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Original Article

The Efficacy of Topical Oliban Oil (Boswellia Carterii B.) in Relieving the **Symptoms of Knee Osteoarthritis**

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Seyede Zahra Emami Razavi¹, Mehrdad Karimi², Mohammad Kamalinejad³

Keywords

Knee injuries; Osteoarthritis of knee; Pain; Boswellia carterii; Traditional medicine; Iran; Visual analog pain scale

Abstract

Background: Oliban oil is frequently used in daily musculoskeletal practice in traditional Iranian medicine, but its benefit remain to be evaluated. The use of oliban oil offers an alternative to oral treatment and topical nonsteroidal anti-inflammatory drug (NSAID) therapy. The objective of this trial was to assess the efficacy and safety of topical oliban oil in relieving the symptoms of knee pain.

Methods: We identified 154 men and women with knee pain who had the clinical criteria of the American College of Rheumatology for the classification of osteoarthritis and the inclusion criteria. The participants were randomly assigned to three groups to receive topical treatment for their painful knee for 6 weeks; oliban oil as intervention group, sesame oil as control group, and diclofenac gel as usual and positive control group. The degree of knee pain was quantified using the visual analog scale (VAS) and Knee Injury and Osteoarthritis Outcome Score (KOOS). The side effects of oliban oil were evaluated using the Common Terminology Criteria for Adverse Events (CTCAE).

Results: In terms of KOOS, the intervention group showed an improvement in pain and symptoms compared with the control group (P = 0.04), but activities of daily living (ADL), sport and recreation (Sport/Rec), and knee-related quality of life (QOL) did not improve significantly. The VAS scores were significantly better for the patients who applied oliban oil and topical diclofenac gel than for those who applied sesame oil (P = 0.02). Furthermore, the intervention group showed an improvement in pain compared with the diclofenac group (P = 0.03). Safety assessments showed that topical oliban oil caused skin pruritus in 0.02% of individuals.

Conclusion: This controlled clinical trial study demonstrates the potential efficacy and safety of topical oliban oil in the symptomatic treatment of knee pain with only minor local skin pruritus.

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¹ Assistant Professor, Department of Physical Medicine and Rehabilitation, Imam Khomeini Hospital, Tehran University of Medical Sciences, Tehran, Iran

² Assistant Professor, School of Traditional Medicine, Tehran University of Medical Sciences, Tehran, Iran

³ Department of Pharmaceutics, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Introduction

Osteoarthritis is one of the most common causes of disability among the elderly over the age of 65 years.¹ This complication is more common before and after the age of 50 among men and women, respectively.² The knee is one of the most common joints involved in osteoarthritis, and knee pain is suffered by approximately 10% of the individuals over 65 years old.³ In addition, a history of knee pain has been reported in about 25% of individuals aged 55 years and older in the past few years. Among half of them, changes in the knee joint have been observed in radiography.⁴

The increasing elderly population, sports injuries and impacts, obesity and excessive weight in youth, and early elderly age are among the risk factors for developing knee pain and its complication over the age of 70 years.

Reducing pain in order to prevent matter (one of Iranian traditional medicine bodily substances) intake is one of the foundations for treating knee pain in traditional medicine, which is used orally or topically. Topical compositions, in addition to reducing pain, are also effective in substance resolving and organ strengthening.

Knee pain, through decreasing activity, causes imbalance of movement and rest, and also sleep problems.

