

THE CONDROPROTECTOR ROLE IN THE OSTEOARTHRITIS OF THE KNEE

Il ruolo del condroprotettore nell'osteoartrosi del ginocchio

M. BIONDI, M. CRISPINO*,
G. IMPROTA**, M. TRIASSI**

*Clinic of Orthopaedics, District 39 and 40 ASL NA 2
NORD, Naples; * Hygiene and Preventive Medicine -
District 39 of the Prevention Department ASL NA
2 NORD, Naples; ** Department of Public Health,
University of Naples "Federico II"*

Address for correspondence:

M. Biondi
Clinic of Orthopaedics, District 39 and 40 ASL NA 2
NORD, Naples
E-mail: masbiondi@libero.it

Received on November 13, 2012

Accepted on April 17, 2013

SUMMARY

This work is a clinical study designed with the aim to assess the effects of a packet containing 500 mg of glucosamine sulfate, 400mg of chondroitin sulfate, 100mg of Vitamin C, 2 mg of manganese, 100 mg of curcuma in some patients affected by primary osteoarthritis (OA). Our research was conducted during eighteen months from 2010 to 2011 in some patients affected by primary osteoarthritis of the knee. The study evaluated 300 patients. 150 patients were enrolled and divided into three subgroups. Most patients enrolled were female (60%), with a mean age of 54 years old and weight about 70kg. We assessed the pain, the joint functions adverse events, the joint noise. We measured the pain according to the VAS scale (from 0 to 10). The VAS score reduction was statistically significant after 12 weeks. The pain related to the joint load, also measured according to the VAS score, showed a significant reduction during the fourth week. Improvements in the rigidity and in some difficulties related to the normal physical activities were observed during the ninth week. It was really important the arrangement of the elements constituting the integrator, because they are responsible for the evident improvement of daily physical activities.

Key words: condroprotettore, osteoarthritis, glucosamine sulfate, chondroitin sulfate, cartilage degeneration

RIASSUNTO

Il presente lavoro è uno studio clinico che ha lo scopo di valutare una compressa contenente 500 mg di glucosamina solfato, 400 mg di condroitina solfato, 100 mg di vitamina C, 2 mg di manganese, 100 mg di curcumina in soggetti affetti da osteoartrosi (OA) primaria. La ricerca è stata condotta per 18 mesi dal 2010 al 2011 in soggetti affetti da OA del ginocchio. Lo studio ha esaminato 300 pazienti, tra i quali ne sono stati selezionati la metà, divisi in tre sottogruppi. La maggior parte dei pazienti inclusi nello studio sono state donne (60%) con un'età media di 54 anni e un peso corporeo di 70 kg. Sono stati valutati dolore, funzione articolare, eventi avversi e rumore articolare. In particolare il dolore è stato valutato secondo la scala VAS (da 0 a 10). È stata osservata una riduzione statisticamente significativa del punteggio VAS già dopo 12 settimane. Il dolore, durante il carico articolare, valutato dal punteggio VAS ha mostrato un miglioramento significativo alla quarta settimana. Inoltre, alla nona settimana sono stati osservati miglioramenti nella rigidità e nella difficoltà ad eseguire le normali attività fisiche. È risultato importante la combinazione degli elementi che compongono l'integratore, poiché sono responsabili dell'evidente miglioramento delle attività fisiche giornaliere.

Parole chiave: condroprotettore, osteoartrosi, glucosamina solfato, condroitina solfato, degenerazione della cartilagine

INTRODUCTION

The osteoarthritis (OA) is a chronic disease affecting the joints, due to the articular cartilage degeneration and to the chemical and mechanical functional alterations, as recognized by Euler ¹.

According to the Literature, the OA is determined by a complex interaction between biological and pathological processes, where numerous factors – such as age, obesity, muscle strength, fractures and/or luxations, repeated microtraumas and instability – are playing.

Although the osteoarthritis etiology is not yet clear, it is certain that the cartilage damage is critical in the occurrence of OA. The osteoarthritis of the knee is the first cause of pain and of disability in Western Countries ². The related diagnosis is assessed through radiological methods. The radiography shows a joint space reduction, an osteophyte formation and a subchondral sclerosis ³. The OA is an heterogeneous condition, so the risk factors, the clinical manifestations and the related prognosis could vary according to the corporal region involved. Generally, joints most frequently affected are the knees, followed by the hip, the hands and the facet vertebral joints.

