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Original Article

Effects of Foot Dry Cupping in Diabetic Distal Polyneuropathy: A Pilot Controlled Clinical Trial

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Abstract

Background: Distal polyneuropathy is a common complication of diabetes mellitus with a considerable negative impact on the quality of life. This study aimed to evaluate the effect of dry cupping on distal polyneuropathy in diabetic patients.

Methods: This controlled clinical trial was performed on 34 patients with diabetic polyneuropathy (DPN) for eight weeks. The non-invasive dry, fixed cupping therapy was performed on the sole of the right foot in the patients three times a week for 10 minutes, and the left foot of the same patient was considered as a control. The severity of diabetic neuropathy was measured using the modified Toronto Clinical Neuropathy Score (mTCNS), and the symptom and sensory test scores were determined.

Results: Twenty patients (40 feet) completed the study. There was a significant difference between the control foot and the treated foot in terms of the mTCNS after four and eight weeks (*P* values = 0.004 and 0.001, respectively), in terms of the sensory test scores after four and eight weeks (*P* values = 0.007 and 0.005, respectively), and in terms of the symptom scores after eight weeks (*P* value = 0.002).

Conclusion: For the first time, this study demonstrated that cupping therapy might be effective as a complementary treatment in alleviating the symptoms of DPN, although understanding the underlying mechanism requires further investigation.

Keywords: Diabetes, Neuropathy, Dry cupping, Persian medicine

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Introduction

One of the prevalent complications of diabetes mellitus is neuropathy. The most common type of diabetic neuropathy is distal symmetric polyneuropathy, which is seen in one-third of diabetic patients (1). Diabetic polyneuropathy (DPN) presents with pain, tingling, or numbness (2). The pattern of involvement is 'stocking and glove', which indicates damage to the longest sensory axons; hence, the distal leg epidermal axons are involved before the more proximal limbs (3). DPN reduces the protective sensation and impairs the normal function of the leg muscles. Disabling neuropathic pain, gait instability, ulcers, recurrent infections in the lower limbs, and amputation have a negative effect on quality of life (4,5). Thus far, no effective treatment has been reported for DPN (5). Cupping is a widely accepted traditional therapy that has been used as a safe method with minimal side effects to reduce pain in different diseases (6). Dry cupping applies vacuum by heat or suction using a cup over soft tissue. Unlike wet cupping, dry cupping does not require incisions or penetrating the skin (7). Although the underlying mechanism of action of cupping therapy is still unknown, it has been demonstrated that dry cupping can promote blood microcirculation and oxygenation at the site, accelerate the repair, and improve the function of local tissue (8,9). Studies have shown

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that cupping therapy could decrease the severity of the symptoms of distal neuropathy of the median nerve in carpal tunnel syndrome (10,11). However, to this date, the effect of cupping on diabetic neuropathy has not been investigated. This study aimed to evaluate the effect of dry cupping on distal polyneuropathy in diabetic patients.

Materials and methods

Trial design

The current study was designed as a controlled clinical trial. This study was in compliance with the Declaration of Helsinki (1989 revision) (12) and was approved and monitored by the Ethics Committee of Kerman University of Medical Sciences (License number: IR.KMU.AH.REC.1397.2656). The trial was registered in the Iranian Registry of Clinical Trials with the following code: IRCT20131214015790N4 (https://en.irct.ir/trial/57055).

Participants

This study was performed on patients with DPN, who were referred to Besat Clinics, Kerman University of Medical Sciences, Kerman, Iran from August to December 2021. The inclusion criteria were as follows: patients aged 20 to 80 years with type 2 diabetes who complained of any of the following symptoms: foot pain, numbness, tingling, weakness, or ataxia. The Exclusion criteria were non-diabetic neuropathy (thyroid disease, cervical or lumbar radiculopathy, and alcoholism), any sores on the soles of the feet, and coagulation disorders. All patients signed the informed consent form.

Intervention

This study was conducted for eight weeks. The non-invasive dry, fixed cupping therapy was performed on the sole of the right foot in patients three times a week for 10 minutes, and the left foot of the same patient was considered as a control. To carry out cupping therapy, a special plastic cup (6 or 7 cm in diameter) was placed in the area between the toes and the sole and connected to the suction pump through the connection hose, and suction was performed with a negative pressure of 300 mm Hg (13).

