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Comparison of Leech Therapy with Medical Treatment on Clinical Symptoms and Nerve-Muscle Changes in Patients with Moderate Carpal Tunnel Syndrome: A Protocol Study

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Abstract

Background: This study aimed to compare the severity of clinical symptoms and nerve-muscle alterations in patients with moderate carpal tunnel syndrome (CTS) between leech therapy and medical treatment.

Methods: This study is a randomized clinical trial protocol. The research population consists of patients with moderate CTS, as determined by clinical symptoms and electrodiagnostic tests (EMG-NCV). A total of 60 patients will be selected through convenience sampling and randomly assigned to two groups: 1) control group (medical treatment) and 2) intervention group (medical treatment and leech therapy). Data were collected using a personal information questionnaire, a visual analog scale (VAS) for pain assessment, and the Boston Carpal Tunnel Questionnaire. The questionnaires were completed by patients at four time points: baseline, day 15, day 30, and day 60. The severity of clinical symptoms and NCV-EMG test results at baseline were compared with those at day 60. Data were analyzed using SPSS version 16 software, with statistical tests including mean, standard deviation, frequency, repeated measures ANOVA, Bonferroni, and Mann-Whitney U tests.

The Clinical Trials.gov identifier for the trial is IRCT20180909040977N1. The trial was registered on January 8, 2019.

Discussion: The findings of this clinical trial may demonstrate the effectiveness of leech therapy as a complementary treatment for CTS and its potential to prevent complications associated with conventional medical treatment.

Keywords: Leeching, Carpal tunnel syndrome, Nerve, Muscles, Pain

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Introduction

Carpal Tunnel Syndrome (CTS) is the most common compressive neuropathy, resulting from median nerve compression within the carpal tunnel (1). It affects approximately 6–12% of adults (2), with a higher prevalence in women and individuals aged 65–74 (3). Occupations involving repetitive hand use, poor posture, and work-related musculoskeletal disorders (WMSDs) increase the risk of CTS (4, 5).

The primary clinical symptoms of CTS include pain, numbness, and tingling in the thumb, index, and middle fingers, often disrupting sleep and hand function (6). These symptoms can lead to psychological distress, including anxiety and depression (7). Diagnosis is typically based on clinical signs (e.g., Tinel's sign, Phalen's test) and nerve conduction velocity (NCV) studies (8, 9). Sonography is also used for imaging peripheral nerves and the carpal tunnel (10).

CTS is classified into mild, moderate, and severe grades based on electrodiagnostic findings (11). Conservative management is recommended for mild to moderate CTS, while surgery is preferred for severe cases (12). However, some studies suggest surgery for moderate to severe CTS (13). Conservative treatments include splinting, manual therapy, corticosteroid injections, and orthotics (14, 15). Approximately 61% of patients avoid surgery due to complications and costs, opting for conservative treatments instead (16). Nonetheless, non-surgical treatments may not prevent recurrence (17), and surgery can lead to adverse effects such as pain, tenderness, and scarring (18).

Leech therapy has emerged as a potential treatment for CTS. Medical leeches were approved by the FDA in 2004 (19).

In a study, the effectiveness of leech therapy on diabetic neuropathy was evaluated in a clinical trial, which

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showed a significant reduction in anesthesia ($P=0.0001$) and paresthesia ($P=0.01$) in patients undergoing leech therapy compared to those receiving gabapentin (20). Additionally, leech therapy can significantly aid in the treatment of dermatophytosis without causing side effects and exhibiting high effectiveness (21).

A systematic review study conducted up to April 2023 yielded successful results of leech therapy in patients with cardiovascular, inflammatory, hormonal, and metabolic diseases (22).

Leech therapy is indicated for skeletal and joint diseases (23).

Leech saliva contains anti-inflammatory compounds (e.g., Eglin, bdellin) and enzymes (e.g., triptase) that promote wound healing and modulate inflammatory responses (19, 23). Additionally, nitric oxide synthase in leech saliva aids nerve repair (24).

This study aimed to compare leech therapy with medical treatment for CTS, focusing on clinical symptom severity and nerve-muscle conduction changes. By exploring the synergistic effects of leech-derived enzymes, this study may contribute to the development of novel therapeutic products.

Methods

Ethical Statements

The study protocol was approved by the Research and Technology Office and the Ethics Committee of Golestan University of Medical Sciences. The study was registered on the Iranian Clinical Trials website (IRCT20180909040977N1).

Participants received information about the goals and methods of the study and were assured that their privacy would be protected. Since participation is entirely voluntary, there are no consequences if a participant decides to stop at any moment.

Study Design

This is a randomized controlled trial protocol. Patients with moderate CTS will be recruited and randomly assigned to either the control group (medical treatment) or the intervention group (medical treatment and leech therapy) using block randomization with blocks of four.

