Journal of Traditional and Complementary Medicine 6 (2016) 199–203

Contents lists available at ScienceDirect

Journal of Traditional and Complementary Medicine

journal homepage: http://www.elsevier.com/locate/jtcme

Original article

Effect of ginger powder supplementation on nitric oxide and C-reactive protein in elderly knee osteoarthritis patients: A 12-week double-blind randomized placebo-controlled clinical trial

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ARTICLE INFO

Article history:
Received 27 July 2014
Received in revised form
3 September 2014
Accepted 18 September 2014
Available online 28 January 2015

Keywords:
C-reactive protein
Ginger
Nitric oxide
Osteoarthritis
Elderly

ABSTRACT

There is limited evidence that ginger (生薑 shēng jiāng) powder consumption can relieve pain and inflammation because of its special phytochemical properties. This study is aimed at investigating the effect of ginger powder supplementation on some inflammatory markers in patients suffering from knee osteoarthritis. This is a double-blind randomized placebo-controlled clinical trial with a follow-up period of 3 months that was conducted on 120 outpatients with moderately painful knee osteoarthritis. Patients were randomly divided up into two groups: ginger group (GG) or placebo group (PG). Both groups received two identical capsules on a daily basis for 3 months. Each ginger capsule contained 500 mg of ginger powder; the placebo capsules had 500 mg of starch in them. Serum samples were collected prior to and after the intervention and were stored at −70 °C until the end of the study. Serum concentration of nitric oxide (NO) and hs-C reactive protein (hs-CRP) were measured using enzyme-linked immunosorbent assay kits. There was no significant difference between the two groups in terms of inflammatory markers (i.e., NO and hs-CRP) prior to the intervention. However, after 3 months of supplementation, serum concentration of NO and hs-CRP decreased in the GG. After 12 weeks, the concentration of these markers declined more in the GG than in the PG. Ginger powder supplementation at a dose of 1 g/d can reduce inflammatory markers in patients with knee osteoarthritis, and it thus can be recommended as a suitable supplement for these patients.

1. Introduction

Arthritis is a prevalent condition affecting millions of people around the world.[1] Osteoarthritis (OA) or degenerative arthritis is the most common form of arthritis that is defined by degeneration of articular cartilage, joint pain and inflammation, and dysfunction particularly in older people.[2,3] Knee joints bear the largest part of the body weight, and they are most likely to be at risk of OA.[4] As the prevalence of OA is high, and the nature of the disease is progressive, it is not surprising that it has had an important effect on the global economy.[3,5] Factors that can predispose people to OA of the knee are age, weight, body mass index (BMI), genetics, occupational activities, history of trauma, and physical work activities, especially kneeling, squatting, lifting, and climbing.[6–9]

Treatment programs commonly involve nonpharmacological and pharmacological measures. If pain becomes debilitating, joint replacement surgery is to be used to ameliorate the quality of life.[10] Generally, exercise and lifestyle modification are considered nonpharmacological measures,[11] and analgesics are prescribed to relieve pain. However, there is increasing concern that some analgesics may cause serious complications. For instance, some cyclooxygenase-2 (COX-2) inhibitors such as nonsteroidal anti-inflammatory drugs have been shown to increase the risk of

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Peer review under responsibility of The Center for Food and Biomolecules, National Taiwan University.

http://dx.doi.org/10.1016/j.jtcme.2014.12.007

adverse cardiovascular and gastrointestinal events.[12] Moreover, findings of two *in vitro* studies demonstrated that naproxen, indomethacin, and ibuprofen, which are the most frequently prescribed nonsteroidal anti-inflammatory drugs, block the synthesis of human cartilage matrix, and this is likely to increase the rate of degeneration of articular cartilage in OA.[13,14] This has led many researchers to attempt to find a remedy or modalities with negligible side effects and significant improvement in the symptoms.[15] Ginger (生薑 shēng jiāng) is an underground rhizome of the plant *Zingiber officinale*, belonging to the family Zingiberaceae, which is one of the most popular herbs used in traditional medicine to remedy diseases such as pregnancy-induced nausea and vomiting, motion sickness, and arthritic conditions. It is thought that ginger might be useful to human health owing to its anti-inflammatory properties. The mechanism of its action is not clear, but it seems to inhibit the activation of tumor necrosis factor-alpha (TNF-α), interleukin-1β (IL-1β), and inducible nitric oxide synthase (iNOS).[16]

C-reactive protein (CRP) is a plasma protein that increases in the systemic response to inflammatory events. Its rapid increase in synthesis within hours after tissue injury or infection suggests that it contributes to host defense and that it is part of the innate immune response. There is an association between elevation of this protein and future major cardiovascular events.[17] Considering the role of ginger in reducing inflammation and given the fact that we could not find any study in the literature on the long-term effects of ginger on inflammation, this study was designed to determine the effect of daily supplementation of 1 g ginger powder for 3 months on inflammatory markers in older patients with knee OA.

