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A Review of the Progress in the Treatment of Osteoarthritis

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Abstract

Osteoarthritis (OA), a common chronic joint disease, significantly affects the quality of life of patients. This article comprehensively reviews the treatment progress of osteoarthritis, covering multiple aspects such as non-pharmacological treatment, pharmacological treatment, surgical treatment, and emerging treatment methods, aiming to provide references for clinical treatment and promote further development in the field of osteoarthritis treatment.

Keywords

Osteoarthritis, Progress in Treatment, Emerging Treatment Methods

1. Introduction

Osteoarthritis (OA) is a chronic joint disease characterized by degenerative changes of articular cartilage and secondary bone hyperplasia. It is widely prevalent globally and severely affects the quality of life of patients and imposes a heavy burden on society and the economy [1]. With the intensification of population aging, the incidence of OA is on the rise. According to the latest research, more than 500 million people worldwide suffer from osteoarthritis [2], posing a significant challenge to public health. Therefore, it is of great clinical significance and social value to have an in-depth understanding of the treatment progress of osteoarthritis.

2. Overview of Osteoarthritis

Osteoarthritis is more common in weight-bearing areas such as the knee joint, hip joint, spine, and distal interphalangeal joint. Its pathological features include wear and tear of articular cartilage, subchondral bone sclerosis, cystic degeneration, and osteophyte formation at the joint edge. The clinical manifestations are diverse, mainly including joint pain, which is initially mild to moderate intermittent dull pain, aggravated after activity, and relieved after rest; Morning stiffness generally lasts for a short period of time, not exceeding 30 minutes; Joint swelling can be caused by joint effusion, bone hyperplasia, or synovial hypertrophy; Bone fricative sounds (sensations) can occur during joint movements; Joint weakness, patients often feel that joint movement is not flexible; In severe cases, it can lead to activity disorders, affecting daily life and work.

The pathogenesis of OA is relatively complex, involving multiple factors such as age, obesity, trauma, genetic factors, congenital joint abnormalities, joint deformities, etc. Age is one of the most important risk factors for osteoarthritis. As age increases, the metabolism and repair ability of joint cartilage gradually decreases, making it more prone to degeneration. Obesity increases joint weight-bearing and alters the biomechanical environment of joints, leading to cartilage damage and inflammatory reactions. In addition, genetic factors also play a certain role in the onset of OA, and certain gene polymorphisms are associated with susceptibility to OA.

3. Progress in the Treatment of Osteoarthritis

3.1. Non-Pharmacological Therapy

1) Exercise therapy

Exercise therapy works through mechanical stress in the treatment of osteoarthritis. Mechanical stress is a key environmental factor in maintaining cartilage homeostasis. Chondrocytes can regulate the anabolic/catabolic signaling axis and the inflammatory response by activating a complex network of mechanical signal transduction, and are involved in the development of OA. Therefore, in this study, we found that mechanical stress can downregulate the cartilage catabolism-related factor MMP13, and downregulate the cartilage anabolism factor COL2A1 both *in vitro* and *in vivo*. However, mechanical stress is a double-edged sword. Moderate mechanical stimulation is a chondroprotective factor for maintaining cartilage homeostasis. Nevertheless, excessive mechanical stress is one of the important risk factors in the pathogenesis of OA. Research shows that cyclic tensile stress (CTS) is an effective antagonist of IL-1β and can inhibit IL-1β-induced chondrocyte catabolism. Excessive CTS can also lead to chondrocyte damage. Studies have found that chondrocytes exhibit a significant fibroblast-like morphology under 0.5 Hz 10% CTS, while 5% stretch maintains the chondrocyte phenotype. In our study, we also found that 0.5 Hz 5% CTS for 4 h can effectively alleviate IL-1β-induced chondrocyte degeneration. However, 8-h CTS intervention exacerbates chondrocyte degeneration. Therefore, it is of great value to deeply explore the internal mechanical signal transduction network of chondrocytes, which is helpful for scientifically formulating exercise prescriptions and improving clinical treatment [3]-[5].

