A Comprehensive Review of Osteoarthritis: Current Understanding, Pathophysiology, Diagnosis, and Management

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ABSTRACT

Osteoarthritis (OA) is a painful condition affecting bones and joints, characterised by abnormal changes and symptoms in the joint tissues. It primarily focuses on cartilage damage over time, causing swelling, tenderness, or stiffness in the joints. It is perhaps the biggest contributor to tormenting and afflicting patients suffering from joint disability. It is expected that the incidence of OA will steadily increase due to aging population and an increasing incidence of obesity. In recent years, there has been notable positive progress in the treatment of OA due to an improved understanding of its pathogenesis and mechanisms of diagnosis and treatment. At this period, the diagnosis mainly relies on the physician's experience and judgment, combined with precise differential diagnosis of other forms of arthropathy. Self-care and exercise regimen customization form the basis of OA treatment and must be taught to the patient. These are usually done together with a myriad of pharmacological care, mainly directed towards analgesia. In extreme cases, prosthetic surgery becomes necessary as the last option and is always accompanied by short-lived effectiveness, along with many adverse effects. To enhance the care of patients with OA, it is necessary to evaluate the modulation or substitution of traditional pharmacologic therapies with natural drugs and extracts. Such compounds have a much greater safety profile and act on perturbed pathways involved in the pathophysiology of OA, creating an integrative approach to this multifactorial disease.

Keywords: Osteoarthritis; Pathophysiology, Diagnosis; Non-Pharmacological approaches; Pharmacological approaches

INTRODUCTION

Osteoarthritis (OA) is a chronic, disabling disorder that affects millions of people globally[1]. It is the leading cause of disability and the most prevalent form of arthritis in various countries[2]. OA is largely defined by its characteristics, which include the severity of articular cartilage breakdown, subchondral bone remodeling, synovitis, and altered extracellular matrix within the joint[3]. Weight-bearing joints primarily affected by this disease exhibit stiffness, functional impairment, pain, and a poor overall quality of life. Populations above a certain age are highly susceptible to OA, making it a critical healthcare concern today[3]. OA also imposes a significant economic burden on society due to direct costs associated with medical care, such as hospitalization, drug therapy, and healthcare support, as well as indirect costs such as reduced productivity due to long-term disability[1]. According to the World Health Organization, the number of people with osteoarthritis is expected to exceed 300 million as a result of increasing obesity, declining life expectancy, and an aging population, with no signs of stabilization over the next few decades. Healthcare costs are rising due to the burden of osteoporosis, as well as other comorbidities such as diabetes, depression, and cardiovascular disease. As a result, OA places a significant burden on healthcare systems globally, highlighting the urgent need for effective treatments and preventive approaches[4,5].

The name "OA" comes from the Greek words "*ostheo-*," meaning "bone," and "-arthritis," a compound of the words "*arthr-*" and "-itis," meaning "joint" and "inflammation," respectively[6]. Osteoarthritis is a broad group of diseases affecting biarticular joints. They share similar biological characteristics and clinical manifestations, making them one of the most common and disabling medical conditions in adults. Due to their unique structural composition, the body's articular cartilage acts as a pressure absorber at the ends of bones within a joint. It consists of an extracellular matrix (ECM) mostly consisting of collagen and proteoglycans, as well as chondrocytes, which are cells that generate and sustain the turnover of the cartilaginous matrix[7]. This mixture gives the cartilage a high-water content, which gives it resilience and mechanical resistance. However, the cartilage's ability to properly regenerate following damage or gradual natural degradation is limited by the tissue's poor vascularization and the chondrocytes' notably low metabolic activity[8].