2. Materials and methods

2.1. Study design and participants

This study was a double-blind randomized placebo-controlled clinical trial, with a 3-month follow-up, of 120 patients with knee OA visiting Khatam-ol-anbia Polyclinic in the city of Yazd in Iran. This study was performed in the period spanning November 2011 to May 2012.

Criteria for inclusion were age (between 50 years and 70 years) and diagnosis of OA verified by a rheumatologist according to the classification criteria of the American College of Rheumatology.[18] Patients with any of the following were excluded: rheumatoid arthritis, inflammatory diseases, metabolic disorders (such as diabetes, cancer, or other serious diseases), signs or history of liver or kidney failure, treatment with oral corticosteroids within a period of 4 weeks prior to the trial, corticosteroids injection within 6 months prior to the experiment, fever > 38°C at screening, permanent consumption of ginger (生薑 shēng jiāng), allergy to ginger, unwillingness to continue the protocol, avoidance of consumption of > 20% of the ginger supplements, any serious complications, consumption of multivitamin, minerals, or other nutritional supplements, and consumption of analgesic medications.

A total of 120 patients meeting the above-mentioned criteria were randomly assigned to two groups (n = participants each): ginger group (GG) and placebo group (PG). Randomization was done via tables of random numbers that were sequential list prepared. The patients were asked to take two 500-mg capsules per day for 3 months. The GG and PG capsules contained powdered ginger and starch, respectively. Placebo and ginger capsules were similar in terms of color, odor, weight, and packing. All the capsules were manufactured in the Institute of Medicinal Plants in Tehran, Iran. Patients were examined at the beginning of the study and then again after 3 months in order to measure anthropometric indices. Moreover, the participants filled out a researcher-made questionnaire with questions on age, occupation, education, and obesity status. The patients were asked not to change their normal diet. The patients were also instructed to keep their daily use of the stairs to a minimum. Furthermore, a rheumatologist taught them some kinds of knee exercises.

2.2. Measurements

Anthropometric indices were obtained by a trained dietitian. The patients' weights were measured using digital scales with a readability of 0.1 kg and with the patients being minimally clothed, without shoes. Height was measured using a stadiometer with a readability of 0.5 cm and with the patients being in a standing position without shoes. To determine the obesity status, the BMI was calculated as weight (kg) divided by the square of height (m). All anthropometric measurements were obtained on the same day when blood specimens were taken.

2.3. Biochemical assessment

Both at the start of and 3 months after the experiment, 5 mL peripheral blood was taken from each patient in a nonfasting state through venipuncture of an antecubital vein (Suha, Iran). Serum samples were stored at −70°C until the end of the study. Serum CRP concentrations were measured using enzyme-linked immunosorbent assay kits (Biocore, Hamburg, Germany). Serum concentration of nitric oxide was measured using a colorimetric assay kit (Biocore).

2.4. Dietary assessment

Dietary intake was assessed by trained dietitians. Data on 24-hour recalls were collected from all 120 participants prior to and after the intervention. The 24-hour recall is based on actual intake and may be used to estimate absolute rather than relative intake.[19] However, this method is susceptible to recall bias, both for identification of foods eaten and for quantification of portion sizes. In order to reduce this type of error in this study, dietary data were collected by highly trained interviewers.[20] Individuals were asked whether the day of recalls was a usual day or not. To enter the data into the computer, standard reference tables were used to convert household portions to grams.[21] After coding, the dietary recall form was linked to a nutrient database (Nutritionist IV, Bruno, CA, USA). For mixed dishes, food groups were calculated taking account of their ingredients. The data related to Nutritionist IV were modified in accordance with the Iranian Food Composition Table.

2.5. Ethical considerations

The protocol was explained to all patients. The participants volunteered to participate in this study and had the possibility of withdrawing from the study at any moment. The Ethics-in-Research Commission of Shahid Sadoughi University of Medical Sciences, Yazd, Iran approved the study, and all patients gave written informed consent.

2.6. Statistical analysis

Data were submitted to SPSS 16.0.2 (2008; SPSS Inc., Chicago, IL, USA).[22] Prior to the statistical comparison, a Kolmogorov–Smirnov test was used to demonstrate the distribution of quantitative data. Furthermore, the t test was used to draw a comparison between the data obtained from the two groups (i.e., between-groups comparison). In addition, Student t test was used for comparing the data obtained from each group before and after the intervention (i.e., within-groups comparison). The results of the protocol are