Recent Advances in Diagnosis and Treatment of Osteoarthritis

Essay

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INTRODUCTION

Osteoarthritis (OA) is a joint disease characterized by the gradual loss of articular cartilage accompanied by bony remodeling, atrophy of periarticular muscles, and capsular stretching. At present, approximately 40% of adults aged over 70 suffer from OA of knee,of these 80% suffer from limitation in movement and 25% are impaired in carrying out their daily activities **(Roy, 2009).**

The ability of degradation products of the extracellular matrix to regulate cartilage homeostasis and influence (OA) disease progression has been extensively studied. For instance, different types of matrix fragments derived from fibronectin or collagen can signal and amplify catabolic processes in chondrocytes that act to either remove tissue components for repair or to initiate reparative signals. Chondrocytes will additionally respond to biomechanical perturbation such that mechanical loading on normal or diseased tissue will contribute to signaling cascades and up regulate synthetic activity or increase the levels of inflammatory mediators **(Tina et al., 2010).**

Osteoarthritis (OA)-associated cartilage degradation is mediated in part by cytokines and growth factors,excreted into the intra-articular environment by synoviocytes,activated immune cells, or by the articular

cartilage itself. Therapies interfering with these cytokines may influence disease progression and improve the patient's quality of life. A pivotal role in the progression of (OA) has been assigned to the pro-inflammatory cytokine interleukin-1β (IL-1β), which induces a cascade of inflammatory and catabolic events **(Marijn et al., 2010).**

Osteoarthritis (OA) is characterized by an imbalance between cartilage anabolism and catabolism. The local production and release of pro-inflammatory cytokines interleukin-1β(IL-1β), interleukin-6 (IL-6) and tumor necrosis factor-α(TNF-α) play a central role in the pathogenesis of (OA) **(Constanze et al., 2010).**

Molecular markers in (OA) have been the object of growing attention due to their potential usefulness in formulating early diagnosis, in assessing disease activity, severity and in evaluating drug effects. It has been observed that serum CRP levels are higher in patients with erosive osteoarthritis than in non-erosive osteoarthritis patients. The molecular markers most useful in identifying cartilage synthesis or degradation originate from different articular sources such as cartilage, bone and synovial tissue. Serum hyaluronan (HA), a marker of synovial proliferation and hyperactivity, appears to reflect (OA) progression. Other interesting biochemical markers are serum keratin sulphate

(KS), Cartilage oligomeric matrix protein (COMP), YKL-40, and urinary C-terminal crosslinking telopeptides of collagen types I and II (uCTX-II) **(Leonardo et al., 2010).**

Conventional radiographs were the standard for diagnosing (OA) over many years, and the radiograph based Kellgren-Lawrence Scale is still a standard of reference for grading osteoarthritis. MRI gives substantial information beyond radiographs as it also demonstrates degenerative changes in the cartilage, menisci, ligaments, bone marrow, and synovial tissue. **(Thomas, 2009).**

Recently new trends have been established in diagnosis of (OA), The American college of rheumatology has established clinical criteria for diagnosing (OA) of the hands,hips and knees **(Roy, 2010).**

As the number of individuals with (OA) increases, effective strategies to manage the pain and disability of (OA) will become even more important. Guidelines for the management of (OA) have been published recently by both the osteoarthritis Research Society International (OARSI) and the European League Against Rheumatism (EULAR). Experts from multiple disciplines, who analyzed and weighted the scientific and clinical evidence as well as previous guidelines, developed recommendations for the management of knee, hip, and hand (OA). The guidelines

indicate that combination of pharmacological and nonpharmacological modalities is the most effective strategy to manage the pain **(Francis, 2008).**

A number of drugs for osteoarthritis are intended to counteract the pro-inflammatory, matrix-destroying effect of cytokines. Further treatment approaches include the administration of antibodies against TNF-α (which are currently available) or the use of anti-inflammatory enzymes such as IL-4, IL-10, IL-13 and TGF-β **(Joern et al., 2010).**

Patients with cartilage defects in the knee form an important category in (sports) medicine. Various techniques are described for restoration of full-thickness articular cartilage defects. Resurfacing techniques where the defect is filled with hyaline cartilage, like the Osteochondral Autograft Transplant System (OATS) technique, are more physiological and durable than fibrocartilagous remodeling treatments. Literature on the treatment of cartilage defects with osteochondral autologous transplantation shows encouraging results **(Sandra et al., 2010).**

Cell therapy based on autologous mesenchymal stem cells (MSCs), which have a vast proliferative capacity and differentiation potential, is an attractive strategy for treating

OA. In vivo implantation of undifferentiated MSCs has led to unexpected results. MSCs with the capacity to differentiate into the mesenchymal lineage can be isolated from the bone marrow, fat tissue, umbilical cord blood, and amniotic fluid. It has been reported that the chondrogenic abilities of MSCs could be triggered with various growth factors **(Wei-Hong et al., 2009).**

AIM OF THE REVIEW

The aim of this study is to review the most recent literatures and researches concerning the recent advances on pathogenesis, diagnosis and treatment of osteoarthritis in attempt to improve patients outcome.

