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Original article

Effect of L-carnitine supplementation on clinical symptoms in women with osteoarthritis of the knee: A randomized, double-blind, placebo-controlled trial

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Abstract

Introduction: L-carnitine has been reported to be helpful in the treatment of osteoarthritis due to its prophylactic role in cartilage degradation. The aim of this study was to investigate the effect of L-carnitine supplementation on clinical symptoms of females with knee osteoarthritis (OA).
Methods: In this randomized double-blind placebo-controlled trial, 72 females with mild to moderate osteoarthritis of the knee were randomly assigned into two groups to receive 750 mg/day L-carnitine ($n = 36$) or placebo ($n = 36$) for 8 weeks. Clinical symptoms were assessed using the WOMAC Osteoarthritis Index and 50% improvement was considered as the threshold for clinical significance. Data were analyzed by paired *t*-test, independent *t*-test, and analysis of covariance.
Results: Sixty-nine patients completed the trial. L-carnitine supplementation led to significant reduction of 46.9%, 54.1%, 48.4% and 44.4% in the WOMAC total score and sub-scores of pain, stiffness and physical function, respectively ($p < 0.001$); whilst in the placebo group, significant reductions were only observed in WOMAC total score and pain sub-score ($p < 0.05$). Comparison of changes between two groups indicated significant differences in WOMAC total score and all sub-scores ($p < 0.05$). These significant differences were also observed between the two groups after adjusting for baseline scores ($p < 0.001$). The number needed to treat (95% CI) for patients who consumed L-carnitine for at least 50% reduction in WOMAC sub-scores of pain and stiffness were 3.3 (2.0, 14.90) and 2.1 (1.6, 4.13), respectively.
Discussion: Although further studies are needed to confirm positive effects of L-carnitine on clinical symptoms in knee OA patients, it seems that L-carnitine may provide a new complementary approach for patients with osteoarthritis of the knee.

Keywords: L-Carnitine; Females; Osteoarthritis; Clinical symptoms, Nutritional supplementation

Introduction

Osteoarthritis (OA) is generally considered as a degenerative disorder involving cartilage degradation, accompanied by local inflammation that accelerates the joint destruction [1]. Symptoms include pain, stiffness, and decreased motion which lead to the limited activity and poor quality of life [2]. OA represents the most common joint disorder among adults [1], affecting an approximately 12–15% of the population between 25 and 74 years of age [3]. The prevalence of this debilitating disease increases significantly with age [3] and is more prevalent in women than men [4]. OA of the knee is more common than in any other joint as knees are the primary weight-bearing joints [5].

It has been suggested that an imbalance between synthesis and degradation of the cartilage matrix components leads to OA [6]. Cartilage degeneration is triggered by loss of matrix proteoglycans, changes in collagen-type production, and at later

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stages, chondrocytes can lose viability due to apoptosis or senescence [6]. Chondrocytes, the only cells present in the cartilage, play an important role in maintaining the cartilage tissue through the production and secretion of collagens, proteoglycans and enzymes affecting cartilage metabolism [7]. Furthermore, mitochondria have a main role in energy production necessary for chondrocyte activity. The inflammation which accompanies OA, targets mitochondria activity resulting in a reduction of ATP synthesis and cellular activity [8]. This decrease in cellular activity can explain the high rate of apoptosis, which is found in osteoarthritic cartilage [9].

Currently there is no apparent cure for OA; however, several approaches including lifestyle modifications, medications or surgery have been suggested for managing the symptoms of OA [2].

Traditional medical treatments for OA usually involve the use of analgesics (i.e., acetaminophen, tramadol), non-steroidal anti-inflammatory drugs (NSAIDs) (i.e., ibuprofen, diclofenac), or cyclooxygenase-2-specific (COX-2) NSAIDs (i.e., celecoxib) alone or in combination. Many of these treatments have shown limited effectiveness in randomized controlled clinical trials [10–13] and they are associated with cardiac risks and gastrointestinal complications, particularly with long-term use [14,15].

