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Meriva®+Glucosamine versus Condroitin+ Glucosamine in patients with knee osteoarthritis: an observational study

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Abstract. – OBJECTIVE: Osteoarthritis (OA) is a major cause of physical disability and impaired quality of life. Non-steroidal anti-inflammatory drugs are the most used treatment for OA, but they are frequently associated to adverse events.

Alternative therapies are under investigation for the treatment of OA. Meriva® is a lecithin delivery form of curcumin, a powerful promoter of anti-oxidant response studied in a number of conditions related to chronic inflammation and pain.

PATIENTS AND METHODS: This 4-month observational study, conducted in a 'real-life' scenario, compares the association of Meriva and glucosamine (n=63) with chondroitin sulphate+glucosamine (n=61) in 124 patients with grade 1-2 OA of the knee.

RESULTS: Patients treated with Meriva+glucosamine had significantly higher Karnofsky Index and WOMAC score (both in the physical and emotional domains), compared to those in the chondroitin+glucosamine group. Noteworthy, the walking distance at the treadmill test after 1 month was also significantly higher in the meriva+glucosamine group; this advantage was sustained until the end of the study. Although the need for concomitant drugs and medical attention decreased in both groups, this reduction was more evident for patients treated with Meriva+glucosamine.

CONCLUSIONS: Taken together, the results of this study shows that the 4-month administration of the association of Meriva and glucosamine can result in a faster onset of action and improved outcomes than the administration of an association of chondroitin sulphate and glucosamine in patients with OA.

Key Words:
Curcumin, Glucosamne, Meriva, Osteoarthritis.

Introduction

Osteoarthritis (OA) is a major cause of physical disability and impaired quality of life in industrialized and in developing countries, with a dramatic impact on healthcare costs[1]. Typically, osteoarthritis is managed with palliative measures that focus on the reduction of symptoms such as lifestyle modification and analgesics[2,3]. Non-steroidal anti-inflammatory drugs (NSAIDs) remain the most used treatment option for OA, but these drugs are frequently associated with adverse events. On these bases, alternative therapies are widely used for the treatment of OA[4].

As a constituent of turmeric (*Curcuma longa L.*), curcumin (diferuloylmethane) has been used for centuries in traditional medicine of India and the Far East[5,6]. Curcumin is a powerful promoter of anti-oxidant response[7], and is now commercially available in a lecithin delivery system (Meriva®, Indena SpA, Milan) that improves the bioavailability of curcuminoids. This formulation has been extensively investigated in a number of conditions triggered and/or sustained by chronic inflammation and associated with pain, like diabetic microangiopathy and retinopathy[8], central serous chorioretinopathy[9], benign prostatic hyperplasia[10], chemotherapy-related adverse effects in cancer patients[11], pain[12], muscle soreness[13], and OA[14,15].

With respect to OA, a three-month registry study in 50 patients showed improved symptoms and joint function with the administration of Meriva, as assessed by the Western Ontario and McMaster Universities (WOMAC) score and the treadmill walking performance[14]. In another larger study (n=100), Meriva improved both clinical endpoints and the inflammatory profiles of OA patients[15]. However, additional evidence is required to fully evaluate the potential role of Meriva in the management of OA.

The aim of the present observational study, conducted in a 'real-life' scenario, is to compare the association of Meriva and glucosamine, a widely used compound in the treatment of OA[16] with the association of chondroitin sulphate+glu-

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cosamine, which has been shown to provide significant relief of the symptoms of OA[16].

Patients and Methods

Patients

The 4-month study enrolled patients with grade 1-2 OA of the knee (either one or two joints), according to the criteria or the American College of Rheumatology and confirmed by x-ray analysis.

All subjects were required to be able to perform the treadmill walking test and to understand all questions from the WOMAC questionnaire[17]. Exclusion criteria were as follows: cardiovascular disease requiring drug treatment, diabetes, body mass index >25, severe metabolic disorders, surgery or arthroscopy within three months prior to inclusion, any oncological condition, or severe bone or joint deformation or condition making the patient unable to walk. Pregnancy, breast feeding, and planned conception were also exclusion criteria.

