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DEGENERATIVE ARTICULAR CARTILAGE DISEASE, OSTEOARTHROSIS

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ABSTRACT

Introduction: *Osteoarthrosis (OA), degenerative articular cartilage disease is a chronic inflammatory arthropathy involving joint elements (subchondral bone, synovial membrane, hyaline cartilage and others). It is due to a disorder in the regulation between degradation and synthesis of the extracellular matrix of cartilage, involving bone and synovial membrane in a biochemical process mediated by growth factors and cytokines which, in turn, intervene in the course of bone remodeling and joint destruction.*

Objective: *to detail the current information related to osteoarthrosis, description, etiology, classification, imaging classification, management and current treatments.*

Methodology: *a total of 52 articles were analyzed in this review, including review and original articles, as well as clinical cases, of which 38 bibliographies were used because the other articles were not relevant for this study. The sources of information were PubMed, Google Scholar and Cochrane; the terms used to search for information in Spanish, Portuguese and English were: arthrosis, osteoartrose, bones, osteoartrosis, articular cartilage.*

Results: *The prevalence of osteoarthrosis increases directly with age 25-35 years 0.1 % 35-65 years 30 % and over 80 years 80-100 %. An improvement of pain and sensitivity is observed with local treatment with capsaicin. Paracetamol can be considered as the basic analgesic in the treatment of most chronic osteoarticular pain in doses of 1 gram four times/day. Opioids have an analgesic effect that almost completely eliminates all kinds of pain regardless of its intensity or site of affection. Short-term and long-term parenteral corticosteroid use is effective in controlling pain and stiffness. Systemic use of corticosteroids in OA is not warranted and only intra-articular injections are advised. Diacerein decreases IL 1Beta production in cartilage as well as nitric oxide levels by antagonizing the catabolic process and stimulates the anabolic process of cartilage. Chondroitin sulfate does not present a clinically relevant effect on joint pain or joint space reduction.*

Conclusions: *osteoarthritis should be considered as a chronic, irreversible and progressive lesion. There are factors that aggravate its prognosis. Many measures are recommended to the patient and his family, especially if it is an elderly patient, in order to avoid the progression of joint damage. Surgical treatment is reserved for patients with severe pain or marked deformity, which occurs in advanced OA. Among the most frequently used procedures are: valgus osteotomy of the proximal tibia, arthroplasty, arthrodesis and amniotic membrane implantation. Bone tissue regenerative currents using tetracyclines that prevent the activation of metalloproteases, autologous chondrocyte implants, hypoxia inducible factor (HIF-1/2a), parathyroid hormone that stimulates chondrocyte multiplication and the use of in situ stem cells, cartilage regeneration and a better understanding of the developmental protein ancestor of osteogenesis, will be part of the medical management protocol, being a promising therapy for future therapy.*

KEY WORDS: *Osteoarthrosis, osteoartrose, bones, osteoartrosis, articular cartilage.*

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INTRODUCTION

With the increase in life expectancy, the incidence of degenerative bone and joint diseases has increased proportionally. Osteoarthritis can be conceptualized as a heterogeneous group of conditions leading to joint symptoms and signs that are associated with alterations in the integrity of articular cartilage, as well as changes related to the subchondral bone and joint margins. This disease usually presents with joint stiffness, pain and often shows joint effusion with varying degrees of localized inflammation(1).

Osteoarthrosis (OA), also called degenerative articular cartilage disease, is a chronic inflammatory arthropathy involving the joint elements (subchondral bone, synovial membrane, hyaline cartilage and others). It affects almost all vertebrate animals, and it is suggested that it was formed in evolution when the bony skeleton appeared. In 1909 Nichols and Richardson established two major groups of rheumatic diseases, degenerative or osteoarthrosis and the second proliferative or inflammatory rheumatism at the level of the synovial membrane whose basis is rheumatoid arthritis. The most recent evidence suggests that there are several clinical phenotypes of OA that represent different disease mechanisms(1,2).

OA is due to a disorder in the regulation between degradation and synthesis of the extracellular matrix of cartilage, which involves bone and synovial membrane in a biochemical process mediated by growth factors and cytokines that, in turn, intervene in the course of bone remodeling and joint destruction. Ancestrally it was considered as an ailment only of the cartilage, however nowadays it is known that it affects the articular organ in all its extension. It presents with progressive loss of cartilage, in addition to a new formation of subchondral trabecular bone and cartilage at the articular borders(1).

METHODOLOGY

A total of 52 articles were analyzed in this review, including review and original articles, as well as cases and clinical trials, of which 38 bibliographies were used because the information collected was not important enough to be included in this study. The sources of information were Cochrane, PubMed and Google Scholar; the terms used to search for information in Spanish, Portuguese and English were: arthrosis, osteoartrose, bones, osteoartrosis, articular cartilage.

The choice of bibliography exposes elements related to osteoarthrosis; etiology, presentation, evaluation, diagnosis, classification and management of the disease.