For a long time, osteoarthrosis (OA) was known as "osteoarthrosis," with the Greek word "-osis" signifying a degenerative process devoid of inflammation, because it was thought to be mostly a wear-and-tear process of the joint cartilage. However, it has been clear since the 1980s that the pathogenic process involves an inflammatory component. As a result, the disease's name has been changed to reflect this new knowledge[9]. According to the factors linked to its onset, there are currently two primary or idiopathic kinds of OA and secondary. Age, sex, ethnicity, and genetics are the main causes of primary OA[10]. Approximately 73% of patients over 55 have OA, and around 60% of them are women, according to the WHO, which states that it usually occurs in the late 40s and mid-50s[10]. This is clarified by the natural aging process, which leads to a reduction in synovial fluid and alterations to its contents and quality.

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Furthermore, as individuals age, their bodies experience substantial traumatic stress and wear, which activates inflammatory processes that modify cartilage and bone and result in osteophytes[8]. Hormonal factors are thought to be the main reason for the greater incidence of OA in ladies. Hormonal variations during menstrual cycles and, most significantly, postmenopausal changes are among these factors[11]. Estrogens are essential for promoting bone metabolism, reducing inflammation, and protecting cartilage[12,13]. Furthermore, pregnancy weakens joints, especially those in the spine and lower body, due to the weight gain and protracted hormonal changes that accompany it[9]. Women often have a greater quadriceps angle, a lower arch height index, and a wider range of internal and external rotation in the hip joint. These sex variations also extend to joint alignment. Over time, these variables cause the knee and hip joints to experience sustained stress[9]. On the other hand, secondary types of OA might be linked to causes that can erode the joint's structure[12]. These include articulation-level trauma, sports or physically demanding occupations, obesity or overweight, metabolic disorders like diabetes or gout, joint malalignment, congenital deformities, body length, bone inequality, and decreased structural support because of weak ligaments or surrounding muscle tissue[6].

It may be promising to tailor future treatment strategies for each patient by choosing the right treatments for certain disease time points and patient subgroups. Finding new targets and developing treatments that will improve the quality of life and restore the ability to work of OA patients requires figuring out the biochemical and biomechanical processes and mechanisms underlying the crosstalk between the various joint tissues. The importance of new methods, natural-type materials, nutraceuticals, and different types of herbal extracts have been acknowledged within the past years. These compounds, as described, have been demonstrated to work via complementary actions to conventional medications, which may enable greater precision in the targeting of pathophysiological processes of osteoporosis and its treatment[14].

To provide a comprehensive understanding of the disease, this review describes the range of treatments available and used to treat osteoarthritis and the mechanisms underlying the structural and mechanical changes in joint tissues that lead to osteoarthritis.

