CURRENT CONCEPTS IN OSTEOARTHRITIS

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ABSTRACT

Osteoarthritis (OA), the most common form of joint disease, affects mainly the hips, knees, hands and feet, leading to severe disability and loss of quality of life, particularly in the elderly population. Its importance grows every year with the aging of the population, with a large increase in the elderly population compared to younger patients. The progressive understanding of the pathophysiology of OA, the perception that the process is not purely mechanical and / or aging, and clarification of the inflammatory pathways involved led recently to the clinical application of various drugs and other measures. This update aims to expose the current concepts on the pathophysiology and treatment of OA.

Keywords: Osteoarthritis. Arthritis. Osteoarthritis, knee. Osteoarthritis, hip. Osteoarthritis/physiopathology.

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INTRODUCTION

Osteoarthritis (OA) is the most common form of articular disease[1] and affects mainly hips, knees, hands, and feet. In USA, it is estimated that 36.4% of the individuals aged 60 and over present OA in the knees[2] In Brazil, the population of individuals over 60 years old, today nearly 19 million, will increase in 2050 to over 64 million.[3] It is alarming data, considering disability, loss of quality of life and the costs to the health system generated by this disease.[4]

Until some decades ago, the treatment for OA was limited to the use of simple analgesic drugs, anti-inflammatories, physical procedures, infiltration with corticoids and, in unsusceptible cases, surgical treatment. The progressive understanding of physiopathology of OA, the perception that the process is not purely mechanical and/or due to aging, and the clarification of the involved inflammatory paths lead to the clinical application of several other drugs and procedures.[5]

PATHOLOGY

The importance of inflammation

Risk factors such as gender, age, trauma, excessive use, genetics, and obesity help to initiate the process of injury in different components of the articulation.[6] It is already well established that the synovia, the bone and the cartilage are the three main tissues affected by the pathological mechanisms of the OA.[6]

The cartilage traditionally receives the main attention in OA studies, due to the massive destruction found in pathological specimens and image studies, as well as due to the large amount of activated biological processes in it. Key events that occur in the cartilage include metabolic unbalance and the emergence of degradation indicators, promoted by cytokine cascades, and the production of inflammatory mediators.[7]

In patients with OA, the chondrocytes, as well as the synovial cells, produce increased levels of inflammatory cytokines, as interleukin 1β (IL-1β) and the alpha tumor necrosis factor (TNF-α), that, in turn, decrease the collagen synthesis and increase catabolic mediators, such as metalloproteases (MMPs) and other inflammatory substances as interleukin 8 (IL-8), interleukin 6 (IL-6), prostaglandin E2 (PGE2) and nitric oxide (NO).[7] In addition, mechanical stress, as by static compression as by dynamic, increases the production of NO by chondrocytes, as well as the expression of nitric oxide synthase (NOS).[8]

Oxidizing agents, among them NO, promote apoptosis of chondrocytes, catabolic processes and degeneration of the matrix, therefore, causing two important pathogenic events characteristic of the osteoarthritic chondrocytes - premature senescence and apoptosis. These events help build up the concept that OA is a disease of premature aging of the articulation.[9]

Synovitis occurs even in the initial stages of OA and can be subclinical. Arthroscopic studies demonstrate alterations in the synovia in up to 50% of the patients with OA, many of which did not present clinical signs of synovitis.[10] Recent techniques using 3 Tesla nuclear magnetic resonance (NMR) demonstrated that the synovial inflammation is more common than previously estimated.[6] Differently from Rheumatoid Arthritis (RA), the

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synovial inflammation in OA is usually found close to areas of pathologically damaged bone and cartilage. This hyper-reactive synovia can release proteinases and cytokines capable of accelerating the articular damage.[6]

TREATMENT

The growing importance of non-pharmacological handling

Over the years, various national and international guidelines were developed in order to help the physicians, health professionals and patients in treatment selection for knee and hip OA treatment. In Brazil, the Brazilian Society of Rheumatology (SBR), through Projeto Diretrizes, formulated in 2003 a consensus for OA treatment.[11] More recently, the Osteoarthritis Research Society International (OARSI) published a recommendation guide[12] with more rigid methodology, based on higher quality papers, which relies on regular reviews, as long as new clinical trials are being published on this topic.[12]

The better treatment for OA requires a combination of pharmacological and non- pharmacological procedures.[12] All knee OA patients should have access to information and education concerning the objectives of the treatment and the importance of changes in lifestyle, exercises, adequation of activities, weight reduction and other measures to diminish the impact on the damaged articulations. The initial focus should be on self-care and treatments directed to the patient instead of passive therapies realized by health professionals.[12] Emphasis should be given on the incentive for adherence to the therapeutic not-pharmacological regimen. Patients should be encouraged to practice and maintain regular aerobic exercises, of muscular strengthening and gain of movement amplitude. Patients with symptomatic OA can benefit from physiotherapy referral for evaluation and instruction to perform appropriate physical exercises to reduce pain and increase the functional capacity.[12]