DEVELOPMENT

In the past, the World Health Organization (WHO) defined it as a disease resulting from mechanical and biological phenomena that destabilize the balance between the synthesis and degradation of cartilage and subchondral bone. In industrialized countries, this disease covers almost 80% of the population over 65 years of age and is the most prevalent rheumatic disease in the world and the most frequent among the adult population. It is also the most important cause of locomotor system disability in people over 60 years of age. Its prevalence increases directly with age 25-35 years 0.1% 35-65 years 30% and over 80 years 80-100%(1,3).

Usually this disease has a higher prevalence in knees, hips, cervical and lumbosacral spine and ankle respectively; however the distal interphalangeal, proximal and carpometacarpal joints are also affected. Among the most representative symptoms are pain of gradual evolution that aggravates or is triggered by activity, stiffness upon awakening and after inactivity, and inflammation of the joints. Although the etiology is not fully clarified, it is considered multifactorial with genetic, constitutional and environmental elements. Standard radiographs of symptomatic joints are used to diagnose OA and generally show marginal osteophytes, decreased joint space, increased subchondral bone density, as well as subchondral cyst formation, bone remodeling and effusion. OA is generally classified as primary or idiopathic and secondary to trauma, processes that alter the structure, endocrine and neuropathic alterations, congenital and metabolic defects, normal articular cartilage function and intense or incongruent work or sports activities and infections. Among the risk factors most implicated in the development of the disease are genetic predisposition, age, sex, obesity, previous joint injuries and mechanical factors(4-8).

In order to be clear on the subject of osteoarthritis, it is important to know the structure and function of articular cartilage, which cushions the pressure overload on the articular surfaces, in addition to preventing bone friction when joint displacement occurs.

Cartilage is formed by highly differentiated cells called chondrocytes that have low metabolic activity and survive in hypoxic conditions (<5% pO 2), surrounded by an extracellular matrix (ECM) which is responsible for the mechanical characteristics of cartilage, allowing cartilage deformation according to stress. Water, collagens, large aggregates of proteoglycans (mostly aggrecan) and other non-collagenous proteins such as binding proteins, fibronectin and cartilage oligomeric matrix protein (COMP) are the predominant components of the ECM(1,4,9,10).

Collagen accounts for 10-20%, the largest being type II, 90-95%, which provides strong tensile strength and is an indispensable component of the extracellular matrix of cartilage and is of great importance in the formation, growth and normal joint function of the endochondral bone. There is also a smaller amount of collagen types I, V, VI, IX, X and XI(1,11).

Proteoglycans (PGs) represent between 10 to 15% of the total, these are structurally complex macromolecules responsible for the compressive strength of cartilage. Proteoglycans consist of a core protein and one or more glycosaminoglycan chains linked

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by covalent bonds. Almost all mammalian cells generate proteoglycans and release them into the ECM, place them on the plasma membrane or store them in secretory granules(1,12).

Extracellular glycoproteins: such as ancorin CII, fibronectin, laminin and integrin. They have different responsibilities between the junction of the ECM and chondrocytes. Integrin interacts with cell receptors and regulates migration, proliferation and differentiation of chondrocytes(1).

In the initial stages of OA, the attempt to repair itself generates a hypertrophic reaction with increased synthesis of the cartilaginous matrix by the chondrocytes. Subsequently, there is a rapid replacement of matrix elements and a clear depletion of proteoglycans, and then a loss of the structure of the collagen network. It also causes the activation of fibroblasts, synovial membrane and macrophages producing large amounts of IL-1β (Interleukin 1 beta) and, to a lesser extent TNF-α (interferon alpha). In late stages synovial inflammation usually persists because of articular cartilage fragments, calcium pyrophosphate crystals, hydroxyapatite crystals and monosodium urate crystals released from the damaged cartilage. The subchondral bone is responsible for up to 30 percent of the shock forces, it is subjected to abnormal pressures, due to the loss of articular cartilage which causes a progressive development in the ossification or sclerosis as protection, leading to the affirmation of osteophytes in the articular margins. In the synovial membrane there is development of sinviocytes, activated B and T cells and secretion of pro-inflammatory cytokines IL 1, TNF alpha, IL 6 and 8 and proteases that increase due to chondrocyte lesion, which leads to a vicious circle maintaining degeneration in OA. Another point is that the facts originated by the increase in the production of interleukin 1-beta, amplifies the elaboration of prostaglandins E2 and nitric oxide, substances directly related to pain and inflammation. Indeed, the intensity of synovitis is related to the severity of pain in patients with OA, which is usually relieved by intra-articular corticosteroid treatment(1).

Effusion synovitis may be the consequence of another joint injury or appreciable stress on a joint or contribute to additional abnormal structural alterations(13-15).

Table 1. Biological phases, mediators responsible for joint tissue destruction in osteoarthrosis and therapeutic potentials.

