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A systematic review of the effects of platelet rich plasma on outcomes for patients with knee osteoarthritis and following total knee arthroplasty

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ABSTRACT

Introduction: Platelet rich plasma (PRP) has been suggested to be effective in the management of knee osteoarthritis. Review of current literature reveals conflicting evidence regarding the benefits of PRP in treating knee OA. Preclinical evidence supports the use of PRP injections to promote a favorable environment for joint tissue healing, targeting not only cartilage but also synovial and meniscal tissues which has a positive effect on delaying the progression of OA. Growth factors found in platelet granules are postulated to influence outcomes in knee OA and after total knee arthroplasty (TKA).

Methodology: A systematic review of studies investigating the use of PRP in knee osteoarthritis and following TKA, was performed by searching the following databases for randomised clinical trials and pseudo-randomised clinical and comparative trials comparing the use of PRP to treat knee osteoarthritis and following TKA: MedLine, EMBASE, Science Direct, PubMed, and the Cochrane Library. The primary outcomes were patient reported measures including pain (visual analog scale (VAS)), quality of life scores, and knee function.

Results: A total of 2328 participants were analyzed across 17 included studies and pooled results showed a statistically significant reduction in pain in favor of PRP following TKA but not in non-surgical management of knee OA ($P < 0.0001$ and 0.13 respectively). No clinical benefit of PRP was found on quality of life and knee function ($P = 0.07$ and 0.05) following TKA, although a statistical improvement in knee function was demonstrated in patients with knee OA after PRP injection ($P < 0.0001$). There was no statistically significant clinical benefit of PRP on secondary outcomes including wound scores and length of hospital stay ($p = 0.33$ and 0.31, respectively). There was no statistically significant difference in respect to blood loss and overall symptoms in favor of PRP compared to control group following TKA ($p = 0.37$).

Conclusion: This systematic review demonstrated no long-term statistically significant improvement in patient validated outcomes and secondary outcomes both in patients with

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knee OA or following TKA for OA. However PRP has been shown to have short to medium-term benefits in pain control after TKA and activities of daily living in patients with OA.

Introduction

Osteoarthritis (OA) is the most prevalent form of arthritis worldwide. The progressive aging of the population has resulted in the increase in the incidence and prevalence of OA and it has become a major public health problem.[13] Several agents, such as nonsteroidal anti-inflammatory drugs, glucosamine, chondroitin-sulfate, hyaluronic acid, and glucocorticoids have been proposed as non-invasive therapies for pain treatment for knee OA, improvement in function, disability, and ultimately modification of severe chondral degeneration and osteoarthritis with varying success rates. According to the survey of the causes of productive work time loss in the United States, OA is the second most common cause of work performance loss after low back pain.[8] The **Kellgren and Lawrence system** is a method of classifying the severity of knee osteoarthritis (OA) using five grades as follows:

Kellgren and Lawrence grading system

- **grade 0**: No radiographic features of OA are present.
- **grade 1**: Doubtful joint space narrowing (JSN) and possible osteophytic lipping.
- **grade 2**: Definite osteophytes and possible JSN on anteroposterior weight-bearing radiograph.
- **grade 3**: Multiple osteophytes, definite JSN, sclerosis, possible bony deformity.
- **grade 4**: Large osteophytes, marked JSN, severe sclerosis and definite bony deformity.

The goals in treating OA include patient satisfaction through pain decrement, function and mobility increment, a better quality of life, prevention and/or correction of deformities through restoration of biomechanics, and slowing the progression of the disease.

Rationale: The effectiveness of PRP is debated[21] and the purpose of this study was to carry out a systematic review of the results of its use in treating knee OA and following TKA. It has been suggested that the cost associated with preparing PRP outweigh the benefits it may provide to patients with OA in the long term as most patients return to baseline knee function within a year of PRP injection. Despite its widespread use, high quality studies are lacking in the literature to demonstrate the real efficacy of PRP. This is still a developing area in the management of musculoskeletal disorders. Postulated hypotheses are that PRP is effective in the non-surgical management of OA by delaying disease progression through stimulating bone regeneration. According to Raeissadat,[8] the rationale for the use of PRP is to stimulate the natural healing cascade and tissue regeneration by a "supraphysiologic" release of platelet-derived factors directly at the site of treatment. It is also postulated that PRP used intra-operatively reduces post-operative bleeding, hospital stays through rapid wound healing and attainment of range of motion (ROM) with patients mobilizing early hence reducing complications associated with reduced mobility, like thromboembolism, pneumonia, urinary tract infections, muscular atrophy and physical deconditioning.

In recent years, there has been significant interest in the use of biologic treatment of muscle, tendon, ligament, and bone injuries in orthopedic and sports medicine. PRP has been used in dermatology, ophthalmology, dentistry, cosmetic and plastics, and maxillofacial surgery, and in the management of sport-associated injuries, such as tendinopathies, muscular lesions, and cartilage damages.[2] In a study by F. Blanke et al.,[22] the authors concluded that percutaneous injections of PRP have the ability to achieve pain relief and halt progressive changes as detected by MRI over 6 months in patients with grade 2 meniscal lesions. Therefore, PRP may be considered as a treatment option in patients with persisting pain from intrasubstance meniscal lesions.

Mechanism of action of PRP: Platelets contain two unique types of granules – alpha granules and dense granules. Alpha granules in platelets function as storage units containing a variety of hemostatic proteins, inactive growth factors, cytokines, and other proteins such as adhesion proteins. Dense granules store and release bioactive factors that promote platelet aggregation, tissue modulation, and regeneration including adenosine diphosphate (ADP), adenosine triphosphate (ATP), calcium, serotonin, histamine, and dopamine. Growth factors found in these granules include platelet derived growth factor (PDGF), transforming growth factor-β_1 (TGF-β_1), vascular endothelial growth factor (VEGF), basic fibroblastic growth factor (bFGF), insulin-like growth factor (IGF-I, IGF-II), endothelial cell growth factor (ECGF), and epidermal growth factor (EGF).[2] It is these growth factors which are postulated to stimulate tissue repair and regeneration in OA and following TKA. These growth factors are cytokines and have an important role in cell proliferation, chemotaxis, cell differentiation and angiogenesis. According to M. Sanchez et al., the pool of growth factors obtained from platelet-rich plasma decreases nuclear factor-kB activation, a major pathway involved in the pathogenesis of OA, which is characterized by a catabolic and inflammatory joint environment. Moreover, the supernatant of autologous proteins also inhibits matrix metalloproteinase 13 production by interleukin 1B- and tumor necrosis factor a-stimulated human articular chondrocytes.

Additional issues are lack of standardization of the platelet concentration for injection, the role of white blood cell (WBC) filtering during preparation, the site of injection into the knee, and most importantly, the number and frequency of injections

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