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Original Article

COMPARING THE EFFECTS OF GINGER (*ZINGIBER OFFICINALE*) EXTRACT AND IBUPROFEN ON PATIENTS WITH OSTEOARTHRITIS

Masoud Haghighi PhD•*, Ali Khalvat MD**, Tayebeh Toliat PhD***, Shohreh Jallaei MSc†

Background: **Ginger (*Zingiber officinale*) extract supplementation has been shown to improve the severity of symptoms and decrease the nonsteroidal antiinflammatory drug (NSAID) requirements in patients with osteoarthritis (OA).**

Objective: **To assess the effects of ginger extract as an alternative to NSAIDs and as a supplement drug in the symptomatic treatment of OA.**

Methods: **Between April and October 2002, 120 outpatients with OA of moderate to severe pain, requiring only the use of NSAIDs, were enrolled into a double-blind, randomized, placebo-controlled clinical trial. These patients were randomized into three groups of 40, including the placebo (PL), ginger extract (GE), and ibuprofen (IBP) groups. After a washout period of one week (week 0), patients received either 30 mg ginger extract in two 500 mg capsules, placebo, or three 400 mg ibuprofen tablets daily for one month. Acetaminophen tablet was prescribed as a rescue analgesic during the study. The clinical assessments included a visual analog scale (VAS) for pain, gelling pain, joint swelling measurement, and joint motion slope measurement. Joint motion slope was measured by goniometry (normal = 130°, limited = 120°, and very limited = 110°).**

Results: **The improvement of symptoms (defined as reduction in the mean change) was superior in the ginger extract and ibuprofen groups than the placebo group. VAS scores and gelling or regressive pain after rising the scores were significantly higher in the PL group than both the GE and IBP groups, a month after the treatment ($P < 0.0001$). However, there was no significant difference in VAS and gelling pain scores between the ginger extract and the ibuprofen groups.**

Conclusion: **Ginger extract and ibuprofen were significantly more effective than the placebo in the symptomatic treatment of OA, while there was no significant difference between the ginger extract and ibuprofen groups in a test for multiple comparison.**

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Keywords: Ginger extracts • ibuprofen • inflammation • osteoarthritis • pain

Introduction

There is an increasing awareness, both in the medical community and among public, for the use of unconventional or alternative treatment modalities by patients.[1, 2] Patients with chronic painful disease often seek alternative therapy,[3] and currently ginger is one of the most popular herbal medications for rheumatic diseases. Ginger (*Zingiber officinale*) has been used for medicinal purposes since antiquity. In particular, it has been an important plant for the traditional Chinese and Indian medicines. Although one of its indications has been historically to treat rheumatic disorders, and although ginger extracts have shown the ability to inhibit arachidonic acid metabolism and have antiinflammatory action and/or anti-rheumatic properties,[4, 5] there are very limited published reports on the efficacy of this herb.[4, 6 – 8] The currently available treatment for osteoarthritis (OA) afford only palliative care. The prescription of simple analgesics, such as acetaminophen to

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reduce pain, generally precedes the treatment with nonsteroidal antiinflammatory drugs (NSAIDs). NSAIDs use is limited by the risk of adverse effects, particularly gastrointestinal and renal toxicity.

The purpose of this study was to assess the effects of ginger extract as an alternative to NSAIDs and as a supplement drug in the symptomatic treatment of OA.

Patients and Methods

Plant material and preparation of extract

Fresh rhizome of ginger (*Zingiber officinale* Rosce) was purchased from a local market in India and authenticated by a botanist (Institute of Medicinal Plants, Jahad-e-Daneshgahi). The plant was dried in the shade. The dried rhizome was powdered mechanically and extracted by cold percolation with 95% ethanol for 24 hr. The extract was recovered and 95% ethanol was further added to the plant material and the extraction continued. The process was repeated three times. The three extracts were pooled together and the combined extract was concentrated under reduced pressure (22 – 26 mm Hg) at 45 – 60˚C. Thirty gram of solvent-free extract was equivalent to one kilogram of the dried ginger (W/W) powder. The concentrate was weighed and combined with the necessary exipients, and then filled into 500-mg capsules, each containing 15 mg of the ginger extract. Lactose (placebo) was also capsulated similarly (all of the above-mentioned procedures were undertaken in the industrial pharmacy department of the Faculty of Pharmacy, Tehran University of Medical Sciences).