Biological phases	**Mediators responsible**	**Therapeutic potentials**
Matrix degradation	MMP-1,-3,-9,-13, ADAMTs-4, -5, cathepsin K, serine proteases (Htra1) driven by cytokines (IL-1,-6,-7,-8,-17,-18 , OSM), chemokines (IL-8, GRO-α,-γ, RANTES, MCP-1) and others (S100 proteins, TGFα, matrix fragments, leukotrienes and prostaglandins).	Protease inhibitors, TIMPs, anti-cytokine therapy, TLR inhibition, MAP kinase inhibition, NFκB inhibition, lipoxygenase and cyclooxygenase inhibitors
Reduced matrix repair	↓ IGF-1, TGF-β, BMP-7 (OP-1), FGF-18 activity.	Growth factors (IA or by gene therapy)
Cell death	↓ HMGB2, ↓ autophagy, reactive oxygen and nitrogen species.	Caspase inhibitors, antioxidants, iNOS inhibitors
chondrocyte hypertrophy	RUNX2, HIF2α, WNT/β-catenin, IL-8	PTH, calcitonin
Calcification and crystals	Transglutaminase, inorganic pyrophosphate, TLR, NLRP3	Phosphocitrate, TLR and NLRP3 inhibition
Subchondral bone sclerosis	WNT/β-catenin, ↓ sclerostin (SOST), BMP, IGF-1	Wnt or BMP antagonists, retarding bone remodeling with bisphosphonates or anti-RANKL
Osteophyte formation	TGF-β, BMP-2	Since these can stabilize the joint, they probably should not be aimed directly at the joint.
Focal bone remodeling (bone marrow lesions)	RANGO, VEGF	Bisphosphonates, anti-RANKL
Synovitis	IL-1β, TNFα, IL-17, IL-15, IL-7, CCL19, MCP-1, MIP-1β, S100 proteins/alarmins.	Anti-cytokine therapy, TLR antagonism, complement inhibition

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MMP=Matrix Metalloproteinase; ADAMTS=Disintegrin A and Metalloproteinase with Thrombospondin Motifs; IL=Interleukin; OSM=Oncostatin M; GRO=Growth-Related Oncogene; RANTES=Regulated on activation, normal T cells expressed and secreted; MCP-1=monocyte chemotactic protein-1; TGF=transforming growth factor; TIMP=tissue inhibitor of metalloproteinase; TLR=Toll-like receptor; MAP=mitogen-activated protein; IGF=insulin-like growth factor; BMP=Bone Morphogenetic Protein; FGF=fibroblast growth factor; IA=Intra-articular; HMGB=High Mobility Group Box Protein; iNOS=inducible nitric oxide synthase; RUNX=Runt-related transcription factor; HIF=Hypoxia Induced Factor; PTH=parathyroid hormone; NLRP3=NOD-like receptor family, pryin domain containing 3; RANKL=Receptor Activating Ligand for Nuclear Factor Kappa-B; VEGF=vascular endothelial growth factor; TNF=Tumor Necrosis Factor; CCL=chemokine ligand (CC motif); MIP=Macrophage Inflammatory Protein.

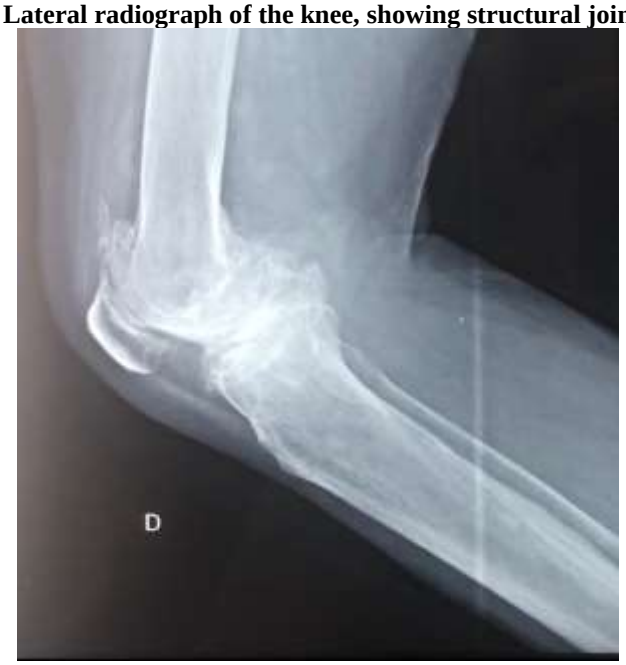
Source: Loeser RF, Goldring SR, Scanzello CR, Goldring MB. Osteoarthritis: A disease of the joint as an organ(7).