Oliban is topically applied to prevent moisture from falling into the eye, and for the treatment of moisture in wounds and toothache,^{5,12} and with olive oil and honey for the treatment of osteoarthritic and bone pain.^{12,13}

Methods

Preparation of oliban oil: Oliban oil was prepared according to methods mentioned in traditional medicine books. In order to reduce the effect of heat on the oil base and oliban oil, an indirect heat and a method equivalent to the Ben-Marie method were used. In some traditional medicine books, olive oil was mentioned as an oil base, which due to the

possible effect of olive oil in reducing pain; in order to prevent bias, sesame oil was used according to traditional medicine texts.^{14,15}

Pulverized olibanum and pharmaceutical sesame oil were poured into a glass container with a weight ratio of one to two. The container was then placed in water, and the water was heated until boiling, and then, placed under indirect heat for 12 hours. Subsequently, the oil was passed through a filter, and then, used. The olibanum sample with species of Boswellia carterii B. was identified at the School of Pharmacy of Shahid Beheshti University of Medical Sciences, Tehran, Iran. Diclofenac gel was also prepared from an Iranian pharmaceutical company.

Clinical trial method: This clinical trial study was performed with placebo control on 154 patients with knee pain who referred to Ganj Teb and Tabiat Institute, Tehran, Iran, from September 2010 to June 2011. Patients entered the study if they met the inclusion criteria, and after signing an informed written consent. At the beginning of the study, the vital signs and weight and height of the patients were recorded.

Inclusion criteria:

- 1. Age between 18 and 80 years
- 2. Pain in at least 1 knee during the last month
- 3. Radiological changes over the past 6 months [Kellgren-Lawrence (K-L) grading] osteophyte presence of the bones and reduced joint space
- 4. Clinical symptoms (local pain, crepitation, and no warmth)
- 5. At least, having moderate knee pain according to the visual analog scale (VAS) of more than 4 during the week before entering the random sampling and research treatment, based on the consequences of the Knee Injury and Osteoarthritis Outcome Score (KOOS)
- 6. Negative pregnancy test among women of childbearing age

Exclusion criteria:

- 1. Active infectious disease
- 2. Lesions and skin disease on the knee
- 3. Renal failure

- 4. Knee surgery during the last 2 months
- 5. History of trauma to the knee during the last 3 months
- 6. Secondary knee pain due to infectious diseases such as gonorrhea
 - 7. History of alcohol and narcotic drugs use
 - 8. Lactation
- 9. Sensitivity and allergy to sesame and oliban oils
 - 10. Use of oral drugs effective on the pain
- 11. History of injection intervention on the knee during past 3 months
- 12. Increased severity of symptoms during the treatment period

In order to reduce the effect of seasonal changes on the body, the sampling and intervention were carried out from mid-September to December 2010 and from April to mid-June 2011 in the first and second stages, respectively.

No drug was prescribed to change the body's cleansing due to traditional medicine.

Patients were divided into 3 groups of intervention, control, and positive control using stratified random sampling method, and were exposed to topical treatment of the knee for 6 weeks. The intervention, control, and positive control groups were treated with oliban oil, topical diclofenac sesame oil, and to differences in respectively. Due appearance of diclofenac drug and oliban oil, there was a potential bias. The researchers attempted to reduce this bias by separating the patients' visit site and delivering the drug to the 3 groups. The information was collected by individuals who were not aware of the drugs; in addition, the individuals' results evaluator was selected from outside the treatment group.

The patients completed the KOOS questionnaire. The questions of this questionnaire include 5 related options with scores ranging from 0 to 4. The total score of the questionnaire ranges from 0 to 100. In this questionnaire, knee pain, knee disease symptoms, daily functions, recreation and exercise, and quality of life (QOL) were evaluated in 5 sections and through 42 questions. The maximum possible raw score

of each individual is 100. Moreover, scores were examined separately in each of the 5 categories of questions.¹⁷ Knee pain is assessed through 9 questions.

The patients were evaluated using the VAS numerical-visual scale in rest and activity. In each stage, the previous questionnaire was out of the reach of patients. This scale has been designed in the range of 0-100 mm to measure pain, in which the lack of a sign indicates a score of 0 for the patient.

Possible side effects were recorded by patients every day. In addition, skin side effects were evaluated each week by the physician based on the Common Terminology Criteria for Adverse Events (CTCAE) (version 4, 2010). Patients were eliminated from the plan in the event of moderate to severe skin complications.