Osteoarthritis

Definition:

Osteoarthritis (OA) is a joint disease characterized by the gradual loss of articular cartilage accompanied by bony remodeling, joint space narrowing, atrophy of periarticular muscles, and capsular stretching **(Roy, 2009)**.

Osteoarthritis (OA) involve degenerative changes in the joint, multifactorial in origin; leading to loss of function, pain and significant disability. The initiation of cartilage breakdown is stimulated with mechanical stress or injury, and the degenerative processes slowly progress over many years. In the advanced stage of OA, the abnormal remodeling of cartilage and subchondral bone sclerosis, subchondral cyst, synovial inflammation and marginal osteophyte formation. at the joint surface and margins, which irreversibly destroys the affected joint **(Joon et al., 2010).**

OA is characterized by an imbalance between cartilage anabolism and catabolism,with the local production and release of pro-inflammatory cytokines. OA is not only common joint diseases in the elderly population but increasingly it affects young individuals. Collectively,

it represents a large proportion of orthopaedic cases **(Constanze et al., 2010).**

OA is associated with impaired quality of life (QOL) as well as high economic costs. Direct treatment costs include physician visits, medications, hospitalizations, surgery, and transportation costs.Indirect costs relate to comorbid conditions and lost productivity at home and work **(Roy, 2010).**

Epidemiology of osteoarthritis:

Osteoarthritis is the most common disease of joints in adults around the world. About one-third of all adults have radiological signs of osteoarthritis, although in an epidemiological study, it was found clinically significant osteoarthritis of the knee, hand, or hip in only 8.9% of the adult population. Knee osteoarthritis was the most common type (6% of all adults). The likelihood of developing osteoarthritis increases with age. Studies have shown that knee osteoarthritis in men aged 60 to 64 is more commonly found in the right knee (23%) than in the left knee (16.3%), while its distribution seems to be more evenly balanced in women (right knee, 24.2%; left knee, 24.7%) **(Joern et al., 2010).**

The prevalence of osteoarthritis of the knee is higher among 70- to 74-year-olds, rising as high as 40%. When the diagnosis is based on clinical signs and symptoms alone, the prevalence among adults is found to be lower, at 10% **(Andrianakos et al., 2006).**

The radiological demonstration of typical signs of osteoarthritis of the knee is not correlated with symptoms: Only about 15% of patients with radiologically demonstrated knee osteoarthritis complain of knee pain. The incidence of the disorder among persons over 70 is estimated at 1% per year. Epidemiological studies have revealed that there are both endogenous and exogenous risk factors for osteoarthritis. Genetic factors unquestionably play a role **(Joern et al., 2010).**

Cross-sectional studies have shown that the risk of knee osteoarthritis is 1.9 to 13.0 times higher among underground coal miners than in a control population. presumably, the main risk factor in this occupational group is frequent work in the kneeling or squatting position. Construction workers, too, particularly floorers, have a significantly elevated prevalence of knee osteoarthritis **(D'Ambrosia et al., 2005).**

In another epidemiological study, it was found a significant dose-effect relationship for overweight (BMI

>30) as a risk factor for knee osteoarthritis, but not for hip osteoarthritis **(Andrianakos et al., 2006).**

OA is the leading cause of disability in the United States, arthritis is a chronic disease with a significant impact on the population. Based on 2003–2005 data from the National Health Interview Survey (NHIS),an estimated one in five or 46.4 million of U.S. adults have self-reported doctor-diagnosed arthritis.Almost 41% (19 million) of these 46 million adults report limitations in their usual activities due to their arthritis. In addition to activity limitations, 31% (8.2 million) of working age adults with doctordiagnosed arthritis report being limited in work activities **(Susan et al., 2009).**