Patients were informed about the aim of the study and treatment procedure according to the Declaration of Helsinki and provided informed consent. Patients were informed that they could leave the study at any time and were allowed to use NSAIDs as needed.

Interventions

All patients received the best management for OA[2]. Patients on an association formulated in tablets (1 tablet/day), each tablet containing 500 mg Meriva® (Indena SpA, Milan, curcumin phospholipids complex) and 500 mg Regenasure® (Cargill, vegetarian Glucosamine HCl) were compared with those on an association formulated in capsules (2 capsules/day), each capsule containing 400 mg Chondroitin sulphate and 415 mg Glucosamin HCl.

Both formulations were purchased on the Italian market and are currently sold through pharmacies.

Evalutations

The Karnofsky Performance Scale Index was used to classify patients as to their functional impairment. The Karnofsky Performance Scale Index can be used to compare effectiveness of different therapies and to assess the prognosis in individual patients. The lower the Karnofsky score, the worse the functional impairment[18]. This parameter was evaluated at baseline and at the end of the study.

The WOMAC questionnaire was also applied, in order to describe and rate the symptoms of OA[17]. The status of OA signs/symptoms was evaluated by the investigator together with the patient at inclusion and at the end of the study.

Patients were trained to perform the treadmill test in two tutorials. Performance was evaluated by the treadmill test at a speed of 3 km/hour and an inclination of 10 percent. The total distance that could be covered without pain (inducing patients to slow down the pace or stop) was noted at the beginning, after 1 months, after 2 months and at the end of the trial.

A diary was kept to record the use of any drug prescribed by the patient's physician, the use of which was free (with only a warning not to use an excess of treatment). The treatment and other costs (including work disruption and hospital admission) occurring during the trial period were recorded in a specific file.

Safety and Tolerability

Safety and tolerability were assessed by weekly phone and mail contacts. All clinical adverse events were evaluated in terms of intensity: mild, moderate, or severe.

Statistical Analysis

All data were analyzed by descriptive statistics. Intra- and inter-group comparisons were performed by the Student's t test or the ANOVA test, as appropriate. A p value < 0.05 was considered statistically significant.

Results

Patient Population

In total, 124 patients were evaluated (61 men; mean age 56.4±5.2 years). Of these, 63 received Meriva+glucosamine and 61 chondroitin+glucosamine.

Baseline characteristics are depicted in Table I. No differences were reported between the two groups in any characteristics. In total, 10 patients withdrew from the study for personal reasons. No adverse events were reported.

Effectiveness Evaluation

At the end of the study, the Karnofsky Index was significantly higher in the Meriva+glucosamine than in the chondroitin+glucosamine group (Table II). A similar finding was report-

Table I. Baseline characteristics.

Patient Data	Meriva+glucosamine	Chondroitin+glucosamine
Total completing 3 months	63	61
Dropouts	4	6
Age (years)	56.6 ± 4.7	55.8 ± 5.8
Males	31	30
Mean global inclusion WOMAC score	83.6 ± 5.3	82.7 ± 4.5
Treadmill test (meters)	85.6 ± 12.0	88.3 ± 18.4

WOMAC: Western Ontario and McMaster Universities

Table II. Karnosfki index.

	Baseline	4 months
Meriva+Glucosamine	71.2 ± 5.4	93.4 ± 6.4*+
Chondroitin+glucosamine	71.6 ± 6.2	79.6 ± 6.6+

*$p < 0.05$ vs chondroitin+glucosamine; +$p < 0.05$ vs baseline.

ed for the WOMAC scores, both in the physical and emotional domains (Tables III and IV).

Noteworthy, the walking distance at the treadmill test was significantly higher in the meriva+glucosamine group than in the control group already at 1 month; this advantage was sustained until the end of the study (Table V).

Need for Concomitant Drugs and Medical Attention

The need for concomitant drugs and medical attention decreased in both groups: however, the use of Meriva+glucosamine was associated with a reduced need for concomitant drugs and medical attention than the association of chondroitin+glucosamine (Table VI).

