The Egyptian Rheumatologist (2015) 37, 85–91

HOSTED BY

Egyptian Society of Rheumatic Diseases

The Egyptian Rheumatologist

www.rheumatology.eg.net
www.elsevier.com/locate/ejr

ORIGINAL ARTICLE

Clinical and biochemical study of the comparative efficacy of topical versus oral glucosamine/ chondroitin sulfate on osteoarthritis of the knee

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Received 18 June 2014; accepted 19 June 2014
Available online 29 August 2014

KEYWORDS

Osteoarthritis;
WOMAC;
COMP;
Glucosamine sulfate;
Chondroitin;
Structure modifying drug

Abstract *Aim of the work:* The aim of this study was to detect and compare the efficacy of topical and oral glucosamine/chondroitin sulfate on knee OA (OAK), and to prove their efficacy on sparing the articular cartilage among the Egyptian patients.

Patients and methods: 180 patients with OAK were included and randomly divided into 2 groups, each of 90 patients. One group took 1500 mg oral glucosamine/chondroitin sulfate and the other group used topical glucosamine/chondroitin sulfate for 3 months. The diagnosis was based on the American College of Rheumatology (ACR) criteria for OAK. Age, duration of OA, and body mass index (BMI) of the patients were recorded. Knee radiographs were assessed with the Kellgren–Lawrence scale. The severity of knee pain, stiffness, and disability were measured using the visual analog scale (VAS) and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). The serum C-reactive protein (CRP) and Cartilage oligomeric matrix protein changes (COMP) were measured.

Results: No statistical difference was found between the 2 groups regarding age, sex, duration of OA, and Kellgren–Lawrence grading scale. Both VAS and WOMAC subscores showed significant equal relief of pain and joint function between the 2 groups regardless of the severity or duration of knee OA. Topical glucosamine was superior to the oral route in improving stiffness and function.

Conclusion: Topical and oral glucosamine/chondroitin sulfate are safe and equally effective on improving knee pain, stiffness and function. Glucosamine/chondroitin sulfate is beneficial as a symptomatic treatment and not as a cartilage sparing drug in the treatment of OAK.

1. Introduction

Osteoarthritis (OA) is the most common musculoskeletal problem in individuals above 50 years of age. It is a progressive disease that can worsen physical function over time. Worldwide

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Peer review under responsibility of Egyptian Society of Rheumatic Diseases.

http://dx.doi.org/10.1016/j.ejr.2014.06.007

estimates indicate that 9.6% of men and 18% of women ⩾60 years have symptomatic OA. In 1990, OA was estimated to be the eighth leading non-fatal burden of disease, accounting for 2.8% of total individuals living with disability [1]. OA can affect the quality of life; mainly walking and climbing stairs [2]. Osteoarthritis has a significant negative impact on the economy, with its total cost estimated as equivalent of 1% of the gross national product (GNP) per year in the UK [2]. Over a 1-year period in the UK, there were 114,500 hospital admissions, in 2000, there were over 35,000 knee replacements performed at a cost of £405 million and also, 36 million working days were lost due to OA alone, at an estimated cost of £3.2 billion in lost production. At the same time £215 million was spent on social services for OA [3].

OA is often associated with the knee, hip, spine, and fingers [4,5]. It involves all tissues of the diarthrodial joints including the bone, cartilage and supporting elements. OA is characterized by focal degeneration of joint cartilage and formation of new bone in the form of osteophytes at the base of the cartilage lesion in the subchondral bone and at the joint margins [6].

Our joints are cushioned by cartilages and lubricated with synovial fluid such that we can move and twist any joint freely without pain. The principal lubricating substances in our cartilage, tendons, ligaments, synovial fluid and mucous membranes are proteoglycans and glycosaminoglycans (GAGs). Glucosamine which is naturally produced by the body is the main ingredient needed to produce GAGs. Glucosamine stimulates the chondrocytes to produce proteoglycans and increase the production of hyaluronic acid resupply of synovial fluid to act as a lubricant, while chondroitin sulfate attracts water into the cartilage and acts as a shock absorber. The proteoglycans are subjected to continuous metabolic turnover, undergoing constant breakdown and resynthesis. The imbalances in these processes that occur with aging or with other medical conditions are partially responsible for the development of arthritis. In old men, the body loses the capacity to produce sufficient glucosamine causing thinning of the cartilage and leads to joint degeneration [7].