The association between the Body Mass Index (BMI) and knees OA is of great importance, since knees OA has a strong correlation with the highly inflammatory metabolic environment found in obesity.[13] Cytokines associated to the adipose tissue, including adiponectine, leptine and resistine, can influence OA through the direct degradation of the articulation or by controlling local inflammatory processes. A recent systematic review evaluated 36 studies on this correlation and found positive risk of BMI for OA development in all of them.[14] Weight loss reduces the pain and improves the physical function of the OA patients, and should be encouraged.[13]

The use of canes and walkers is also recommended for symptomatic OA of the knees, promoting improvement of the pain and lowering energy expenditure.[15] The patients should be educated to correctly use a cane or crutch in the counter side hand, walkers being preferable for patients with bilateral disease. The use of orthosis or socks is also indicated to patients with axis bypass in valgus and varus.[12]

Acupuncture is treatment modality with proved benefit in the relief of OA pain.[16] Other body and mind therapies, such as yoga, tai chi and qi gong also can be used in OA treatment, with improvement evidences.[17]

The use of drugs is to complement non-pharmacological procedures. Among the available drugs, there are those essentially analgesic drugs, that do not interfere in the course of the disease; as well as the anti-inflammatory drugs, controversial due to their side effects; and, finally, the drugs modifiers of the osteoarthritis disease (DMOOAD), those capable of reversing, stabilizing or at least delaying the course of OA.[5]

Among DMOOAD of oral use diacerein[18], glicosamine[19], chondroitin[20], the association of glucosamine with chondroitin[21], the non-saponifiable extracts of soybean and avocado[22] and chloroquine are pointed out. Glucosamine and chondroitin are, unquestionably, the most popular "chondroprotectors". It has been recently discussed the relationship between the effectiveness of these substances and the type of used molecule, in addition to its isolated or associated use. Recent metanalysis[24], as well as a Cochrane systematic review[19] reported benefits with the use of sodium glucosamine sulfate (Rotta type glucosamine) alone. A recent study also revealed that the chondroitin, when combined, can compromise the absorption of glucosamine.[25] Meanwhile, there is not yet consensus in the literature in this regard.

Hyaluronic acid (HA) is an intra-articular DMOOAD, and its application is called visco-supplementation (VS).[26] It has an important modulating action, mainly through interaction with CD44 receptors present in type B "fibroblast-like" synoviocytes.[27] Therefore, besides the mechanical effect of promoting better distribution of forces, reduce the pressure due to weight and recovering the rheological properties of synovial fluid, hyaluronic acid also acts biochemically, reducing the gene expression of cytokines and enzymes associated from the OA.[27] From the economic point of view there is an increasing number of studies showing that, if incorporated into the treatment of knee OA, VS can be cost-effective, including being able to delay the completion of a total prosthetic knee.[28]

Currently it is recommend the addition of 1 ml triamcinolone to visco-suplementation.[29,30] The addition of corticosteroids makes pain and function improvements occur earlier and in greater intensity, without compromising long term outcomes.[30] It is also possible to maximize the benefits of VS through a prior joint lavage. One should not wait for the failure of other treatment options to consider VS, since it is known that patients who will benefit most from this treatment are those whose disease is in early stage (lower grade OA) and use the joints more actively.[31]

FINAL CONSIDERATIONS

It is crucial to keep in mind that the treatment of OA is not scaled but multimodal. The patient should be educated about his disease and encouraged to take an active behavior in his treatment. The disease has no cure, but it can be controlled through diet, exercise, use of orthosis, and medication administration. We must use the entire available therapeutic arsenal, and in case of failure, do not hesitate to indicate surgical treatment. The joint replacement surgery still plays an important role in OA treatment. The total hip replacement surgery was considered the surgery of the 20th century by Lancet[32], due to the strong positive impact that it can bring to the patient's quality of life .

FUTURE DIRECTING

Comprehensive and individualized OA treatment

Currently there is a major global effort to identify biomarkers of OA disease. These markers, found in blood, urine, or even

in the cell genome, would be able to produce information on the characteristics of the disease in a given individual, its relationship with various risk factors, as well as control over the evolution of the disease, and why not, on the response intensities to the most various types of used treatments.

The most recent genetic studies, which present the most appropriate approach for identifying susceptibility genes among the complex genetic spectrum, have revealed some most convincing signals, such as the 7q22 loci, which contains multiple potential genes such as the growth differentiation factor 5 (GDF5) gene and the frazzled protein (FRZB).[33] Just 10 years ago, the cost to sequencing and individual's genome was about $ 100 million. Currently, this value is around ten thousand dollars, and soon, it is estimated that we can ask for a genome a study to our patients as we ask, for example, for a MRI.

In the future, therefore, we will be able, through a blood test, or even a hair, to define the best treatment strategy, the best drugs and non-pharmacological procedures to be used by each of our patients, offering thus a comprehensive and individualized treatment. Will this be true?

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