Outcome measurement

The severity of diabetic neuropathy was measured using the modified Toronto Clinical Neuropathy Score (mTCNS). The mTCNS is a reliable and valid clinical tool to evaluate the symptoms of DPN in clinical trials (14); the questionnaire consists of 11 items. Six items are related to the symptom scores including foot pain, numbness, tingling, weakness, ataxia, and upper limb symptoms, and five items are related to the sensory test scores including pinprick, temperature, light touch, position sense, and vibration. Each item is graded from 0 to 3 and the total score is calculated from their sum. In the case of symptom scores, 0 indicates absence, 1 indicates presence but no interference with the sense of well-being or the activities of daily life, 2 indicates presence and interference with the sense of well-being but not with the activities of daily life, and 3 indicates presence and interference with both the sense of well-being and the activities of daily life. In the case of sensory test scores, 0 indicates normal, 1 indicates reduced at the toes only, 2 indicates reduced to a level above the toes but only up to the ankles, and 3 indicates reduced to a level above the ankles and/or absent at the toes (14). This score was measured by a trained physician for each patient at the beginning of the study and the fourth and eighth weeks.

Sample size

The sample size was determined by G*Power software. Considering type-I error = 5% and type-II error = 20%, and a medium (0.25) effect size, the minimum sample of 10 subjects in each group was calculated to be sufficient. Taking into account the 20% probability of sample loss, the sample size was increased to 12.

Safety assessment

Patients were asked to report any cupping complications or exacerbation of neuropathic symptoms.

Statistical methods

We used repeated measures one-way ANOVA, Bonferroni post-hoc test, and paired t-test for analyzing parametric data. *Friedman* and Wilcoxon tests were employed to compare nonparametric data. Statistical analysis was performed using SPSS software version 21. Statistical significance was set at $P < 0.05$.

Results

In this study, 58 patients were initially screened for eligibility. Subsequently, 34 patients with DPN were enrolled in the study. During the study, five individuals refused to continue the study due to dissatisfaction with the cupping procedure. Nine participants were also withdrawn from the study due to irregular visits. Finally, 20 patients completed the study. A detailed description of the patient's enrolment, allocation, and analysis is illustrated in Figure 1.

The demographic characteristics of the participants in the study are shown in Table 1. The studied variables were similar in the two groups at the baseline. Patients' medications included insulin, glibenclamide, metformin, and pioglitazone for DM and gabapentin for neuropathy.

As shown in Table 2 and Figure 2, the control group showed no significant changes in the mTCNS, sensory test scores, and symptom scores during the study. In the cupping therapy group, the mTCNS and sensory test scores improved in the fourth week, and the symptom

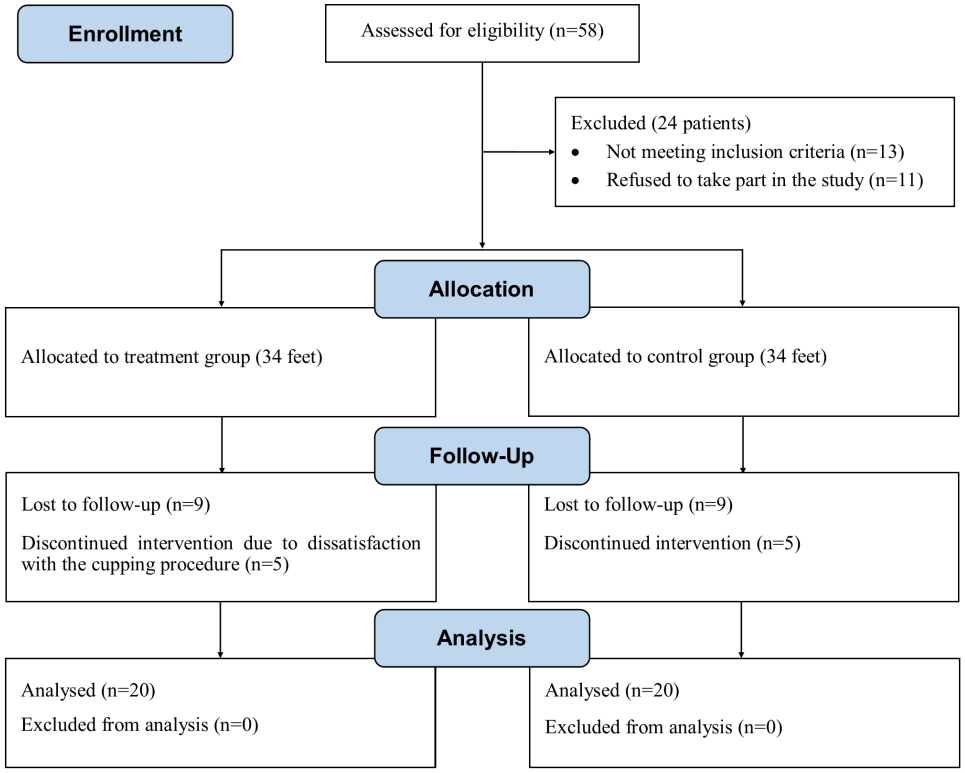

Figure 1. Flow diagram of the patients' enrolment, allocation, and analysis

Table 1. Demographic data of the patients participating in the study.

