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EFFICACY AND TOLERABILITY OF GINGER (*ZINGIBER OFFICINALE*) IN PATIENTS OF OSTEOARTHRITIS OF KNEE

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Abstract : Osteoarthritis (OA) is a chronic degenerative disorder of synovial joints and a common cause of locomotor disability. NSAIDs are routinely used for symptomatic treatment and are associated with side effects which have led to the increased interest towards alternative treatment options. This study was conducted to evaluate the safety and efficacy of ginger in management of OA. Sixty patients of OA of knee were enrolled in randomized open label study and divided into three groups of 20 each. Group I received tab. Diclofenac 50 mg and cap. placebo, group II received cap. ginger 750 mg and cap. placebo and group III received cap. ginger 750 mg and tab. diclofenac 50 mg. The assessment of efficacy was done at every 2 weeks till 12 weeks, by using Western Ontario and McMaster Universities osteoarthritis (WOMAC) index, Visual Analogue Scale (VAS) and the safety assessment was done by noting adverse events during the study. The analysis of WOMAC score and VAS score in all the three groups showed statistically significant improvement with time in all groups. On comparison among three groups, group III patients who received both ginger and diclofenac showed numerically superior improvement than the individual treatments. There was no statistically significant difference among three groups in case of adverse events. Ginger powder has add-on effect on reducing the symptoms of OA of knee with acceptable safety profile.

Key words : Osteoarthritis Ginger Zingiber officinale

INTRODUCTION

Osteoarthritis (OA) is a disorder characterized by progressive destruction of articular cartilage having prevalence of about 22% to 39% in India (1, 2, 3). It affects more commonly elderly population and is a common cause of locomotor disability. The pathophysiology of OA involves degeneration of articular cartilage which is mediated by various factors like inflammatory mediators, biomechanical factors, chemical injury, changes with aging and metabolic factors. It causes major disability in patients characterized by recurrent episodes of pain, stiffness, loss of function and disability to perform day to day activities and its signs comprise of crepitus, tenderness and joint swelling (4, 5).

The goal of treatment is to relieve pain, improve mobility of joints and minimize

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disability. The treatment comprises of non-pharmacological, pharmacological therapies and surgical treatment. The non-pharmacological modalities include patient education, brief period of rest, weight reduction in obese individuals and graduated exercise. The pharmacological treatment provides symptomatic relief with non-steroidal anti-inflammatory agents such as Acetaminophen, Aspirin, Diclofenac, selective COX-2 inhibitors e.g. Celecoxib etc. The available drugs have various limitations like gastrointestinal side effects such as dyspepsia, gastritis etc., (6) and cardiac adverse effects of selective COX-2 inhibitors (7).

Geriatric population is most commonly affected as they are already taking many other medications for the chance of drug interactions and non-compliance increases. Cost factor is also important in developing countries like India and pharmacological therapy adds to financial burden to the patients. Due to above limitations; there is a need to provide alternative therapies with reduced incidence of adverse effects. Ginger is one of the most commonly used natural products and a promising agent for treatment of osteoarthritis. It has been seen in various animal and human studies that ginger has property of relieving inflammatory symptoms in patients of osteoarthritis. The anti-inflammatory action of ginger is due to inhibition of COX-1, COX-2 and LOX. In addition it, also inhibits several genes encoding cytokines, chemokines and inducible enzyme COX-2, thus providing evidence that ginger modulates the biochemical pathway which are activated in chronic inflammation (8, 9, 10, 11, 12, 13). Based on this concept, the present study was conducted to evaluate the safety and efficacy of ginger in the treatment of osteoarthritis.

MATERIALS AND METHODS

This study was randomized, open label which was undertaken at the Orthopaedics OPD of Sri Guru Ram Das Charitable Hospital, attached to Sri Guru Ram Das Institute of Medical Sciences and Research, Vallah, Sri Amritsar. The time period of study in which patients were enrolled was from April 2010 to January 2011. Patients of osteoarthritis of knee attending Orthopaedics OPD and meeting the inclusion and exclusion criteria were enrolled for the study.