Clinical doctors will develop appropriate exercise intensity, frequency, and duration based on factors such as the patient's age, severity of illness, physical condition, and exercise habits. For example, for elderly patients or those with severe illnesses, low-intensity, long-term exercise methods such as slow walking, water exercise, etc. may be chosen; For young and mild patients, the intensity and complexity of exercise can be appropriately increased, such as jogging, cycling, and other exercises. At the same time, exercise therapy also focuses on combining rehabilitation training, such as joint mobility training, balance training, etc., to improve patients' joint function and self-care ability.

2) Physical therapy

Physical therapy is an important part of comprehensive treatment of osteoarthritis, including hot compress, cold compress, massage, acupuncture and moxibustion, physiotherapy and other methods. Hot compress uses heat transfer to dilate local blood vessels, promote blood circulation, relieve muscle spasms and pain. Common hot compress methods include hot towel wet compress, hot water bag hot compress, infrared irradiation, etc. Cold compress is the use of low temperature to constrict local blood vessels, reduce inflammation, swelling, and pain. It is commonly used in the treatment of acute attacks or sports injuries, such as ice packs and cold therapy patches. Massage and acupuncture and moxibustion are traditional physical treatment methods of traditional Chinese medicine. Massage stimulates the muscles, tendons and acupoints around the joints through manipulation to promote the movement of qi and blood, relieve pain and muscle tension; Acupuncture and moxibustion is to regulate the function of qi and blood in human meridians through acupuncture points, so as to relieve pain, reduce swelling and improve joint function. Physiotherapy, such as ultrasound, electrotherapy, magnetic therapy, etc., uses different forms of physical energy to act on joint tissues, improve tissue metabolism, promote inflammation absorption, and tissue repair. In recent years, a new type of physical therapy method, shock wave therapy, has gradually been applied in clinical practice [1] [6]. Shock wave is a mechanical pulse wave that is transmitted through a physical mechanism medium (air or liquid). It can stimulate the cell activity of tissues such as bones, muscles, and tendons, promote angiogenesis and cell proliferation, thereby relieving pain and promoting tissue repair. It has a good therapeutic effect on early to mid stage osteoarthritis.

3) Weight management

Obesity is one of the important risk factors for the occurrence and development of osteoarthritis. Research has shown that for every 1 kg increase in weight, the risk of knee osteoarthritis increases by approximately 50%. Overweight can cause additional pressure on joints, especially weight-bearing joints such as knee and hip joints, accelerating the wear and degeneration of joint cartilage. Therefore, weight management is crucial for the prevention and treatment of osteoarthritis. The way of weight management is no longer limited to simple dietary control, but adopts comprehensive measures, including reasonable dietary structure adjustment, appropriate exercise, behavioral intervention, and nutritional counseling. In terms of diet, it is advocated for patients to reduce their intake of high calorie, high-fat, and high sugar foods, and increase the proportion of foods rich in dietary fiber and nutrients such as vegetables, fruits, and whole grains [7]. Exercise combines aerobic exercise and strength training to help patients burn excess calories, increase muscle mass, and improve basal metabolic rate. At the same time, through behavioral interventions such as setting reasonable weight goals, recording diet and exercise, cultivating good lifestyle habits, etc., help patients maintain long-term weight management effectiveness. Nutritional counseling provides personalized nutritional advice to patients, supplementing vitamins, minerals, and other nutrients according to their physical condition and nutritional needs, in order to promote physical health and joint function recovery.