A pathologic feature that helps differentiate OA is the loss of articular cartilage, which is usually seen on plain radiographs as joint space narrowing. Joint breakdown and cartilage breakdown correlate with attempts at repair with new bone synthesis and the development of subchondral sclerosis and osteophytes. OA is recognized as a disease that affects the entire joint, including ligaments, menisci, synovium and joint capsule, thanks to imaging studies, especially magnetic resonance imaging (MRI). MRI may show evidence of abnormal bone structure at the subchondral border with cysts and bone marrow lesions; represented as hyperintense areas in proton density or T2 with fat suppression(3,7).

The American College of Rheumatism in 1984 divided OA into: primary (without apparent cause) and secondary, however this classification is under discussion. A better system of classification could help to go deeper into the discernment of bone and cartilage interrelationships in order to enrich therapeutics by being more specific, so Herrero-Beaumont has proposed a subclassification of patients with primary osteoarthritis depending on the main mechanism(1):

a. Genetically induced osteoarthritis.
b. Arthritic disease related to estrogenic deficit.
c. Arthrosis essentially associated with aging.

Figure 1. Lateral radiograph of the knee, showing structural joint damage.



Source: The Authors.

As for imaging studies, nuclear magnetic resonance is the technique of choice in the evaluation of the disease, such as T2 mapping, gadolinium enhancement technique, short time projection/reconstruction and cartilage spectroscopy. Another useful study is the ultrasound which evaluates with great precision the bony erosions in the joints in the initial stages, this presents benefits such as its ease of access, speed, efficiency, innocuousness, besides being a dynamic study, in real time and comparative, being considered a primordial annex in the examination of the pathology. It is used to verify the presence of osteoarthritis and to know if there is a joint effusion, which is responsible for the pain, and its presence reveals a torpid evolution of the disease(1,16).

Regarding X-rays, the Kellgren and Lawrence classification is used, which is divided into grades as follows:

Grade 0: normal.

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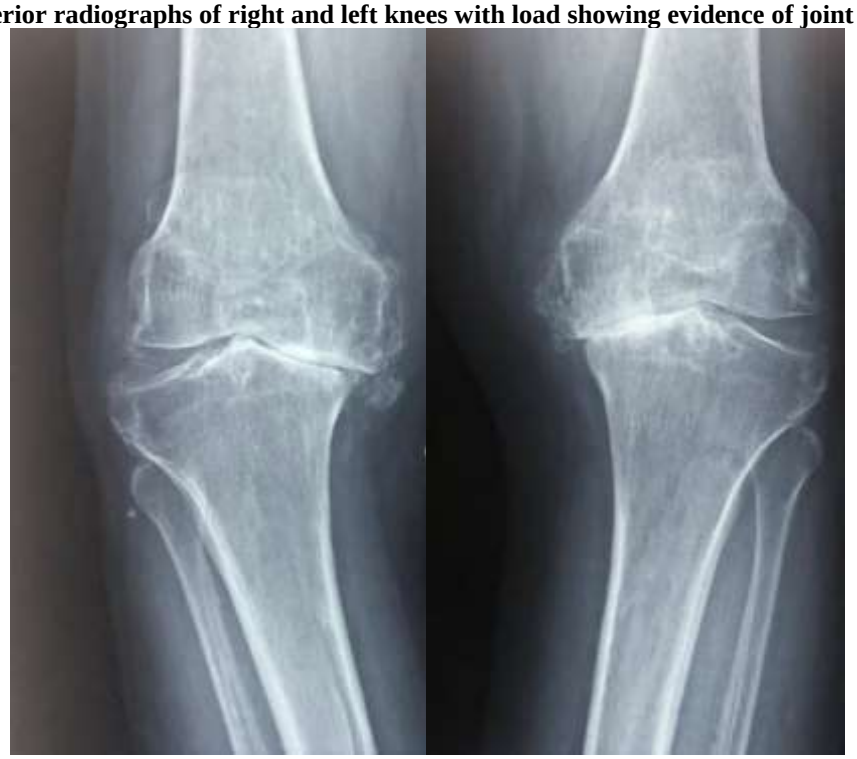
Grade 1: doubtful (possible osteophytes, doubtful joint narrowing).
Grade 2: mild (confirmed osteophytes, possible space narrowing).
Grade 3: moderate (multiple moderate osteophytosis, evident space narrowing, slight sclerosis, possible extreme bone deformity).
Grade 4: severe (abundant osteophytes, marked space narrowing, severe sclerosis, bone end deformity)(1,16-19).
Arthroscopy is currently a reliable procedure which, in addition to diagnosis, also examines the seriousness of the lesions for their treatment(1).

Figure 2. Anteroposterior radiographs of right and left knees with load showing evidence of joint structural alteration.



Source: The Authors.

Osteoarthrosis should be considered as a chronic pathology, by now irreversible and progressive. Its prognosis will depend on several factors such as(1):
Age: the younger, the worse the prognosis.
Genetics.
Location and extension of the lesions.
Work activity that favors its progression.
Evolution, according to the speed of progression.
Obesity.
Aggregate diseases.
Existence of non-remediable determinant diseases.
Some recommended measures with the purpose of delaying or avoiding the evolution of the articular damage are(1):
The use of contralateral cane.
Avoid constant squatting.
The use of appropriate footwear.
Avoid frequent use of stairs.
Avoiding low chairs and beds.
Use long tongs to pick up objects from the floor.
Sitting work if it is of long duration.