Inclusion criteria comprised of patients of either sex with symptomatic osteoarthritis of knee who fulfilled American college of rheumatology criterion for the diagnosis of osteoarthritis (14) and those who had knee pain between 40 mm and 90 mm on a 100 mm Visual Analogue Scale (VAS) at the time of diagnosis were enrolled for the study. Patients with cardiovascular diseases, hypertension, gastro-duodenal disorders, diabetes mellitus, hepatic or renal impairment, bleeding disorders and pregnant females were excluded from study.

The botanical name of ginger is *Zingiber Officinale Roscoe* which belongs to family *Zingiberaceae*. The Zingiber officinale rhizome powder was purchased from Tulsi Amrit private limited, Indore, Madhya Pradesh and encapsulation of powder was done by Inteck Research Institute, Hisar, Haryana. Each capsule contained 750 mg of ginger powder. Placebo used was lactose and it was also encapsulated by Inteck Research

Institute, Hisar, Haryana. A total of 60 patients of either sex were randomly divided in three groups of 20 each.

Group I received Tab. Diclofenac 50 mg and Cap. placebo orally BD.

Group II received Cap. Ginger 750 mg and Cap. placebo orally BD.

Group III received Cap. Ginger 750 mg and Tab. Diclofenac 50 mg orally BD.

Patients received treatment for a total duration of 12 weeks. Rescue medicine Acetaminophen 500 mg was given to patients complaining of severe pain as required up to a maximum of 6 tablets/day. The consultation of Ayurvedic physician Dr. Jatinderjit Singh (B.A.M.S consultant at KD hospital, Amritsar) was taken during the study. This study was conducted in accordance with the principles of good clinical practice and the Declaration of Helsinki. The approval of Institutional ethics committee was obtained. Written, informed, signed consent was taken from all patients before inclusion in the present study and all the risks and benefits were explained to them in their own language.

Assessment

The assessment of efficacy was done using the Western Ontario and McMaster Universities Osteoarthritis (WOMAC) index and Visual Analogue Scale (VAS). Safety was assessed by noting any adverse event occurring during the study. Follow up of the patients was done at 2 weeks, 4, 6, 8, 10 and 12 weeks. Patients were given a proforma to record the frequency and timings of the rescue medication if consumed.

Statistical analysis

The values are expressed as Mean±S.D. Data was statistically analyzed using Kruskal-Wallis Test and Friedman test. Statmate freeware software v1.0 was used.

RESULTS

The age group of the patient in Group I, II and III in group I was 54.8±9.67 yrs, in group II it was 52.85±8.1 yrs and in group III was 50.05±11.3 yrs. In group I six were male and 14 females, in group II, 8 were male and 12 females and in group III, 6 were males and 14 females. There was no significant difference among three groups in the demographic profile of the patient (Table I).

The baseline WOMAC scores were 44.90±9.21, 46.40±9.80 and 45.45±11.06 respectively in groups I, II and III. The baseline VAS scores were 80.00 ± 12.98, 78.25±12.80 and 80.50±10.25 in groups I, II and III respectively. There was statistically no significant difference among three groups in WOMAC and VAS score at baseline (Table I).

The consumption of rescue medication in group I was 35 tablets consumed by four patients, 68 tablets in group II consumed by eight patients and 5 tablets in group III consumed by one patient only (Table II). The untoward events such as nausea, vomiting, epigastric distress, heart burn, rash, allergic reaction, edema, diarrhea, fluid retention, abdominal bloating, irritation of mouth and if any others were observed to assess the

TABLE I: Patient's demographics and baseline levels of WOMAC & VAS Score among three groups.

Parameter	*Group–I*	*Group–II*	*Group–III*
Age (years)	35-40=01 41-50=07 51-60=05 >61=07	35-40=01 41-50=06 51-60=10 >61=03	35-40=07 41-50=04 51-60=04 >61=05
Sex	Males-06 Females-14	Males-08 Females-12	Males-06 Females-14
Duration of illness	0-6 months=06 7-12 months=05 >1 year=09	0-6 months=08 7-12 months=04 >1 year=08	0-6 months=07 7-12 months=06 >1 year=07
Baseline WOMAC Score	44.90±9.21	46.40±9.80	45.45±11.06
Baseline VAS Score	80.00±12.98	78.25±12.80	80.50±10.25

N=20 in each group.

safety. The untoward events among three groups were found to be statistically non-significant when compared with Chi-square test (Table II).

