

Outstanding scientific accomplishment

Abstract

In recent years, platelet-rich plasma (PRP) rich in growth factors (PRGF) has emerged as a promising autologous biological therapy alternative for use in cosmetic and regenerative medicine. PRGF is a high concentration of platelets extracted from whole blood, and platelet-containing plasma is separated and concentrated from red blood cells by centrifugation. The hundreds of bioactive proteins that make up PRGF, including cytokines, peptides, and growth factors, aid in the healing of skin and soft tissues. PRGF has several attractive features, including tissue regeneration and healing capabilities, the extended release of several growth and differentiation factors from activated platelets, and the lack of immunogenicity problems. Because of its unique biological properties, PRGF has a wide range of clinical uses in regenerative and cosmetic medicine. This paper's main objective is to highlight a fantastic, effective method for treating osteoarthritis (OA) in the knee (KOA). It also highlights the significant influence that our exceptional M.Sc. thesis has had.

Keywords: Egypt, knee osteoarthritis (KOA), MSc thesis, PRP, PRGF

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Introduction

It is thought that inflammation results from cartilage damage, and inflammation is a key factor in the development and progression of OA.¹ Musculoskeletal impairments are largely caused by OA.² A common ailment that frequently interferes with daily life is KOA.³ Primary KOA continues to be a degenerative disease that is difficult to control. Primary KOA is still a difficult degenerative disease to treat, putting an increasing financial and physical burden on people as a result of rising average life expectancy and obesity rates.⁴

A biological therapy called autologous PRP is created from the patient's own plasma and contains a significant amount of platelets. Because they release cytokines and growth factors, these platelets are essential for both inflammation and the healing process. Diagrammatic of PRGF therapy process is imagined in Figure 1.

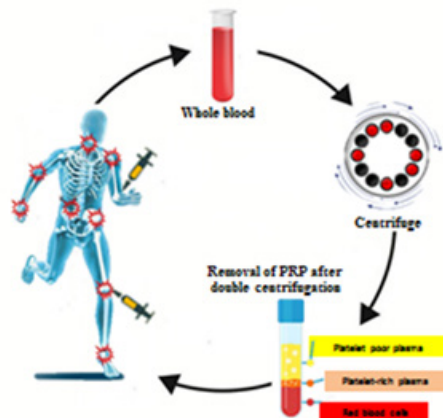


Figure 1 Schematic diagram showing the platelet-rich plasma rich in growth factors therapy process.

Regretfully, OA-related musculoskeletal impairments currently lack an effective treatment.⁵ PRP is a solution made from a person's own blood that has a small amount of plasma and a high concentration of platelets. The numerous growth factors and anti-inflammatory proteins found in platelets have the potential to support blood vessel formation, cell growth, migration, specialization, and the formation of supportive tissue.^{1,6,7}

Alpha-granules (α -granules), dense granules, and lysosomal granules are the three types of granules found in platelets. Growth

factors can be found in α -granules. PRP's growth factors primarily function to either recruit and activate additional immune cells or cause inflammation in endothelial cells. Chemokines and cytokines are other components of α -granules that stimulate cell chemotaxis, proliferation, and maturation, as well as modulate inflammatory molecules.^{1,8}

Objective

Highlighting a remarkable, effective method for curing KOA was the main target, and it highlights the enormous influence that our fantastic thesis has had.

Methodology and theoretical orientation

PRP was made from blood using the Olivier et al. 2012 method,⁹ which was modified in 2020 using a technique that our lab had calibrated and improved.¹⁰ Following two centrifugations of the blood, PRP was extracted. As a result, this promising PRP method is now a routine, reasonably priced test used for patient treatment in the clinical pathology, hematology, and blood banking labs of Menoufia University hospitals. The criteria established by the coaching of the Clinical Pathology and Hematology Departments served as the basis for choosing this approach. A certificate of proclamation (Figure 2) of precious perspective worthy publication from the CPQ Medicine journal certifying the announcement of precious perspective entitled "A Therapeutic Approach from Lab to Clinic in the Domain of the Disease Caused by the Novel Coronavirus From the Perspective of an Egyptian Scientist" was presented by Prof. Laila M. Montaser on May 7, 2020.



