The Journal for Nurse Practitioners 16 (2020) 11–14

Contents lists available at ScienceDirect

The Journal for Nurse Practitioners

journal homepage: www.npjournal.org

Examination of the Role of Platelet-Rich Plasma in Meniscal Tears

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Keywords:
knee
meniscal tear
meniscus
orthopedics
platelet-rich plasma

A B S T R A C T

The role of platelet-rich plasma in meniscal tears in humans has yet to be fully examined in the literature. Meniscal tears remain a prevalent and common orthopedic injury. Numerous methods of treatment for this condition are available, ranging from conservative methods to surgical options. Platelet-rich plasma is a biologic agent that is minimally invasive, can have regenerative properties, and may aid healing for patients. This article offers a current review of the literature examining platelet-rich plasma in meniscal tears and recovery.

Introduction

Orthopedic injuries are some of the most ubiquitous conditions seen by nurse practitioners (NPs) in acute and primary care settings. Specifically, knee pain is a common complaint, and the prevalence continues to rise—about 65% during the past 20 years.[1] Knee pain can be due to an unidentified meniscal tear. Meniscal tears are a common injury, with an incidence of approximately 66 per 100,000 people annually.[2] Meniscal tears remain a prevalent knee injury in the young and in the elderly and are one of the most frequent reasons for knee surgery.[3,4]

Risk factors for a meniscal tear include repetitive mechanical movement, such as squatting and climbing stairs, male sex, and advanced age.[3] Management of meniscal tears includes operative measures, such as meniscectomy and meniscal repair/reconstruction, and more conservative measures, namely, analgesics, activity modification, physical therapy, and intra-articular corticosteroid injections.[3] Rest, physical therapy, and nonsteroidal anti-inflammatories (NSAIDs) are typically the initial choice of treatment for meniscal tears.[5] Intra-articular injections present another, less-invasive option for meniscal tear management.

Intra-articular injections have numerous advantages over systemic treatments. They can be safer because they are minimally invasive compared with surgical intervention, can be performed in the office, and have increased bioavailability compared with systemic treatment, allowing for lower doses.[6] Corticosteroids, hyaluronic acid, and platelet-rich plasma (PRP) are more common components of intra-articular injections. Used since the 1950s in other disciplines, such as dermatology and maxillofacial conditions, the use of biologic agents, such as PRP, in health care has increased over time.[7]

In the evolving landscape of regenerative medicine, NP awareness of various treatment options for common complaints and ailments, including orthopedic injuries, is important. To this end, very few clinical studies have evaluated the efficacy and use of PRP in meniscal tears. This thorough review of the literature aims to explore the use of PRP in meniscal tears.

Background

Menisci are C-shaped fibrocartilaginous structures between the tibiofemoral areas of the knee.[3] Menisci help to cushion the knee joint.[5] Unfortunately, tears can occur in the meniscus from a variety of causes, including mechanical force, such as plant/pivot injuries, or degeneration caused by a weakened meniscus due to advanced age, osteoarthritis, or both.[5]

The location of a meniscal tear is important with regard to healing. A tear can occur within this cartilage structure in a vascularized ("red") or avascularized ("white") zone, or across both zones.[8] These zones are particularly important in reference to blood supply and healing of a meniscal tear. Typically, a tear within the red zone may heal on its own, whereas tears in the white zone do not have a rich blood supply and more often need further management.[5] Most meniscal tears are centrally located in the white zone and thus poorly vascularized. A tear may be vertical radial, vertical longitudinal, oblique, complex, or horizontal.[2] Further, there are different grades of severity of meniscal tears, from 0 (normal) to 3 (a complete tear).[2]

More common symptoms of a meniscal tear can include pain or tenderness, typically along the medial or lateral joint line of the knee, stiffness, swelling, mechanical symptoms, such as the knee "locking" or "giving way," or decreased range of motion.[5] Provocative tests, including Thessaly and McMurray, can help with a meniscal tear diagnosis.[4] In the Thessaly maneuver, the patient bears weight on the affected extremity at approximately 5° and then 20° flexion while externally and internally rotating the knee and body. Pain medially or laterally, with or without the sensation of locking or popping, is considered positive.[4] The McMurray maneuver requires the provider to flex the patient's knee while either internally or externally rotating the patient's tibia while extending

https://doi.org/10.1016/j.nurpra.2019.08.018
1555-4155/

the knee; a palpable click or pop with discomfort or pain is positive.[4]