Eligibility Criteria

Patients will be examined by a specialized neurosurgeon, undergo clinical examinations, and have their NCV and EMG strips reviewed. Written consent will be obtained from those who meet the study criteria. If they are unwilling to cooperate or meet any of the study withdrawal criteria, they will be excluded and receive routine treatment (Table 1).

Control Group

Patients in the Control group will receive medical treatment (Celecoxib 100 mg twice daily, Gabapentin 100 mg twice daily, Vitamin B1 300 mg once daily, and a short cock-up splint during sleep)

Intervention Group Protocol

Patients in the intervention group will receive medical treatment (Celecoxib 100 mg twice daily, Gabapentin 100 mg twice daily, Vitamin B1 300 mg once daily, and a short cock-up splint during sleep) and leech therapy. Leeches will be applied along the median nerve pathway on day 1 and, if necessary, on day 15. Side effects will be monitored using ESR and CRP tests.

In a similar study titled "The Effectiveness of Leech Therapy in the Severity of Diabetic Neuropathy: A Randomized Controlled Trial," the researcher placed 3 to 5 average natural leeches on the back of each foot in three sessions with a 15-day interval to investigate the effectiveness of leech therapy. In the control group, each patient consumed one 300 mg gabapentin capsule for 30

Table 1. Study inclusion and exclusion criteria

Inclusion criteria:
• Age between 30-60 years. • The presence of clinical symptoms and positive tests such as Tinel, Phalen and carpal compression. • Positive paraclinical findings (NCV-EMG) detected by the electrodiagnosis device, and their grades are in the middle level as diagnosed by a neurosurgical specialist and neurologist (25). • Satisfaction with using one of the two methods. • Lack of diseases such as: rheumatism, rheumatoid arthritis, other upper limb disorders, coagulation problems, diabetes, hypothyroidism, gout, lupus erythematosus, acromegaly, chronic kidney disease, and diseases that mimic CTS symptoms such as: neuropathy, cervical radiculopathy, thoracic outlet syndrome, and Double-crush syndrome. • No recent pregnancy and mental retardation and anemia. • No repeated wrist fracture or trauma and wrist surgery. • No corticosteroid injection into the wrist joint in the past 3 months. • No immune system disorders and severe allergic reactions • No use of neuropathy drugs and the consumption of non-steroidal anti-inflammatory drugs in the past two weeks (26,27). • No history of stroke syndrome
Exclusion criteria:
• Becoming pregnant during treatment. • Developing severe allergic reactions during treatment. • Fear of leech application after observing leech. • Severe visual problems in filling out the visual pain questionnaire.

nights before sleep(20).

Clinical Management

The device used for EMG and NCV tests to determine diagnosis, disease grade, and compare symptom severity is the Nihon Kohden model, which will be used at a skin temperature above 31-32 degrees Celsius and following the AAEM standard (28). These tests will be used in two stages, before and after CTS treatment (60 days).

Blinding

In this study, the conditions for providing services make it impossible to blind the participants. In this study, the neurologist and the interviewer conducting the telephone interview will be unaware of the study groups.

Sample Size

Based on Michalsen et al's study (29,30), the sample size was calculated with an error rate of 5% and a power of 80%. A 20 percent sample loss was taken into account, meaning that each group had 25 patients, for a total of 30 patients per group.

$$n = \frac{\left(s_1^2 + s_2^2\right)\left(z_{1-\frac{\alpha}{2}} + z_{1-\beta}\right)^2}{\left(\bar{x}_1 - \bar{x}_2\right)^2}$$

Data Collection Tools

1. Visual Analog Scale (VAS): Indicates the degree of pain.
2. The Boston Carpal Tunnel Questionnaire: measures the degree of symptoms and the level of function.
3. Personal Information Questionnaire: Collects demographic and clinical data.

Questionnaires will be administered at baseline, day 15, day 30, and day 60. NCV-EMG tests will be performed at baseline and day 60. (Fig.1 Trial flowchart)

The following criteria were used: mild pain was defined as 1–3, moderate pain as 4–7, and severe pain as 8–10. • A score of at least two points is considered clinically significant (31).

