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Is Glucosamine/Chondroitin Sulfate effective in the Long-Term on the Progression of Structural Changes in Knee Osteoarthritis?

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To the Editor,

Osteoarthritis (OA) is the most common and disabling disease on the autonomy of older people and it affects the quality of life (1) in the over 70 years population (2). OA has no cure and becomes an important problem of public health. The main goals are to ameliorate pain, inflammation and rigidity, and to diminish articular damage and joint destruction (3, 4).

Glucosamine and Chondroitin sulfate (G/CS) have proven symptomatic slow acting effects on the knee OA; however, its disease modifying drug effect for OA is controversial (5, 6). To demonstrate the disease modifying effect (slowing/reversal of OA progression), it is necessary to perform prospective studies in long periods of time, ideally 1 - 2 years or more (5).

OA affects the cartilage and subchondral bone. The joint space width (JSW) narrowing is not symmetrical. JSW is an indicator of OA progression. In fact, there is a linear negative correlation between cartilage volume loss and OA severity. The lower the JSW, the greater the knee OA severity (7). That correlation is only valid for the medial compartment, due to the fact that for the lateral compartment, the greater the JSW, the greater the OA severity (8). The JSW narrows usually in the weight bearing compartment (mainly medial) and it widens on the contralateral compartment (frequently lateral), which is a phenomena known as the yawn sign (1). Boegard, in a 2-year follow-up study (55 patients, age range 35 - 54), has noticed that the mean minimal JSW diminishes in the medial tibiofemoral compartment, while the same space increases in the lateral tibiofemoral compartment (9). Ledingham, in a 2-year follow-up study (knee OA patients), observed that an increase in JSW was only seen in the lateral tibiofemoral compartment and corresponded with narrowing of the contralateral (medial) worst affected compartment (10). Lanyon, in a 3-year follow-up study reported the narrowing of both medial and lateral tibiofemoral compartments (51 patients, age average 71) (11). These anatomical changes reveal the natural history of knee OA. Besides, the poorer accuracy and precision of measurement on lateral compartment progression is attributable to the variable degree of subluxation in this compartment as a result of medial compartment disease (12).

In a recent brief report (13) published at the arthritis care and research entitled "Long-term effects of Glucosamine/Chondroitin Sulfate on the progression of structural changes in Knee Osteoarthritis: 6-year follow-up data from the Osteoarthritis Initiative", these conclusions have been stated: 1) G/CS had no effect on the medial compartment when assessed by radiographic parameters; 2) G/CS diminished cartilage volume loss in global knee and lateral compartment, however, not on the medial compartment; 3) the protective effect on cartilage was not associated to symptom improvement measured by WOMAC.

In this study, there are some issues to comment. First, the volume of the medial compartment was similar in both groups. The volume of the lateral compartment was greater in the treatment group (G/CS) than in the not-exposed group, but without difference. Indeed, the not-exposed group had a greater JSW than the treatment group ($P = 0.049$). Second, the evolution on X-rays and cartilage volume loss, at 6-year for the medial compartment, showed an even lower loss on the not-exposed group than in the treatment group (G/CS), although not significant ($P = 0.496$). Third, the protective effect of G/CS was only seen on the lateral compartment ($P < 0.001$). As it was stated (1, 9-11), the collapse of the medial compartment produces abnormal forces that could contribute to changes in the lateral compartment, and increase the JSW as a result. Finally, the actual dose of G/CS and the adherence rate of the population could not be determined. Moreover, the protective effect on cartilage was not associated to the symptom improvement measured by WOMAC. On that scenario, the protective effect of G/CS on the lateral compartment and the non-protective effect in the medial compartment could just be a result of progression in the natural history of Knee OA as stated by Boegard, Ledingham, Lanyon, and Fernandez-Cuadros (1, 9, 10).

Due to the fact that all of the arguments exposed the Long-term effects of G/CS on the progression of struc-

tural changes in knee OA, specially the asseveration that G/CS protects the lateral but not the medial compartment, based on radiographic assumptions, it should be taken with caution.

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