Radiographic images may be useful in determining the presence of degenerative disease and may provide indirect evidence of degenerative changes to the meniscus but will not show a meniscal tear.[5] Magnetic resonance imaging is a more sensitive test for evaluation of a meniscal tear and should be considered if the diagnosis is unclear.[5]

PRP and Review of Literature

Derived from autologous blood, pure PRP consists of a higher platelet concentration than whole blood and is isolated by centrifugation, blood filtration, and plateletpheresis.[9] There are 4 variants of PRP based on cell content and fibrin makeup: pure PRP, leukocyte and PRP, leukocyte and platelet-rich fibrin, and pure platelet-rich fibrin.[10]

The goal for such a biologic therapy is to "influence and reverse the catabolic environment... [and] restore joint homeostasis."[11(p1006)] The mechanism of action of PRP can be linked to its release of numerous growth factors that encourage bone and tissue healing via activation of various signaling pathways.[6] PRP injections are considered a newer and more unconventional method of treatment. Currently, they remain investigational, and the United States Food and Drug Administration has yet to regulate PRP. As a result, patients are required to pay for this treatment without insurance reimbursement. It is important to be cognizant when determining the most efficacious treatment and most cost-effective treatment for patients.

Most research to date advises a minimum of 2 to 3 doses.[9] Moreover, PRP cannot be stored or frozen and must be drawn immediately before each injection, which can lead to greater variability in PRP injection composition.[6] There remain inherent risks associated with intra-articular injections, including infection (approximately 1 in 3,000 injections).[12] There is also a 2% to 25% possibility of a postinjection flare or local inflammatory response that can last 2 to 3 days and range from mild to severe.[13] Milder injection reactions are typically treated with ice, compression, elevation, and NSAIDs. More severe injection reactions, exhibited by erythema, warmth, edema, and even systemic symptoms, such as fever, require laboratory tests, arthrocentesis, antibiotics, and possibly hospitalization.[13]

Google Scholar, PubMed, Cumulative Index of Nursing and Allied Health Literature, and Embase were used in a reproducible search method to review the literature. Inclusion criteria comprised articles published between 2014 and 2019, research performed on patients, PRP (1 of the 4 variants) as the sole biologic agent used, confirmation of a meniscal tear, and research written in English. Exclusion criteria included research performed on animals, use of 2 or more PRP formularies, and concomitant use of other biologics, such as mesenchymal stem cells, bone marrow, or hyaluronic acid. The search terms "meniscus" and "meniscal injury," rather than "meniscal tear," were used to ensure a robust search for this study. PRP is also known as thrombocyte-rich plasma in some research, so this term was included where applicable in the literature search (Supplementary Table and Figure, available online at http://www.npjournal.org).

The literature search yielded 6 articles.[14-19] Most articles comprised active patients with a mean age of 28 to 29 years. The articles include case studies, 1 retrospective cohort study, and 1 longitudinal cohort study. Results were measured in pain scores, functional outcome measures, and healing of meniscal tissue via second-look arthroscopy or magnetic resonance imaging. Assessment tools include the visual analog scale (VAS), International Knee Documentation Committee (IKDC), Knee Injury and Osteoarthritis Outcome Score (KOOS), the Global Rating of Change (GROC), and the Tegner Activity Level Scale.

The VAS grades a patient's intensity of pain using a numeric measurement. The IKDC and KOOS are subjective questionnaires evaluating knee function, pain, and symptoms, comprising swelling, and stiffness in the IKDC and knee flexion, extension, grinding/clicking of the knee, and quality of life in the KOOS.[20] The GROC score evaluates a patient's perception of improvement before the date of injury and after treatment, and the Tegner Activity Level Scale assesses knee function, including limping, support, instability, stair climbing, and squatting.[20]

Betancourt et al[14] detailed a case study of a 29-year-old woman with a grade 3a medial meniscus tear confirmed on magnetic resonance imaging. She had pain with weight bearing, clicking, squatting, and changing positions from seated to standing and had previously tried hyaluronic acid injections. The article evaluated the use of 1 ultrasound-guided injection of leukocyte-poor PRP in a grade 3a degenerative medial meniscus tear. Results from this article showed an improvement in VAS, GROC, and KOOS pain scores at a 30-month follow-up; specifically, VAS improved from 70 mm to 40 mm, and KOOS improved from 39 to 63.1.[14]

Griffin et al,[15] in a retrospective cohort study, evaluated the use of PRP in arthroscopic meniscal repair in subsequent meniscectomy and functional outcome measures, including IKDC, Tegner Lysholm Knee Scoring Scale, return to work, and return to sport. Over the course of 3 years, surgeons performed arthroscopic meniscus repairs on 35 patients, of which 15 were performed with PRP augmentation. No difference was found in reoperation rates or functional outcome measures between the PRP and non-PRP group. The types of tear examined in this study were wide ranging, from longitudinal to peripheral horizontal to vertical.