Considering the limitations of the established osteoarthritis medications, and the recent interest in complementary and alternative medicine (CAM), many patients have turned their attention to CAM such as dietary supplements in order to find safer alternatives to manage their symptoms. Over the last decade many dietary supplements such as glucosamine sulphate, chondroitin sulphate, and antioxidants have been introduced for the management of OA. L-carnitine is one of the dietary supplements that has been reported to have beneficial effects in managing different chronic diseases including non-alcoholic steatohepatitis, type 2 diabetes mellitus, heart and renal failure [16–20]. Recently, L-carnitine was reported to be effective in management of arthritis [21,22] due to its role in cellular metabolism and anti-inflammatory activity. Previous studies have demonstrated that L-carnitine stimulates protein synthesis, proliferation and differentiation of human primary osteoblasts [23,24]. In addition, findings from in vitro study indicated that L-carnitine can stimulate both cartilage matrix glycosaminoglycan production and ATP synthesis leading to high proliferation rate in human primary chondrocytes; Therefore it might induce the regeneration of cartilage tissue and help chondrocytes to counteract the physiological consequences of osteoarthritic processes [21]. To the best of our knowledge, there are few reports about the effects of L-carnitine on clinical signs and symptoms in OA patients, so this study aimed to evaluate the effects of L-carnitine supplementation on clinical symptoms in females with knee OA.

Methods and materials

Subjects selection

This randomized, double-blind, placebo-controlled trial was conducted between November 2013 and November 2014. The study protocol was approved by the Ethics Committee of Tabriz University of Medical Sciences (Iran) and registered on the Iranian Registry of Clinical Trials website (code: IRCT201311231197N17). All subjects were made aware of the content of the study and a written informed consent was obtained from each subject.

The sample size was calculated based on information obtained from studies by Farid et al. [5] and Geraci et al. [22] on the intensity of knee pain. Considering a confidence level of 95% and power of 80%, the sample was determined at least 30 cases in each group. The sample size was increased to 36 cases in each group for a possible dropout of 20%. Seventy-two volunteer women aged 40–60 years with the diagnosis of mild to moderate bilateral primary knee OA according to the American College of Rheumatology criteria [25,26] and body mass index (BMI) of 25–34.9 kg/m^2 were recruited from the rheumatology clinic of Tabriz University of Medical Sciences. The exclusion criteria were: secondary OA (due to a known disorder), arthroscopy, surgery, or a joint injection of the target knee within the previous 6 months, history of knee joint replacement, any serious systematic disease, cardiovascular disease, diabetes mellitus, liver, renal and/or thyroid disorders and any other chronic inflammatory disease, pregnancy and lactation, smoking, alcohol intake, currently taking omega-3-fatty acids (e.g., fish oil) and antioxidant supplements, use of NSAIDs two weeks prior to and during the intervention. Since the use of NSAIDs was not allowed during the trial, patients were permitted to use acetaminophen for relieving pain and symptoms if it was needed.

Study design

The eligible participants were randomly allocated into intervention and placebo groups based on random block procedure consisting of four subjects per block, which matched subjects to each block based on menopausal status, BMI and age, produced by Random Allocation Software, version 1.0 (M. Saghaei, Department of Anesthesia, Isfahan University of Medical Sciences, Isfahan, Iran) [27]. A computer-generated random sequence was kept in a remote secure location and administered by an independent third party who was not involved with the clinical conduct of study until all data were collected and verified. Patients and those who involved in enrolling participants, administering interventions and assessing outcomes were blind to group assignments. The experimental group ($n = 36$) received 750 mg L-carnitine tartrate per day divided into three equal doses of one 250 mg tablet after each meal for 8 weeks (L-carnitine, *Karen Pharmaceutical & Nutrilife* Co., Yazd, Iran). The control group ($n = 36$) received placebo according to the same regimen and for the same duration (Placebo, *Karen Pharmaceutical & Nutrilife* Co., Yazd, Iran). The placebo pills contained inactive ingredients with no therapeutic activity and had an identical appearance. The participants were asked to keep their usual dietary intake and physical activity during the study period. Patients were monitored weekly for any side effects of L-carnitine supplementation. A diagram of the study design is shown in Fig. 1.

At the onset of the study, all patients underwent routine physical examinations. Body weight was recorded to the nearest 0.1 kg