



A Topical Gel From Flax Seed Oil Compared With Hand Splint in Carpal Tunnel Syndrome: A Randomized Clinical Trial

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Abstract

This study compared the therapeutic effect of flax seed oil topical gel and hand splint in the treatment of carpal tunnel syndrome. This study was a randomized clinical trial. Forty-nine patients, 96 hands, with mild to moderate idiopathic carpal tunnel syndrome were divided into 2 groups randomly. One group was treated by topical gel and the other group by hand splint. Intensity of symptoms and function before and after intervention was measured via Boston Carpal Tunnel Questionnaire. After intervention, the ANCOVA showed a significant difference between the symptom and function scores of the 2 groups. In both cases, recovery was higher in the gel group ($P < .001$). The topical use of flax seed oil gel is more effective in the improvement of symptoms and function of patients with mild to moderate carpal tunnel syndrome as compared with hand splint, and it can be introduced as an effective treatment.

Keywords

Persian medicine, carpal tunnel syndrome, flax seed oil

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Carpal tunnel syndrome (CTS) is one of the major debilitating diseases of the hand and one of the most common causes patients visit orthopedics and rheumatology clinics.¹ Carpal tunnel syndrome was first described as a nocturnal hand pain around 1850, followed by the term *acroparesthesia* until 1950,² and nowadays it is defined as a median nerve compression neuropathy at the wrist.³ Carpal tunnel syndrome is the most common form of median nerve entrapment^{1,4,5} and is responsible for 90% of all entrapment neuropathies.^{6,7} The prevalence of carpal tunnel syndrome in different societies and general population varies between 3.8% and 16%, and the incidence of the disease is reported variably from 1 to 2.3 out of 100 individuals per year.^{1,3,4,8-11} The disease occurs mainly in females and in both hands, and it may affect all ages; however, the mean age of most patients is between 40 and 60 years.^{1,12} Carpal tunnel syndrome is one of the most frequent and costly upper extremity disorders among the working population,¹³ and it has the greatest days away from work of 27 days.¹⁴

The most common diagnosis is the idiopathic type of the disease.^{5,12,15} However, occupational risk factors including repetitive movements of the wrist flexor muscles have been recognized with the disease.¹⁶ Other medical risk factors

include diabetes, pregnancy, oral contraceptive consumption, alcoholism, hypothyroidism, morbid obesity, renal failure, long-term hemodialysis, severe heart failure, lupus, scleroderma, dermatomyositis, acromegaly, nerve tumors, fractures, and posttraumatic arthritis.^{6,15}

Symptoms vary depending on the disease severity. The sensory component of a nerve is engaged first and the patient suffers from nocturnal pain, tingling, numbness, and paresthesia in the median nerve area. Then motor symptoms occur in the form of weakness or hand motion and grasping dysfunctions.^{6,15} Although some studies suggested electrodiagnosis as

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the gold standard for carpal tunnel syndrome diagnosis¹⁷ a more accurate diagnosis is based on a combination of clinical evaluation and electrodiagnosis study.

The consensus is that the mild to moderate carpal tunnel syndrome should be subjected to conservative treatment,¹⁴ and hand splint is considered as one among the effective and standard treatments.¹⁸ On the other hand, a study that examined 20 clinical trials and 2 review studies showed that the efficiency of most existing conservative methods is short term.¹⁹ Therefore, it seems necessary to take advantage of all treatment capacities for reducing the severity of symptoms of this costly and debilitating disease.

According to a report of the World Health Organization, traditional and complementary medicine is extensively used in the developing countries due to its availability, affordability, and naturalness. It is also expanding in the developed countries rapidly.^{20,21} Persian medicine is based on the scientific experiences and observations passed down from generation to generation.²² Avicenna was one of the greatest and most famous polymath and physician in the world who described the sensory symptoms caused by the dysfunction of a nerve (neuropathy).^{23,24} Persian medicine prescribed the topical use of some herbal oil products,^{25,26} such as flax seed oil,^{24,27,28} as a tonic for neural tissues and remedy for their diseases. *Linum usitatissimum* L (Flax) is an inexpensive plant native to Asia, Europe, and the Mediterranean. Several studies have reported its anti-inflammatory, antioxidant, and analgesic effects.²⁹⁻³³ It is also beneficial for arthritis and some skin lesions.^{32,34}

This study is a randomized clinical trial that examines the effectiveness of flax seed oil gel versus hand splint, a mild to moderate carpal tunnel syndrome common treatment.