It is characterized by some damaged areas of the cartilage surfaces and synovial joints, associated with such remodeling of the underlying bone and with a synovitis. It could be defined in different ways due to the numerous clinical and radiological features. The clinical features are: the pain (joint pain and joint crepitus); in serious cases the feature is the joint space reduction and the osteophytes formation, that could be seen by radiology. The gonarthrosis often occurs: it determines significant pain, and instability, so it could often leads to physical disability ⁴. Patients are often examined on radiological and not clinical bases; pain is a decisive factor in the assessment of the disease progression. A series of treatments could support the manage of the symptoms associated with the osteoarthritis of the knee.

Non-pharmacological interventions include weight loss, physical exercise and physiotherapy. Pain control is achieved with the mobility, the classic analgesia, NSAIDs and opioids. We can also associate some physical therapy cycles (TENS, TECAR therapy, LASERJAG). If the noninvasive interventions fail in the pain control, intra-articular infiltrations (Hyaluronic ac.), arthroscopic lavages, and finally the arthroplasty could be performed.

These treatments have the aim to manage the pain and to avoid the joint function loss.

Almost the interventions doesn't affect the disease progression and the arthroplasty of the knee is the only way to manage the pain and return to the function. Several international studies showed that the glucosamine (GS) and the chondroitin (C) – two cartilage's components – can reduce the pain related to the osteoarthritis and contribute to the cartilage's reconstruction in the starting OA ^{5,6}.

Glucosamine is a natural amino-sugar; it is a main element of the complex proteins called glycosaminoglycans, which are an integral part of the cartilage structure. Hyaline cartilage is composed for the 50% by collagen and for the rest by proteoglycan which give her a viscoelastic resistance with bearing function ^{7-10,12}.

Chondroitin is a large molecule; it generates a gel constituting part of the cartilage, increasing her compression resistance ¹¹.

Several studies showed that nutraceutical supplements are effective in reducing symptoms and some of them affected the course of osteoarthritis ¹³.

The C Vitamin is an excellent antioxidant that preserves the cells by the damaging effects due to the antioxidants. Curcumin is the main biologically active component of the turmeric, also known as diferuolmetano; particularly, at least 400 scientific publications in the last four years confirm its significantly anti-inflammatory, antioxidant and anticarcinogenic properties ¹⁴. Also the interest in the potential of the curcumin as a neuroprotective factor is increasing, because, unlike the other antioxidant elements, curcuminoids are able both to prevent the free radicals creation, and to neutralized the existing ones. Several studies showed that the curcumin is not toxic for humans up to 8000 mg/day.

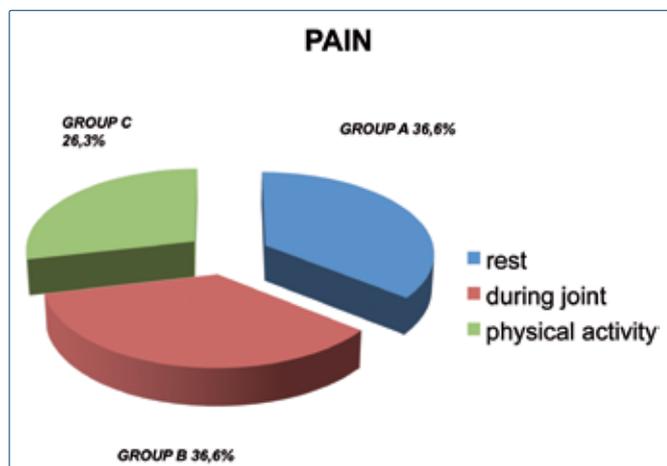
The US FDA (food and drug administration) classifies the curcumin as a GRAS (General Recognition and Safety) substance, also named "generally recognized as safe". It acts against arthritis as it is able to stop both the NF (tumor necrosis factors) and the TNF action ¹⁴.

The aim of this study is to clinically evaluate the use of one dietary integrator dose containing glucosamine sulphate, chondroitin sulphate and curcumin.

MATERIALS AND METHODS

This work is a clinical study that has the aim to evaluate a tablet containing GS, C, MN, 100 mg of curcumin and C vitamin in patients affected by primary osteoarthritis. This search was performed in a period of 18 months; it was started on the 5th of January 2010 in the two laboratories of the Local Agency NA2 North (district 42) and was finished on the 5th of July 2011. 300 patients were considered; 150 were excluded because they did not meet the radiographic criteria (70) and were older than 56 years old (80). Most patients included in this study were female (60%), with a mean age of 54 years old, weight of 70 kg; patients affected by OA of the knee gave their informed consent. 150 patients both male and female between 35 and 65 years old were enrolled. The inclusion criteria were the primary OA of the knee, diagnosed both clinically and radiologically with synovitis signs, persistent pain from at least two months and VAS score of at least 4 during the gait (Rating Scale Painful). The exclusion criteria were the presence of rheumatic factors (rheumatoid arthritis), allergies to chondroitin and selfish, serious medical conditions (AIDS, terminally renal disease), pregnancy, chronic assumption of FANS, hepatic disease, diabetes, corticosteroids assumption until three months before the beginning of the study. After the inclusion selection, the study group was divided into three subgroups, particularly the first characterized by rest pain (55 patients), the second by pain during load joint (55 patients), and the third by pain during physical activity (40 patients) (Fig. 1).