The purinergic system is an essential modulator in metainflammation and its involvement in the pathogenesis of OA opens more scope for future treatment of the disease. The importance of the purinergic system in osteoarthritic cartilage is recognized, as well as how the components of the metabolic syndrome related to OA impact this system. Adenosine-mediated A2AR action is involved in the maintenance of articular cartilage balance and is an essential modulator in OA. Stimulation of the previously mentioned receptor developed by obesity could lead to cartilage depletion and OA formation in obese patients. Further study on the contribution of nucleotide receptors in OA and metabolic syndrome is needed to better understand the underlying processes that turn on purinergic signaling in the pathogenesis of OA and to clarify the confounding results(20-24).

Diabetes mellitus (DM2) presents a pathogenic effect on osteoarthrosis via 2 primary pathways comprising oxidative stress and chronic mild inflammation as a consequence of chronic hyperglycemia and insulin resistance. DM2 is presented as one of the risk factors for the progression of OA, as well as

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having a negative impact on the success of arthroplasty. There are increasing findings and concerns about the safety of various medications in diabetics with OA including acetaminophen, non-steroidal anti-inflammatory drugs and corticosteroid injections. However, other medications can be safely prescribed in patients with OA and DM2, such as glucosamine and intra-articular hyaluronic acid. However, more research is needed to clearly understand whether diabetes control and prevention can modulate the onset and progression of OA(25-28).

In the absence of a definitive cure, the treatment of OA usually relied on symptom relief focused on reducing pain and increasing mobility. Some ointments such as the one containing a chemical compound called capsaicin act on substance P, which is linked to the origin of the transmission of the pain stimulus, thus influencing the relief and improvement of pain, sensitivity and functionality of the patient with OA according to some studies, however, it frequently presents a local burning sensation as a side effect(1).

Paracetamol is the drug of first choice recommended by most international guidelines in the treatment of OA. The American College of Rheumatology (ACR) Good Clinical Practice Guidelines (GBPC) suggest starting with paracetamol up to 1 g four times per day in situations where pain is mild to moderate in intensity. NSAIDs have more analgesic effect but also more toxicity compared to paracetamol(1,29).

Opioids have an analgesic effect that almost completely eliminates all kinds of pain regardless of its intensity or site of affection. They are non-ceiling drugs, which means that the higher the dose, the greater the effect; however, it should be clear that the higher the dose, the greater the risk of presenting side effects such as respiratory depression, physical dependence, tolerance and other symptoms that lead to drug dependence. Within this group is popular the use of tramadol, which is an effective drug compared to placebo in several studies, generally used when pain therapy does not respond adequately to NSAIDs.

Short-term and long-term parenteral corticosteroid use is effective in controlling pain and stiffness. However, the benefits are usually seen in high doses, which entails some undesirable effects, therefore, corticosteroids are recommended in very specific cases. Most authors agree that the use of corticosteroids in OA systemically is not justified and is only recommended in intra-articular injections. Intra-articular injection of a preparation of betamethasone acetate and phosphate provides a notable improvement in the WOMAC score when compared to the values seen with hyaluronic acid. Some bibliographies show that there is a significant decrease in short-term pain in knee osteoarthritis (7-30 days) after intra-articular corticosteroid injection(1,30).

NSAIDs inhibit the cyclooxygenase enzyme (COX), thus stopping the synthesis of prostaglandins which are responsible for hyperalgesia due to sensitization of the nociceptive nerve endings. They generally have an important adverse effect on the gastrointestinal mucosa, which may perforate or bleed, increasing morbimortality. Chronic use of NSAIDs increases the risk of complications(1,30).

There are two COX isoforms, COX-1 and COX-2; the first is constitutional and maintains homeostasis of the internal environment, renal and gastric integrity and the second is found at the site of inflammation. Nowadays, attempts are being made to synthesize NSAIDs that selectively deprive the latter isoenzyme, without altering the production of prostaglandins in the kidney and stomach. The possibility of causing gastrointestinal complications varies greatly from group to group. Ibuprofen is one of the least harmful to the gastric mucosa; among the most gastrodamaging are piroxicam and ketoprofen, with a medium lesion of the gastric epithelium we have acetylsalicylic acid, naproxen, sulindac and indomethacin. Within this group of drugs, the concept of specific COX-2 inhibitors was proposed, which initially included Rofecoxib (Viox) and Celecoxib (Celebrex), which showed greater inhibition of COX-2 than of COX-1(1,30,31).