Boston Questionnaire

Scores for functional status and symptom severity range from 1 (mild) to 5 (severe). The patients were categorized

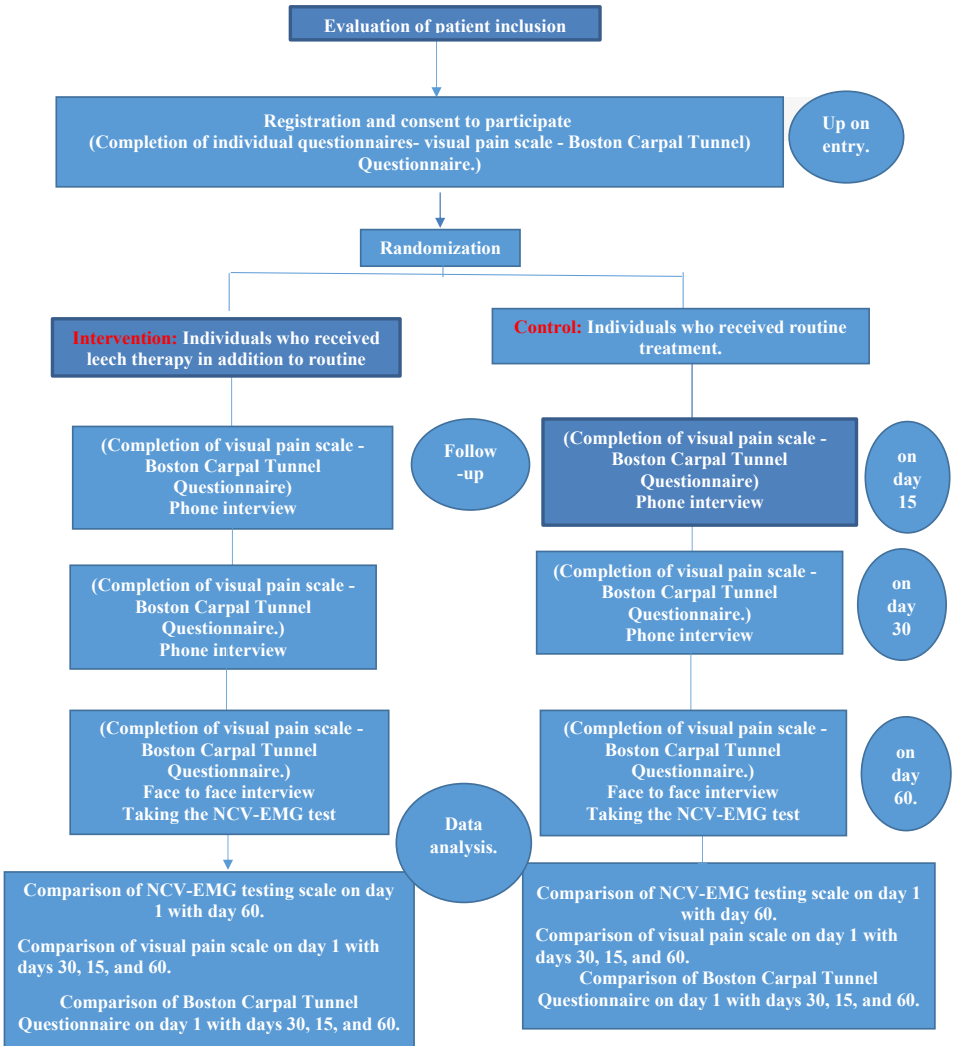

Figure 1. Trial flowchart

into five groups according to their scores: mild (1.1-2), moderate (2.1-3), severe (3.1-4), very severe (4.1-5), and healthy (0-1).

A decrease in Scores Indicates Improvement

The Boston Questionnaire has also been validated in Iran several times, with reliability, sensitivity to clinical changes, and internal consistency (symptom severity questionnaire) being 0.853, 2.35, and 0.94, respectively, and (functional status questionnaire) being 0.86, 1.7, and 0.96, respectively (32).

Statistical Analysis

SPSS 16 will be used to analyze the data. Inferential tests (repeated measures ANOVA, Bonferroni, and Mann-Whitney U) and descriptive statistics (mean, standard deviation, and frequency) will be employed. A *P* value of less than 0.05 will be deemed significant.

Discussion

A randomized controlled trial is described in this study protocol to assess the effectiveness of leech therapy for moderate CTS. This study attempts to offer important insights into the possible advantages of leech therapy as a supplemental treatment for CTS, notwithstanding limitations like the inability to blind participants and assessors.

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Authors' Contribution

Conceptualization: Ali Akbar Aghaeinezhad, Mehdi Zarvandi.
Investigation: Ali Akbar Aghaeinezhad, Mehdi Zarvandi.
Methodology: Mehdi Zarvandi, Ali Akbar Aghaeinezhad.
Project administration: Ali Akbar Aghaeinezhad.
Supervision: Ali Akbar Aghaeinezhad.
Writing–original draft: Ali Akbar Aghaeinezhad, Mehdi Zarvandi.

Competing Interests

The authors declare that they do not have any conflict of interest.

Ethical Approval

The researcher obtained the code of ethics number IR. GOUMS. Rec. 1397.098 date:2018/08/29 from the Ethics Committee of Golestan University of Medical Sciences.

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