Materials and Methods

Study Design

This study was a randomized open-label clinical trial. The allocation ratio was 1:1.

Ethical Issues

All the patients were included in the study voluntarily after signing informed consent forms and were provided with free flax oil topical gel and hand splint. Patients' personal information was kept confidential. This study is in accordance with the Helsinki Declaration and was conducted after obtaining approval from the Committee of Ethics of Tehran University of Medical Sciences (Approval No. 9021309002-132293). The study was registered with the Iranian Registry of Clinical Trials (Number IRCT201411210023N1).

Preparation of Medicine and Splint

Brown flax seeds were purchased from the market in Kerman Province, and they were confirmed by a botanist of Kerman University. Voucher specimens (No. 1628) were deposited at the Herbarium of the Department of Pharmacognosy (KER Herbarium) in the Faculty of Pharmacy, Kerman University of Medical Science, for future reference. Flax seed oil was extracted through the cold press method in

Table 1. Composition of Fatty Acids of Flax Seed Oil (According to GC-MS Analysis of the Methyl Esters).

Fatty Acids	Retention Times (Minutes)	Content %
Palmitic acid (C16:0)	18.34	6.5
Oleic acid (C18:1) (omega 9)	21.35	17.5
Stearic acid (C18:0)	21.45	5.5
Linoleic acid (C18:2) (omega 6)	21.50	15
Linolenic acid (C18:3) (omega 3)	21.85	53.5

Kerman Oil Extraction Company and stored in closed dark containers. The obtained oil was analyzed in the laboratory of the Kerman School of Pharmacy (Table 1).

The medicine was made in the Faculty of Pharmacy of Shahid Beheshti University in Tehran. The obtained oil was gradually mixed with carbomer 937 by controlling the pH and the physical properties of the product in such a way that the pH of the final product was kept within a range of minimum irritant effects for the skin and the gel becomes uniform without having sediments and without becoming biphasic. For this purpose, 10% gel was prepared and packaged in 80-g double-shell tubes. The carpal tunnel syndrome hand splints had external and internal angles of 20° and 5°, respectively, as well as 2 adjustable Velcro fastening straps in the dorsal section.

Setting

This study was carried out on 96 hands belonging to 49 patients who were referred to Besat Specialized Clinic affiliated to Kerman University of Medical Sciences. After being admitted to the clinic, the patients were visited by an orthopedic specialist. They were then introduced to the researcher after a clinical and electrodiagnostic diagnosis of carpal tunnel syndrome. Finally, they were included in the study in case they met the eligibility criteria.

Randomization

The eligible patients were divided randomly into 2 groups using random digit numbers. One group was prescribed the splint and the other group was prescribed the topical gel. The patients with the disease affecting both hands had one type of treatment.

Inclusion and Exclusion Criteria

Patients of both genders aged 20 to 60 years with a diagnosis of mild to moderate idiopathic carpal tunnel syndrome were included in the study.

Inclusion Criteria. Clinical diagnosis by an orthopedic specialist as exhibiting at least 2 symptoms from among the following: nocturnal pain, tingling, numbness, hypoesthesia, paresthesia; or exhibiting a symptom plus a sign (positive Tinel or Phalen)^{35,36}; electrodiagnostic evidence of mild to moderate carpal tunnel syndrome.

Exclusion Criteria. Inability to fill out the questionnaire, history of trauma or fracture or surgery or direct injection into the carpal tunnel area during the past 6 months, pregnancy, diabetes, hypothyroidism, alcoholism, median nerve entrapment in the areas other than carpal tunnel area with clinical diagnosis or electrodiagnosis, severe skin complications resulting from the use of a topical gel, rheumatic

diseases such as rheumatoid arthritis, scleroderma, amyloidosis, systemic lupus erythematosus, any history of hypersensitivity to topical or oral compositions of flax, having serious diseases such as an advanced cancer simultaneously, renal failure and long-term hemodialysis, heart failure, body mass index-based morbid obesity or emaciation, recent chemotherapy and radiotherapy, consumption of anticancer drugs and corticosteroid, thenar atrophy, and report of a severe type of carpal tunnel syndrome in electrodiagnostic study.

Electrodiagnosis

Electrodiagnostic assessment of the patients was performed by a physical medicine and rehabilitation specialist using a Medelec Synregy Viasis electromyography system. The method for electrodiagnosis was the same as that in the study by Ashraf et al.³⁷ Considering the possibility of the daily changes of the electrodiagnostic assessment result,³⁸ all the patients were assessed at a similar time of the day (5-8 PM).

