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KNEE OSTEOARTHRITIS - A MINI REVIEW

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ABSTRACT

Knee osteoarthritis (OA) is one of the main reasons for debilitating signs and symptoms like pain, limitation of joint movement, muscle wasting and muscle tightness in aging adult. As there is a growing prevalence and high impact of knee osteoarthritis symptoms, it is necessary to find low-price, easy-to-administer management to relieve its symptoms. This review focuses on recent studies of knee osteoarthritis prevalence, incidence, pathophysiology and its associated risk factors.

KEYWORDS: Knee, Osteoarthritis, Pathophysiology, Risk factors, Radiography, Drugs.

INTRODUCTION

Around 654.1 million individuals aged 40 years and above suffer with knee osteoarthritis (OA) globally in 2020.The global prevalence of knee osteoarthritis based on systematic and meta-analysis study reported 16.% in individuals aged 15 and over and 22.9% in individuals aged 40and over.[1] Due to different diagnostic methods, the estimate rate of knee osteoarthritis varies among different populations. A paper published by World Health Organization (WHO) suggests that around 9.6% of men and 18.0% of women over the age of 60 have symptomatic knee osteoarthritis and is more common among elderly women. Around 40 million will be severely disabled with knee osteoarthritis by 2050.

Prevalence and Incidence of Knee Osteoarthritis

In Asia, prevalence rates of knee osteoarthritis were found to be high in elderly people. The risk factors for knee osteoarthritis include obesity, old age, lack of exercise, high bone density, hormonal factors, genetic predisposition and occupation involving prolonged squatting and kneeling.[2-9] With about 11% of women aged 60 years and above frequently reporting symptoms of knee osteoarthritis, it has emerged as a major cause of physical disability among aging people. A population-based prospective study in Melbourne assessed 438 healthy, middle-aged Australian women over 11 years to study factors affecting osteoarthritis and the results of the study showed that 21.6% had evidence of radiological knee osteoarthritis. In another study conducted in China among farmers, it was found that prevalence of radiographic knee osteoarthritis and symptomatic knee osteoarthritis in rural men was double that of their urban counterparts. Rural women also had a higher prevalence of both severe radiographic and symptomatic knee osteoarthritis. Physical activity, BMI, and aging may be the risk factors for radiological knee osteoarthritis and modification of these factors could prevent further development of osteoarthritis. Most of the population ran the risk of developing osteoarthritis after the age of 45 years.[10-11]

It has been reported that osteoarthritis is the second most familiar rheumatologic disease found in India, with an estimated population from 22% up to 39%.[12] A study carried out in the suburbs of Bangalore among 342 patients diagnosed with knee osteoarthritis, based on the modified American College of Rheumatology (ACR) criteria, reported that osteoarthritis was present in about 15.5% of the male population and in 18.8% of the female population.[13] In a research performed in villages and cities around Chandigarh, revealed that about 56.6% of aged persons had osteoarthritis and a lower prevalence of osteoarthritis among elderly people in rural areas, attributing this to high mobility, social interaction, and less obesity.[14]

Risk Factors For Knee Osteoarthritis

Unmodifiable factors like old age, ethnicity, female gender and genetic inheritance are risk factors. Modifiable factors like occupation, overweight, knee injury ,weakness of muscles and obesity affects the loading and contribute to the development of knee OA.[1,15,16] Excess adipose tissue produces humoral factors, leading to changes in the cartilage metabolism. It may be that the leptin system could be a link between metabolic abnormalities in obesity and greater risk of osteoarthritis.[5] Local mechanical factors that contribute to the progression of

knee osteoarthritis are varus or valgus deformity, joint laxity, muscle weakness, repeated kneeling and squatting, loss of structural integrity of the joint, and microfracture.

Pathophysiology of Knee Osteoarthritis

The articular cartilage mainly contains the extracellular matrix (ECM) with scarce population of cells and lacks in nerves, lymph and blood vessels. Knee osteoarthritis was initially considered to be involved with the articular cartilage, but is now seen as a degenerative joint disorder due to complex changes that occur in response to underlying pathophysiology. Initially the inflammation would not be prominent and increased stress beyond the strength of articular cartilage leads to the advanced condition of joint degeneration.[17-19]

Apart from the disintegration of the articular cartilage in knee osteoarthritis, there could be subchondral bone restructuring with sclerosis, cyst formation, muscle atrophy, synovial inflammation, ligamentous involvement and spasm. Joint effusion and thickening of the synovium and capsule may also occur. Osteoarthritis is considered a biological and chemical process, where loss and restructure of joints occurs. C-reactive protein is found to be the inflammatory marker of early knee osteoarthritis. The formation of osteophyte usually appears at the margins of the synovial membrane and hyaline cartilage due to changes in knee joint loading. Osteophyte formation is viewed as the body's reaction to self-repair and redistribute the impact across the joint. The incompetent repair of cartilage could be due to the disturbance of anabolic and catabolic mechanisms that force the inflammatory cytokine proteins, leading to unusual increase in pressure of subchondral bone layer and cartilage. Chondrocyte cells, synovium leukocytes, and bone osteoblast cells/osteoclast cells produce cytokine molecules, an inflammatory moderator.[20-24]

Classification of Osteoarthritis

Knee osteoarthritis may be classified as primary or secondary knee osteoarthritis. Primary knee osteoarthritis is a process in which articular degeneration occurs in the absence of an obvious underlying abnormality. Secondary osteoarthritis of the knee is often the result of injury (trauma) or repetitive motion such as found in certain occupations. It may also happen due to congenital conditions and underlying diseases, systemic metabolic diseases, endocrine diseases, and bone dysplasias.[15,25,24]

