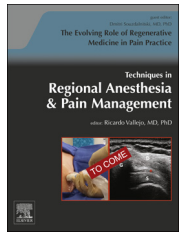
Techniques in Regional Anesthesia and Pain Management ▮ (▮▮▮▮) ▮▮▮–▮▮▮

Available online at www.sciencedirect.com

ScienceDirect

www.elsevier.com/locate/trap



Platelet-rich plasma injections for knee osteoarthritis: Systematic review of duration of clinical benefit

Dmitri Souzdalnitski, MD, PhD[a,*], *Samer N. Narouze, MD, PhD, FIPP*[a], *Imanuel R. Lerman, MD, MS*[b], *Aaron Calodney, MD*[c]

[a]*Center for Pain Medicine, Western Reserve Hospital, Cuyahoga Falls, Ohio*
[b]*Department of Anesthesiology, University of California, San Diego, La Jolla, California*
[c]*Texas Spine & Joint Hospital, Tyler, Texas*

ARTICLE INFO

Keywords:
Platelet-rich plasma
Injections
Knee
Osteoarthritis
Regenerative medicine

ABSTRACT

Both researchers and clinicians have exhibited growing interest in the use of platelet-rich plasma (PRP) and other autologous products for a variety of clinical conditions. Newly published data suggest that PRP injections can be an effective complement to conventional management strategies for knee osteoarthritis (OA) and chondropathy. Using a systematic review approach, we sought to synthesize the published data on the duration of clinical effect of PRP on knee OA and chondropathy. We systematically searched PubMed for all reports published in any language between the earliest available date and July (fourth week) of 2015 using the following key words: platelet, rich, plasma, knee, and osteoarthritis. If double-blind randomized, controlled trials were not available, we included other clinical trials and observational studies. We further searched for the association of the same keywords (platelet, rich, plasma, knee) and chondropathy. After reviewing abstracts, we acquired full-text papers where appropriate. We categorized the level of evidence for the duration of treatment efficacy according to Guyatt and coauthors. Twenty-four relevant studies encompassing 2,385 patients were included in the review. Studies reported clinical outcomes from intra-articular injection of PRP or recounted autologous products. The results showed a consistent improvement in patient pain scores and functional indexes for 6 months after initiation of injections. The residual clinical effect was typically observed beyond 6 months of follow-up in most of the studies. Pain and functional scores decreased after 12 months of follow-up but remained higher than the base scores in the majority of studies. Some suggested that annual injections improved treatment outcomes after 18 months of follow-up. Data from available clinical reports suggest that the PRP administration results in decreased pain and enhanced functional status. The duration of beneficial clinical effects after administration of PRP or recounted autologous products for patients with knee OA and chondropathy was stable up to 6 months following completion of regenerative therapy. The pain and functional scores worsened after 12 months of follow-up but were still better than pre-injection scores according to the majority of publications. The analysis is limited by the wide variability of available studies.

*Corresponding author.
E-mail address: ds241014@ohio.edu (D. Souzdalnitski).

http://dx.doi.org/10.1053/j.trap.2016.09.012
1084-208X/

Introduction

Knee cartilage counteracts pressure to bony parts of the joint when exposed to compressive and shearing forces that are inevitably present with movement in the knee joint.[1] Radiography, magnetic resonance imaging, ultrasonography, arthroscopy, and other diagnostic modalities can detect degenerative changes in cartilage (chondropathy).[2] Degenerative changes in cartilage, synovia, and bony elements of the knee joint are typically asymptomatic in early stages.[3] Progression of chondropathy and underlying bone pathology, commonly secondary to aging, overuse, or trauma, usually results in symptomatic knee osteoarthritis (OA).

Knee OA is a disease of the entire joint, not just cartilage, that involves synovia, menisci, ligaments, and subchondral bone.[2] The exact causes are not completely identified, but are believed to be a consequence of biomechanical forces, metabolic disarrays, overuse, or trauma.[1] The pain and joint stiffness experienced by patients result from damage to these tissues. Disease onset is gradual. Progression of knee OA is associated with a worsening structural and metabolic environment in the knee joint, accompanied by knee pain, joint effusion, and local hyperthermia in advanced cases.