Intervention

The patients were divided randomly into 2 groups of *splint* and *gel*. The Boston Carpal Tunnel Questionnaire was filled by the patients. One group was given the standard splint to wear at night. The other group was given topical gel of flax seed oil. The topical gel was applied twice a day in the morning and in the evening to an appropriate tip of finger unit on wrist palmar area, 2-3 cm above and below wrist crease of the affected hand/hands without massage. Intervention duration in both groups was 3 weeks. The patients were then revisited and the Boston Carpal Tunnel Questionnaire was completed.

In this study, outcome measurement tool was the Boston Carpal Tunnel Questionnaire, which is one of the most reliable and the most widely used tools for measuring the outcome of interventions in carpal tunnel syndrome.³⁹ Each question contains 5 options of the mildest (1) to the most severe (5) state. This study used the Persian version of Boston Carpal Tunnel Questionnaire whose validity was assessed and which had proved acceptable consistency, reliability, and sensitivity.³⁴

Statistical Analysis

We calculated that 48 patients in each group would be required for the study to have 80% power to detect a difference of 40% between groups with a significance level of .05. The independent *t* test and χ^2 test were used for quantitative and qualitative comparisons, respectively, between the 2 groups. We analyzed the principal dependent variable, namely, the severity of symptoms and function after the intervention, using the scores obtained by the 2 groups; and assuming as the covariate the initial score, we subsequently implemented ANCOVA. SPSS 20 (IBM SPSS, Version 20.0, Armonk, NY) was used for data analysis. *P* values >.05 were considered as significant.

Results

The first and the last patients were visited in December 2014 and August 2015, respectively. Fifty-eight patients with 110 affected hands were evaluated for inclusion in the study, and 103 affected hands were eligible to be included in the study. Finally, 96 affected hands were statistically analyzed (Figure 1).

In total, 48 hands were allocated to the gel group and 48 hands were allocated to the splint group. Both groups were comparable with regard to age and sex, and the 2 groups were

not significantly different in terms severity of carpal tunnel syndrome (Table 2).

Using ANCOVA, the scores of symptom and function after intervention showed a significant difference (Table 3), and improvements of symptoms and function in the gel group were greater than that observed in the other group (*P* < .001).

The topical gel was tolerated well by the patients and no complaints were reported. There was no serious local or general side effects in the follow-up physical examination.

Discussion

To the best of our knowledge, this was the first study to compare the effectiveness of flaxseed oil topical gel and hand splint in the conservative treatment of mild to moderate carpal tunnel syndrome. The results of this randomized trial showed that this gel can improve sensory and functional symptoms of carpal tunnel syndrome effectively as compared with the splint.

Neuropathy in the Persian Medicine

In Persian medicine sources, symptoms of sensory neuropathy, which is due to the dysfunction of a branch of a nerve, are referred to as *khader*.^{23,24} Carpal tunnel syndrome can be considered as a *khader* through a comparative study of sensory symptoms. Persian medicine has proposed several treatments through different methods, including topical medications, for this clinical state.²⁴ Conducting a clinical trial is essential for making these options evidence-based. One of the therapeutic suggestions is flax seed oil. This herbal product has long been used for several therapeutic purposes in Persian medicine.⁴⁰

Flax seed oil has anti-inflammatory effects^{32,33} since it contains considerable amounts of α -linoleic acid.⁴¹ Also, several studies have pointed out its antioxidant and analgesic effects.²⁹⁻³¹ From the standpoint of Persian medicine, topical oils having a “warm” temperament are able to increase local blood supply.²⁴ On the other hand, oxidative stress, ischemic injury, and inflammation occur in carpal tunnel syndrome pathophysiology.^{17,42} Therefore, flax seed oil is expected to have therapeutic effects for carpal tunnel syndrome.

In 2014, the randomized double-blind trial of Hashempur et al proved the effectiveness of flax oil in reducing sensory and functional symptoms of carpal tunnel syndrome.²⁸ In this study, one group received medicine (flax seed oil) and another group received placebo, in addition to splint as a standard treatment for both groups. Therefore, the trial of Hashempur et al was merely to study the medicine’s effectiveness on disease symptoms and no comparison was made between flax seed oil and splint.

