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A pilot randomized double-blind placebo-controlled trial on topical chamomile (*Matricaria chamomilla* L.) oil for severe carpal tunnel syndrome

Mohammad Hashem Hashempur [a, b], Zeinab Nasiri Lari [c, d], Parissa Sadat Ghoreishi [c, d], Babak Daneshfard [d, e], Mohammad Sadegh Ghasemi [f], Kaynoosh Homayouni [d, *], Arman Zargaran [g, h]

[a] Noncommunicable Diseases Research Center, Fasa University of Medical Sciences, Fasa, Iran
[b] Department of Traditional Medicine, School of Medicine, Fasa University of Medical Sciences, Fasa, Iran
[c] Department of Traditional Persian Medicine, School of Traditional Medicine, Shiraz University of Medical Sciences, Shiraz, Iran
[d] Research Center for Traditional Medicine and History of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran
[e] Essence of Parsiyan Wisdom Institute, Traditional Medicine and Medicinal Plant Incubator, Shiraz University of Medical Sciences, Shiraz, Iran
[f] Student Research Committee, Shiraz University of Medical Sciences, Shiraz, Iran
[g] Pharmaceutical Sciences Research Center and Department of Phytopharmaceuticals (Traditional Pharmacy), School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran
[h] Research Office for the History of Persian Medicine, Shiraz University of Medical Sciences, Shiraz, Iran

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ABSTRACT

Objective: To assess the effectiveness of standardized topical Chamomile (*Matricaria chamomilla* L.) oil in patients with severe carpal tunnel syndrome, as a complementary treatment.
Method: A pilot randomized double-blind placebo-controlled trial was conducted. Twenty six patients with documented severe carpal tunnel syndrome were treated in two parallel groups with a night splint plus topical chamomile oil or placebo. They were instructed to use their prescribed oil for 4 weeks, twice daily. Symptomatic and functional status of the patients and their electrodiagnostic parameters were evaluated when enrolled and after the trial period, as our outcome measures.
Results: A significant improvement of symptomatic and functional status of patients in the chamomile oil group was observed ($p = 0.019$ and 0.016, respectively) compared with those in the placebo group. However, electrodiagnostic parameters showed no significant changes between the two groups.
Conclusion: Chamomile oil improved symptomatic and functional status of patients with severe carpal tunnel syndrome.

1. Introduction

"Symptomatic compression neuropathy of median nerve", known as carpal tunnel syndrome (CTS) is the most common type of entrapment neuropathy accounted for about 90% of them [1,2]. The most common symptoms of CTS are pain, weakness, numbness, burning sensations, and tingling in the median nerve territory [3,4].

There are both conservative and surgical treatment options for the patients. Surgery is used for patients with severe CTS or cases of conservative treatment failure [5]. However, failure of surgical intervention is not uncommon (up to 19%) where outcome is not satisfactory [6,7]. Additionally, patients may avoid it because of their concerns about safety, inconvenience and the cost of surgery [2]. Therefore, further investigations required to find out more feasible and efficient treatments.

At the present time, complementary and alternative medicine (CAM) is more popular and acceptable than the past. It may be due to its accessibility, feasibility and low cost [8,9]. There are many treatment options suggested by different schools of CAM, some of which could be helpful for CTS patients.

Matricaria chamomilla L. (Asteraceae) is one of the most common herbs used worldwide [10,11]. The main ingredient from the essential oil of its flowers is α-bisabolol and its oxides and also chamazulene which is accountable for its medical properties [10,12]. Chamomile

* Corresponding author. Department of Physical Medicine and Rehabilitation, Shahid Faghihi Hospital, Zand Street, Shiraz 7134845794, Iran.
E-mail address: kayhomayouni@gmail.com (K. Homayouni).

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essential oil is shown to have anti-microbial [13], anti-inflammatory [14] and anti-cancer properties [15]. Moreover, positive effect of chamomile on acute pains [16] including joint pain [17] has been reported. Not only no toxicity was reported in the topical use of chamomile [18], but it has been approved by German E commission for inflammatory and bacterial skin diseases [11].

In addition to modern-day science, the school of Traditional Persian Medicine (TPM) has introduced chamomile as an analgesic and used it for treating variety of medical conditions. Based on *The Canon of Medicine* written by *Ibn-e-Sina* or Avicenna (980–1037 AD) [19] and *The Storehouse of Medicaments* of *Aghili* (written in 1772 AD) [20], topical use of chamomile oil could be beneficial as analgesic for joint pain and as tonic agent for neural tissue [21,22].

Accordingly, after we found out the effectiveness of linseed oil on mild and moderate CTS [23], we decided to conduct this pilot study to investigate the possible effect of topical chamomile oil on severe CTS.