4) Auxiliary equipment

The use of assistive devices is one of the important means to reduce joint load and improve joint function. Common assistive devices include canes, walkers, knee braces, knee pads, etc. [8]. Crutches and walking aids can help patients share some of their weight, reduce joint burden, alleviate pain, and improve walking ability [9]. For patients with knee osteoarthritis, wearing knee braces or knee pads can provide additional support and stability, limit abnormal joint movement, reduce joint pressure, and improve the joint's mechanical environment. In recent years, with the continuous advancement of technology, new intelligent assistive devices have emerged. These intelligent assistive devices are equipped with advanced technologies such as sensors and microprocessors, which can monitor joint activity data in real time, such as joint angle, motion speed, force situation, etc., and provide personalized rehabilitation advice and treatment plans for patients through data analysis. For example, some smart knee braces can automatically adjust the support force based on the patient's movement status, providing more precise protection and support for the joint.

3.2. Drug Therapy

1) Non steroidal anti-inflammatory drugs (NSAIDs)

Non steroidal anti-inflammatory drugs are commonly used painkillers in the treatment of osteoarthritis, and their mechanism of action is mainly to inhibit the activity of cyclooxygenase (COX) and reduce the synthesis of prostaglandins, thereby exerting anti-inflammatory and analgesic effects [10]. NSAIDs can be classified into non selective COX inhibitors and selective COX-2 inhibitors based on their selectivity towards COX isoenzymes [11]. Traditional non selective NSAIDs such as aspirin, ibuprofen, naproxen, etc., although having good anti-inflammatory and analgesic effects, also inhibit COX-1 in tissues such as the gastrointestinal tract and kidneys, leading to an increased risk of gastrointestinal adverse reactions (such as stomach pain, nausea, vomiting, ulcers, bleeding, etc.) and cardiovascular adverse reactions (such as hypertension, heart attack, stroke, etc.) [2] [12]. In order to improve the safety of NSAIDs, new selective COX-2 inhibitors have emerged, such as celecoxib and etoposide. These drugs have a strong selective inhibitory effect on COX-2 and a relatively small impact on COX-1, thereby reducing the incidence of gastrointestinal adverse reactions to a certain extent [13] [14]. However, there are still potential cardiovascular risks associated with long-term use of selective COX-2 inhibitors, so it is necessary to strictly control the indications and dosage of medication in clinical applications, and closely monitor adverse reactions in patients.

2) Corticosteroids

Corticosteroids have strong anti-inflammatory effects, which can reduce capillary permeability, inhibit leukocyte chemotaxis and phagocytosis, reduce the release of inflammatory mediators, and thus alleviate joint inflammation and pain [15]. Intraarticular injection of glucocorticoids is a commonly used method for treating osteoarthritis, which can directly deliver drugs to the affected area, quickly exerting anti-inflammatory and analgesic effects, especially suitable for patients in acute exacerbation or other treatment methods with poor efficacy [16] [17]. However, frequent and long-term intra-articular injections of glucocorticoids may lead to adverse reactions such as cartilage damage, osteoporosis, and infection. Therefore, currently clinical practice pays more attention to the application of precision injection technology, ensuring accurate injection of drugs into the joint cavity through ultrasound guidance or X-ray fluoroscopy, while strictly controlling the dosage and injection frequency to reduce the occurrence of adverse reactions.

3) Antirheumatic drugs (DMARDs) to improve the condition

Glucosamine sulfate, chondroitin sulfate, and other commonly used anti rheumatic drugs to improve the condition [18] play an important role in the treatment of osteoarthritis. Glucosamine sulfate is a natural amino monosaccharide that is an essential component for the synthesis of proteoglycans in the cartilage matrix of joints. It can promote the synthesis of proteoglycans and collagen fibers by chondrocytes, increase the content of cartilage matrix, and inhibit the activity of cartilage degrading enzymes such as matrix metalloproteinases, thereby protecting joint cartilage and delaying the progression of osteoarthritis. Chondroitin sulfate is an acidic mucopolysaccharide that can bind with collagen to form a stable cartilage structure, while also having anti-inflammatory and inhibitory effects on cartilage degradation [19]. Research has found that the combined use of glucosamine sulfate and chondroitin sulfate may have better therapeutic effects [20], and can more effectively improve symptoms such as joint pain, swelling, and functional impairment. In addition, some new DMARDs such as diacerein are gradually being applied in clinical practice. Diacerein is an interleukin-1 (IL-1) inhibitor that reduces joint inflammation and cartilage damage by inhibiting the activity of IL-1, and has good therapeutic effects on early to mid stage osteoarthritis.

