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Efficacy of topical chamomile oil for mild and moderate carpal tunnel syndrome: A randomized double-blind placebo-controlled clinical trial

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ABSTRACT

Objective: To evaluate the efficacy of topical chamomile oil in patients with mild and moderate carpal tunnel syndrome (CTS).
Method: Eighty six patients with electrodiagnostic criteria of mild and moderate CTS were enrolled in this randomized double-blind placebo-controlled clinical trial and received wrist splint plus topical chamomile oil or placebo for 4 weeks. They were evaluated at the baseline and end of the study regarding functional and symptomatic scores, dynamometry, and electrodiagnostic indexes.
Results: Dynamometry, functionality, and symptom severity scores of the patients were significantly improved in the chamomile oil group compared with the placebo group ($P = 0.040$, $P = 0.0001$, $P = 0.017$, respectively). Additionally, compound latency of the median nerve in the chamomile oil group significantly decreased ($P = 0.035$) compared to the placebo group. Other electerodiagnostic measurements did not change significantly.
Conclusion: Complementary treatment with topical chamomile oil may have some benefits for patients with mild and moderate CTS, both subjectively and objectively.

1. Introduction

Entrapment of the median nerve in the carpal tunnel causes the most common type of entrapment neuropathy known as carpal tunnel syndrome (CTS) [1,2]. The disease has posed a considerable burden worldwide and still remains a problem in healthcare systems [3]. Annual incidence rate of CTS is considered to be 276:10000 with a peak incidence rate in the age range of 40–60 years old [4].

Although CTS is categorized as idiopathic etiopathogenetically [5], the median nerve entrapment in the carpal tunnel is known to be the basic pathophysiology of the disease. It causes various symptoms, among which numbness at night is the main characteristic [6].

Among available conservative and surgical treatment options, non-surgical treatments such as splinting and steroid therapy are usually used for management of mild and moderate CTS. However, their long term effectiveness is under question besides possible complications [7].

Abbreviations: BFR, Bach flower remedies; BMI, Body mass index; CAM, Complementary and alternative medicine; CL, Compound latency; CTS, Carpal tunnel syndrome; EMG, Electromyography; GC, Gas chromatography; HPLC, High performance liquid chromatography; MDL, Motor distal latency; MS, Mass spectrometry; NCV, Nerve conduction velocity; PDA, Photodiode Array; SDL, Sensory distal latency; SPL, Sensory proximal latency; TPM, Traditional Persian Medicine; UV, Ultra violet.

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In recent years, complementary and alternative medicine (CAM) has become more popular all around the world [8,9]. A more recent academically introduced brand of CAM, Traditional Persian Medicine (TPM), has some suggestions including herbal remedies for neuropathic pains such as CTS [10].

German chamomile, *Matricaria chamomilla* L. (*Asteraceae*) has a wide range of applications worldwide [11,12]. Previous studies show that the reported compounds in the chamomile flowers like azulenes and α-bisabolol (in essential oil) and flavonoids (mostly apigenin and its derivates) have anti-inflammatory, anti-oxidant, and analgesic properties [13–15]. Not only the modern-day documents, but also TPM has considered chamomile as an analgesic agent. Its topical application as a painkiller in the joint pain and a neural tissue strengthening agent is mentioned by Avicenna (980–1037 AD) [16] in "Canon of Medicine" [17] and *Aghili Alavi Shirazi* (1670–1747 AD) [18] in "Storehouse of Medicaments" [19]. Moreover, its topical use has shown to have no toxicity beside the validation of German E commission and FDA [11,12,20].

One of the popularly reported traditional dosage forms of chamomile in TPM and Iranian ethno-medicine is its traditional oil. Traditional chamomile oil is the infusion of chamomile aqueous extract in an oily vehicle (sesame oil). We standardized traditional chamomile oil dosage form [21]. Our previous study revealed positive effect of this oil in severe CTS so that significant functional and symptomatic improvement of the patients was observed [22]. Therefore, we aimed to investigate the effect of standardized traditional chamomile oil on mild and moderate CTS.

2. Materials and methods

2.1. Study design

This randomized placebo-controlled clinical trial had a two-arm parallel design with allocation ratio of 1:1 for the control and intervention groups. Also, the protocol of the study has not been modified after the trial's commencement.