In OA, the rate of synthesis and secretion of matrix-degrading metalloproteinases by the chondrocyte are greatly increased leading to a loss of the proteoglycans from the extracellular matrix. Also, lysosomal enzymes can cleave both hyaluronic acid and chondroitin 6-sulfate. It is to be noted that proteoglycan and collagen synthesis continue to rise in proportion to the severity of the lesion [8]. It is tempting to believe that ingestion of these agents would somehow provide beneficial help to the cartilage [9].

An important biomarker of cartilage degradation is termed cartilage oligomeric matrix protein (COMP). The serum levels were found to reflect the extent of cartilage matrix turnover in patients with OA [7,10–12]. COMP is a pentameric glycoprotein which is highly expressed in the cartilage. It binds collagens I, II and IX accordingly, this abundant cartilage matrix protein might have several roles in cartilage tissue homeostasis, including regulation of collagen fibril formation and maintenance of the integrity and properties of collagen network [13]. The rate of synthesis of COMP is enhanced in the human cartilage with early OA lesions and rising levels of COMP have been found to correlate with progression of the disease [14]. COMP was initially thought to be cartilage specific, over the past few years it has been identified in all structures of the joint, including ligaments, meniscus, tendons, and synovium. Serum level of COMP was found also to be increased after physiological cyclic loading [15].

Previous studies have demonstrated an association between OA progression and inflammation as measured by systemic C-reactive protein (CRP) levels. The more aggressive disease seen in OA patients with elevated CRP levels may be linked to a more inflammatory synovial response in the diseased joint [16].

For decades, the traditional pharmacologic management of OA has been mainly symptomatic without well-documented influence on the duration of the disease and its progression. Dietary supplements have become mainstream products in the management of OA like glucosamine sulfate [17]. Glucosamine sulfate, the pharmaceutical derivative of the naturally occurring aminomonosaccharide glucosamine, a constituent of glycosaminoglycan in the cartilage matrix and synovial fluid, has been used orally for the treatment of OA since the early 1980s. After oral administration, glucosamine sulfate is bioavailable and reaches the articular cartilage. It is preferentially incorporated by the chondrocytes into the components of the glycosaminoglycan chains in the intact cartilage, stimulates the synthesis of physiological proteoglycans, and decreases the activity of catabolic enzymes, including metalloproteases [18].

In addition, the compound may reverse some of the negative effects of interleukin-1 on cartilage metabolism [19]. Also, there is a mild anti-inflammatory effect exerted by the suppression of superoxide radical generation or the inhibition of inducible nitric oxide synthesis and selectively, of the cyclooxygenase-2 pathway.

Contradictory researches were published regarding the efficacy of glucosamine and chondroitin sulfate in OA. Some researchers found that glucosamine has no value in the management of OA [20,21]. Others found that oral glucosamine and chondroitin sulfate may relieve the pain and joint stiffness, physical function, overall questionnaire score, and analgesic use associated with OA [22]. Moreover; they may act as a disease-modifying agent in patients with mild to moderate OA showing delayed radiographic progression of OA of the knee [23–28]. Most currently available glucosamine-based drugs and supplements are taken orally at a dosage (1500 mg daily). The dose reaching the articular cartilage is a fraction of a percentage of the oral dose (10–20%) [29]. Lately; an emulsion matrix [obalin] was available. It can hold up to 20% glucosamine compounds in a stable emulsion which can deliver glucosamine transdermally to the joints [19]. Chondroitin sulfate acts as a carrier substance to enhance dermal penetration [30]. Unfortunately, no data are available comparing the efficacy of the two products in managing OA of the knee [31].

The aim of this study was to detect, compare the efficacy of topical and oral glucosamine/chondroitin sulfate on knee OA and to prove their efficacy on sparing the articular cartilage among the Egyptian patients.

2. Patients and methods

One hundred eighty outpatient females aged 32 to 62 years, diagnosed as OA of the knee based on the criteria of the American College of Rheumatology [31] were included. The following predetermined exclusion criteria were considered on enrollment: Pregnant females; other rheumatologic disorders causing erosive arthritis of the knee; cases with severe osteoarthritis or with moderate or marked knee effusion; regular