Patient selection and study design

This study was approved by the local committee for medical ethics and prior written informed consent was obtained from all patients. One hundred and twenty outpatients with OA (89 men, and 31 women), aged 52 to 64 years (mean: 58.5 years) were recruited for this study, which was carried out in the rheumatology clinic of Imam Khomeini Hospital. All the patients had complaints of clinical dysfunction and pain due to OA. Radiologically, it was verified that they had OA in the hip or knee with pain on movement of >30 mm on a 100-mm visual analog pain scale[9] (VAS, mean 69 mm) on their first visit for this study. The study was a double-blinded randomized placebo-controlled clinical trial. Exclusion criteria were rheumatoid arthritis, metabolic disorders (diabetes), gastrointestinal disorders (gastritis or duodenum ulcer), neurological disorders, and dementia. The patients were then randomized into three treatment groups of 40, receiving either 30 mg ginger extract in two 500 mg tablets; placebo daily, or three 400-mg ibuprofen capsules daily for one month. Acetaminophen was used as a rescue medication throughout the study (1 to 3 tablets daily). Treatment with analgesics and NSAIDs was discontinued during the one-week wash-out period.

The following measurements were taken from the above-mentioned agents:

- One hundred-mm VAS for assessing the severity of pain;
- Gelling pain;
- Joint swelling measurements; and
- Joint motion slope measurements.

Statistical analysis

The data expressed as mean±SEM were statistically analyzed by the analysis of variance (ANOVA) followed by the Kruskal-Wallis non-parametric test for between-group differences and Dunn's correction of the significance level for multiple comparison. The level of significance adopted was $P < 0.05$. Calculations were performed on a personal computer, using the Instat program, before breaking the code.

Results

Characteristics

A total of 120 patients with OA were enrolled in three treatment groups: ginger extract, placebo, and ibuprofen group. Table 1 shows a brief characteristical comparison of the study groups before the start of the treatment (baseline). There was no significant difference between the groups for mean age, pain, joint swelling measurement, joint motion slope measurement (one-way ANOVA), and sex (Chi-square).

Efficacy

During the treatment period, no patient was excluded from this study. At the end of one month of treatment, VAS and gelling or regressive pain after rising changed in comparison to the baseline

Table 1. Baseline characteristics of patients evaluated at the end of the washout period.

Characteristic	Treatment groups			*P* Value
	Ginger extract *n* = 40	Placebo *n* = 40	Ibuprofen *n* = 40	
Mean age (years)	58.3 ± 0.33	58.4 ± 0.36	58.8 ± 0.35	$P > 0.05$
Range	(55 – 64)	(52 – 62)		
Sex (man : woman)	29 : 11	28 : 12	32 : 8	$P > 0.05$
VAS	71.7 ± 3.5	64.2 ± 2.8	71.2 ± 2.4	$P > 0.05$
Gelling or regressive pain after rising score	3.65 ± 0.18	3.22 ± 0.27	3 ± 0.20	$P > 0.05$
Joint swelling scores	1.25 ± 0.06	1.07 ± 0.04	1.15 ± 0.05	$P > 0.05$
Joint motion slope scores	1.62 ± 0.07	1.37 ± 0.07	1.45 ± 0.07	$P > 0.05$