This study took the second step. This time, the therapeutic effect of flax seed oil—as an independent treatment, not as an adjuvant—was trialed and compared with the effect of wrist splint, which is among the main and standard treatments for mild to moderate idiopathic carpal tunnel syndrome. In addition, the pharmaceutical form of the intervention was changed from a fatty oil product to a topical gel. The topical gel has no problems caused by the storage and use of a fatty product and it is more

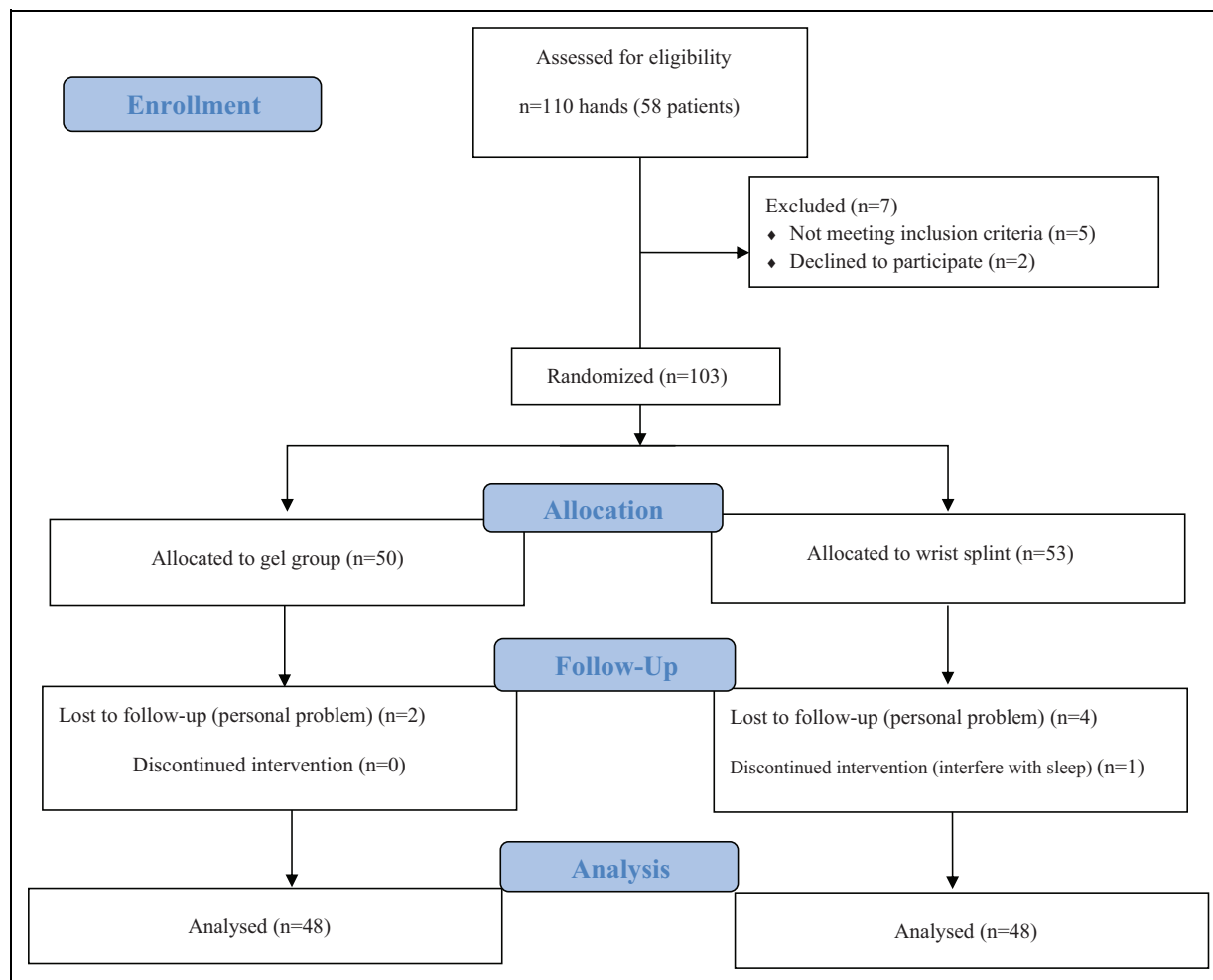


Figure 1. CONSORT flow diagram.

Table 2. Baseline Information of the Participants in Splint and Gel Groups.

