in a severe tendon injury.
Krauss, et al. 2016	PROSPECTIVE CASE CONTROL STUDY	14 adult patients with chronic high hamstring tendinopathy who	I:PRP + Rehabilitation program	1) Questionnaire assessing both average pain on a visual analog scale	The use of PRP injections shows promising results in treating chronic high hamstring tendinopathy

		previously failed physical therapy. Mean patient age was 46.6 yrs.		and functional levels, including the Lower Extremity Functional Scale (LEFS). 2) On follow up completed the same questionnaire.	
Y. Guillodo, et al. 2015	COHORT STUDY	Study included 34 patients, Mean age was 26.3±3.7 years in the PRP group and 28.8±7.4 years in the control group (NS).	I:PRP + Rehabilitation program C: Rehabilitation program	1) Physical examination and ultrasonography by the same physician 10 and 30 days after the injury. 2) Patient was then contacted by telephone to determine the TTRTP at the pre-injury level.	Single local PRP injection failed to decrease the TTRTP at the pre-injury level in athletes with grade III acute hamstring in- juries.
Levy GM, et al. 2018	PILOT PROSPECTIVE COHORT	The study sample consisted of 22 females and 7 males with a mean age of 45.2 years	I:PRP + Rehabilitation program	1) Victorian Institute of Sport Assessment-Proximal Hamstring Tendons (VISA-H) questionnaire	Patients with PHT receiving a PRP injection did not improve on clinical outcomes at 8-weeks follow-up.
R.R. Fader, et al. 2014	CASE SERIES	Total of 18 consecutive patients which included 12 females and 6 males. The average age at the time of the injection was 42.6 yrs .	I:PRP + Rehabilitation program	1) Questionnaire evaluating previous treatments 2) Visual analog scale (VAS) for pain 3) Subjective improvement, history of re-injury, and return to activity.	For refractory cases of chronic insertional proximal hamstring injuries, platelet-rich plasma injections are safe and show benefit.
Zanon, et al. 2016	CASE SERIES	18 players with twenty-five hamstring injuries with mean age of 24.2 yrs	I:PRP + Rehabilitation program	Sport participation absence (SPA), in days, was considered to correspond to the healing time, re-injury rate, and tissue healing on MRI and USG.	Study confirmed the safety of PRP in treating hamstring lesions. PRP-treated lesions did not heal more quickly than untreated lesions, but they showed a smaller scar and excellent repair tissue.
Rettig, et al. 2013	CASE CONTROL STUDY	5 patients in each of the treatment and control groups. The	I:PRP + Rehabilitation program	Time to RTP	There were no significant differences in recovery from hamstring injury between treatment with PRP and routine

		median age was 23 years in the treatment group versus 26 years in the control group.	C: Rehabilitation program		rehabilitation.

Table 1 Characteristics of Studies

REFERENCES:

1. Rossi LA, Molina Rómoli AR, Bertona Altieri BA, Burgos Flor JA, Scordo WE, Elizondo CM. Does platelet-rich plasma decrease time to return to sports in acute muscle tear? A randomized controlled trial. *Knee Surg Sports Traumatol Arthrosc*. 2017;25(10):3319-3325. doi:10.1007/s00167-016-4129-7

2. Connell DA, Schneider-Kolsky ME, Hoving JL, et al. Longitudinal study comparing sonographic and MRI assessments of acute and healing hamstring injuries. *AJR Am J Roentgenol*. 2004;183(4):975-984. doi:10.2214/ajr.183.4.1830975

3. Ahmad CS, Redler LH, Ciccotti MG, Maffulli N, Longo UG, Bradley J. Evaluation and management of hamstring injuries. *Am J Sports Med*. 2013;41(12):2933-2947. doi:10.1177/0363546513487063

4. Hussain N, Johal H, Bhandari M. An evidence-based evaluation on the use of platelet rich plasma in orthopedics - a review of the literature. *SICOT J*. 2017;3:57. doi:10.1051/sicotj/2017036

5. Yan R, Gu Y, Ran J, et al. Intratendon Delivery of Leukocyte-Poor Platelet-Rich Plasma Improves Healing Compared With Leukocyte-Rich Platelet-Rich Plasma in a Rabbit Achilles Tendinopathy Model. *Am J Sports Med*. 2017;45(8):1909-1920. doi:10.1177/0363546517694357

6. 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):203-210. doi:10.1177/1941738110366385

7. Borrione P, Fossati C, Pereira MT, et al. The use of platelet-rich plasma (PRP) in the treatment of gastrocnemius strains: a retrospective observational study. *Platelets*. 2018;29(6):596-601. doi:10.1080/09537104.2017.1349307

8. Terada S, Ota S, Kobayashi M, et al. Use of an antifibrotic agent improves the effect of platelet-rich plasma on muscle healing after injury. *J Bone Joint Surg Am*. 2013;95(11):980-988. doi:10.2106/JBJS.L.00266

9. Tsai WC, Yu TY, Lin LP, et al. Platelet rich plasma releasate promotes proliferation of skeletal muscle cells in association with upregulation of PCNA, cyclins and cyclin dependent kinases. *Platelets*. 2017;28(5):491-497. doi:10.1080/09537104.2016.1227061

10. Seow D, Shimozono Y, Tengku Yusof TNB, Yasui Y, Massey A, Kennedy JG. Platelet-Rich Plasma Injection for the Treatment of Hamstring Injuries: A Systematic Review and Meta-analysis With Best-Worst Case Analysis. Am J Sports Med. 2020 May 19:363546520916729. doi: 10.1177/0363546520916729. Epub ahead of print. PMID: 32427520.