values (before treatment), but not in the remaining outcome parameters, including joint swelling measurement and joint motion slope measurement (Table 2). There was no significant difference between the three groups in terms of the pain level at study entry ($P > 0.05$), as examined by the Kruskal-Wallis nonparametric test. VAS changed from the entry median value of 64.2 ± 2.8 mm to 56.5 ± 3.6 mm in the placebo group, 71.7 ± 3.5 mm to 30 ± 3.7 mm in the ginger extract group, and 71.2 ± 2.48 mm to 28 ± 3 mm in the ibuprofen group (Figure 1). There was a significant difference between the three groups in VAS at the end of one month treatment ($P < 0.0001$), as examined by the Kruskal-Wallis nonparametric test. The Dunn's test for multiple comparisons showed a significant difference in these tests between the ginger extract and placebo ($P < 0.001$), as well as ibuprofen and placebo ($P < 0.001$), but not between the ginger extract and ibuprofen ($P > 0.05$) at the end of one month of treatment (Figure 1). Also gelling or regressive pain after rising the scores changed from the entry median values of 3.22 ± 0.27 to 1.77 ± 0.11 in the placebo group, to 3.65 ± 0.18 to 1.3 ± 0.13 in the ginger extract group, and 3.0 ± 0.2 to 0.97 ± 0.1 in the ibuprofen group (Figure 2). There was a significant difference between the three groups in the gelling pain at the end of one month treatment ($P < 0.0001$), as examined by the Kruskal-Wallis nonparametric test. The Dunn's test for multiple comparison showed a significant difference in these tests, between the ginger extract and placebo ($P < 0.05$) as well as the ibuprofen and placebo ($P < 0.001$), but not between the ginger extract and ibuprofen ($P > 0.05$) at the end of one month of treatment (Figure 2).

These results also showed a significant difference between both the ginger extract and ibuprofen groups with the placebo group, but not between the ginger extract and ibuprofen group.

The number of acetaminophen used in these treatment groups could not be assessed, because the majority of the patients did not fill in this form correctly.

Discussion

The findings of this study demonstrate a ranking of efficacy in pain level in patients with osteoarthritis, with ginger extract and ibuprofen being more effective than placebo. Nonetheless, there is an identical efficacy between the ginger extract and ibuprofen.

Although the use of NSAIDs in osteoarthritis is highly controversial,[10] the fact is that many physicians and patients favor these agents for short- and long-term use. However, the therapeutic utility of these agents is frequently limited by the development of side effects, especially gastrointestinal ulceration and ulcer complications. Ulcer complications, such as bleeding and perforation, associated with NSAID therapy often occur without warning and could be life threatening.

The active components of ginger are not known with certainty, but studies of the lipophilic rhizome extracts have yielded the potentially active

Table 2. The change in outcome parameters after a month of treatment.

Parameters	Treatment groups			*P* Value
	Ginger extract *n* = 40	Placebo *n* = 40	Ibuprofen *n* = 40	
VAS	30 ± 3.7	56.5 ± 3.6	28 ± 3.4	$P < 0.0001$
Gelling pain score	1.30 ± 0.13	1.77 ± 0.11	0.97 ± 0.11	$P < 0.0001$
Joint swelling scores	1.12 ± 0.52	1.02 ± 0.02	1.10 ± 0.04	$P > 0.05$
Joint motion slope scores	1.55 ± 0.07	1.30 ± 0.07	1.40 ± 0.07	$P > 0.05$

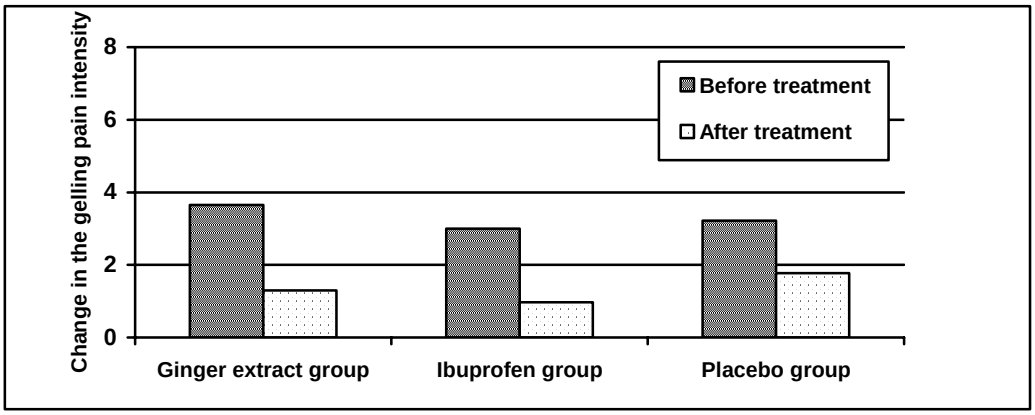

Figure 1. The effects of ginger extract, ibuprofen, and placebo on the change in the mechanical pain intensity. There was no significant difference between the groups before treatment ($P > 0.05$). There was a significant difference between the ginger extract and placebo groups ($P < 0.001$) and also, between the ibuprofen and placebo groups ($P < 0.001$) after treatment. There was no significant difference between the ginger extract and ibuprofen groups ($P > 0.05$).
Before treatment:
Ginger extract group = 3.65 ± 0.18; ibuprofen group = 3 ± 0.2; placebo group = 3.22 ± 0.27.
After treatment:
Ginger extract group = 1.3 ± 0.13; ibuprofen group = 0.97 ± 0.1; placebo group = 1.77 ± 0.11.

