

Research Progress of PRP and Chinese Medicine in the Treatment of Knee Osteoarthritis

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Abstract: Knee osteoarthritis is a common and frequently occurring disease in clinic, and degeneration of articular cartilage is one of the main causes of this disease. Delaying cartilage degeneration and promoting cartilage repair are important ways to relieve pain and improve function. PRP is an autologous product derived from highly centrifugal blood, which contains a high concentration of effective factors, which can maintain tissue homeostasis and regulate the body's inflammation and coagulation. The product can regulate bone and blood vessel remodeling, inhibit chondrocyte apoptosis, inhibit inflammatory reaction and promote collagen synthesis by injection into the joint. PRP has unique advantages in the treatment of knee osteoarthritis, and has become one of the feasible methods for clinical treatment of KOA. Based on this, through this review, the author will elaborate the preparation of PRP, the mechanism of ACTION of KOA, the safety evaluation, the advantages of PRP and other treatment methods, and the combination of PRP and TRADITIONAL Chinese medicine in the treatment of knee osteoarthritis, aiming to provide new ideas, new methods and new methods for clinical diagnosis and treatment.

Keywords: Knee osteoarthritis, PRP, Mechanism of action

1. Introduction

The main clinical manifestations of knee osteoarthritis (KOA) are pain, popping and effusion in the medial side of knee joint. Narrowing of medial space, genu varus deformity, changes of lower limb force lines, and functional limitations are among the common degenerative changes of articular cartilage at present. Some patients have articular cartilage destruction or subchondral bone marrow edema as indicated by knee magnetic resonance imaging (MRI), and the incidence rate can reach 50% in the elderly over 60 years old [1]. Due to the lack of blood vessels in adult knee cartilage, lack of blood nutrition and moisture, and low regeneration ability, it is difficult to treat KOA, thus limiting the healing potential of the joint. Knee progressive destruction of articular cartilage causes include joint damage, degenerative changes, joint imbalance of internal stress, but in its essence the reason is because the articular cartilage matrix decomposition and synthesis in a state of imbalance, and the cause of imbalance and joint trauma, joint deformity, age, physical factors, physical condition, and some genetic characteristics and related[2]. Exact mechanisms and pathophysiological mechanism of KOA is unclear, but the KOA is due to the result of the accumulation, and not just the joints of "wear" [3], loss and damage of articular cartilage is the end of this process, in the whole process of KOA and progress involves a combination of mechanical, cellular and biochemical process, KOA happened early joint destruction causes joint inflammation medium imbalance, Further lead to cartilage degeneration, extracellular matrix degeneration, systemic inflammation, chondrocyte apoptosis, osteophyte formation, bone remodeling[4].

So far, there is no clear treatment for osteoarthritis, and the American College of Rheumatology has proposed a classification in which conservative treatment includes pharmacotherapy and non-pharmacotherapy. Non-pharmacotherapy includes total body exercise and muscle exercise, but non-pharmacotherapy is often heavily dependent on patient compliance and difficult to control [5]. Major drug treatments include analgesics, nonsteroidal anti-inflammatory drugs, hyaluronic acid (HA), ozone, and corticosteroid injections. Although the above drug treatments have certain efficacy, they also have large side effects [6]. This means that treatment focuses on treating the patient's symptoms and slowing the progression of the degenerative process. Thus, the treatment goals of KOA focus on limited movement, pain and stiffness relief, improved joint function, improved quality of life, correction of

potential joint malformation, and delay or avoidance of total knee replacement (TKA) [7]. Although TKA is effective in the treatment of advanced KOA, it is estimated that the 10-year and 20-year survival rates are about 95% and 85%, respectively [8], and more than one-third of TKA patients have postoperative adverse reactions such as intraoperative pain. Therefore, it is of great significance to delay the degeneration rate of articular cartilage before TKA. In recent years, growth factors have attracted people's interest because of their properties of repairing tissue damage and maintaining normal tissue structure, especially platelet-rich plasma (PRP) injection [9-11]. PRP can release various growth factors and cytokines, accelerate cartilage matrix synthesis, inhibit synovial inflammation and promote cartilage healing.

2. PRP

2.1. The preparation of PRP

Artificial preparation method of PRP: sterile, suitable room temperature, humidity, room temperature. Extract 0.2mL heparin sodium with a 1ml syringe, then moisten with a 50ml syringe. The tourniquet was bound, the elbow was disinfected 2-3 times, and 30 ml of peripheral blood was drawn from the elbow vein with a 50ml syringe, followed by the first centrifugation. During centrifugation, the peripheral blood was evenly divided into two 50mL sterile centrifuge tubes. The two tubes were placed in the horizontal rotor, and then placed in the centrifuge under sterile conditions for 6 minutes. After putting on sterile gloves, the centrifuge tubes were removed and stratified to ensure that the peripheral blood was stratified into two layers. After that, the supernatant in the two centrifuge tubes was collected into the clean centrifuge tubes with a clean 10mL syringe for the second centrifuge. Use a clean 10ml syringe to balance another clean centrifuge tube by adding an equal amount of sterile water or normal saline. The tube was placed in a horizontal rotor, marked on the supernatant layer with adhesive plaster, centrifuged for 5 minutes and removed by observing the stratification, checking that the liquid in the marked tube was divided into three layers. A 10ml syringe was used to extract 4ml of fluid from the middle layer (leukocyte rich layer, PRP layer) and bottom supernatant of granulosa cells. If the amount of the middle layer is sufficient, 4ml is extracted from it. 0.4mL liquid was placed in a sterile anticoagulant tube for evaluation [12-14].