PATHOPHYSIOLOGY

Osteoarthritis is an intricate disorder of the muscles and skeleton, marked by inflammation of synovial tissue, reduction in the joint space, changes in the underlying bone, and the gradual decline of the cartilage which covers the joints. Mechanical pressure, family history, and inflammation are some of the causes that can lead to the onset of OA[15]. In addition, the progression of osteoarthritis is influenced by changes due to aging, sex, and immune system factors. However, a clear pathogenesis remains difficult to understand for all cases[15]. Genetic analyses have shown that multiple risk alleles are spread across the genome, confirming the polygenic nature of osteoporosis[15]. Histone changes and DNA methylation affect tissue integrity and gene expression[16]. These changes have several variables that include inflammatory mediators (IL-1b, IL-8) and stress-causing factors attributed to reactive oxygen species[16]. Additionally, by disturbing the balance between catabolic and anabolic processes in articular cartilage, genetic modifications occur in principal pathways such as the TGF-β family[17]. Increased production of matrix metalloproteinase, disintegrin, and metalloproteinase with thrombospondin patterns results from these reactions, which involve elevation of inflammatory mediators and destruction of the extracellular matrix of cartilage[16]. People may also be at risk for the disease due to mechanical causes such as joint instability, trauma, and abnormal joint alignment[18]. The association between systemic weakness and local biomechanical variables leads to the development of OA[18]. When the biomechanical loads exceed the osteochondral structure's natural resistance, cartilage loss and degradation progress[19]. According to biomechanics, injury to bone and cartilage reduces their capacity to support aberrant stresses, which results in more serious structural damage[19]. Joint load distribution is changed by fractures and joint misalignments, such as varus and valgus deformities, which cause incongruent joint lines and mechanical axis deviation[20]. In addition to meniscal protrusions increasing local loading, meniscal injuries cause aberrant load transfer, raising peak loads on joint cartilage and hastening the course of osteoarthritis in the knee[21]. Joint instability brought on by weak muscles and loose ligaments increases shear stresses on joint surfaces, causing cartilage degradation and the advancement of osteoarthritis[22]. In OA, inflammation plays a crucial role, and synovitis is becoming increasingly well-acknowledged as a crucial characteristic. The pathophysiology of OA is significantly influenced by inflammatory cytokines, particularly IL-1b, which are released in greater amounts from synovial fibroblasts in afflicted individuals[23]. TNF-a and IL-6 levels rise as a result of this increase, which also helps to create an inflammatory pattern[23]. The inflammatory condition often causes a proinflammatory state, which can rapidly progress to systemic inflammation, in addition to its local effects. With the advancement of the disease, subchondral bone and articular cartilage undergo deformation, and the tissues that are meant to heal get further damaged due to destructive activities[24,25]. Moreover, OA is said to have some correlation with the innate and adaptive immune systems, and it seems that immune cells of the system, like lymphocytes, may have some responsibility for the illness progression. Albeit, precisely how is still vague[26].

One more investigative work pointed out the contribution of oxidative stress (OS) in OA pathogenesis. The triggering of oxidative stress-induced processes like inflammation, extracellular matrix degradation, and cartilage cell death is some of the better-understood consequences of the pathological level of imbalance between reactive oxygen species (ROS) and antioxidant output known as oxidative stress[27]. Furthermore, the level of OS and cellular dysfunction in OA may be elevated owing to the degenerative activity of mitochondria in the cartilage cells. Complications within the constellation of OA epitomize the multitude of processes emerging from changes at molecular, cellular, and tissue levels[5]. The highlighted results provide multiple options for new therapeutic strategies, especially for designing gene therapies and biological medications that would aim to alter these disease processes. Still, more investigation is needed to fully understand the pathways which stem OA and to focus these findings on more effective disease-modifying treatments[28].

SYMPTOMS

The most common symptom among people with osteoarthritis is pain. According to 2008 research by Hawker and colleagues, people with OA often report two types of pain: periodic, acute pain and persistent, background agonizing pain[29]. It is also observed that OA pain gradually and subtly worsens with time. Early in the course, certain (often high-impact) activities are the cause of the expected discomfort. As time passes, joint pain and other symptoms grow more consistent and less predictable, starting to interfere with day-to-day activities. Advanced stages include unexpected, severe, and ongoing dull and agonizing discomfort that causes people to avoid specific activities[7,29]. A comprehensive list of patient-reported symptoms and their frequency is listed. It is important to remember that the level of pain and the structural pathology seen on MRI do not necessarily match the symptoms of OA. On imaging, some people with excruciating