4) Biological agents

In recent years, biologics have made significant progress in the treatment of osteoarthritis, bringing new hope for the treatment of osteoarthritis. Biological agents are a class of drugs prepared using biotechnology, mainly including cytokine antagonists, monoclonal antibodies, etc. [21]. In the treatment of osteoarthritis, commonly used biologics include interleukin-1 (IL-1) antagonists, tumor necrosis factor alpha (TNF-α) inhibitors, etc. IL-1 and TNF-α are important cytokines involved in the inflammatory response of osteoarthritis, which can promote the infiltration of inflammatory cells, apoptosis of chondrocytes, and expression of matrix metalloproteinases, leading to the destruction of articular cartilage and exacerbation of inflammation. IL-1 antagonists and TNF-α inhibitors specifically bind and block the biological activity of IL-1 and TNF-α, thereby reducing joint inflammation, inhibiting cartilage degradation, and protecting joint function. However, biologics are expensive and may cause adverse reactions such as immunosuppression, infection, and allergies. Therefore, in clinical applications, it is necessary to strictly screen patients and closely monitor the occurrence of adverse reactions.

5) Traditional Chinese Medicine Treatment

Traditional Chinese medicine classifies osteoarthritis as "bone obstruction" and "obstruction syndrome", and believes that its onset is related to factors such as liver and kidney deficiency, insufficient qi and blood, invasion of wind cold dampness, and blood stasis. Traditional Chinese medicine has unique advantages in treating osteoarthritis, including oral and external use of traditional Chinese medicine, acupuncture and moxibustion, massage and other treatments [22]. Traditional Chinese medicine is administered orally through syndrome differentiation and treatment. Based on the patient's specific symptoms, signs, tongue and pulse information, personalized prescriptions are formulated for regulation. Common treatment methods include nourishing the liver and kidneys, dispelling wind and dampness, promoting blood circulation and removing blood stasis, unblocking collaterals and relieving pain, etc. For example, Duhuo Parasitic Decoction is a classic formula for treating liver and kidney deficiency, wind cold dampness type osteoarthritis, with the effects of tonifying the liver and kidney, nourishing qi and blood, dispelling wind dampness, and relieving rheumatism and pain. For external use of traditional Chinese medicine, the drug is directly applied to the affected area and exerts its efficacy through skin penetration. Commonly used dosage forms include plasters, ointments, and fumigants. Such as pain relieving plaster, Yunnan white ointment, etc., have the effects of promoting blood circulation, removing blood stasis, reducing swelling and relieving pain; Traditional Chinese medicine fumigation detergent promotes local blood circulation, relieves pain and muscle spasms through the warm and medicinal effects of hot steam. As traditional Chinese medicine therapies, acupuncture and moxibustion and massage are also widely used in the treatment of osteoarthritis. Acupuncture and moxibustion can regulate the movement of qi and blood in meridians through acupuncture at specific points, so as to relieve pain, reduce swelling and improve joint function; Tuina involves massaging the muscles, tendons, and acupoints around the joints using manual techniques to release adhesions, relieve pain, and improve joint mobility. Modern research has shown that the mechanism of action of traditional Chinese medicine in treating osteoarthritis may be related to various factors such as regulating immune function, antioxidant stress, inhibiting the expression of inflammatory factors, promoting chondrocyte proliferation and matrix synthesis.