11. Pas HI, Reurink G, Tol JL, Weir A, Winters M, Moen MH. Efficacy of rehabilitation (lengthening) exercises, platelet-rich plasma injections, and other conservative interventions in acute hamstring injuries: an updated

systematic review and meta-analysis. Br J Sports Med. 2015 Sep;49(18):1197-205. doi: 10.1136/bjsports-2015-094879. Epub 2015 Jul 21. PMID: 26198389.

12. A Hamid MS, Mohamed Ali MR, Yusof A, George J, Lee LP. Platelet-rich plasma injections for the treatment of hamstring injuries: a randomized controlled trial [published correction appears in Am J Sports Med. 2015 May;43(5):NP13]. *Am J Sports Med*. 2014;42(10):2410-2418. doi:10.1177/0363546514541540

13. Hamilton B, Tol JL, Almusa E, et al. Platelet-rich plasma does not enhance return to play in hamstring injuries: a randomised controlled trial. *Br J Sports Med*. 2015;49(14):943-950. doi:10.1136/bjsports-2015-094603

14. Reurink G, Goudswaard GJ, Moen MH, et al. Rationale, secondary outcome scores and 1-year follow-up of a randomised trial of platelet-rich plasma injections in acute hamstring muscle injury: the Dutch Hamstring Injection Therapy study. *Br J Sports Med*. 2015;49(18):1206-1212. doi:10.1136/bjsports-2014-094250

15. Bezuglov, Eduard & Maffulli, Nicola & Tokareva, Alyssa & Achkasov, Evgeny. (2019). Platelet-rich plasma in hamstring muscle injuries in professional soccer players. A pilot study. Muscle Ligaments and Tendons Journal. 09. 112. 10.32098/mltj.01.2019.20.

16. Krauss J, Nugent R, Bodor M, Fredericson M (2016) Therapeutic Eficacy of Platelet- Rich Plasma Injections in Treating Chronic High Hamstring Tendinopathy. Clin Med Rev Case Rep 3:084

17. Fader RR, Mitchell JJ, Traub S, Nichols R, Roper M, Mei Dan O, McCarty EC. Platelet-rich plasma treatment improves outcomes for chronic proximal hamstring injuries in an athletic population. Muscles Ligaments Tendons J. 2015 Feb 5;4(4):461-6. PMID: 25767784; PMCID: PMC4327356.

18. Wetzel RJ, Patel RM, Terry MA. Platelet-rich plasma as an effective treatment for proximal hamstring injuries. *Orthopedics*. 2013;36(1):e64-e70. doi:10.3928/01477447-20121217-20

19. Zanon G, Combi F, Combi A, Perticarini L, Sammarchi L, Benazzo F. Platelet-rich plasma in the treatment of acute hamstring injuries in professional football players. Joints. 2016 Jun 13;4(1):17-23. doi: 10.11138/jts/2016.4.1.017. PMID: 27386443; PMCID: PMC4914369.

20. Rettig AC, Meyer S, Bhadra AK. Platelet-Rich Plasma in Addition to Rehabilitation for Acute Hamstring Injuries in NFL Players: Clinical Effects and Time to Return To Play . Orthop J Sports Med. 2013 Jun 24;1(1):2325967113494354. doi: 10.1177/2325967113494354. PMID: 26535233; PMCID: PMC4555507.

21. Guillodo Y, Madouas G, Simon T, Le Dauphin H, Saraux A. Platelet-rich plasma (PRP) treatment of sports-related severe acute hamstring injuries. Muscles Ligaments Tendons J. 2016 Feb 13;5(4):284-8. doi: 10.11138/mltj/2015.5.4.284. PMID: 26958537; PMCID: PMC4762640.

22. Brukner P. Hamstring injuries: prevention and treatment—an update.Br J Sports Med. 2015;49:1241–1244. PubMed ID: 26105015 doi:10.1136/bjsports-2014-094427

23. Karli, David & Robinson, Brent & Bs,. (2010). Platelet Rich Plasma for Hamstring Tears. Pract Pain Manage. 10.

24. Levy GM, Lucas P, Hope N. Efficacy of a platelet-rich plasma injection for the treatment of proximal hamstring tendinopathy: A pilot study. J Sci Med Sport. 2019 Mar;22(3):247-252. doi: 10.1016/j.jsams.2018.08.001. Epub 2018 Aug 9. PMID: 30145035.