Chondroitin sulfate (CS) is a natural biomacromolecule widely distributed in almost all vertebrates and invertebrates. Leeb et al (2008) in their meta-analysis shows that it decreases the need for analgesics or NSAIDs, on the other hand the team of Prof. Jean-Pierre Pelletier (March 2011), presents a study which confirms the structure modifying effect of chondroitin sulfate through a quantitative MRI, which has determined the result of therapy with CS on the decrease in cartilage volume, subchondral bone lesions and synovitis in people with osteoarthritis of the knee. However, a study by the Cochrane Controlled Trials Register, Medline, Embase and CINAHL Group (June 2010) concludes that it does not produce a clinically relevant impact on joint pain or joint space narrowing(1,32,33).

Glucosamine sulfate (GS) is a component that is part of the fundamental substance of articular cartilage, the proteoglycans. In many studies, SG at a dose of 1500 mg/day has been shown to be effective in the control of knee and hip osteoarthritis symptoms. Trials comparing SG with NSAIDs suggest that SG causes symptomatic benefits similar to NSAIDs, but with a lower possibility of adverse reactions. Both SG and CS do not appear to adequately eliminate subchondral bone modifications, synovial inflammation or osteophyte formation. More studies focused on the assessment of their potential disease-modifying effects and long-term therapy are needed(1,32).

Intra-articular hyaluronic acid (HA) is an expensive treatment that has been used in large numbers since its approval by the Food and Drug Administration (FDA). Regarding the efficacy of HA, several meta-analyses concluded that it is an effective drug for the treatment of pain and symptom control in OA, especially in gonarthrosis(1,29).

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Diacerein at 50 mg decreases IL 1Beta production in cartilage and also nitric oxide levels. By selectively inhibiting IL-1 it antagonizes the catabolic process and stimulates the anabolic process of cartilage, preventing the degradation of articular cartilage.

Silver/soy isaponifiables (IPS) increase collagen synthesis by the chondrocyte without modifying collagen proportions. They stimulate the expression of transforming growth factor and activated plasminogen inhibitor, stimulating and intervening in the repair of the cartilage matrix. Bone tissue regenerative currents using tetracyclines that prevent the activation of metalloproteases, autologous chondrocyte implants, hypoxia-inducible factor (HIF-1/2a), parathyroid hormone that stimulates chondrocyte multiplication and the use of stem cells 'in situ', cartilage regeneration and the better understanding of the developmental osteogenesis progenitor protein, will be part of the medical management protocol, being a promising therapy for future therapy(1,34).

Physiotherapeutic treatment in osteoarthrosis plays a fundamental role in the improvement of pain, muscle dysfunction and functional impotence secondary to pain. The physical technique with the most evidence of effectiveness is exercise. It has been shown that strengthening and toning exercises, performed under aerobic conditions, have better results on pain and fatigue than stretching exercises. In addition to this, massage, currents, ultrasound, thermotherapy, kinesitherapy and hydrotherapy are often used. Pain frequently favors voluntary immobilization, which leads to an impairment of mobility and consequently of function, in addition to leading to muscular complications(1).

The use of orthoses should be prescribed in a correct and timely manner to avoid pain, joint complications and soft tissue retractions. There are studies showing that isometric quadriceps exercise increases the amount of hyaluronic acid in the knee in patients with gonarthrosis, as well as clinical trials showing that an exercise program in people at risk of suffering knee osteoarthritis increases the content of glycosaminoglycans in the articular cartilage. Muscle weakness and reduced joint proprioception are risk factors for the formation of osteoarthritis. The exercise plan should be individualized and individually adapted. An exercise plan with a minimum of three sessions per week is recommended, without exceeding two sessions per day. Strengthening of the quadriceps in the prevention of the progression and frequency of painful crises in this disease is the gold standard(1,32,35).

Figure 3. Knee surgery for gonarthrosis.

Source: The Authors.

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Surgical treatment is reserved for patients with severe pain or marked deformity, which occurs in advanced OA. There is a wide range of procedural therapies to be performed in these cases, among them we have:
Arthroplasty.
Valgus osteotomy of the proximal part of the tibia.
Arthrodesis.
Amniotic membrane implant.
There are also several techniques to repair the cartilage, these are used according to the phase in which the lesion is presented. An example of this is the injection of proteoglycans supported by oxygen-ozone therapy with the capacity to revitalize the chondrocytes and the infiltration of autologous plasma rich in platelets used for the inhibitory capacity of the transforming growth factor beta (TGFß), contained in the platelets, on the origin of the inflammatory cascade(36-38).

CONCLUSIONS

Osteoarthritis should be considered as a chronic, irreversible and progressive lesion. There are factors that aggravate its prognosis. Many measures are recommended to the patient and his family, especially if it is an elderly patient, in order to prevent the progression of joint damage. Surgical treatment is reserved for patients with severe pain or marked deformity, which occurs in advanced OA. Among the most frequently used procedures are: valgus osteotomy of the proximal tibia, arthroplasty, arthrodesis and amniotic membrane implantation. Bone tissue regenerative currents using tetracyclines that prevent metalloproteinase activation, autologous chondrocyte implants, hypoxia inducible factor (HIF-1/2a), parathyroid hormone that stimulates chondrocyte multiplication and the use of in situ stem cells, cartilage regeneration and a better understanding of the developmental protein ancestor of osteogenesis, will be part of the medical management protocol, being a promising therapy for future therapy.