Samples size was estimated at a minimum of 30 individuals in each group based on the strength of 80% and the first type error of 0.005 in the two-domain test. Accounting for about 10% sample loss, about 40 individuals were selected in each group.

Data analysis: Data were statistically analyzed using SPSS software (version 12, SPSS Inc., Chicago, IL, USA). The Mann-Whitney statistical test was used for comparison of age, weight, sex, and VAS and KOOS scores among men and women.

The one-way analysis of variance (ANOVA) was used to measure the effect of the intervention on different severities of pain and changes in VAS and KOOS scores. In addition, repeated measures ANOVA was exploited to investigate the variations in each individual.

The chi-square and t tests were used to analyze the qualitative and quantitative variables between the two groups, respectively.

The significance level of all tests was considered to be P < 0.05.

Results

In the present study, 154 patients with knee pain participated, among whom 63 (41%) and 91 (59%) were men and women, respectively.

Table 1. Demographic features of the studied patients

Group	Oliban oil	Sesame oil (Control)	Diclofenac	P
Variable	$(Mean \pm SD)$	$(Mean \pm SD)$	$(Mean \pm SD)$	
Age (year)	52.1 ± 9.4	50.8 ± 9.4	52.5 ± 9.7	> 0.05
Weight (kg)	84.9 ± 18.5	83.1 ± 18.9	81.3 ± 16.4	> 0.05
Height (m)	1.65 ± 0.10	1.67 ± 0.11	1.65 ± 0.09	> 0.05
Heart rate	74.1 ± 10.0	74.3 ± 9.1	73.5 ± 8.5	> 0.05
Systolic blood pressure (mmHg)	127.6 ± 13.3	131.2 ± 11.2	133.6 ± 15.3	> 0.05
Diastolic blood pressure (mmHg)	71.7 ± 8.7	79.7 ± 8.7	81.4 ± 9.1	> 0.05
Duration of suffering from knee pain (months)	4.7 ± 5.1	4.1 ± 3.7	3.5 ± 5.5	> 0.05
	Number (%)	Number (%)	Number (%)	
One-sided knee pain	25 (52)	12 (27)	18 (40)	-
Two-sided knee pain	23 (48)	33 (73)	27 (60)	-

SD: Standard deviation

There was no statistically significant difference in age, duration of suffering from knee pain, weight, height, and body mass index (BMI) between the 3 groups (Table 1).

Patients were evaluated on the basis of K-L osteoarthritis imaging grading at the beginning of the trial, and 26, 90, 35, 2, and 1 patients were at zero, first, second, third, and fourth grade, respectively. The severity of the symptoms of osteoarthritis grading of 116, 35, and 3 patients was in the normal, moderate, and severe stages, respectively.

At the beginning of the study, 183 patients were screened and examined; 5 and 24 individuals were excluded from the study due to tendency to receive oral treatment and non-compliance with the entry criteria, respectively. The remaining 154 patients were randomly divided into 3 groups; 51 patients were allocated to the intervention group treated with oliban oil and diclofenac, and 52 patients were assigned to the control group. For 6 weeks, the patients used 10 drops of the oils and a unit of the fingertip index (FTI) of diclofenac gel twice a day.

During the study, 1 patient exited the study due to the lack of effect of oliban oil and 1 patient was excluded due to the incidence of itching and 48 patients remained in the intervention group until the end of the study. In addition, 7 and 6 patients, respectively, in the sesame oil and diclofenac gel groups were excluded due to lack of effect.

Evaluation of the effect of the oliban oil on the pain, stiffness, and discomfort indices of the KOOS questionnaire showed significant difference after 6 weeks of continuous use (P = 0.04). However, it did not have a significant effect on daily functions, recreation and exercise, and QOL. Moreover, there was no statistically significant difference between the two groups of oliban oil and diclofenac gel in terms of pain. However, the oliban oil showed a statistically significant difference relative to diclofenac gel in terms of stiffness and symptoms of knee discomfort (P = 0.03).