Figure 2 A certificate of worthy publication honored to Prof Laila Mahmoud Montaser on behalf of CPQ medicine, certifying the publication of precious perspective.

Because cartilage lesions have a limited capacity to heal on their own, KOA presents a challenge. KOA can be treated with oral non-steroidal anti-inflammatory medications, physical therapy, braces, activity modifications, and, as a last resort, surgery. When non-surgical therapy fails and surgery is not yet required, intra-articular (IA) injections are frequently used. Biologic adjuncts, such as PRP, have been the subject of recent research to enhance IA homeostasis. Because it can be difficult to translate non-clinical study results and methodological recommendations into human clinical cure guidelines, *in vitro* and animal research findings frequently produce different clinical outcomes.¹

Results

According to the research's findings, PRGF treatment was designed to help KOA patients with their soreness support and function progression. Through IA injection, PRGF has been demonstrated to enhance joint function and lessen discomfort in patients with KOA. It can also improve the metabolic processes of damaged structures and initiate a regenerative response, which can have a beneficial effect on the inflammatory and catabolic processes linked to KOA.

Discussion

In the comment to a unique master science's thesis conducted in the Department of Clinical Pathology, Faculty of Medicine, Menoufia University, then discussed in February 2016 entitled "Platelet-rich plasma preparation applications in KOA" and published as a paper in an international Journal (Menoufia Medical Journal 2017 July; 30(1):139-146), by Prof. Laila M. Montaser and group¹¹ under the title of "Application of platelet-rich plasma preparation rich in growth factors in knee osteoarthritis", the authors accorded an ideal fitter avenue in preparing PRP that evidenced to be a perfect election for osteoarthritic patients with a success rate 92.8% for the first time in Egypt. As a result, the dissertation discussion committee went to the Menoufia Faculty of Medicine Council to request approval for its use as a novel clinical therapeutic approach for the first time in Egypt. In addition to using it for KOA, this outstanding thesis inspired many of our faculty members and researchers, as well as those at other colleges, hospitals, and private clinics in the Delta and throughout Egypt, to use it in research and clinical settings for regenerative and aesthetic medicine diseases like musculoskeletal regeneration, hair restoration, wound healing, skin and face rejuvenation, breast augmentation, shoulder and hand renovation, and the regeneration and reconstruction of skeletal and connective tissues in cases of sports-related injuries, periodontal, and maxillofacial diseases. The authors then concluded that autologous PRP-rich in growth factors injected IA is a safe, minimally invasive, and low-risk procedure that provides growth factors for cartilage regeneration and healing. In order to lessen pain and enhance knee function and quality of life, it is beneficial for treating KOA. The platelet count and TGF- β levels in PRP were important markers of improvement. This study recommended adjusting the initial blood draw amount based on the patient's blood platelet count in order to achieve a sufficient high PRP platelet count ($\geq 1001.25 \times 10^9$ platelets/l in 5 ml). This will enable later administration of a higher dose of growth factors to improve OA.¹¹

Montaser wrote extensively about this esteemed thesis in her two Editorials from 2016 and 2018.^{12,13} Although the laws and regulations requiring the award to be given within two years of the dissertation's completion prevented this unique thesis from receiving the Best Thesis Award, the Master of Science thesis deserves to be honored by Menoufia University on its anniversary.