Eventually, knee OA becomes a disease of the entire body because progressive degeneration in the knee joint negatively affects physical performance and creates limitations in routine activities. These changes, in turn, may trigger a chronic pain disorder. The chronic pain is typically much more than a painful sensation; it is accompanied by anxiety, depression, occupational and social problems, dependence on medications, and potential adverse effects of treatment. There is currently no cure for OA.[1]

Knee OA typically is discovered in middle age and affects 50% of the population aged 65 years and older. According to a report from the centers for disease control and prevention, the prevalence of symptomatic OA is as high as 16.7% in all individuals older than 45 years.[1] It is 1 of the 5 top causes of disability.[4] Estimated hospital expenditures of total knee joint replacements are $28.5 billion in the United States.[1] The direct health care costs likely represent only a small portion of the economic effect of OA. Estimating the overall economic effect of knee OA on workforce efficiency, absenteeism, and necessary help within households as well as the effect of decreased physical activity on cardiovascular, endocrine, and other organ systems is difficult.[5] Published causes of death secondary to knee OA do not include, for example, the number of people who die of the complications of nonsteroidal anti-inflammatory drugs used for the knee OA.[2]

Management of knee OA remains less than satisfactory, despite the use of comprehensive treatment that includes physical rehabilitation, manipulation, and oral and parenteral drugs. Benefits of arthroscopic surgery are unclear, and, even if present, last less than 2 years.[6] The definitive treatment remains knee replacement, which is not without adverse effects and limitations.[7]

Intra-articular knee injections have been used for the treatment of knee arthritis for more than a century. The first available report of intra-articular knee injection was published in 1897, approximately 3 centuries after initial experiments on injections in humans and approximately 40 years after invention of the hollow needle.[8] Corticosteroids and hyaluronic acid are the most commonly injected agents for knee OA.[9] Despite their widespread use, corticosteroid injections appear to be predominantly appropriate for knee OA with synovitis. Their clinical effect is typically only a few weeks, according to most studies,[9] and, according to some reports, up to 24 weeks.[10]

Viscosupplementation has been considered a safe and efficacious treatment for symptomatic knee OA. Effects characteristically are sustained up to 6 months after injection, according to most of the systematic reviews, including a recent evidence-based summary of high-quality, placebo (normal saline)-controlled trials.[11] Viscosupplementation has insignificant and clinically inapt benefit and unfavorable side effects according to other systematic reviews.[12] Dissatisfaction with treatment outcomes for knee OA has prompted an intensive search for alternative injectable treatment agents that can intensify the restorative reactions in synovia, cartilage, bone, meniscal tissue, ligaments, and knee joint tissues affected by injury or degeneration.[13]

Platelet-rich plasma (PRP) and recount autologous products (eg, platelet lysates, conditioned serum, selected growth factors, and peripheral blood stem cells) have garnered attention because they use the patient's own cells and PRP growth factors are contained in platelet alpha-granules. Agents prepared from a patient's own cells are believed to provide an environment that may be beneficial to reparative processes because of supraphysiologic concentrations of these products.[14] Intra-articular use of autologous biologic products applied directly to the synovia, cartilage, bone, meniscal tissue, or ligament is expected to stimulate a natural regenerative process.[15] Experimental studies propose that PRP injections may foster regeneration of the entire joint environment, including, but not limited to, cartilage, bone, and synovia.[15-19] Newly published data suggest that PRP injections can effectively complement conventional management strategies of knee OA and chondropathy.[13-15,20-31] However, the duration of clinically meaningful benefits remains unclear.

Objectives

We used a systematic review methodology to analyze available clinical studies reporting on the duration of clinical effects of PRP in patients with knee OA and knee chondropathy.

Methods

We systematically searched PubMed for all reports published in any language between the earliest available date and July (fourth week) of 2015 using the following keywords: platelet, rich, plasma, knee, and osteoarthritis. The following is an example of the primary query performed for the PubMed database: ("platelet-rich plasma"[MeSH Terms] OR ("platelet-rich"[All Fields] AND "plasma"[All Fields]) OR "platelet-rich plasma"[All Fields] OR ("platelet"[All Fields] AND "rich"[All Fields] AND "plasma"[All Fields]) OR "platelet rich plasma"[All Fields]) AND ("osteoarthritis, knee"[MeSH Terms] OR ("osteoarthritis"[All Fields] AND "knee"[All Fields]) OR "knee