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File: ■ Turmeric (*Curcuma longa*)
■ Meriva®
■ Osteoarthritis

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RE: Turmeric Complex with Phosphatidylcholine Safe and Effective as Adjunct in Mild to Moderate Osteoarthritis

Belcaro G, Cesarone MR, Dugall M, et al. Efficacy and safety of Meriva®, a curcumin-phosphatidylcholine complex, during extended administration in osteoarthritis patients. *Altern Med Rev*. 2010;15(4):337-344.

Turmeric (*Curcuma longa*) root has a long history of use for treating inflammation and arthritis.[1] Within the compounds isolated from turmeric root, curcumin has been extensively investigated and shown to be effective in treating inflammation, in part, by suppressing the expression and function of a series of cellular agents (enzymes, cytokines, transcription factors) associated to this condition.[1,2] Despite this and evidence of other bioactivity, the clinical exploitation of curcumin has lagged behind because of poor bioavailability.[1] The researchers in this two-armed study have addressed curcumin's potential in alleviating osteoarthritis (OA) symptoms, capitalizing on the improved bioavailability of curcuminoids formulated with phospholipids, as in Meriva® (Indena S.p.A.; Milan, Italy).

The researchers recruited 100 patients with x-ray diagnosed OA in either or both knees. The patients included had mild to moderate pain, were not fully responding to non-steroidal anti-inflammatory drugs (NSAIDs), and were allowed to use NSAIDs, analgesics, and other treatments throughout the study. Patients who were under medical treatment for cardiovascular disease or diabetes, or had a body mass index >25, were excluded, as were those who were suffering from a severe metabolic disorder, had undergone surgery or arthroscopy in the 3 months prior to the study, or had oncologic or severe bone or joint conditions. Patients unable to walk were also excluded from the study. In addition, female patients breastfeeding, pregnant, or planning on a pregnancy were not included. The researchers split the 100 patients into 2 study groups; group A, the control group, used the best available treatment according to their doctor and specialist's directives. Group B, the treatment group, received the best available treatment along with Meriva.

While Meriva was developed by Indena S.p.A., it was made for this study by Sigmar Italia S.p.A., Almè, Italy. The treatment was 1,000 mg daily in the form of two 500 mg

pills consumed after morning and evening meals for 8 months. This regimen corresponded to an overall intake of 200 mg of curcuminoids per day. The composition of each pill was 20% curcuminoid mixture (75% curcumin, 15% demethoxycurcumin, and 10% bisdemethoxycurcumin), 40% phosphatidylcholine, and 40% microcrystalline cellulose. No use of placebo is mentioned in the control group.

The symptoms and severity of OA were measured in various ways at the beginning and end of the study. Patients' functionality was assessed using the Karnofsky Performance Scale Index and patients answered the Western Ontario and McMaster Universities (WOMAC) questionnaire for symptom evaluation. Also, patients were asked to conduct a treadmill test, in which patients' ability to walk without pain at 3 km/hour at a 10% inclination for as long as possible was evaluated. The researchers also required the patients to document their use of other drugs during the study, as well as certain quality of life indicators like time off of work or hospitalization due to OA. Lastly, the patients' blood was collected, and oxidative stress was measured in Carr units, in addition to a set of inflammatory markers that included erythrocyte sedimentation rate (ESR), interleukin-1β (IL-1β), IL-6, soluble CD40 ligand (sCD40L), and soluble vascular cell adhesion molecule-1 (sVCAM-1).

From the 100 total patients enrolled in the study, 11 dropped out due to logistical conflicts, leaving a final n=44 for the control group and n=45 in the treatment group. The treatment group's Karnofsky Performance Scale Index was significantly improved after 8 months from 73.3 at baseline to 92.2 ($P<0.05$). No difference in the index was observed in the control group. The overall WOMAC score in the treatment group significantly improved by decreasing from 80.6 to 33.3 ($P<0.05$). The WOMAC scores for the treatment group's pain dropped significantly from 16.6 to 7.3 ($P<0.05$) at the study's conclusion. In addition, the WOMAC scores for stiffness were significantly reduced from 7.4 to 3.2 ($P<0.05$). The WOMAC scores for physical function also improved significantly in the treatment group from baseline to the end of the study by decreasing from 56.6 to 22.8 ($P<0.05$). The scores for emotional and social function were also significantly improved, 33.9 vs. 10.2 and 24.4 vs. 10.3 from baseline to endpoint, respectively ($P<0.05$ for both). No significant differences were seen in any of the control group's WOMAC scores at the end of the study, and all treatment scores were improved significantly compare to control ($P<0.05$).

At the end of the study, the researchers also report a significant 3.87-fold improvement in the treatment group's treadmill test results over the control group ($P<0.05$ compared to baseline and controls). Also, the treatment group's inflammation markers ESR, IL-1β, IL-6, sCD40L, and sVCAM-1 were significantly reduced ($P<0.05$ for all), while no significant difference in these markers was observed in the control group. A notable result reported in the treatment group was the 63% reduction in the use of NSAIDs (e.g., celecoxib) and doctor-recommended painkillers (e.g., acetaminophen) as compared with a 12% reduction in the control group ($P<0.05$). The researchers also report significant reductions in gastrointestinal complaints, distal edema, and hospital services related to OA in the treatment group vs. the control group at the end of the study ($P<0.05$ for each). The reported percentages for all of these changes differed from the presumed mean decreases in the text and the given median decreases in Table 8.

The authors conclude that the association of Meriva to conventional anti-inflammatory therapy improves the management of a multitude of symptoms and lifestyle indicators associated with OA. The authors mention that a dosage of 1 g Meriva/day

(corresponding to 200 mg/day curcuminoids and ca.150 mg/day curcumin) is much less than the 10 g/day or even larger doses of unformulated curcumin used in other pre-clinical or clinical studies on curcumin.

This study confirms the beneficial effect of Meriva evidenced in a previous smaller and shorter study.[3] Of notable interest is the documentation of a positive effect of Meriva on OA at a low daily dosage of curcumin. This observation supports the dramatic increase in bioavailability of curcumin from Meriva observed in a previous animal study.[4] Another additional important result of this study is the significant decrease of NSAID and analgesic usage by patients also taking Meriva, along with an associated significant reduction in gastrointestinal adverse effects and costs. The decrease of various inflammatory markers, especially IL-1β, IL-6, suggests a generalized downregulation of the inflammatory status.

One weakness of this study is the absence of a placebo pill for the control group; thus, any placebo effect is not accounted for or addressed. Despite this problem, the study furthers the knowledge of curcumin use via Meriva as an adjuvant for OA treatment. Furthermore, the observed benefits provide a basis for the study of Meriva as a stand-alone agent in future comparative studies with NSAIDs for the treatment of OA, at least in its milder form.

—Amy C. Keller, PhD

References

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