3.3. Surgical Treatment

1) Arthroscopic surgery

Arthroscopic surgery is a minimally invasive procedure suitable for patients with early to mid stage osteoarthritis. It directly observes and operates the joint cavity by establishing small incisions around the joint, inserting arthroscopes and surgical instruments [23]. Under arthroscopy, diseased tissues within the joint can be cleaned, such as removing free bodies, hypertrophic synovium, damaged meniscus, etc., thereby reducing joint pain and improving joint function. In addition, arthroscopic surgery can also be combined with some cartilage repair techniques, such as microfracture surgery, autologous chondrocyte transplantation, etc., to repair and reconstruct damaged joint cartilage. Micro fracture surgery involves drilling holes in the subchondral bone to stimulate the release of bone marrow mesenchymal stem cells, promote fibrocartilage formation, and repair cartilage defects; Autologous chondrocyte transplantation involves culturing and expanding the patient's own chondrocytes *in vitro*, and then transplanting them into the cartilage defect site to achieve cartilage repair. With the continuous development of arthroscopy technology, surgical instruments and equipment are becoming increasingly advanced, surgical operations are more precise and minimally invasive, postoperative recovery time is significantly shortened, and patients can recover joint function and daily life faster.

2) Osteotomy

Osteotomy is an effective treatment for patients with osteoarthritis who have abnormal lower limb force lines. Common osteotomy techniques include high tibial osteotomy, femoral condyle osteotomy, etc. [3] [24]. Expected outcomes of medial compartment osteoarthritis treated with proximal tibial wedge osteotomy in young and middle-aged adults [4] [6]. High tibial osteotomy is mainly used to correct varus or valgus deformities of the knee joint. By changing the force line of the tibia, the load on the knee joint is transferred from the more severely affected side to the relatively normal side, thereby reducing the pressure on the joint compartment and delaying the process of joint degeneration [5] [25]. Femoral condyle osteotomy is mainly used to treat knee osteoarthritis caused by femoral deformity. Traditional osteotomy mainly relies on the experience of the surgeon and X-ray fluoroscopy for operation, which has certain errors. In recent years, with the development of computer-aided navigation technology, the accuracy of osteotomy has been significantly improved. The computer-aided navigation system performs CT or MRI scans on patients before surgery, establishes a three-dimensional model, and then tracks the position and direction of surgical instruments in real time during the surgery, guiding doctors to perform precise bone cutting operations, ensuring that the angle and position of the bone cutting conform to preoperative planning, thereby improving surgical effectiveness and reducing the occurrence of complications.

3) Joint replacement surgery

Joint replacement surgery is the ultimate treatment for advanced osteoarthritis and one of the most effective treatment methods currently available [6] [26]. It mainly includes total knee arthroplasty, total hip arthroplasty, etc. Joint replacement surgery involves removing the affected joint surface and implanting artificial joint prostheses to restore the normal shape and function of the joint. After years of development and improvement, artificial joint prostheses have become more rational in material properties and design, and their service life has been continuously extended. Joint replacement surgery can significantly improve patients' symptoms such as joint pain and functional impairment, and enhance their quality of life. In recent years, the surgical techniques for joint replacement have been continuously improved, and minimally invasive surgical approaches have gradually been applied, such as the minimally invasive small incision technique for knee joint replacement and the direct anterior approach technique for hip joint replacement [7] [27]. These minimally invasive surgical approaches have the advantages of minimal trauma, less bleeding, and faster postoperative recovery, which can reduce patients' pain and hospitalization time. At the same time, the application of rapid rehabilitation concept in joint replacement surgery is becoming increasingly widespread. Through a series of measures such as preoperative optimization of patients' physical condition, intraoperative fine operation, and early postoperative rehabilitation exercise, the rehabilitation process of patients is accelerated and patient satisfaction is improved.