As the U.S. population ages, these numbers are likely to increase considerably. Each year, arthritis results in 750,000 hospitalizations and 36 million outpatient visits. In 2003, direct medical costs for arthritis were $81 billion while indirect costs were another $47 billion. This economic burden explains the increasing attention that is being directedarthritis and to finding pharmacological agents to help control the disease **(Susan et al., 2009).**

Pathogenesis of Osteoarthritis

I- Etiologic factors in osteoarthritis:

1-Age:

Age is the risk factor most strongly correlated with OA.OA is in fact, the most chronic disease in later life; more than 80 percent of persons over age 75 years are affected, and OA increases progressively with age to all joint sites. Radiological changes in OA increase as individuals age, although these changes do not always correlate with clinical symptoms or disability, and therefore understanding age-related changes is essential **(Martin and Buckwalter, 2002).**

Age-related morphological and structural changes in articular cartilage include fraying, softening, and thinning of the articular surface, decreased size and aggregation of matrix proteoglycans, and loss of matrix tensile strength and stiffness **(Martin and Buckwalter, 2002).**

Mechanical stress on joint cartilage may arise from a number of factors, including altered gait, muscle weakness, changes in proprioception, and changes in body weight. In addition, age-related morphologic changes in articular cartilage are most likely due to a decrease in chondrocytes'

ability to maintain and repair the tissue. This is because chondrocytes themselves undergo age-related decreases in mitotic and synthetic activity, exhibit decreased responsiveness to anabolic growth factors, and synthesize smaller and less uniform large aggregating proteoglycans and fewer functional link proteins **(Steven and Mukundan, 2009).**

Age also appears to be an independent factor that predisposes articular chondrocytes to apoptosis, because the expression levels of specific proapoptotic genes (those encoding Fas, Fas ligand, caspase-8, and p53) are higher in aged cartilage. Cultured chondrocytes have been shown to exhibit an age related decline in response to insulin-like growth factor-I (IGF-I), a growth factor that stimulates the production of proteoglycans, collagen, and integrin cell receptors. Progressive chondrocytes senescence (as reflected in expression of the senescence-assosiated enzyme β-galactosidase), erosion of chondrocyte telomere length, and mitochondrial degeneration due to oxidative damage also contribute to the age-related reduction in chondrocyte function **(Steven and Mukundan, 2009).**

2- Joint location:

Although OA occurs most commonly in weight-bearing joints, age affects joints differentially. A study

comparing tensile fracture stress of cartilage in femoral head and in the talus showed that it decreased progressively with age in the former but not in the latter. Joint specific, age-related changes in articular cartilage may explain why OA is more common in hip and knee joints with increasing age but occurs rarely in the ankle **(Cole and Kuettner, 2002).**

Alterations in chondrocyte responsiveness to cytokines also appear to vary depending on the joint. For example, studies show that knee chondrocytes exhibit more interleukin-1 (IL-1) receptors than ankle chondrocytes and that knee chondrocytes express mRNA for matrix metalloproteinase-8 (MMP-8),whereas chondrocytes from the ankle do not **(Cole and Kuettner, 2002).**

3-Joint malalignment and trauma:

Joint malalignment or trauma may lead to rapid development of OA, or it may initiate a slow process that results in symptomatic OA years later. Probably as a result of progressive reduction in periarticular blood flow and the resultant decrease in rate of remolding at the osteochondral junction, joints become increasingly congruent with age. Altered joint geometry may interfere with nutrition of the cartilage, or it may alter load distribution, either of which may result in altered biochemical composition of the

cartilage, irrespective of age. Local factors, such as stresses related to joint use and joint deformity, also influence the development of OA. A previously injured joint is very susceptible to development of OA **(Conghan, 2002).**

Joint incongruence (e.g., malreduced intra-articular fractures, developmental dysplasia of the hip, recurrent dislocation of the patella) can lead to early-onset OA. Repetitive, high-impact sports are strongly associated with injury and increase the risk for lower limb OA. Repetitive trauma at a subfracture level has been shown to accelerate remolding in the zone of calcified cartilage, with reduplication of the tidemark and thinning of the noncalcified zone resulting in stiffening of the subchondral bone, increased wear of the overlying cartilage, and ultimately development of OA. Regular exercise is important in maintaining articular cartilage structure and metabolic function.Running and low-impact activities have not been shown to increase the risk of OA **(Conghan, 2002).**

Articular cartilage is remarkably resistant to damage by shear forces; it is, however, highly vulnerable to repetitive impact loading when joints are subjected to in vitro cyclic loads that are easily borne by subchondral bone, cartilage degeneration still results. This vulnerability