Variable	Value
Sex (male/female) [a]	11/9
Age (year) [b]	66.05 ± 1.85
BMI (kg/m^2) [b]	26.65 ± 1.01
HbA_1C [b]	7.50 ± 0.17
Duration of DM (year) [b]	15.95 ± 1.63

[a] Data are expressed as numbers.
[b] Data are expressed as mean ± SD.
BMI: body mass index; DM: diabetes mellitus.

scores improved in the eighth week. Moreover, there was a significant difference between the control foot and the treated foot in terms of the mTCNS and the sensory test scores in weeks four and eight, and in terms of the symptom scores in the eighth week. This indicates that the effect of cupping therapy on sensory tests is observed earlier than the symptoms of DPN. No side effects were reported during cupping therapy on the soles of patients' feet.

Discussion

In this controlled clinical trial, the efficacy of cupping therapy in DPN was investigated. The results of the present study showed that dry cupping therapy was effective in reducing the symptom and sensory test scores in the treated foot in comparison with the control foot.

Only a few studies have reported the efficacy of cupping on neuropathy. In a study by Michalsen et al, performed on 52 patients, it was found that a single wet cupping application could significantly reduce the severity of carpal tunnel syndrome symptoms compared to the control group (10). In another randomized clinical trial, Mohammadi et al showed that the incorporation of ten sessions of cupping therapy in a routine physical therapy program could improve the severity of distal neuropathy of the median nerve compared with physiotherapy alone (11).

The current study is the first to evaluate the effect of dry cupping therapy on diabetic neuropathy. Patients with neuropathy experience a combination of microvascular and neurological complications in their feet, which result in decreased blood flow and impaired sensation in the legs. Microcirculatory dysfunction leads to peripheral nerve dysfunction, and impaired peripheral nerve blood flow is considered a possible additional pathological mechanism of diabetic neuropathy (1). It was demonstrated that cupping therapy can lead to soft tissue repair and pain relief by improving local blood and lymphatic flow (13). Depending on the level of negative pressure applied and its duration, vascular perfusion in the vacuum area can increase by up to five times (9). Wang et al demonstrated that 300 mm Hg of negative pressure applied for a duration of 5 or 10 minutes caused a significant increase in the peak skin blood flow (13). In the current study, suction with a pressure of -300 mm Hg for 10 minutes was used to evaluate the therapeutic response.

There are several theories about the mechanism of

Table 2. Comparison of mean outcome measures between the two groups before the treatment and at weeks 4 and 8.

Variable		Time			*P* value[a]	
		Baseline	Week 4	Week 8	Week 4	Week 8
mTCNS	Control group	17.30 ± 1.25	17.25 ± 1.25	17.40 ± 1.28	0.99	1
	Treatment group	17.25 ± 1.24	14.70 ± 1.21	13.40 ± 1.19	0.007[c]	0.002[c]
	P value[b]	0.72	0.004[c]	0.001[d]		
Sensory test scores	Control group	9.90 ± 1.09	9.90 ± 1.09	9.95 ± 1.08	1	0.31
	Treatment group	9.85 ± 1.07	7.85 ± 0.88	7.25 ± 0.93	0.007[c]	0.003[c]
	P value[b]	0.70	0.007[c]	0.005[c]		
Symptom scores	Control group	7.40 ± 0.63	7.35 ± 0.62	7.45 ± 0.65	0.99	1
	Treatment group	7.40 ± 0.63	6.85 ± 0.67	6.15 ± 0.55	0.18	0.004[c]
	P value[b]	1	0.96	0.002[c]		

mTCNS: Modified Toronto Clinical Neuropathy Score.
Data are presented as mean ± SEM.
[a] Within-group comparison (compared to the baseline); [b] Between-group comparison; [c] *P* value < 0.01, [d] *P* value < 0.001.