pain show few results, and vice versa. A person's sense of pain may be influenced by several elements, including past pain experiences, expectations for treatment, psychological aspects, and the sociocultural context[30]. Joint swelling, clicking, locking, grating, crepitus, cramping, decreased range of motion, and deformity are other nonpain signs of osteoarthritis. Symptoms of instability, buckling, or "giving way" are also mentioned. Morning stiffness that goes away in half an hour is a complaint of OA patients. In contrast, rheumatoid arthritis usually lasts longer. Additionally, OA pain gets worse as the day goes on and as one's level of activity increases[19]. The absence of systemic signs is expected. Fever, weight loss, or abnormal blood tests are examples of this. Such symptoms would notify the doctor of further illness processes, such as infection or cancer[19]. It has been observed that OA symptoms cause people to lose their independence and become less able to engage in the activities they like[31]. 81.5% of patients with OA reported limitations in their activities of daily living, according to an extensive study of 10,000 patients[32]. Of these, 61.1% reported limited mobility outside the home, and 12.8% reported limited mobility within the home (compared with 10.2% and 2.8% in the general population, respectively). Additionally, OA patients reported far greater disability in dressing, housekeeping, and food shopping than the general population. Sports and gardening were among the leisure pursuits that were greatly impacted. In comparison to a control group, those with OA also missed more work[33]. Overall, OA substantially impacts quality of life (QOL) across several dimensions. There is undoubtedly a lower quality of life in terms of physical functioning, but there have also been reported negative impacts on mental health.

TREATMENT OF OSTEOARTHRITIS

OA management entails a thorough strategy catered to the requirements of each patient and the severity of their ailment. Although there isn't a cure for OA at this time, therapy mostly aims to reduce modifiable risk factors before the disease manifests and ease its symptoms once it does. One of the most effective ways to reduce the risk of developing OA in the lower limbs and spine joints is to take proactive steps, such as losing weight or changing postural or orthopaedic abnormalities[34]. When OA appears, weight loss is also the initial line of therapy, particularly for knee-related disorders[31]. However, patients frequently need a pharmaceutical strategy to improve their quality of life during the acute pain phases of OA[35]. Managing symptoms effectively becomes crucial, signaling a change to focused therapies meant to reduce discomfort and enhance general wellbeing[36]. Given the degenerative nature of OA and its significant impact on a patient's quality of life, managing this condition requires a comprehensive strategy. While rehabilitation and physical therapy are important, they may not always be sufficient to alleviate the disabling pain associated with OA. Therefore, it becomes necessary to combine pharmacological treatments such as analgesics and nonsteroidal anti-inflammatory drugs (NSAIDs)[37,38]. Furthermore, it is essential to address the psychological effects of osteoarthritis-related pain, given its chronic and potentially excruciating nature. Along with physicians and physical therapists, collaboration with medical professionals, such as psychologists, can provide patients with valuable support in managing pain and any associated depressive symptoms[39].

Non-Pharmacological approaches

A range of non-pharmacological methods are used to treat osteoarthritis (OA) to relieve pain, improve joint function, and improve overall quality of life without the use of medication. A more detailed review of non-pharmacological OA treatments can be found here:

Exercise and Physical Activity

One of the most important components of osteoporosis management is following exercise programs specifically designed to meet each person's needs and abilities. Walking, swimming, and cycling are examples of low-impact exercises that help build stronger muscles around affected joints, increase flexibility, and reduce stiffness. Exercise also encourages weight loss, which relieves stress on weight-bearing joints and reduces discomfort[40].

Physiotherapy

Targeted exercises, stretching, and manual therapies are used in physical therapy to increase joint function, strength, and mobility. Physical therapists collaborate closely with patients to develop individualized treatment programs that target specific areas of weakness or restriction[41]. To relieve pain and stimulate healing, therapeutic modalities, including electrical stimulation, ultrasound, heat, and cold, may also be applied[41].

Occupational Therapy

To reduce joint stress and increase independence, occupational therapists help people with osteoarthritis modify their daily activities. To lessen joint stress during activities like dressing, cooking, and grooming, they could suggest assistive technology like braces, splints, or ergonomic gadgets[42]. For people with OA, occupational therapy seeks to maximize functional capacities and improve quality of life.

Weight management

Since excess weight puts additional strain on weight-bearing joints, maintaining a healthy weight is crucial for treating the symptoms of osteoarthritis. In addition to lowering pain and enhancing joint function, nutrition counselling, dietary adjustments, and lifestyle modifications can assist people in reaching and maintaining a healthy weight[40].