3.4. Emerging Treatment Methods

1) Stem cell therapy

Stem cell therapy has become one of the research hotspots in the field of osteoarthritis treatment in recent years. Stem cells have the potential for self-renewal and multi-directional differentiation, and can differentiate into various cell types such as chondrocytes, osteoblasts, and adipocytes, providing a new pathway for the repair and regeneration of articular cartilage. At present, the most extensively studied type of stem cells in the treatment of osteoarthritis is mesenchymal stem cells (MSCs) [28] [29]. MSCs have a wide range of sources and can be obtained from tissues such as bone marrow, fat, and umbilical cord. They have various biological functions such as immune regulation, anti-inflammatory, and promoting tissue repair. The application of MSCs in the treatment of osteoarthritis through intra-articular injection and other methods has shown certain therapeutic effects in clinical trials. MSCs can differentiate into chondrocytes under the induction of the joint microenvironment, secrete extracellular matrix, and repair damaged joint cartilage; Meanwhile, MSCs can also regulate immune responses, inhibit the activation of inflammatory cells and the release of inflammatory factors, alleviate joint inflammation, and promote joint tissue repair and regeneration by secreting various cytokines and growth factors. However, stem cell therapy still faces some issues, such as the source of stem cells, isolation and culture techniques, optimal transplantation dose and timing, long-term safety, etc., which require further in-depth research and exploration.

A: After stem cell therapy (side view), B: Before and after view (AP) after stem cell therapy, C: Before and after (AP) view of stem cell therapy.

2) Gene therapy

Gene therapy is an emerging treatment method that aims to treat osteoarthritis by introducing target genes into joint tissue cells and regulating their biological behavior. At present, research on gene therapy for osteoarthritis mainly focuses on the following aspects: firstly, introducing genes that promote the synthesis of matrix by chondrocytes, such as insulin-like growth factor-1 (IGF-1) gene, transforming growth factor-β (TGF-β) gene, etc., to enhance the synthesis and metabolism ability of chondrocytes and promote the synthesis of cartilage matrix; The second is to introduce genes that inhibit the expression of inflammatory factors, such as the IL-1 receptor antagonist (IL-1Ra) gene, TNF-α soluble receptor gene, etc., to suppress the inflammatory response and reduce the damage to joint cartilage; The third is to introduce genes that regulate cell apoptosis, inhibit chondrocyte apoptosis, and maintain the quantity and function of chondrocytes [30]-[32]. Although gene therapy has broad application prospects, it is still in the clinical trial stage and faces many technical challenges, such as vector selection, efficient gene transfection, regulation of gene expression, and evaluation of safety and efficacy. In addition, the high cost of gene therapy also limits its clinical promotion and application.

3) Treatment with platelet rich plasma (PRP)

Platelet rich plasma (PRP) is a platelet rich concentrate extracted from autologous whole blood by centrifugation [33]. PRP contains various growth factors, such as platelet-derived growth factor (PDGF), transforming growth factor-β (TGF-β), insulin-like growth factor-1 (IGF-1), etc. These growth factors can promote cell proliferation, differentiation, and tissue repair. The mechanism of intra-articular injection of PRP for the treatment of osteoarthritis mainly includes: promoting the proliferation of chondrocytes and matrix synthesis, repairing damaged articular cartilage; Inhibit the activation of inflammatory cells and the release of inflammatory factors, alleviate joint inflammation; Promote angiogenesis and provide sufficient nutritional supply for joint tissue repair. Clinical studies have shown that PRP treatment for osteoarthritis has certain effects in reducing joint pain and improving joint function, and is relatively safe [34]-[36]. However, the influence of factors such as preparation method, platelet concentration, injection frequency, and dosage on the therapeutic effect of PRP is still controversial, and further research is needed to optimize the treatment plan.

4. Conclusion

In summary, significant progress has been made in the treatment of osteoarthritis, ranging from traditional non-pharmacological, pharmacological, and surgical treatments to emerging stem cell therapy, gene therapy, and more. Multiple treatment methods provide osteoarthritis patients with more choices. In clinical treatment, various treatment methods should be comprehensively applied according to the specific situation of the patient, and personalized treatment plans should be formulated to achieve the best treatment effect.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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