In their presentation at SPIE Nanoscience + Engineering: August 19–23, 2016, San Diego, CA, USA, Montaser and colleagues¹⁴ discussed "Articular cartilage tissue engineering with plasma-rich in growth factors and stem cells with Nano *scaffolds*" and it was published in the Proc. Of SPIE 9930, Biosensing and Nanomedicine IX, 99300V. The potential to cure smooth tissue damages and rejuvenate cartilage is the sacred cup of musculoskeletal medicine. Articular cartilage mend and renovation is theorized to be broadly ungovernable due to the needy correlated characteristics of that tissue. Due to their little self-restoration capacity, cartilage faults widely outcome from joint harm, senility, or OA, are the ultimate oftentimes irreparable and are a significant origin of joint distress and recurrent inability. Yet, existing procedures do not excellently replace hyaline cartilage and might conduct to the occurrence of fibro- or persist hypertrophic cartilage. The scarcity of dynamic manners of curing has motivated study for tissue engineering collecting stem cells, *scaffold* substances and ecological agents. Also the authors explained that the range of articular cartilage tissue engineering, what points to rectify, repeated, and/or recover impaired or ill cartilage working, has outraged keen attention and retains massive scope for enhancing cartilage remedy. PRGF and/or stem cells might be effectual for tissue restore besides cartilage remedial approaches. There is an appreciable commitment to precede present cartilage treatments on behalf of finishing a consistently felicitous way for handling cartilage maladies. Tissue engineering might be the greatest strategy to gain that target by means of the implement of stem cells, modern biologically insufflated *scaffolds* and, emanating nanotechnology. In this manuscript, contemporary and developing strategy in the area of cartilage tissue engineering is showed for certain application in goat as an experimental animal model. Within the upcoming years, the spread of novel techniques applying stem cells, in *scaffolds*, with the addition of an extra element of culture milieu possible raise the value of novel established cartilage.¹⁴

In line with our findings, the authors of the study by Garbin and Olver⁵ pointed out that PRP therapy has shown promising clinical outcomes in reducing pain and enhancing joint function in KOA patients. PRP may offer a more practical and accessible alternative to other biological therapies for the treatment of OA. Compared to ordinary whole blood, PRP has a higher concentration of platelets. Because of its abundance of growth factors, it is commonly used to control inflammation and promote healing in musculoskeletal disorders. The authors also pointed out that although there were still difficulties with the clinical application of PRP, its beneficial unofficial effects had increased interest in its use in orthopedic surgery and sports medicine.⁵

Li et al.⁴ stated that primary KOA remains a degenerative disease that is difficult to treat. As obesity rates and average life expectancy rise, people were experiencing a greater financial and physical burden from OA. When compared to many other treatment options, the authors concluded that IA-PRP injection has been shown to be a safe and effective method of improving the quality of life for patients with KOA.⁴

The prevalence of KOA was estimated to be over 10% of the population, with a 45% lifetime risk, according to Rodríguez-Merchán in 2022.¹⁵ Current guidelines recommended controlling body weight, therapeutic exercise, medication treatment (oral non-steroidal anti-inflammatory drugs, paracetamol, opioids), and mechanical assistance (braces, orthoses, walking aids). Nevertheless, these treatments were typically only short-term. Despite the fact that IA corticosteroids are typically advised, their benefits are typically transient and ought to be limited to treating pain. The efficacy of hyaluronic acid is questionable.

When the previously listed treatments fail, total knee arthroplasty is typically recommended as an effective course of action. However, it can be costly and have medical and surgical repercussions. Finding safe and effective alternative treatments for knee OA is essential. PRP treatment for KOA has been investigated. The effectiveness of IA-PRP injections in the knee joint is still up for debate, despite the fact that most studies recommend temporary pain relief. Although there is conflicting clinical evidence and basic research knowledge, PRP is becoming more and more popular among orthopedic surgeons who treat patients with OA. Furthermore, the authors noted that knee arthropathy causes pain for people with hemophilia (PWH). One of the current areas of debate is the efficacy of IA-PRP injections in treating PWH knee pain.¹⁵

Evaluation of inflammatory activity, bone/cartilage biomarkers, and changes in clinical outcome (pain and knee activity) in patients with KOA following a single IA-PRP injection or a combination of IA and intraosseous PRP (IA+IO-PRP) was the aim of the 2023 study by Barman et al.¹⁶ After receiving IA-PRP and IA+IO-PRP injections, the authors concluded that there were significant clinical benefits. However, deterioration of the subchondral bone structure was a crucial element in the etiology of KOA, as stated by Barman and associates in 2022.¹⁷ An IA injection was not a suitable treatment for the diseases affecting the damaged subchondral bone structure. The purpose of their study was to assess the therapeutic effects of a single IA injection, either alone or in combination with IO-PRP injections.