Kaminski et al[16] outlined a prospective, randomized, parallel-group, double-blind, placebo-controlled study examining 37 patients with unstable complete vertical tears in the red-white zone of the meniscus. Patients treated with intraoperative repair and injection of PRP showed an 85% increase in healing rate via second-look arthroscopy or magnetic resonance imaging at 18 weeks compared with 47% in the control group that received a placebo injection during surgery. Both groups showed an increase after 42 months in functional outcome measures, including IKDC, the Western Ontario and McMaster Universities Arthritis Index, a self-administered questionnaire evaluating pain, stiffness, and physical function, and KOOS scores.[19] Although the difference in VAS scores between the 2 groups was not significant, the KOOS score improved significantly in the PRP-treated group.[16]

Pujol et al[17] detailed a study evaluating the use of PRP in open meniscal repair surgery in grade 2 or grade 3 horizontal tears extending into the avascular (white) zone. Over the course of 3 years, 34 patients underwent open meniscal repair surgery, 17 with an in situ injection of PRP and 17 without. Outcomes measured included KOOS and IKDC scores, healing via magnetic resonance imaging performed 1 year postoperatively, and subsequent meniscectomy (deemed "clinical failure"). Ultimately, functional clinical outcomes were slightly higher in the PRP-group than in the control group seen in median active flexion, IKDC, and KOOS scores. Failure rates were higher in the control group, at 11.8% vs 5.8%.

A longitudinal cohort study evaluated PRP in medial meniscal and lateral meniscal tears in military personnel with a mean age of 34.6 years.[18] Outcome measurements include KOOS, Tegner Activity Level, IKDC, and VAS scores. Of note, an injection of 10% calcium gluconate was used before the PRP injection. Evaluation at the time of injection and at 4 and 12 weeks after treatment showed improvement in KOOS and IKDC scores: "The IKDC subjective score improved from 41.3 ± 4.83 before to 48.7 ± 3.2 and 49.6 ± 3.3 after 4 and 12 weeks of PRP injection respectively."[18(p700)] The article did

not clarify the reason or utility of calcium gluconate. Some studies have shown that the addition of calcium gluconate or calcium chloride can act as a platelet activator and potentiate its effect, namely, tissue healing, through increased availability of various bioactive molecules.[21,22]

Urzen and Fullerton[19] described a case study of a 43-year-old man with a magnetic resonance imaging-confirmed bucket handle meniscal tear. After 3 injections of leukocyte-rich PRP, performed 6, 16, and 27 weeks after the injury, there was complete resolution of pain with ambulation and performing daily activities.[19]

Management Strategies

Various management strategies exist for meniscal tears, including nonoperative management, partial and total meniscectomy, meniscal repair, and meniscal transplantation.[4] Nonoperative management includes rest, physical therapy, and oral medications, namely NSAIDs.[4] A randomized clinical trial comparing arthroscopic partial meniscectomy and physical therapy in the treatment of nonobstructive meniscal tears reported arthroscopic partial meniscectomy was not superior to physical therapy; in fact, the study advocated for physical therapy as a beneficial alternative.[23]

Various injections are used in the management of meniscal injury, including corticosteroid injections and biologic agents such as hyaluronic acid and mesenchymal stem cells. Operatively, partial or total meniscectomy can be performed. Meniscal repair is indicated for peripheral tears in the vascularized zone, vertical and longitudinal tears, and tears 1 to 4 mm in length.[4] Meniscal transplantation is reserved for younger patients with nearly total meniscectomy without comorbidities such as obesity, diffuse arthritis, or significant chondrosis.[4]

Recommendations and Summary

Support for the use of PRP in meniscal healing varies. Pujol et al[17] and Griffin et al[15] do not make a recommendation for or against the use of PRP. Of 6 studies reviewed, 4 studies report PRP improved functional clinical outcomes. In 4 studies, PRP helped to improve psychometric measures, specifically VAS scores before and after administration. KOOS scores improved in 4 studies.