Joint Protection Strategies

To lessen the load on afflicted joints, joint protection strategies include altering movement patterns and utilizing assistive technology. Pain can be reduced and more joint injury can be avoided by employing strategies including timing activities, avoiding repeated motions, and wearing supportive footwear[40].

Pharmacological approaches

Nonsteroidal Anti-Inflammatory Drugs

The second-line therapy for OA includes analgesics and NSAIDs. These substances work by preventing the production of prostanoids from arachidonic acid by blocking prostaglandin-endoperoxide synthase, sometimes referred to as cyclooxygenases (COXs), which are oxidoreductases[43]. Among the many COX isoforms, oxidative stress and inflammatory cytokines like IL-1b and TNF-a are intimately linked to the inducible production of COX-2[44]. These findings are supported by several investigations that have shown that the cartilage of people with OA has higher levels of these inflammatory mediators, pro-inflammatory nitric oxide (NO), and COX-2[45]. These findings highlight the relationship that exists between oxidative stress, inflammatory processes, and clinical disorders. However, there are a number of disadvantages to using NSAIDs since they limit the production of prostaglandins. The stomach mucosa is impacted by non-selective COX inhibitors, which target both COX-1 and COX-2 isoforms. Notably, COX-1 has a critical role in preventing stomach bleeding and ulcers[46]. COX-2-specific inhibitors, on the other hand, are associated with a higher risk of thrombosis since they are made to spare isoform 1 activity[46]. Although both COX-1 and COX-2 aid in the body's production of prostaglandins, COX-2 is the main source of prostacyclins, which are involved in vasodilation and inflammation[47]. In the meantime, COX-1 has a strong vasoconstrictive impact by catalyzing the production of thromboxanes[48]. Therefore, the balance

is shifted in favor of enhanced vasoconstriction and prothrombotic activity when COX-2 is inhibited[49]. Using NSAIDs in cream or gel form is the preferable method of treating OA, particularly in older adults. These topicals have similar pharmacological action to oral equivalents, although perhaps having a slower rate of absorption[49]. The primary worldwide recommendations for the treatment of OA in the hands and knees advocate their usage due to their improved safety profile. For those with knee OA who are 75 years of age or older, the American College of Rheumatology strongly recommends topical administration of NSAIDs rather than oral ingestion. For those with concomitant diseases and increased risk of cardiovascular, gastrointestinal, or renal side effects, which are frequently seen in this age range, this guideline is especially important[50].

Steroidal Anti-Inflammatory Drugs

Corticosteroids are among the most potent substances that can reduce inflammatory reactions in the human body. This family of medications, which is derived from cortisones, works by interacting with the transcription factors of many genes to downregulate their expression[51]. Long-term use of corticosteroids, however, is linked to serious adverse effects, such as weight gain, edema, diabetes, hypertension, and an increased risk of infection[52]. Inadequate information on the enteral usage of this class of compounds in OA settings can be found in the literature. Although time-limited, the few studies that are now available have demonstrated only modest improvements in pain alleviation for both hand and knee OA[53]. Directly injecting corticosteroid medication into the afflicted region is another treatment approach. In 1951, Hollander and associates conducted groundbreaking research on rheumatoid arthritis of the knee, and seven years later, Miller and associates repeated the procedure for OA patients[6]. Since then, injections have been used to treat other OA-affected joints, and research into this type of treatment is still ongoing[54]. Given that the most recent data suggests a comparatively brief duration, ranging from a few weeks to months, these studies seek to evaluate the duration of the anti-inflammatory and analgesic effects of corticosteroids, which calls for careful consideration when choosing the best course of treatment[54]. There are still several disadvantages to the process even if local corticosteroid administration maintains the drug's effects primarily restricted to the joint while also lowering systemic adverse effects. Infections can occur after the operation, albeit they are currently extremely uncommon; also, some research has linked the therapy to local adverse effects such as cartilage loss, necrosis, and weakening of the tendons[55]. However, even though they are uncommon, some systemic reactions to the medication can be seen, such as iatrogenic Cushing syndrome, headache, sleeplessness, short-term elevation of blood sugar, and suppression of the hypothalamic-pituitary-adrenal axis[56]. While other societies, such as the American Academy of Orthopedic Surgeons, take a more cautious stance on the subject, the Osteoarthritis Research Society International, European League Against Rheumatism, and Royal Australian College of General Practitioners guidelines recommend intra-articular corticosteroid use in conjunction with physical exercise for short-term pain reduction in knee OA, conditionally and limitedly in time[57].