2.2. Mechanism of action

Studies have reported [15] that PRP can release factors to regulate microcirculation and pain control to treat the symptoms caused by knee degeneration. Through literature review, the author found that the current mechanism is relatively clear factor regulation. PRP can release 18 factors to act on the human body [16], and the author only lists those that are closely related. Epidermal growth factor (EGF) can be secreted by platelets, macrophages and monocytes in the blood and can promote mitosis of chondrocytes and osteoblasts. Promote the growth, proliferation and differentiation of mesenchymal cells and epithelial cells, and affect the synthesis and metabolism of extracellular matrix; Promote wound healing; Promote angiogenesis; Enhance the influence of other growth factors; Stimulate endothelial chemotaxis and angiogenesis; Regulate collagenase secretion [17-18]. Transforming growth factors α and β 1 regulate the growth and differentiation of mesenchymal cells, endothelial cells and epithelial cells, and affect bone formation, reconstruction and regeneration by inhibiting collagen synthesis and calcium release. This factor can also regulate other growth factors (including EGF, PDGF, A-FGF, B-FGF) to play a role; Inhibit osteoclast formation and bone resorption; Inhibit proliferation of macrophages and lymphocytes, stimulate endothelial chemotaxis and angiogenesis; Participates in regulating the balance between fibrosis and cardiomyocyte regeneration; On the other hand, by influencing the formation of osteoblasts and bone matrix deposition to adjust the steady state of osteogenesis relations, stimulate fibroblast chemotaxis, increase the synthesis of collagen and fibronectin, stimulate or inhibit endothelial cells, fibroblasts and osteoblasts mitosis, inhibit DNA synthesis of human fibroblasts [16-19]. In addition. Acid fibroblast growth factor (A-FGF, FGF-1, B-FGF, FGF-2) can regulate angiogenesis, promote wound healing at injured sites, promote collagen synthesis, matrix and epithelial formation; In addition, it is responsible for the growth and differentiation of cells, including fibroblasts, myoblasts, osteoblasts, nerve cells, endothelial cells, keratinocytes, and chondrocytes. As a mitotic protocoell, the factor can stimulate the proliferation of myoblasts and increase the number of osteoblasts. In addition, as the myogenic cells of fibroblasts, skin keratinocytes and skin endothelial cells, this cytokine can stimulate the proliferation of myoblasts and mesenchymal cells, hinder the degeneration and differentiation of chondrocytes, and slow down the degeneration of articular cartilage [17-19].

Connective tissue growth factor can promote differentiation, matrix mineralization and osteoblast proliferation. Promote angiogenesis, cartilage regeneration and platelet adhesion [20-21]. Insulin-like growth factor (IGF) stimulates the growth of myoblasts and fibroblasts and activates the synthesis of collagenase and prostaglandin E2 in fibroblasts; This factor increases the utilization rate of the combination of collagen and bone matrix, and through the synthesis of the two, the wound healing can be improved efficiently and quickly. To regulate the metabolism of articular cartilage; In addition, this factor can stimulate chondrogenic preosteoblasts and osteoblast replication, cell growth, and bone matrix formation. Regulates the growth and repair of skeletal muscle [17,22-23]. The interleukin family (IL-1 β , IL-6, IL-8) stimulates fibroblast growth and collagen production; Together with IL-8, IL-6 promotes angiogenesis and epithelial mitosis, and stimulates epidermal mitosis. Support angiogenesis; Target cells (neutrophils, which play a leading role, but also include other granulocytes) are induced to chemotaxis, leading them to migrate to the infection site and play a role in inhibiting the occurrence and development of inflammation and stimulating phagocytosis of the target site [24-25].