TABLE II: Comparison of rescue medication and untoward events among three groups.

	Group I	*Group II*	*Group III*
Total number of tablets consumed	35	68	5
Number of Patients who consumed	4	8	1
Nausea	–	2(10)	–
Epigastric distress	–	2(10)	1(5)
Heart burn	–	2(10)	1(5)
Constipation	–	–	1(5)

N=20 in each group; values within the brackets represent the percentage.

The percentage improvement in WOMAC score from baseline in group I by the end of study i.e at 12th week was 74.83%, in group II was 63.68% and in group III was 79.43%. The percentage improvement in VAS score from baseline in group I was 60.31%, in group II was 59.11 and in group III was 66.77%. The percentage improvement in WOMAC score and VAS score among three groups from baseline was statistically significant ($P<0.001$) in three groups (Figs. I & II).

DISCUSSION

The pharmacological treatment comprises of Acetaminophen and non-steroidal anti-inflammatory agents including selective COX-2 inhibitors for symptomatic relief. As Osteoarthritis commonly affects the elderly people, and if they have associated co-morbid conditions can lead to various drug interactions. NSAIDs will blunt the effect of antihypertensives, if patient is suffering from CVS disorders and if given selective COX-2 inhibitors there is further increased risk of CVS adverse events and if NSAIDs are given to patients of DM, there is increased risk of nephropathy. The available treatment is also associated with gastrointestinal side effects. Hence because of above said limitations the awareness is increasing both in medical community as well as among the public, for

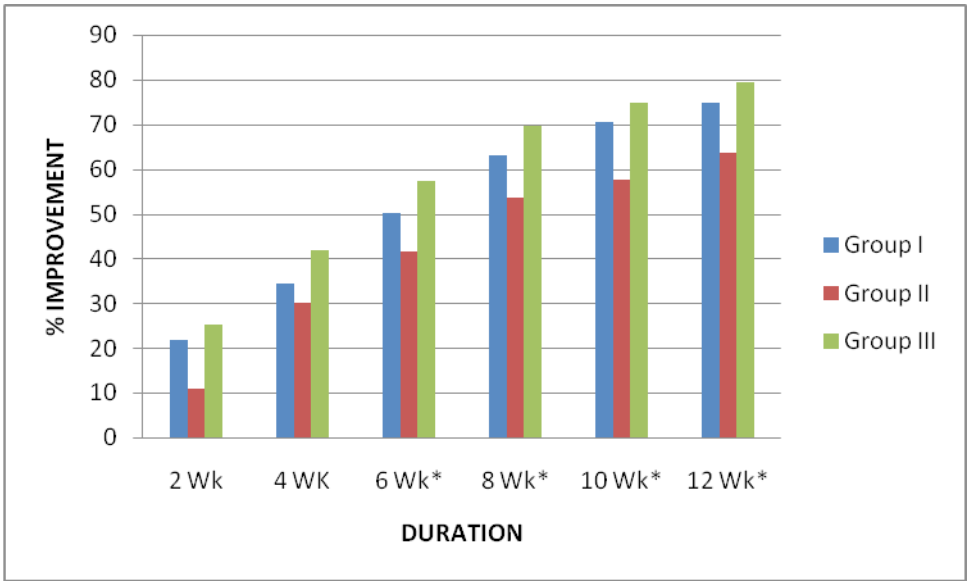

Fig. I: Percentage improvement in WOMAC score from baseline among three groups (N=20 in each group), *P<0.001.

