Prospective, Randomized, Double-Blinded, Sham-Controlled Pilot Study of Intraneural Facilitation as a Treatment for Carpal Tunnel Syndrome

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Abstract

Objective: To perform a pilot study to assess the efficacy of intraneural facilitation, a novel manual technique, in the treatment of carpal tunnel syndrome (CTS).
Design: Patients with clinical and electrodiagnostic evidence of CTS were randomized into intraneural facilitation or sham groups.
Setting: Electrodiagnostic laboratory in a university medical center.
Participants: Patients referred to our electrodiagnostic laboratory were screened based on nerve conduction studies that were diagnostic for distal median neuropathy at the wrist or CTS. A total of 14 participants were enrolled; 4 participants withdrew prior to randomization, with the remaining 10 participants (N=10) divided equally between treatment and control groups. There was a 9:1 female-to-male sex ratio and average duration of symptoms was 28.5 months.
Interventions: Treatment was performed twice weekly for 3 weeks.
Main Outcome Measures: Primary outcomes were the Boston Carpel Tunnel Questionnaire (BCTQ) and Boston Functional Status Scale at enrollment and at 1 week and 3 months after completion of intervention. A secondary outcome was ultrasonography (US) of the median nerve performed at baseline and 1 week after intervention.

Keywords: Carpal tunnel syndrome; Physical therapy modalities; Rehabilitation; Therapeutics

List of abbreviations: BCTQ, Boston Carpel Tunnel Questionnaire; CSA, cross-sectional area; CTS, carpal tunnel syndrome; US, ultrasonography; WFR, wrist to forearm ratio.

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Intraneural facilitation is a novel form of manual physical therapy based on the principle of restoring vascular flow at the arteriae or vasa nervorum in peripheral nerve. Intraneural facilitation has been suggested to improve clinical function in patients with diabetic-associated polyneuropathy, a model for ischemic neuropathy. Carpal tunnel syndrome (CTS) is a common entrapment neuropathy where regional compression in the carpal tunnel leads to edema, increased endoneural pressure, and nerve ischemia. During this feasibility/pilot study, we sought to assess the efficacy of intraneural facilitation compared to sham control on improving symptom severity, functional status, and ultrasonography (US) measurements of the median nerve in patients with CTS.

Methods

This was an institutional review board–approved prospective, randomized, and double-blinded treatment study with informed consent obtained from participants. Patients referred to our electrodiagnostic laboratory were screened based on nerve conduction studies that were diagnostic for distal median neuropathy at the wrist or CTS. All sensory and motor nerve conduction studies were performed using a Viking Quest EMG machine, by the same examiner. Sensory and motor nerve conduction studies of the median nerve were done using standard techniques. A sensory nerve conduction study was performed by stimulating the median nerve at the palm and proximal to the wrist while recording the response over the second digit. The minimum cutoff for normal median sensory conduction velocity across the carpal tunnel was 50 m/s. In persons without CTS, the sensory nerve action potential of the median nerve is at least 20 μV. Motor nerve conduction study of the median nerve was performed by stimulating the median nerve at the wrist and recording over the median eminence using disposable silver surface strip electrodes. The maximum normal limit of terminal motor latency for the median nerve is 4.2 ms. Hand temperature was maintained at 32-34°C by warming the limbs prior to the study.

Inclusion criteria was electrodiagnostic and clinical evidence of CTS in those between the ages of 18 and 75 years. Four participants were excluded with the following exclusion criteria: prior carpal tunnel release, any condition that would prevent nerve conduction studies from accurately diagnosing CTS, workers’ compensation cases, pregnancy, physical or occupational therapy for CTS within 6 months, steroid injections into the carpal tunnel within 3 months, clinically silent distal median neuropathy, clinical symptoms that warranted more aggressive therapy, any medical condition that may affect participation or outcomes, and/or inability to fully participate with the research study because of travel limitations.