Discussion

Taken together, the results of this observational study, conducted on OA patients in a 'real-life' scenario, show that the 4-month administration of the association of Meriva and glucosamine can result in a faster onset of action and improved outcomes than the administration of an association of chondroitin sulphate and glucosamine. Notably, this latter association is widely used for the treatment of OA[16], a widespread inflammatory condition characterized by a significant socio-economical burden for which alternative therapies are widely used. Of note, the Meriva+glucosamine association resulted also in a decreased need for medical attention, with a consequent potential reduction in medical costs.

Meriva® is based on curcumin, a traditional product of traditional Indian medicine. Curcumin is one of the most extensively investigated natural products[5,6] and its broad spectrum of preclinical activity and low toxicity suggests benefit for the treatment of several inflammatory conditions. However, only few successful clinical studies of curcumin have been reported[19], mainly due to its poor oral bioavailability. In fact, unrealistically-high dosages of curcumin (>10 g/day) are required to achieve plasma concentrations corresponding to those suggested in preclinical studies[20]. To overcome these issues, Meriva was developed, a phytosome complexing curcumin with phosphatidylcholine[8]. Studies on Meriva[8-15] encompassed different preclinical or clinical conditions. The focus was however on OA because

Table III. WOMAC score, physical function

	Meriva+glucosamine		Chondroitin+glucosamine	
WOMAC item	Baseline	4 months	Baseline	4 months
Pain	15.6 ± 3.2	6.8 ± 2.0*+	15.4 ± 1.7	10.2 ± 2.2+
Stiffness	7.0 ± 1.8	3.1 ± 1.0*+	7.6 ± 1.8	5.5 ± 1.9+
Physical functions	55.7 ± 7.1	26.4 ± 5.7*+	56.3 ± 4	48.5 ± 2.4+
Totals	83.6 ± 5.3	36.3 ± 5.0*+	88.3 ± 18.4	64.2 ± 7.3+

WOMAC: Western Ontario and McMaster Universities; *$p < 0.05$ vs chondroitin+glucosamine; +$p < 0.05$ vs baseline

Table IV. WOMAC score, social and emotional function.

	Meriva+glucosamine		Chondroitin+glucosamine	
WOMAC item	Baseline	4 months	Baseline	4 months
Social functions	22.7 ± 2.0	9.4±2.2*+	22.7 ± 3.3	17.6 ± 3.2+
Emotional functions	30.3 ± 3.4	13.5±2.0*+	34.2 ± 2.6	28.3 ± 2.7+

WOMAC Western Ontario and McMaster Universities; *$p < 0.05$ vs chondroitin+glucosamine; +$p < 0.05$ vs baseline.

Table V. Treadmill test.

	Meriva+glucosamine	Chondroitin+glucosamine
Baseline	85.6 ± 12.0	88.3 ± 18.4
1 month	213 ± 15.2*+	102 ± 19.6
2 months	278 ± 21.1*+	167.3 ± 16+
4 months	374 ± 31.4*+	224.5 ± 32.6+

*$p < 0.05$ vs chondroitin+glucosamine; +$p < 0.05$ vs baseline.

Table VI. Need for concomitant drugs and medical attention.

	Meriva+ glucosamine	Chondroitin+ glucosamine
Use of NSAIDs or painkillers	-44%*	-23%
Gastrointestinal complications	-56%*	-15%
Use of other drugs/treatments	-38%*	-21%
Management costs	-26%*	-12%
Distal edema	-28%*	-18%
Hospital admissions, consultation, and tests	-32%*	-21%
Non-drug treatment (e.g., physiotherapy), costs due to complications, etc.	-33%*	-18%

*$p < 0.05$ vs chondroitin+glucosamine

of the strong rationale for the use of curcumin in this inflammatory disease[14,15]. Although the lack of randomization, the relatively short follow-up and the overall limited number of patients should be taken into account, we believe that the present study adds further evidence to the use of Meriva in OA by suggesting that this compound can be considered as an effective add-on treatment to glucosamine in OA patients. Larger and longer studies, possibly with a randomized design, are however necessary to either confirm or discard these findings.

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Conflict of Interest

The Authors declare that they have no conflict of interests.

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