FIGURE 1.
Division into subgroups according to pain.



The therapy involved the assumption, every day during a period of 90 days, of one tablet containing 500mg of glucosamine sulfate, 400 mg of chondroitin-sulfate, 100 mg of C vitamin, 2mg of manganese, 100mg of curcumin. Clinical controls were carried out at the 2nd, 5th, 9th, 12th and at the 16th week. Pain, joint function adverse events, joint noise were assessed. Pain was evaluated according to the VAS score (from 0 to 10). Two patients in the first group and three patients in the second group did not complete the study due to adverse events: nausea (affecting two subjects in the first group and three subject in the second group), diarrhea (affecting three subjects in the second group). These patients left the study after 11 days; it was not noticed any difference about the age and the gender distribution between the groups.

Glucosamine and chondroitin sulfate are the most components used in the arthritis therapy; it is considered in the world that the use of such components in the osteoarthritis treatments has a considerable influence on the process of cartilage degeneration in the following way:

- Glucosamine affects the cartilage formation and repair.
- The chondroitin-sulfate is a part of such protein molecule that contributes in providing to the cartilage its elastic properties and has an anti-inflammatory action; this leads to the pain and the joint swelling reduction. Furthermore, the chondroitin-sulfate contributes to the damaged cartilage recovery to better amortize the joints.
- Numerous clinical studies showed that the collagen of the type II protects the cartilage structure and affects

its synthesis, improving both the mobility and the joint. Due to its ability to be hydrolyzed within the intestine it grows in the cartilage, and it is able to stimulate the synthesis of macromolecules in the extracellular matrix through the chondrocytes.

- Curcumin is known for its anti-edemigen, anti-inflammatory and antioxidant functions. Well known is also the anti-cancer activity.

RESULTS

The therapy, delivered as described above, led to a significant VAS score reduction already after 12 weeks; all three subgroups showed a pain reduction particularly during the night. As far as in particular the pain related to the joint load, assessed by the VAS score, it had a significant improvement in the fourth-fifth week only in the first group. In addition, some improvements in the rigidity and in the difficulty associated with any regular physical activities were observed in the ninth week.

Significant was the combination between the elements constituting the integrator, since they are responsible for the noticeable improvement in daily physical activities. It was demonstrated that they could act on the pain related to the OA by reducing it, and that they also support the cartilage reconstruction in the early stages of OA. Muscletonic and growing stimulation properties of these components, in fact, contribute to reduce the joint functions.

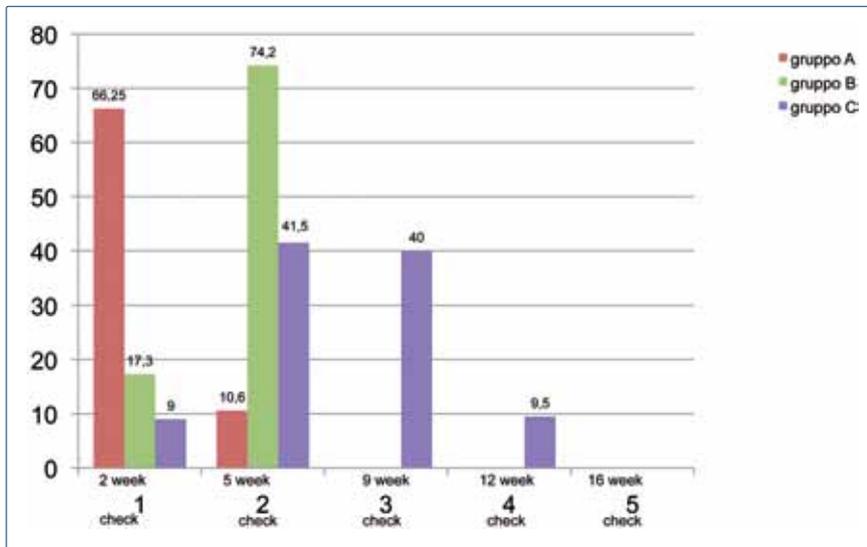
FANS assumption was significantly reduced over few weeks (about two) and since from the fifth weeks patients did not assume them.