In addition, the diclofenac gel changed the pain, stiffness, and discomfort indices of the KOOS questionnaire and showed a significant difference after 6 weeks of continuous use.

The oliban oil significantly altered the VAS scale during 6 weeks of treatment intervention among the patients compared to the sesame oil group (P = 0.02). Diclofenac also significantly decreased pain among the patients; however, oliban oil indicated a statistically significant difference compared to diclofenac (P = 0.03) (Table 2).

Moreover, the patients were evaluated on the basis of CTCAE tables in the section of possible skin complications, and 20 symptoms were found and investigated, with only 1 case of a second-degree topical itching due to oliban oil causing the patient to leave the study.

Concurrent related symptoms in traditional medicine were also evaluated. Catarrh, digestive disorders, and excrement disorder were observed among the patients that were not comparable due to the lack of a non-patient control group.

Table 2. The amounts of the studied variables before and after of intervention

Variable	Group	Oliban oil (Mean ± SD)	Sesame oil (Control) (Mean ± SD)	Diclofenac (Mean ± SD)		
The outcomes based on KOOS questionnaire (0-100)						
Pain	At the beginning	54 ± 9	60 ± 11	52 ± 13		
	The amount of changing after 6 weeks	$18 \pm 9^{*#}$	3 ± 9	$10 \pm 9^*$		
Symptoms	At the beginning	70 ± 9	79 ± 9	75 ± 11		
	The amount of changing after 6 weeks	$15 \pm 8^*$	7 ± 5	11 ± 6		
Daily activities	At the beginning	91 ± 10	83 ± 7	78 ± 6		
	The amount of changing after 6 weeks	7 ± 4	2 ± 5	5 ± 1		
Exercise/recreation	At the beginning	67 ± 25	60 ± 16	63 ± 18		
	The amount of changing after 6 weeks	11 ± 23	3 ± 9	13 ± 8		
Quality of life	At the beginning	68 ± 11	60 ± 7	66 ± 5		
	The amount of changing after 6 weeks	8 ± 16	4 ± 5	7 ± 13		
The outcomes based on VAS (0-100 mm)						
Pain	At the beginning	60.3 ± 15.7	56.7 ± 16.3	59.5 ± 16.2		
	The amount of changing after 6 weeks	$45.3 \pm 17.3^{*\#}$	7.3 ± 8.1	$29.5 \pm 15.7^*$		

SD: Standard deviation; KOOS: Knee Injury and Osteoarthritis Outcome Score; VAS: Visual analog scale

Discussion

It is estimated that about 60% of available drugs are derived directly or indirectly from substances of natural origin. In addition, natural products are a valuable source for inspiring chemists to design new drugs. According to studies, 66% of the elderly use complementary-alternative medicines to treat their osteoarthritic pain. 20

Olibanum is one of the oldest medicinal plants used by mankind. in Ebers Papyrus (about 1550 BC), more than 700 medicinal herbs have been named, one of which is olibanum.²¹ Olibanum is one of the plants used by the ancient Iranians for inhalation, and was named Vahogeoneh in the Avesta.²² Olibanum oil with olive oil and honey are used to treat joint pain and chronic coldemerging pains, and is used with sesame oil to resolve difficulties. 12,13 In addition, it has been added to some topical combinations to increase the speed of the effect.¹⁴ The plants of this genus contain various derivatives of boswellic acid.23 The application hydrogenated extract of olibanum has been patented in the treatment of patients with stroke.23 Oleogam extract of olibanum resin and Indian olibanum have long been used in the treatment of knee inflammation, and trichytic acids have anti-cancer effects.24 The effects of olibanum on reducing pain during labor, with lavender, chamomile, and lemon, have been confirmed through inhalation in a clinical trial.25 In double-blind clinical trials, oral administration of compounds containing boswellic acid has been shown to reduce pain and knee inflammation, and increase knee flexion. A group of triterpenic acids (TTPs) derived from boswellia by inhibiting the 5-lipoxygenase enzyme has an inflammatory effect. Boswellic acid has antiinflammatory effects and is effective on diseases leading to intestine ulceration like ulcerative colitis.26 Another study has shown that boswellic acid of the pentacyclictriterpene acid present in olibanum, in addition to anticancer effects and inhibition of topoisomerase 1 and 2, is also able to seal the blockade of leukotriene 5-lipoxygenase.²⁷