components, gingerols and shogaols.[11]

One of the mechanisms of inflammation is the increased oxygenation of arachidonic acid, which is metabolized by cyclooxygenase and 5-lipoxygenase, leading to prostaglandin E_2 and leukotriene B_4, two potent mediators of inflammation.[4] Ginger contains chemical substances with an antiinflammatory potential, and the effect might be attributed to the actions of gingerols, shogaols, diarylheptanoids, and dialdehyd diterpens, which may inhibit inflammatory prostaglandins.[12 – 14] These agents are dual inhibitors of eicosanoid synthesis, which makes the substances even more interesting in the field of rheumatology.[15 – 17] Thus, antiinflammatory effect of ginger may be due to a decrease in the formation of prostaglandins and leukotrienes.[18] A suppressive effect of ginger compounds in arthritic rats has been reported.[19, 20] A retrospective case series was reported on the use of ginger in 56 patients with rheumatoid arthritis, osteoarthritis, and muscle discomfort.[4] The patients subjectively described symptom relief, with many reporting that they were able to reduce their use of other

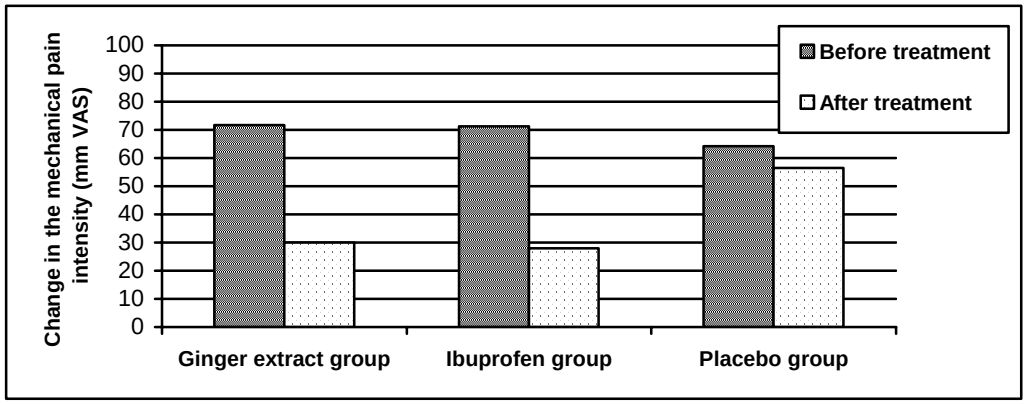

Figure 2. The effect of ginger extract, ibuprofen, and placebo on the change in gelling pain intensity. There was no significant differences between the groups before treatment ($P > 0.05$). There was a significant difference between the ginger extract and placebo groups ($P < 0.05$) and also, between the ibuprofen and placebo groups ($P < 0.001$) after treatment. There was no significant difference between the ginger extract and ibuprofen groups ($P > 0.05$).
Before treatment:
Ginger extract group = 71.7 ± 3.50; ibuprofen group = 71.2 ± 2.48; placebo group = 64.2 ± 2.8.
After treatment:
Ginger extract group = 30 ± 3.7; ibuprofen group = 28 ± 3; placebo group = 56.5 ± 3.6.

antiarthritis drugs. Not long ago, in various randomized, double-blind, placebo-controlled trials ginger was shown to reduce symptoms of osteoarthritis.[7, 8]

A one-month period of therapy with only one dose of ginger extract applied in this study might not have been adequate for all the effects of ginger extract to be detected. Future studies might look into the dose-response and duration of therapy of a standardized and highly concentrated ginger extract in patients with osteoarthritis.

In conclusion, the results of our study indicated that ginger extract could be used as an alternative to the NSAID and as a supplement drug in patients with osteoarthritis.

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