The use of biologic augmentation in orthopedics is gaining momentum. As PRP and its variants continue to be explored, an examination of various aspects deserves consideration. There is variation in PRP type, preparation, injection technique, and injection frequency. This can be due to a number of reasons, paramount of which is the identification of the therapeutic goal for the patient—to lessen inflammation, potentiate meniscal remodeling, or reduce pain. Variation in types of PRP and use of premedications could affect the efficacy of the biologic agent and influence the validity of the results.

Use of PRP as the sole conservative therapy vs augmentation to surgical meniscal repair deserves further attention. The type of meniscal tear is also relevant to the evaluation of PRP's efficacy. The studies include a variety of tears, including bucket handle, horizontal, and lateral tears extending into avascular zones. Studies have yet to extensively evaluate the use of concurrent therapies, comorbidities, co-injuries, and certain aspects of patient demographics, such as body mass index, with PRP injection.[9] Razaq et al[18] found concomitant ligamentous injuries—anterior cruciate ligament and lateral collateral ligament—were present in most of the study participants. This is worth noting, because concomitant anterior cruciate ligament deficiency can negatively affect meniscal healing.[16]

Generalizability within the research is lacking, because a larger and more diverse patient population is needed. Case and cohort studies potentially introduce confounding bias, performance bias, reporting bias, recall bias, and selection bias. Lack of blinding and randomization can particularly affect the internal and external validity of some of the results.

NPs should include PRP in their armamentarium of management strategies for meniscal tears. Specifically, PRP should be considered in cases where other less invasive measures have been exhausted, including physical therapy, NSAIDs, steroid injections, and hyaluronic acid. Because PRP has shown promising efficacy in functional outcome measures, this treatment can potentially improve a patient's quality of life and mobility. Further, there is potential for PRP to promote meniscal healing through regenerative properties. Treatment for a meniscal tear should always be case dependent and individualized for the patient.

PRP is a promising modality for meniscal tears. Standardization of PRP injection has not yet been achieved. Evaluations of the efficacy of PRP in the setting of standardized dosages and preparation will be important. Most of the research has shown it can improve functionality, pain, and healing. However, the relatively small sample of research here potentially introduces bias and lacks a diverse and large patient population, thereby affecting generalizability. The recommendation is for NPs to consider all available resources in the treatment and management of meniscal tears. Consideration of PRP should be case specific, with close monitoring of functionality, pain, and adjunctive treatment encouraged.

Supplementary Data

The Supplementary Table and Figure associated with this article can be found in the online version at https://doi.org/10.1016/j.nurpra.2019.08.018.