2.3. Advantages with other treatments

Conservative approaches are the first choice in the early and middle stages of KOA, and oral nonsteroidal anti-inflammatory drugs are the most widely used drugs in drug therapy. It has obvious relief effect on early mild KOA patients with pain, swelling and other clinical symptoms, but requires long-term use, with many adverse reactions. Intraarticular drug therapy can form a high concentration of drugs locally in the diseased tissue and reduce systemic reactions without long-term use. Therefore, intraarticular drug injection has become the main method to stimulate cartilage regeneration. Currently, the most commonly used intra-articular injection drug is HA, which is an important component of the synovial fluid of the knee joint. HA plays a key role in lubrication of articular surface, stress relief of load-bearing surface, and transport of synovial cartilage nutrients. Navarro-sarabia F [26] followed 306 PATIENTS with KOA for up to 40 months in a randomized controlled trial of intra-articular HA versus placebo. The results showed that repeated intraarticular injections of HA improved clinical symptoms in patients with KOA, but did not reflect whether KOA was in remission or merely a change in the natural course of the disease after a long period of treatment. Their results showed that both treatments were effective in improving knee function and symptoms. Compared with HA, PRP not only has better clinical improvement effect, but also has a lower rate of re-therapy in long-term follow-up, and the overall efficacy is better than that of THE HA treatment group [27-28]. In addition, ozone and corticosteroids are commonly used for knee injections. Babaei-ghazani A [29] performed ultrasound-guided corticosteroid injection and ozonation injection in 62 patients for KOA follow-up of 3 months. The results showed that both corticosteroids and ozone injection were effective in KOA patients, and the ozone group had longer clinical symptoms. This is because ozone has strong oxidation properties [30] and has strong anti-inflammatory and analgesic effects. In this study, Duymus TM [31] and Huang Y [32] treated PRP with ozone and corticosteroids as control groups, respectively. The results showed that the early curative effect of each group was similar, but the intermediate curative effect of PRP group was significantly better than the control group, and the late ozone and corticosteroid failure. This is because ozone and corticosteroids do not improve the cellular microenvironment in the joint and can only achieve good clinical results in the short term. Therefore, they cannot replace the role of HA and PRP in the treatment of KOA. In addition to PRP, researchers are also exploring other biological therapies. Such as amniotic heterogenous suspension transplantation (ASA), mesenchymal stem cells (MSCs), exosomes, botulinum toxin TYPE A, etc. [33]. However, its clinical application is currently limited due to lack of high-quality studies and other reasons.

2.4. Safety evaluation of PRP

At present, PRP in clinical use is obtained by taking patients' own venous blood, adding anticoagulant, and centrifugation in vitro, which does not cause immune rejection and does not have the risk of disease transmission. This also confirms the role of PRP in treating diseases other than KOA. Combined with the randomized controlled trials of Li W et al. [34], adverse reactions caused by adverse PRP were non-specific and mostly related to the injection operation itself. Therefore, these adverse reactions usually resolve spontaneously within a few days, with high safety.

3. Treatment of knee osteoarthritis with PRP and Traditional Chinese medicine

Traditional Chinese medicine has the characteristics of multi - effect, multi - target and multi -

pathway, and has been widely used in clinic. PRP combined with Traditional Chinese medicine can bring benefits in patients with knee osteoarthritis. Yang Chen [35] respectively gave the experimental group three schemes of bone arthralgia analgesic solution, PRP and bone arthralgia analgesic solution combined with PRP to observe which group had the best effect. It was found that oral gubi analgesic solution and PRP injection had good efficacy in the treatment of knee osteoarthritis with liver and kidney deficiency, and the efficacy of gubi analgesic solution combined with PRP in the treatment of knee osteoarthritis with liver and kidney deficiency was superior to that of gubi analgesic solution alone or PRP alone, which could significantly improve the clinical symptoms of patients. He Cuihuan [28] explored the observation of curative effect of PRP and Xianling Gubao capsule on early and middle KOA and evaluated the influence of PRP and Xianling Gubao capsule on the expression of relevant inflammatory factors in serum of KOA patients, and conducted network pharmacology analysis experiment on Xianling Gubao capsule. PRP combined with xianling Gubao capsule can significantly improve the pain and knee function scores in early and middle KOA patients. PRP combined with oral Xianling Gubao capsule can reduce the expression level of cytokines in serum, regulate inflammatory response, effectively improve knee pain and function, and delay the course of KOA [36].

4. Conclusion and outlook

Because PRP from extraction and centrifugal venous blood of the human body, and then applied to the human body itself, its safety can be guaranteed, as a new method for the treatment of knee osteoarthritis, PRP can effectively alleviate the degeneration of articular cartilage, suppress disease clinical symptoms, delay the onset of the knee joint replacement, in degenerative disease, With the degeneration of articular cartilage, inflammatory reactions begin to appear at the degeneration site, and PRP releases related factors to inhibit the occurrence and development of inflammation. The curative effect of TCM combined with PRP in the treatment of KOA is remarkable, but it has its shortcomings. First, there are few prescriptions selected and few articles obtained by the author through literature review. Secondly, the relationship between PRP and PRP is not clear. Whether PRP promotes the function of PRP or PRP changes the function of PRP remains to be proved. In view of this, the author believes that expanding the clinical study of TCM and PRP, and clarifying the corresponding relationship between them on this basis, may provide a new approach for clinical treatment of KOA [37].

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