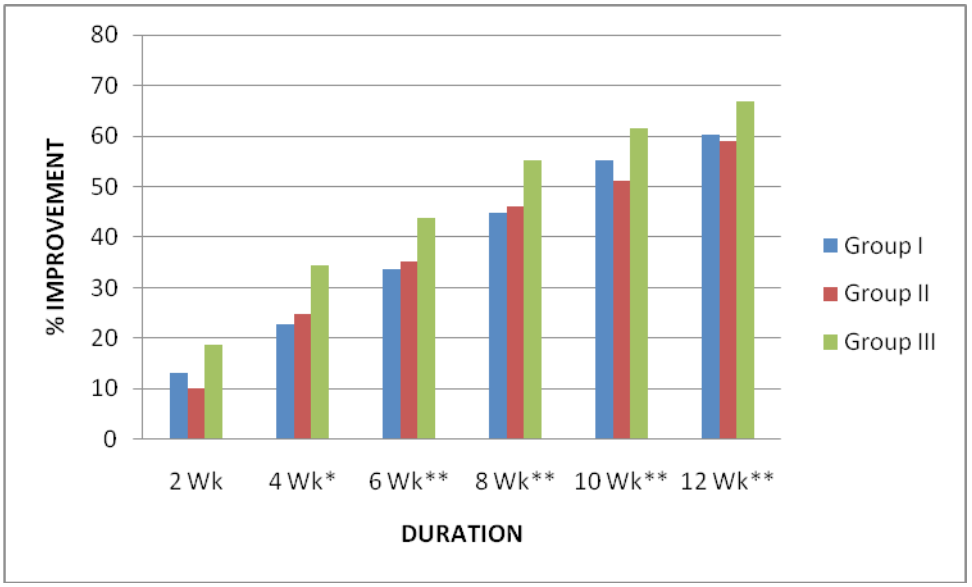

Fig. II: Percentage of improvement in VAS score from baseline among three groups (N=20 in each group), (*P<0.05, **P<0.001).

the use of alternative treatment modality.

In Indian and Chinese medicine, ginger is one of the most popular herbal medication for chronic painful conditions involving joints. It has been an important plant for

traditional Chinese and Indian Ayurvedic medicines. It has been used since long time for treatment of rheumatic disorders due to its ability to inhibit arachidonic acid metabolism, leading to its anti-inflammatory and antirheumatic properties. There are very limited published reports about the efficacy of this herb. Hence this study was planned to evaluate the safety and efficacy of ginger in osteoarthritis.

In group I, significant improvement in WOMAC and VAS scores were seen at 6 week of the study which remained statistically significant till the end of the study. In group II, statistically significant improvement in both WOMAC and VAS scores were seen at 6 week of the study which were highly significant till the end of study. Our study showed statistically significant improvement in VAS in ginger group, which is in conformity with randomized double blind placebo controlled trial conducted by Altman et al., (15). Similar findings as in our study were observed by Haghighi et al., (16), who conducted a randomized double blind placebo controlled trial of one month duration in 129 patients of OA and Acetaminophen was used as rescue medication similar to our study. In another study (17) powdered ginger was given to 56 patients, of which 18 were of OA, 28 of rheumatoid arthritis and 10 of muscular discomfort and the relief in pain was in conformity with the present study.

In group III, significant improvement in VAS score was seen at 4th week of the study and at 6th week significant improvement was seen in both WOMAC and VAS scores which remained highly significant till the end of the study. On comparison of WOMAC score among three groups by the end of the study i.e. at 12th week, group I showed significant difference than that of group II and the difference between group I and group III was not statistically significant but was numerically superior in group III. Moreover, group III showed highly significant difference in comparison with group II.

The percentage improvement in VAS score among all the three groups showed no significant difference till the end of the study. But the difference in group III was numerically superior to group I as well as group II. The overall assessment in WOMAC and VAS scores throughout the study showed numerically superior improvement in group III. The probable reason may be because of the add-on effect of both the ginger and Diclofenac, as both these agents inhibit COX. In addition ginger also inhibits LOX which may be the probable reason for add-on effect. Among the rescue medication, maximum numbers of tablets as well as number of patients who consumed Acetaminophen were in group II and least in group III. The probable reason may be due to add-on effect as explained above. Among the adverse events: Nausea, epigastric distress, heart burn and constipation were observed. In the present study we did not study the effect of ginger on disease progression i.e whether it halts the disease progression or not. For this purpose a study of longer duration may be planned in near future.

Conclusion

Ginger has analgesic and anti-inflammatory properties along with no serious adverse events. It also reduces the intake of rescue medicine. So it can be considered as an add-on therapy in patients of Osteoarthritis.

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