BIBLIOGRAPHY

1. *Arias-Cantalapiedra. Osteoartritis. Rev Cuba Med Física Rehabil [Internet]. 2017;6(2). Disponible en: https://revrehabilitacion.sld.cu/index.php/reh/article/view/171*
2. *Vina ER, Kwoh CK. Epidemiology of osteoarthritis: literature update. Curr Opin Rheumatol. marzo de 2018;30(2):160–7.*
3. *O'Neill TW, Felson DT. Mechanisms of Osteoarthritis (OA) Pain. Curr Osteoporos Rep. octubre de 2018;16(5):611–6.*
4. *Roseti L, Desando G, Cavallo C, Petretta M, Grigolo B. Articular Cartilage Regeneration in Osteoarthritis. Cells. el 23 de octubre de 2019;8(11):1305.*
5. *Kidd B. Mechanisms of Pain in Osteoarthritis. HSS J. febrero de 2012;8(1):26–8.*
6. *Glyn-Jones S, Palmer AJR, Agricola R, Price AJ, Vincent TL, Weinans H, et al. Osteoarthritis. The Lancet. julio de 2015;386(9991):376–87.*
7. *Loeser RF, Goldring SR, Scanzello CR, Goldring MB. Osteoarthritis: A disease of the joint as an organ. Arthritis Rheum. junio de 2012;64(6):1697–707.*
8. *Oteo Álvaro Á. Mecanismos etiopatogénicos de la artrosis. Rev Soc Esp Dolor [Internet]. 2021 [citado el 17 de febrero de 2023]; Disponible en: http://gestoreditorial.resed.es/fichaArticulo.aspx?iarf=22468176 7-749235414274*
9. *Camarero-Espinosa S, Rothen-Rutishauser B, Foster EJ, Weder C. Articular cartilage: from formation to tissue engineering. Biomater Sci. 2016;4(5):734–67.*
10. *Cohen NP, Foster RJ, Mow VC. Composition and Dynamics of Articular Cartilage: Structure, Function, and Maintaining Healthy State. J Orthop Sports Phys Ther. octubre de 1998;28(4):203–15.*
11. *Gregersen PA, Savarirayan R. Type II Collagen Disorders Overview. En: Adam MP, Everman DB, Mirzaa GM, Pagon RA, Wallace SE, Bean LJ, et al., editores. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993 [citado el 16 de febrero de 2023]. Disponible en: http://www.ncbi.nlm.nih.gov/books/NBK540447/*
12. *Merry CLR, Lindahl U, Couchman J, Esko JD. Proteoglycans and Sulfated Glycosaminoglycans. En: Varki A, Cummings RD, Esko JD, Stanley P, Hart GW, Aebi M, et al., editores. Essentials of Glycobiology [Internet]. 4th ed. Cold Spring Harbor (NY): Cold Spring Harbor Laboratory Press; 2022 [citado el 16 de febrero de 2023]. Disponible en: http://www.ncbi.nlm.nih.gov/books/NBK579925/*
13. *Driban JB, Harkey MS, Barbe MF, Ward RJ, MacKay JW, Davis JE, et al. Risk factors and the natural history of accelerated knee osteoarthritis: a narrative review. BMC Musculoskelet Disord. diciembre de 2020;21(1):332.*
14. *Roemer FW, Guermazi A, Felson DT, Niu J, Nevitt MC, Crema MD, et al. Presence of MRI-detected joint effusion and synovitis increases the risk of cartilage loss in knees without osteoarthritis at 30-month follow-up: the MOST study. Ann Rheum Dis. octubre de 2011;70(10):1804–9.*
15. *Wang X, Jin X, Blizzard L, Antony B, Han W, Zhu Z, et al. Associations Between Knee Effusion-synovitis and Joint Structural Changes in Patients with Knee Osteoarthritis. J Rheumatol. noviembre de 2017;44(11):1644–51.*
16. *Taljanovic MS, Graham AR, Benjamin JB, Gmitro AF, Krupinski EA, Schwartz SA, et al. Bone marrow edema pattern in advanced hip osteoarthritis: quantitative assessment with magnetic resonance imaging and correlation with clinical examination, radiographic findings, and histopathology. Skeletal Radiol. mayo de 2008;37(5):423–31.*
17. *Hofmann S, Kramer J, Vakil-Adli A, Aigner N, Breitenseher M. Painful bone marrow edema of the knee: differential diagnosis and therapeutic concepts. Orthop Clin North Am. julio de 2004;35(3):321–33.*
18. *Wilson AJ, Murphy WA, Hardy DC, Totty WG. Transient osteoporosis: transient bone marrow edema? Radiology. junio de 1988;167(3):757–60.*
19. *Kellgren JH, Lawrence JS. Radiological Assessment of Osteo-Arthrosis. Ann Rheum Dis. el 1 de diciembre de 1957;16(4):494–502.*
20. *Gratal P, Lamuedra A, Medina JP, Bermejo-Álvarez I, Largo R, Herrero-Beaumont G, et al. Purinergic System Signaling in Metainflammation-Associated Osteoarthritis. Front Med. el 28 de agosto de 2020;7:506.*
21. *Gharibi B, Abraham AA, Ham J, Evans BAJ. Contrasting effects of A1 and A2b adenosine receptors on adipogenesis. Int J Obes. marzo de 2012;36(3):397–406.*
22. *Tesch AM, MacDonald MH, Kollias-Baker C, Benton HP. Endogenously produced adenosine regulates articular cartilage matrix homeostasis: enzymatic depletion of*