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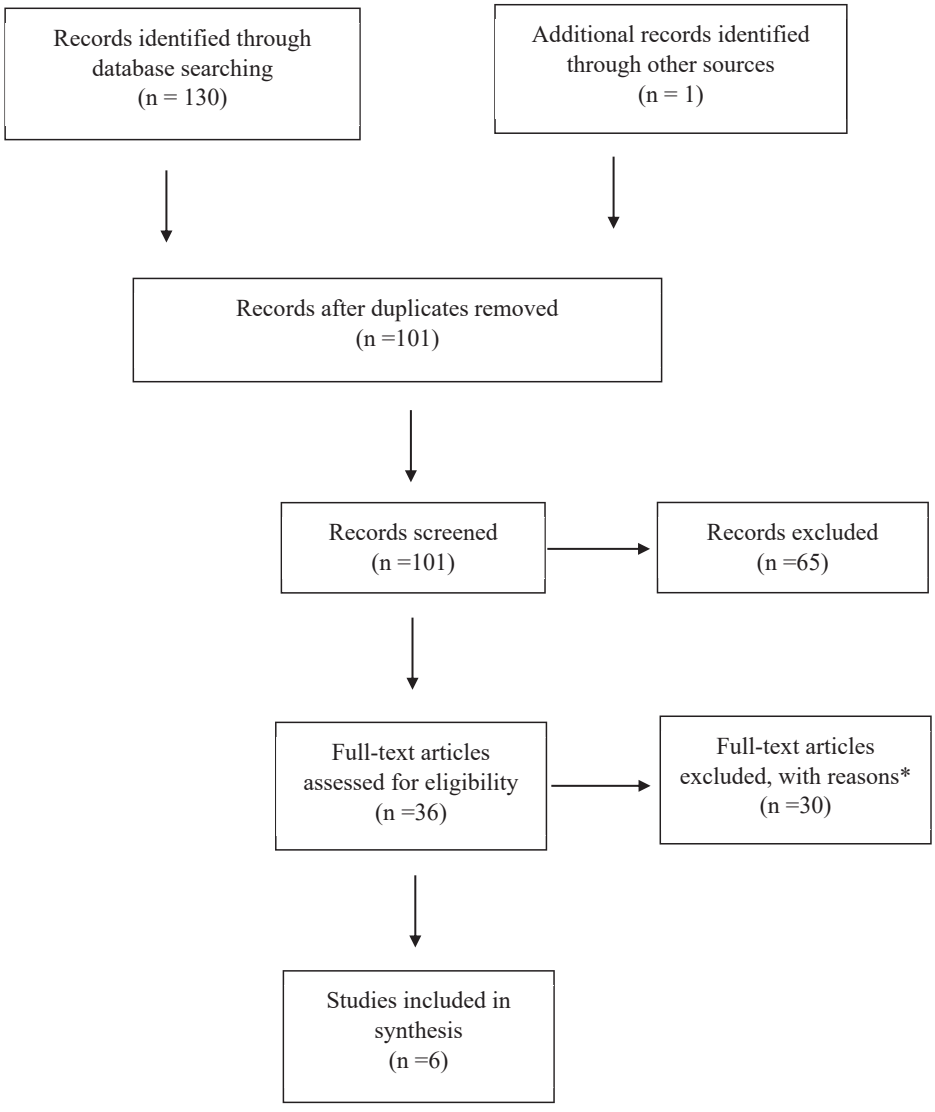
In compliance with national ethical guidelines, the author reports no relationships with business or industry that would pose a conflict of interest.



* Exclusion criteria includes research performed on animals, use of two or more PRP formularies, and concomitant use of other biologics (such as mesenchymal stem cells, bone marrow, hyaluronic acid).

Supplementary Figure. Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Supplementary Table
Search Strategies

Database	Results
PubMed	
Search Meniscus sort by: Best Match Filters: published in the last 5 years; Humans; English	1808
Search "Meniscus"[Mesh] OR meniscus OR menisci OR meniscal. Sort by: Best Match Filters: published in the last 5 years; Humans; English	2162
Search platelet rich plasma. Sort by: Best Match Filters: published in the last 5 years; Humans; English	1673
Search (("Meniscus"[Mesh] OR meniscus OR menisci OR meniscal)) AND platelet rich plasma. Sort by: Best Match Filters: published in the last 5 years; Humans; English	24
CINAHL	
(MH "Meniscal Injuries") Limiters - Published Date: 20140101-20191231; English Language; Human Search modes - Boolean/Phrase	251
(MH "Meniscal Injuries") OR meniscus OR menisci OR meniscal Limiters - Published Date: 20140101-20191231; English Language; Human Search modes - Boolean/Phrase	990
(MH "Platelet-Rich Plasma") Limiters - Published Date: 20140101-20191231; English Language; Human Search modes - Boolean/Phrase	370
(MH "Platelet-Rich Plasma") OR platelet rich plasma OR platelet-rich plasma Limiters - Published Date: 20140101-20191231; English Language; Human Search modes - Boolean/Phrase	427
(MH "Meniscal Injuries") OR meniscus OR menisci OR meniscal AND ((MH "Platelet-Rich Plasma") OR platelet rich plasma OR platelet-rich plasma) Limiters - Published Date: 20140101-20191231; English Language; Human Search modes - Boolean/Phrase	10
Embase	
('knee meniscus'/exp OR meniscus OR menisci OR meniscal) AND [english]/lim AND [humans]/lim AND [2014-2019]/py	5412
((('thrombocyte rich plasma'/exp OR platelet) AND rich AND plasma OR 'platelet rich') AND plasma OR thrombocyte) AND rich AND plasma AND [english]/lim AND [humans]/lim AND [2014-2019]/py	4560
('knee meniscus'/exp OR meniscus OR menisci OR meniscal) AND [english]/lim AND [humans]/lim AND [2014-2019]/py AND ((('thrombocyte rich plasma'/exp OR platelet) AND rich AND plasma OR 'platelet rich') AND plasma OR thrombocyte) AND rich AND plasma AND [english]/lim AND [humans]/lim AND [2014-2019]/py	96