In particular, the group suspended already after a few days the NSAIDs assumption. Most patients in the first and second group did not take FANSs at the fifth week. At the sixteenth the three groups were recalled to verify the therapy effects (Fig. 2).

Glucosamine and chondroitin-sulfate showed an anti-inflammatory action able to improve the pain, by giving to the cartilage structure a chance of strengthen.

Important in these processes is the curcumin action, which acts as anti-inflammatory and constitutes a part of a protein molecule that provides to the cartilage its elastic properties and has an anti-inflammatory action: this allow to obtain the both pain and the joint swelling reduction. Curcumin suppresses the activation of the transcription factor NFkB this leads to inhibition of cyclooxygenase₂ (COX₂) expression and metal prothesis₉ (MMP₉) in human chondrocytes: implications for the treatment of osteoarthritis.

Furthermore, the chondroitin sulfate affects the damaged cartilage recovery in order to better amortize the joints.

FIGURE 2.**Week suspended NSAID assumption.****CONCLUSIONS**

The osteoarthritis is a chronic inflammatory disease characterized by a structural alteration of the articular cartilage. NSAIDs act on the pain in the acute phase. The aim of the glucosamine and chondroitin assumption is to support the metabolism of the articular cartilage structure, by acting on the process modulation of the cartilage degeneration, improving the quality of both cartilage and synovial fluid.

The results of this study showed that the combination of the various components studied may be an effective solution for the pain symptoms in those subjects who are affected by moderate OA.

Therefore, we can conclude that this product may provide an effective aid to reduce the painful symptoms in the osteoarthritis of moderate grade.

REFERENCES

- Jordan KM, Arden NK, Doherty M, et al. *EULAR Recommendations 2003: an evidence based approach to the management of knee osteoarthritis: Standing Committee for International Clinical Studies Including Therapeutic Trials ESCISIT. Report of a Task Force of the Standing Committee for International Clinical Studies Including Therapeutic Trials (ESCISIT)*. Ann Rheum Dis 2003;62:1145-55.
- Bedson J, Jordan K, Croft P. *The prevalence and history of knee osteoarthritis in general practice: a casecontrol study*. Fam Pract 2005;22:103-8.
- Zhang W, Moskowitz RW, Nuki G. *OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expertconsensus guidelines*. Osteoarthr Cartil 2008;16:137-62.
- Sengupta K, Alluri KV, Satish AR, et al. *A double blind, randomized, placebo controlled study of the efficacy and safety of 5-Loxin for treatment of osteoarthritis of the knee*. Arthritis Res Ther 2008;10:R85.
- Ringdahl E, Pandit S. *Treatment of knee osteoarthritis*. Am Fam Physician 2011;83:1287-92.
- Zhang W, Nuki G, Moskowitz RW, et al. *OARSI recommendations for the management of hip and knee osteoarthritis: part III: Changes in evidence following systematic cumulative update of research published through January 2009*. Osteoarthritis Cartilage 2010;18:476-99.
- Towheed TE, Maxwell L, Anastassiades TP, et al. *Glucosamine therapy for treating osteoarthritis*. Cochrane Database Syst Rev 2005;(2):CD002946.
- Richy F, Bruyere O, Ethgen O, et al. *Structural and symptomatic efficacy of glucosamine and chondroitin in knee osteoarthritis. A comprehensive meta-analysis*. Arch Intern Med 2003;163:1514-22.
- Jobanputra P. *Structural and symptomatic efficacy of glucosamine and chondroitin: relevant financial interest?* Arch Intern Med 2004;164:338-39.
- Poolsup N, Suthisang C, Channark P, et al. *Glucosamine long-term treatment and the progression of knee osteoarthritis: systematic review of randomized controlled trials*. Ann Pharmacother 2005;39:1080-87.
- Bana G, Jamard B, Verrouil E, et al. *Chondroitin sulfate in the management of hip and knee osteoarthritis: an overview*. Adv Pharmacol 2006;53:507-22.
- Clegg DO, Reda DJ, Harris CL, et al. *Glucosamine, chondroitin sulphate, and the two in combination for painful knee osteoarthritis*. N Engl J Med 2006;354:795-807.
- Bello AE, Oesser S. *Collagen hydrolysate for the treatment of osteoarthritis and other joint disorders: a review of the literature*. Curr Med Res Opin 2006;22:2221-32.
- Davis JM. *Curcumin effect on inflammation and performance recovery following eccentric exercise-induced muscle damage*. American Physiology 2007;292:R2168-R2173.