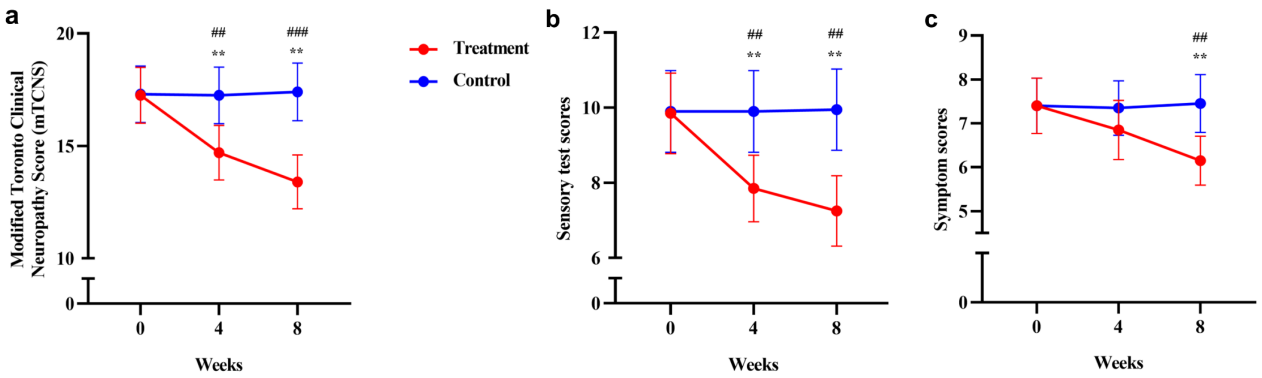

Figure 2. Changes in the outcome measures in the dry cupping group compared to the control group from baseline (week 0) to weeks 4 and 8. (a) mTCNS. (b) Sensory test scores. (c) Symptom scores. $^{**}P$ value < 0.01 compared to the time 0. $^{\#\#}P$ value < 0.01 and $^{\#\#\#}P$ value < 0.001 compared to the control group in similar time

action of cupping therapy, but none of them has been thoroughly studied. One of the most relevant of these hypotheses is the "release of nitric oxide (NO) theory". Nitric oxide is a signaling gas molecule known as a mediator of vasodilatation. Cupping therapy increases local blood flow and lowers vascular resistance by aggregating the release of NO from endothelial cells (15). In diabetic rats, decreased vasodilation of epineurial arterioles has been determined. Furthermore, it has been reported that endoneurial blood flow can be enhanced by vasodilators (1).

Neuropathic pain occurs in more than 50% of patients with DPN and is often severe, leading to impaired quality of life. Tricyclic agents, duloxetine, gabapentin, or pregabalin are the first-line treatments, followed by opioids and topical drugs, which have limitations due to their side effects, the need for frequent administration, and the probability of addiction. Several studies have shown the antinociceptive effects of cupping therapy (16,17). The "pain gate theory" is the most prominent theory presented about the possible mechanism of the pain-alleviating effect of cupping therapy. Accordingly, cupping increases nerve impulses by stimulating pain receptors, which ultimately causes pain gates to close and pain to diminish (18).

In a non-randomized clinical trial, Ludwig-Slomczynska et al demonstrated that negative pressure wound therapy could be effective in the management of diabetic foot ulcerations through epigenetic changes (methylated genes located on chromosomes 6 and 20), resulting in the inhibition of complement system activation (19).

Lee et al indicated that plasma cupping (PC), which is the advanced form of traditional cupping, is useful for treating inflammatory muscle pain by reducing tumor necrosis factor-alpha (TNF-α) -mediated interleukin-1β (IL-1β) and interleukin 6 (IL-6) expression. Plasma cupping stimulates angiogenesis and accelerates wound healing (20). Proinflammatory cytokines TNF-α, IL-1β, and IL-6 aggravate the process of peripheral neuropathy and neuropathic pain in diabetic patients (21).

Finally, this study indicated that cupping therapy could be effective in alleviating the symptoms of DPN, although understanding the underlying mechanism requires further investigation.

One of the most important limitations of the present study was the lack of patient classification based on the

severity of neuropathy. Since the severity of neuropathy, duration and pressure of the vacuum, and the size of the used cup can affect the response to treatment, extensive studies are needed to investigate the impact of these variables on the efficacy of cupping therapy and its possible mechanism of action in diabetic neuropathy. There is no guideline for determining the amount and duration of pressure applied in cupping therapy in different areas of the body for different diseases. Lack of follow-ups after discontinuation of treatment is another limitation of this study.

Conclusion

For the first time, this study showed that cupping therapy, as a complementary treatment, may be effective in reducing the symptoms of diabetic neuropathy. However, to properly interpret the results, it is necessary to conduct clinical trials with larger sample sizes and longer durations after overcoming the limitations of the present study.

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Authors' Contribution

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Competing Interests

The authors declare no conflict of interest.

Data Availability Statement

The data of this study are available on request from the corresponding author upon reasonable request.

Ethical Approval

The current study was in compliance with the Declaration of Helsinki (1989 revision). This study protocol was reviewed and approved by the Ethics Committee of Kerman University of Medical Sciences (License number: IR.KMU.AH.REC.1397.2656). The trial was registered in the Iranian Registry of Clinical Trials with the following code: IRCT20131214015790N4. The informed consent was obtained from all individuals included in this study.

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