Radiological Evidence Of Severity Of Knee Oa

Several biochemical and biomechanical factors are considered for the pathogenesis. Cartilage damage is one of the main pathological changes in osteoarthritis. Synovitis and degenerative changes of articular cartilage are likely to be facilitating factors in the release of osteopontin (OPN) into the synovial fluid. OPN is a multifunctional phosphoprotein secreted by many cell types such as osteoclasts, macrophages, lymphocytes, epithelial cells and vascular smooth muscle cells (SMC) 1, 2 and is present in the extracellular matrix of mineralized tissues and in extracellular fluids at sites of inflammation. A study, based on KL classification radiographic grading of osteoarthritis in the knee, was performed on 39 patients with knee osteoarthritis and 15 as controls.[25] Endoglin concentrations in both plasma and synovial fluid were analysed and it was concluded that endoglin in plasma and synovial fluid is correlated with progressive joint damage in knee osteoarthritis and Endoglin is likely to be useful as a biomarker for determining disease severity. Severity of knee osteoarthritis is based on the KL grading scale. The severity of radiographic knee osteoarthritis may have detrimental effects on functional ability at the later stages of the disease.[26] Due to the effects of knee osteoarthritis, people tend to refrain to participate in behavioural activity of their choice. Knee osteoarthritis, apart from affecting the physical conditions also affects the person's emotional health.[27] There is a shortfall of undefined connection between disease severances and the reported pain and disability. Usually the joint pain increases by activity and reduces at rest. Severe osteoarthritis can result in pain during rest as well as during night time, resulting in restless sleep. Major noticeable changes are not seen in the initial stages of osteoarthritis and the pain and discomfort shall not be recognized till the periosteum membrane, joint sac, peripheral meniscus, or synovium are affected. Osteoarthritis leads to muscle weakness and proprioception can also be affected. The disturbed joint function that occurs because of the changes can ultimately lead to pain.[16]

Knee osteoarthritis pain

Gradual onset of pain seen in knee osteoarthritis. Pain is due to dynamic underlying pathophysiological changes that take place in the peripheral and central nervous system in response to underlying pathology and symptoms. Pain in knee osteoarthritis arises from patellofemoral joints, medial or lateral tibiofemoral compartment and located mostly in and around knee joint and sometimes upper leg or knee.[6,28] Since cartilage is aneural and cannot be the source of pain, the cause of pain could be due to cartilage destruction that might expose the subchondral bone for vulnerabilities, osteophytes rupturing the synovial lining of

the joint capsule or breaking to form fragments of bones in the joint and trabecular microfracture. Pain in knee osteoarthritis patients usually occurs only with motion and only in later stages is the pain experienced at rest also.[29]

In certain cases, jarring of joints due to large stress like holding heavy weights or stressful exercise could also cause the pain. Osteoarthritis pain is normally produced by the stimulation of mechanical or chemical irritation of pain that is conveyed to cerebral cortex through A and C nerve fibres. This involves the activation of thalamic nuclei inside the ventral lateral thalamus and the transmission of message to the cortex, where the noxious stimulus is recognised for location, duration, intensity and quality. Descending pathways originating in the supraspinal centres (somato sensory and limbic cortices) project through the peri-aqueductal gray area to the dorsal horn and modulate the activity in the dorsal horn by controlling spinal pain transmission. The perception of pain is altered by the patient's emotional and cognitive status. Knee osteoarthritis impacts an individual's life in four dimensions: symptoms, loss of function, restricted physical activity, and reduced quality of life. Knee osteoarthritis pain also restricts activities such as walking long distances, climbing stairs, and getting out of a car due to pain leading to functional impairment.[28]

Current pharmacotherapy for osteoarthritis provides only symptomatic relief with drugs such as non-steroidal anti-inflammatory drugs (NSAIDs), opioids, serotonin-norepinephrine reuptake inhibitors, intra-articular injections of corticosteroids and dietary supplements. Also disease-modifying drugs such as monoclonal antibodies, growth factors and cytokine inhibitors are being developed and may be promising alternatives for the management of osteoarthritis.[29] Adjuvant therapy with vitamin supplements, glucosamine, chondroitin sulphate and herb extracts are recommended to reduce pain and improve joint function in osteoarthritis. NSAIDs and capsaicins are being used topically on knees in osteoarthritis patients for relief of pain and inflammation.

NSAIDs exert their analgesic and ant-inflammatory effect by inhibiting cyclooxygenase enzymes but adverse effects such as ulcers, kidney and heart diseases warrant its use for short term only. In patients refractory and contraindicated to NSAIDs narcotic analgesics are used. They act by inhibiting transmission of pain impulses however problem of tolerance, drug dependence has to be addressed. Serotonin norepinephrine reuptake inhibitors such as duloxetine is used to treat depression and chronic musculoskeletal pain in osteoarthritis. This is recommended in patients who are refractory to NSAIDs. Intra-articular injections of

corticosteroids such as methylprednisolone, triamcinolone, betamethasone, triamcinolone and dexamethasone are recommended for patients with moderate to severe osteoarthritis.

Vitamin D supplementation not only improves bone anabolic activity but also reduced pain and loss of function. Glucosamine and chondroitin sulphate induce proteoglycans production by chondrocytes and to suppress inflammatory mediators in synovial fluids. Disease-modifying drugs like growth factors, cytokines, monoclonal antibodies and inhibitors are still in infancy stage of drug development and have been implicated in modulating disease progression by improving regeneration of cartilage and subchondral remodelling, reducing pain, inflammation and matrix degradation.[30]

CONCLUSION

Knee osteoarthritis, a leading musculoskeletal disorder without known cure and having debilitating effect on physical, functional and emotional status of an individual requires a holistic treatment approach.

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Conflict of interest

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