2.2. Compliance with ethical standards

The study design was in compliance with the guidelines of Helsinki Declaration (1989 revision). The ID number of CT-P-9363-6203 has been dedicated to the study protocol, after reviewing and approval, by the Local Medical Ethics Committee of Shiraz University of Medical Sciences (SUMS). Additionally, the study protocol was registered in Iranian Registry of Clinical Trials (registration ID: IRCT2014052811341N2). In addition, participation of the included patients was done after signing the dated, written informed consent form.

2.3. Preparation of the materials

We purchased chamomile flowers from a traditional herbal shop (*Attari* in Persian language) in Shiraz. The flowers were obtained from Kazeroon, a city near Shiraz in Fars province. The plant was identified and approved by a herbalist (Miss. Sedigheh Khademian) in Herbarium center of school of pharmacy, SUMS (Voucher no. PM407). Also, standard Sesame oil was purchased from Golkaran Co.

Preparing traditional chamomile oil was performed according to the historical documents [23,24] as well as our previous works [14,21,22]. In this method, 600 g of cleaned powder of chamomile flowers was boiled in 4.5 L of distillated water for 3 h. Then, the residue of the flower was removed and the remained aqueous extract of chamomile was boiled with 1 L of Sesame oil for 4 h s (until the whole aqueous content was vaporized). The remained oil was used as traditional chamomile oil in this study. Also, placebo was made with 10% (V/V) of Sesame oil in pharmaceutical paraffin (Merck co.) and 0.1% of chamomile essential oil. The essential oil was obtained from chamomile flowers via Clevenger apparatus method (hydro-distillation).

Standard treatment for both groups was a wrist splint that immobilizes the wrist in an extension position with 5-degree deviation. It had three adjustable Velcro fastenings and was made from a 5-mm medical foam covered by fabric and leather layers in the internal and external surfaces, respectively.

2.4. Gas chromatograph analysis

In the aim of measuring volatile components in the final product, the essential oil of the chamomile oil was obtained via hydro-distillation method (using Clevenger apparatus) [21,22]. Then, the obtained essential oil was analyzed by GC/FID (gas chromatograph Bruker technologies model 450-GC) and GC/MS (GC instrument, Agilent 7890 with mass specific detector, Agilent 5975C) instruments [21].

2.5. Total poly-phenol and total flavonoid content

Total poly-phenol and total flavonoid content of the methanolic extraction of traditional Chamomile oil were measured via UV spectrophotometer (PG instrument), based on galic acid and quercetin equivalents per liter of chamomile oil, respectively [21].

2.6. Determination of apigenin as a marker by HPLC method

Apigenin, as the main reported flavonoid of the chamomile flower was chosen to be quantified in the preparation [22]. HPLC analysis was performed with a Knauer technologies model apparatus attached to Eurospher 100-5 C18 column (250 × 4.6 mm with precolumn) and connected to a photodiode array (PDA) detector. There was a mobile phase containing water (with 0.2% phosphoric acid): methanol (58:42). Before operation and extraction, the samples of the chamomile oil were treated by boiling with HCL (2 h) because all apigenin derivates in the sample were free [25].

2.7. Inclusion and exclusion criteria

All of the patients above 18 years old with electrodiagnostic criteria of mild or moderate CTS (from the Outpatient Clinics of *Shahid Faghihi* Hospital and *Imam Reza* Polyclinic, two academic teaching centers, affiliated with SUMS) were enrolled. They should have at least two signs or one sign plus one symptom of: numbness, paresthesia, night pain, tingling, positive Phalen test, positive Tinnel test, and positive compression test. The patients were labeled as mild and moderate CTS, if they had: SDL> 3.7 ms, NCV <40 m/Sec, MDL >4.2 ms, CL > 2.4 ms.

On the other hand, patients with clinical and electrodiagnostic evidence of severe CTS (including: SDL> 5.3 ms OR absent, NCV< 28 m/Sec, MDL >6.5 ms OR absent, CL > 3.2 ms) were excluded. Other exclusion criteria included the history of surgical release of the median nerve and/or trauma and/or fracture of the wrist bones and/or intra-carpal injection in the past 6 months, evidence of cervical radiculopathy in EMG, recent use of analgesic or corticosteroids, hypersensitivity to the drug or placebo, and inability to complete data gathering sheet. In addition, patients with neuropathies, collagen vascular diseases, rheumatoid arthritis, hyperthyroidism, diabetes, renal failure, and alcoholism were excluded.