OA-Modifying Medications

Several potential molecular targets have been identified thanks to the understanding of the pathways involved in the onset and progression of the condition, including matrix-degrading proteases, mechanisms of altered senescence of chondrocytes, cartilage repair mechanisms, bone remodeling processes, and low-grade inflammation mediators[40]. Disease-modifying OA drugs (DMOADs) are a group of molecules capable of intervening in specific molecular mediators of these processes. In recent years, efforts have been directed toward researching novel pharmacological strategies to alleviate patients' pain and stop the progression of OA. Matrix metalloproteinases like MMP-13 protease or ADAMTS-4 and -5 peptidase, growth factors like FGF-18, bone morphogenetic protein (BMP-7), or TGF-β, cytokines, and small molecules like TNF-α or IL-1β are some of the most intriguing targets[58]. Targeting cellular senescence, a process linked to the stress response is another strategy to maintain cartilage health[59]. Oxidative stress is linked to an early aging process of joint cellular components in OA, impacting not only chondrocytes but also musculoskeletal cells, synovium fibroblasts, osteoblasts, and osteoclasts[60]. This significantly releases proinflammatory cytokines and proteases in the joint space, which causes a senescence-associated secretory phenotype (SASP)[61]. The goal of current research is to create compounds having senolytic and/or senomorphic action to pursue a pharmaceutical approach to the phenomenon. Senolytic compounds can inhibit pro-senescence or anti-apoptotic pathways, which are frequently overexpressed in disease. Their targets include pro-senescence proteins p15, p16, p21, and p53, as well as the anti-apoptotic PI3K/Akt pathway and B cell lymphoma family proteins Bcl-2, Bcl-XL, and Bcl-W[62,63]. Senomorphics, on the other hand, work by blocking cells' SASP or counteracting their biological effects; AMPK signaling, IL-6 receptors, IL-8, and IL-1β are interesting targets, which in turn prevent the synthesis of MMP-13 and ADAMTS5. There are also current preliminary investigations for senomorphic preparations that can directly block matrix-degrading enzymes[64].

Regenerative Treatments

In orthopaedic medicine, regenerative treatments are becoming more and more well-liked for treating OA and other joint diseases. Several methods has been established to assess ability to repair the osteochondral damage using bioactive materials[65,66].Among theese, platelet-rich plasma (PRP) treatments and viscosupplementation with HA are two intriguing choices. These treatments provide creative, non-invasive ways to improve joint function and reduce pain, giving patients a higher quality of life again.

Hyaluronic Acid

The use of HA as viscosupplementation, either by injection or enteral supplementation, represents a relatively new treatment technique in OA. The body spontaneously produces HA, a high molecular weight (MW) molecule with a molecular weight of 6.5 kDA to 20 MDa, which is made up of units of N-acetylglucosamine and D-glucuronic acid that alternately repeat[67]. It functions as a lubricant and antioxidant in soft connective tissue, cartilage, and synovial fluid, where it is physiologically present[67]. Furthermore, HA is an important regulator of cytokine release that affects cell migration and proliferation while lowering MMP activity[68]. Both the start and progression of OA are linked to changes in joint HA and the depolymerization that breaks it down. Lower MW forms of HA are produced as a result of this process, which alters the mechanical characteristics and composition of synovial fluid and slows cartilage regeneration. These mechanisms are mostly associated with elevated levels of RONS and hyaluronidase activity[69]. Furthermore, low-MW forms of HA seem to be proinflammatory, whereas high-MW HA protects the joint[70]. While the exogenous supply of HA cannot fully replace the endogenous one, it can still partially restore the synovial fluid's functionality, promoting matrix production and promoting an anti-inflammatory effect by inhibiting the NF-κB and MAPK signaling pathways and lowering the levels of TNF-α, IL-1β, and IL-6 in the joint[71]. Furthermore, while TNF-α stimulates the production of NO and metalloproteinase, lowering it protects the joint from OA-induced deterioration[71].