Variable	Gel (n = 48)	Splint (n = 48)	P
Age, mean (SD)	40.8 (9.5)	41.6 (10.2)	.672
Sex, n (%)			
Female	46 (95.8)	43 (89.6)	.435
Male	2 (4.2)	5 (10.4)	.218
Hand, n (%)			
Right	24 (50)	24 (50)	1
Left	24 (50)	24 (50)	1
Severity, n (%)			
Mild	40 (83.3)	34 (70.8)	.145
Moderate	8 (16.7)	14 (29.2)	.145

convenient for patients to apply. In addition to cosmetic issues, especially for women who are affected more often, the splint may limit daily activities. For this reason, it is used at night, but some patients do not feel comfortable about sleeping while wearing a splint. On the other hand, storing and applying greasy oil products, though effective, may lead to problems caused by oiliness. With due attention to all these reasons, we decided to use a pharmaceutical gel instead of simple and raw flaxseed oil.

Although the hand splint is one of the most effective and well-known treatments of mild to moderate carpal tunnel syndrome, the study results showed that the therapeutic effects of the topical gel of flax seed oil exceed the ones of the splint. Consequently, the splint can be replaced by it as an effective treatment for the patients who are not willing to use a splint.

The hand splint is not commonly used for severe carpal tunnel syndrome cases. Severe cases are usually operated in current medicine. However, the explanation of Persian medicine on the mechanism for reduction of the carpal tunnel syndrome symptoms is the gradual removal of concentrated materials (black bile or phlegm in humorism as a basic theory in Persian medicine) from nerve and its surrounding areas. In the study by Rivas-Suárez et al, a cream based on bach flower remedies was effective in patients during their waiting time for surgical option.⁴³ There is some evidence that chamomile oil improves severe carpal tunnel syndrome.⁴⁴ Subsequent trials will determine whether other topical combinations, proposed by complementary medicine including flax seed oil, may be effective in severe cases and reduce related surgeries and their potential complications and risks.

Table 3. Comparison of Treatment Outcome in Splint and Gel Groups Before and After Intervention.

Group	Symptom Severity		Function Severity		P Value ^a	Between-Group Comparison P Value ^b	
	Before	After	Before	After		Symptom Severity	Function Severity
Gel	26.8 (7.8)	16.5 (6.2)	17.3 (5.8)	12.3 (5.2)	<.001	<.001	<.001
Splint	22.4 (5.9)	17.8 (4.4)	13.5 (5)	12.2 (3.7)	<.001		

^at Test.^bANCOVA.

Study Limitations

Short-term follow-up is one of the limitations of our study. A splint is one of carpal tunnel syndrome's symptomatic and supportive treatments (and not etiologic) with no long-term effects. We aimed at proposing a new herbal topical product instead of the hand splint. Lack of electrodiagnostic assessment of patients after the intervention is another limitation of the study. Similar to the majority of other trials on carpal tunnel syndrome, we were faced with some feasibility problems. Finally, the common pattern of Persian medicine in dealing with diseases, including neurological disorders, aims at offering a package, containing both preventive recommendations and therapeutic measures. The synergy of the package components may lead a patient toward complete and permanent treatment not merely a symptomatic treatment. For example, nutrition has an important basic role in this package.⁴⁵ If the effectiveness of every single part of the proposed package of Persian medicine in treating carpal tunnel syndrome during separate clinical trials is proved, we expect to achieve an effective protocol for the long-term treatment of the disease.

Conclusion

The results showed that for patients with the clinical and electrodiagnostic diagnosis of mild to moderate idiopathic carpal tunnel syndrome, topical application of flax seed oil gel, twice a day for 3 weeks, was more effective than a hand splint for short-term reduction of symptoms and functional improvement. This method can be introduced as an effective and supportive alternative treatment for patients who are unwilling to use a hand splint. It should be mentioned that further studies are needed for determining the long-term effects of the proposed method.

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Author Contributions

Dr M. Setayesh is the principal investigator, and he participated in the overall design of the study, conducted the study, and took primary lead in drafting the manuscript. Dr A. R. Sadeghifar participated in the design of the study, visited all patients for allocation, and contributed to the writing of the manuscript. Dr N. Nakhac provided statistical support and contributed to the writing of the manuscript. M. Kamalnejad is co-investigator, participated in the design of drug, and made dosage form and flax seed oil gel. Dr H. Rezaeizadeh is the main

supervisor of this study as a PhD thesis and provided support and mentorship necessary for the success of this work, including participation in the design of the study and critical review of and contributions to the manuscript.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical Approval

The Committee of Ethics of Tehran University of Medical Sciences approved this study (Approval Number 9021309002-132293).

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