Currently, despite the availability of traditional medicine resources and the clinical experience of traditional medicine drugs, the necessary evidence of its effectiveness, duration of administration, and the scope of their effects, as well as information on how to choose a drug and its

^{*} The differences of the amounts of changing after 6 weeks between oliban oil and diclofenac gel groups with sesame oil (control) group were significant (P < 0.05).

The difference of the amounts of changing after 6 weeks between oliban oil and diclofenac gel groups was significant (P < 0.05).

advantages over a drug with a similar effect are not available. In addition to pain relief, knee pain also involves the analysis of material causes of the disease; moreover, the rapid return of the normal movements of a joint is effective in analyzing the pathogen. Due to its warm and dry nature, olibanum is effective in drying and ripening in preparing and removing the knee phlegm. Perhaps its shrinkage effect has a role in reducing swelling. Combinations of frankincense with different compositions are used to treat diseases associated with inflammation, like breast inflammation. Although its analgesic effect has been documented in traditional medicine, no information is available on its effect on the quality of the disease, daily activities, and the recovery of individuals suffering from knee pain. In the KOOS, in addition to pain, stiffness, and symptoms of the disease, everyday activities, sports, recreation, and QOL are fully considered. With this in mind, it corresponds with some of the therapeutic and health maintaining criteria in Iranian traditional medicine, like motion and rest, and exercise.

In allopathic medicine, the use of topical non-steroidal anti-inflammatory drugs is one of the treatments prescribed for knee osteoarthritis,²⁸ which reduces symptoms of knee osteoarthritis over a 6-week period.²⁹ Therefore, in order to compare and standardize the efficacy of oliban oil, this drug was considered as a positive control.

According to our findings, oliban oil has been effective in decreasing pain and joint stiffness, reducing motor limitation, and increasing the ability to move among patients. Diclofenac was also effective in reducing pain among patients; however, it was not effective in changing the symptoms of knee pain. Hence, oliban oil may be considered as a topical drug. Of course, in other studies, diclofenac has been effective in reducing joint stiffness and pain during walking.³⁰

Perhaps one of the reasons for the lack of impact of oliban oil on daily activities, exercise/recreation, and QOL was the

removal of the principle of cleansing, nonreformation of nutrition, and non-use of manual applications of the treatment plan. Future studies can determine the role of the treatment program for the cleansing and correction of all 6 essential principles of life in combination with local therapies. Particularly since, in previous studies, planned and ongoing exercise and the use of massage and treatment for 3 weeks in a spa and lifestyle changes in VAS had a significant effect on reducing symptoms and the sustainability of the therapeutic effect.³¹ According to the study on the effect of an edible mixture of olibanum and curcumin in the treatment of knee osteoarthritis, the concurrent oral and topical administration of olibanum can be suggested for patients with knee pain.32

Conclusion

According to the findings of this study, topical treatment with oliban oil can be suggested in cases in which the patient complains only of joint pain, and not have baseline illnesses.

Overall, the evaluation of the effect of local treatment with oliban oil showed that this oil was effective in reducing pain and stiffness, and increasing knee motion, but there was no significant effect on daily functions, recreation, exercise, and QOL. The effects of diclofenac were consistent with those of similar clinical reports. Moreover, the intervention with topical oliban oil was more effective than sesame oil, and it also seems that the collaboration of Iranian traditional medicine is likely to be effective in future studies.

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Conflict of Interest

Authors have no conflict of interest.

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