Numerous uses have been developed since the Food and Drug Administration approved the intra-articular use of HA for the treatment of knee OA in 2001[71]. While some, like Economic Aspects

of Osteoporosis and Osteoarthritis or the American College of Rheumatology (ACR), advocate using HA only in the second instance, after previous therapeutic options have failed, European League Against Rheumatism suggest considering it because of its possible longer-lasting benefits[71].

Platelet-Rich Plasma (PRP)

PRP is a concentrated autologous blend of growth factors, platelets, and bioactive substances. To take use of the regenerative qualities of platelets for medicinal purposes, it is obtained by centrifuging whole blood and then reinjected into the same donor[72]. Once activated by collagen or thrombin, it can release growth factors and cytokines like TNF-α and IL-1b, which can reduce inflammation, inhibit the NF-κB pathway, promote matrix deposition and proliferation of mesenchymal stem cells, inhibit metalloproteinase activity, and promote tissue healing[73]. Additionally, PRP has been demonstrated in both in vitro and in vivo studies to stimulate autophagy, which has a cascading impact on the enhanced chondrocytes and promotes, dose-dependently, their proliferation and destruction of the injured ones. Additionally, PRP has been demonstrated in both in vitro and in vivo investigations to stimulate autophagy, which in turn leads to an increase in the synthesis of collagen type II and proteoglycan, therefore promoting, dose-dependently, the proliferation of chondrocytes and the destruction of the injured ones[74].

A meta-analysis of 18 trials evaluating the advantages of intra-articular PRP injection to those of HA usage was published in 2020 by Belk and colleagues. They found that using PRP produced outcomes that were on par with or even better than those from HA treatments[75].

These therapies have a significant degree of heterogeneity because there are several PRP formulations now in use and there are questions regarding their pharmacodynamics. Comparing the outcomes of clinical trials becomes extremely difficult as a result. The primary worldwide recommendations oppose the therapeutic use of PRP because of these factors[74].

CONCLUSION

There are currently no effective treatments for osteoarthritis (OA), a degenerative disorder linked to the degeneration of joint cartilage. The primary issue, however, is the incapacity that results from the loss of joint function as well as the ongoing, rising pain that comes with the process. Painkillers only address the symptoms of OA and not the underlying reasons of the suffering, thus their effects are brief and limited. Over the last several decades, a number of methods have been developed to directly inject into the joint to stop the cartilage from degenerating and to alleviate pain. Additionally, the advantages seem to be restricted in this instance, and clinical trials have not yet demonstrated their usefulness and safety. Because of their advantageous qualities as antioxidants and anti-inflammatories, several natural compounds have been utilized in this situation for a very long time. Joint cartilage is destroyed by OA, a degenerative disorder linked to several causal causes. There is no known cure, and therapeutic approaches focus only on the palliative care of the illness. Since significant pain is caused by incapacity and joint loss of function, medications are frequently given. However, they have a limited and transient effect and have several negative side effects. Furthermore, with little clinical effectiveness, several additional strategies have been modified, such as injecting strengthening elements like PRP or HA. To support the evidence, establish therapeutic guidelines, and create additional therapy groups, more targeted research and trials are required in light of recent advancements.

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