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adenosine stimulates matrix degradation. Osteoarthritis Cartilage. mayo de 2004;12(5):349–59.

23. *Corciulo C, Cronstein BN. Signaling of the Purinergic System in the Joint. Front Pharmacol. el 24 de enero de 2020;10:1591.*
24. *Burnstock G, Gentile D. The involvement of purinergic signalling in obesity. Purinergic Signal. junio de 2018;14(2):97–108.*
25. *Veronese N, Cooper C, Reginster JY, Hochberg M, Branco J, Bruyère O, et al. Type 2 diabetes mellitus and osteoarthritis. Semin Arthritis Rheum. agosto de 2019;49(1):9–19.*
26. *Courties A, Sellam J. Osteoarthritis and type 2 diabetes mellitus: What are the links? Diabetes Res Clin Pract. diciembre de 2016;122:198–206.*
27. *Eymard F, Parsons C, Edwards MH, Petit-Dop F, Reginster JY, Bruyère O, et al. Diabetes is a risk factor for knee osteoarthritis progression. Osteoarthritis Cartilage. junio de 2015;23(6):851–9.*
28. *Schett G, Kleyer A, Perricone C, Sahinbegovic E, Iagnocco A, Zwerina J, et al. Diabetes Is an Independent Predictor for Severe Osteoarthritis. Diabetes Care. el 1 de febrero de 2013;36(2):403–9.*
29. *Charlesworth J, Fitzpatrick J, Perera NKP, Orchard J. Osteoarthritis- a systematic review of long-term safety implications for osteoarthritis of the knee. BMC Musculoskelet Disord. diciembre de 2019;20(1):151.*
30. *Mao L, Wu W, Wang M, Guo J, Li H, Zhang S, et al. Targeted treatment for osteoarthritis: drugs and delivery system. Drug Deliv. el 1 de enero de 2021;28(1):1861–76.*
31. *Solomon DH, Husni ME, Libby PA, Yeomans ND, Lincoff AM, Löscher TF, et al. The Risk of Major NSAID Toxicity with Celecoxib, Ibuprofen, or Naproxen: A Secondary Analysis of the PRECISION Trial. Am J Med. diciembre de 2017;130(12):1415-1422.e4.*
32. *Fernández-Martín S, González-Cantalapiedra A, Muñoz F, García-González M, Permuy M, López-Peña M. Glucosamine and Chondroitin Sulfate: Is There Any Scientific Evidence for Their Effectiveness as Disease-Modifying Drugs in Knee Osteoarthritis Preclinical Studies?—A Systematic Review from 2000 to 2021. Animals. el 29 de mayo de 2021;11(6):1608.*
33. *Volpi N. Chondroitin Sulfate Safety and Quality. Molecules. el 12 de abril de 2019;24(8):1447.*
34. *Grässel S, Muschter D. Recent advances in the treatment of osteoarthritis. F1000Research. el 4 de mayo de 2020;9:325.*
35. *Safran-Norton CE, Sullivan JK, Irrgang JJ, Kerman HM, Bennell KL, Calabrese G, et al. A consensus-based process identifying physical therapy and exercise treatments for patients with degenerative meniscal tears and knee OA: the TeMPO physical therapy interventions and home exercise program. BMC Musculoskelet Disord. diciembre de 2019;20(1):514.*
36. *Everts P, Onishi K, Jayaram P, Lana JF, Mautner K. Platelet-Rich Plasma: New Performance Understandings and Therapeutic Considerations in 2020. Int J Mol Sci. el 21 de octubre de 2020;21(20):7794.*
37. *Bolduc JA, Collins JA, Loeser RF. Reactive oxygen species, aging and articular cartilage homeostasis. Free Radic Biol Med. febrero de 2019;132:73–82.*
38. *Gómez-García F. Historia y desarrollo de la artroplastía de cadera: una visión de sus aciertos, fallas y enseñanzas. (Segunda parte). Acta Ortopédica Mex. 2021;35(5):440–52.*

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