PRP injections for OA had been widely promoted in clinical practice in recent years, despite their questionable effectiveness, according to Xiong and colleagues in 2023.¹⁸ The authors conducted a meta-analysis of relevant randomized controlled trials (RCTs) to determine the safety and efficacy of PRP injections for the treatment of OA. They concluded that PRP injection therapy can safely and effectively increase functional activity in OA patients while also having a positive impact on analgesic outcomes.

Wang et al. conducted a meta-analysis in 2024¹⁹ with the aim of comparing the clinical effectiveness of IA injections of PRP versus corticosteroid (CS) in the treatment of KOA. After a comprehensive search of the PubMed, Embase, and Web of Science databases, literature on IA-PRP and CS injections for the treatment of KOA appeared. Recent studies conducted in 2024 found that IA-PRP injections outperform CS injections in terms of improving functional outcomes and reducing pain in KOA patients. During the short follow-up period, there was no appreciable difference between PRP and CS knee injections.

However, the benefits of PRP injections were most evident in the medium- to long-term management of clinical symptoms, including pain relief, improving patients' quality of life, increasing activities of daily living, and improving sports capabilities.¹⁹

In line with our findings, PRP injection therapy also showed great promise for enhancing knee cartilage healing, as reported by Xiao et al. in 2023.²⁰ Examining the state of research on PRP use for KOA over the past 15 years was the aim of this bibliometric analysis. The Web of Science Core Collection provided all of the papers that looked at PRP's use in KOA applications. Future developments in this area included sports management, the standardization of injectable components, injection sites, and injection techniques, the alteration of growth factor receptor expression, whether it was positive or negative, and the confirmation of PRP contraindications.²⁰

According to Cui and colleagues, PRP had been widely used to treat KOA.²¹ There was a great deal of research on the topic. However,

there were no bibliometric reports in this field's publications. According to the authors of this bibliometric study, the Web of Science database was used to compile a thorough set of articles on PRP and its application in treating KOA that were published between 2011 and 2021. By providing a thorough examination of the clinical developments in the field, this analysis allowed researchers to pinpoint important areas of interest and investigate fresh directions for their study on PRP treatment of KOA.

In 2020, Ren and colleagues²² reported that PRP had been widely used to treat a range of orthopedic diseases. The topic had been the focus of extensive research. However, there were no bibliometric reports on the publications in this field. A very useful method for systematically evaluating the current level of research in a given field is bibliometrics. Using R2 software, the current state, potential applications, and hotspots of PRP in the management of orthopedic disorders over the past 19 years were investigated. The Web of Science Core Collection was searched from 2002 to 2020 to find every article about PRP's application in orthopedics. The authors' keyword analysis revealed that growth factors, PRP composition, and PRP in conjunction with mesenchymal stem cells were the main areas of research interest. The frontiers of PRP research included studies on rotator cuff injuries and cartilage damage, as well as a comparison of the clinical effectiveness of PRP and hyaluronic acid. The authors concluded that there was still debate regarding the efficacy of PRP in treating orthopedic conditions. Low levels of evidence, insufficient sample sizes, inconsistent system names, inconsistent preparation and application procedures, and a lack of comprehensive basic scientific studies were among the remaining shortcomings of the experimental methods. The co-occurrence and cluster maps, along with the analysis of hotspots and frontiers, may help to resolve current problems and open up new research avenues.

Conclusion

In the domain of orthopedics, the use of autologous PRGF is rapidly becoming more and more common. For OA, treatments that focus on controlling inflammation and the progression of the illness offered a bright future. PRGF therapy had shown promise as a safe and efficient treatment for KOA. It was clear from the results of the studies that PRGF therapy needed to be used more effectively, and clinicians should be aware of the practical applications and outcomes of PRGF as a treatment for OA. IA injection of PRGF had been demonstrated to be both safe and effective in enhancing the quality of life for patients with KOA when compared to alternative treatment methods.

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None.

Conflicts of interest

The author declares that there is no conflicts of interest.

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