2. Materials and methods

2.1. Study design

This is a pilot randomized placebo-controlled trial with a two-arm parallel design and allocation ratio of 1:1 for the intervention and control groups.

2.2. Ethical issues

Local Medical Ethics Committee of Shiraz University of Medical Sciences (SUMS) approved the study proposal with the ID number: CT-P-9365-6205. Moreover, all of the participants signed the written informed consent.

2.3. Preparation of the materials

The chamomile flower was purchased from a local herbal shop (*Attari* in Persian language) in Shiraz, south of Iran, and was verified by a botanist at herbarium center of School of Pharmacy, SUMS with voucher number of PM407.

We prepared traditional chamomile oil according to our previous study on standardization of "traditional direct heat method" [24]. In this method, we purified the flowers and turned it to powder form. Then 600 g of the powder was boiled in 4.5 L of distillated water for 3 h. Then, after removing the plant powder from aqueous extract, 1 L of sesame oil was added to it and was boiled until the whole content was evaporated and oil remained. The final product was standardized based on its essential oil content (2.05% of chamazulene as the main pharmacological ingredient and 62.35% of Bisabolone Oxide as the major ingredient), and analyzed with gas chromatographic with Mass detector (GC/MS) method and also 2.7640 ± 0.1776 mg/L total flavonoid and 11.0043 ± 0.4514 mg/L total poly phenol content.

The placebo was prepared with the pharmaceutical paraffin with 10% (V/V) of sesame oil and 0.1% of chamomile essential oil. They were mixed, in order to achieve similar odor and color of our test drug.

An immobilizing wrist splint which holds the wrist in a 5° extension position, with three adjustable Velcro fastenings, was used as standard treatment. It was made of 5-mm medical foam, with internal fabric and external leather layer.

2.4. Inclusion and exclusion criteria

Patients from both genders 18 years and older were enrolled in this study who had clinical signs and symptoms of CTS (from two Physical Medicine and Rehabilitation clinics affiliated with SUMS). All of the patients were diagnosed by electrodiagnostic instrument for evidence of severe CTS. These patients were advised to undergo surgery and if they refused it they were allowed to participate in our study.

Patients with mild or moderate CTS were excluded. The other exclusion criteria were hypersensitivity to chamomile oil, intracarpal injection within the past 6 months, and coexisting proximal median nerve mononeuropathies, cervical radiculopathies, or brachial plexopathies. Patients were also excluded if they had rheumatologic and endocrine diseases, and other conditions that could mimic CTS. Pregnancy, recent or ongoing use of corticosteroids or analgesics was the other important exclusion criteria.

2.5. Electrodiagnosis

Electrodiagnostic study was performed by a Medlec Synergy Viasis electromyography instrument with two 6 mm electrodes and 23 mm pads. The detailed procedure was similar to a previously published article [25]. All of the participants were assessed clinically and electrodiagnostically by the same physician (K.H.) who was blinded about the allocations.

2.6. Intervention

2.6.1. Splint

In this study, placebo and the test drug were added to the standard treatment of wrist splint. The splint was prescribed for the patients to be used at night-only.

2.6.2. Placebo and test drug

A 4 weeks period was considered for administration of the placebo and the test drug. Patients were advised to use 5 drops of the prescribed oils, topically on the palmar zone of the wrist every morning and evening. They were prohibited from massaging the mentioned part of wrist.

2.7. Outcome measures

We used the Persian version of Boston Carpal Tunnel Questionnaire (BQ) as the primary outcome measure, and its reliability, validity, and internal consistency was confirmed previously [26]. It assesses symptom severity score (BQ SYMPT) and functional status score (BQ FUNCT). Median nerve sensory distal latency (SDL), motor distal latency (MDL), sensory nerve conduction velocity (NCV), and compound latency (CL) were secondary outcome measures. We obtained the data of primary and secondary outcome measures at the enrollment and 4 weeks after the intervention.

2.8. Randomization, blinding and concealment of allocation

Using a computer-generated block-randomization list (non-stratified with equal-length blocks), we randomly allocated the eligible patients to two parallel drug and placebo groups.

In bilateral CTS patients, the same intervention was considered for both wrists. All of the researchers, physicians, and statisticians were blind to the patients' allocation. Additionally, patients were also blind to their allocation because of the similar color and odor of the placebo and drug and their same containers' shape and size.

2.9. Statistical analysis

Clinical and demographic properties of the enrolled participants are shown as the mean ± standard deviation or proportions. The statistical analysis was performed by using Fisher exact test, and Mann–Whitney test. The significance value was set at $p < 0.05$. The Statistical Package for the Social Sciences, version 18.0 (SPSS Inc., Chicago, IL, USA), was used for all statistical analyses.