Participants were administered the Boston Carpal Tunnel Questionnaire (BCTQ) and Boston Functional Status Scale at enrollment, 1 week after treatment, and 3 months after treatment. US of the wrist and forearm was performed at enrollment and 1 week after treatment. When bilateral CTS was present the most symptomatic or dominant side was studied.

US training to confirm interrater agreement among 2 sonographers (S.H., B.T.) was completed before the study. USs were performed on LOGIQ e with a 12L-RS 4.2-13.0 MHz linear array transducer. The median nerve was measured in the axial (transverse) plane by continuous tracings just inside the hyperechoic epineural rim of the nerve. The median cross-sectional area (CSA) (mm²) at the distal wrist crease and 12 cm proximally in the forearm was used to calculate the wrist to forearm ratio (WFR). A CSA ≥10 mm² and WFR ≥1.4 was considered positive for CTS. Our technique and yield are derived from 2 US references listed in our article where the sensitivity was increased to nearly 100% by using both criteria instead of just the CSA. The same criteria applied to the intraneural facilitation treatment and control groups. As such, there is no minimal detectable difference other than the cutoff threshold of CSA ≥10 mm² and WFR ≥1.4.

Each patient was randomly assigned to treatment with intraneural facilitation or sham therapy with equal frequency (twice weekly) and duration of visits (45 minutes) for 3 weeks. All intraneural facilitation and sham interventions were performed by the same certified physical therapist (M.B.). Physicians responsible for clinical and US examinations were blinded to the type of treatment delivered. The sham treatments were designed to mimic actual intraneural facilitation but avoid stretching or altering microvascular changes of.
the median nerve (e-online description). No participants missed ≥2 treatment or sham sessions nor withdrew after randomization and therefore were not eliminated from the study.

**Intervention**

We hypothesize that intraneural facilitation can reverse the regional increased pressure and ischemia in CTS by the use of 3 manual holds designed to stretch muscles, mobilize joints, traction skin and connective tissue, and bias blood flow from surface arteriae or vasa nervorum back into intraneural vessels of the median nerve.1,9

**Intraneural facilitation technique**

The first hold gently stretches vessels to enlarge the opening at the junction of the artery and bridging vessel.1 The constriction of transperineural vessels from endoneural edema creates a valve-type mechanism that further decreases endoneural capillary circulation.9 A second hold is intended to drive transperineural blood flow past this stricture into the endoneural capillaries. The third hold involves bolsters and pressure points away from the secondary hold to promote upstream circulatory flow and theoretically create a vacuum to pull microvascular circulation into the now patent intraneural vascular beds.1

**Sham description**

The sham method is a set of passive and active exercises involving the affected shoulder, wrist, fingers, and thumb. Eleven exercises were administered with 3 stretches and 8 active exercises. The total active repetitions for 8 exercises were 640, total stretching time was 10 minutes, and time for total sham treatment 45 minutes.

Intraneural facilitation is different than the sham group in several ways. First, with intraneural facilitation the holds are static and may last several minutes depending on observed changes compared with active and passive exercises in the sham group. Furthermore, intraneural facilitation combines several holds including a “facilitation” hold that conceptually biases circulation to the epineural vessels of the median nerve and a “secondary” or treatment hold that recruits the presurized flow into endoneural capillaries of a median nerve innervated structure, that is, flexor carpi radialis. During intraneural facilitation session, the practitioner monitored extremity color changes for decreased

![Fig 1](Consolidated Standards of Reporting Trials flow diagram. Abbreviation: INF, Intraneural facilitation.)
redness or pallor and decreased stiffness or flaccidity in the finger(s). Further description of the 3 holds and sham techniques are available in the supplemental material section on the e-online description.

**Outcome measures**

The primary outcomes were the validated BCTQ and Boston Functional Status Scale, used as patient self-reported measures in CTS.3,10 The BCTQ consists of 11 individual pain items, while the Boston Functional Status Scale consists of 8 functional items (for both, the lower the score, the lower the pain and functional variables). The secondary outcome was US CSA of the median nerve at the wrist and the WFR.

**Statistical analysis**

The effect of the type of intervention on changes from baseline of the BCTQ and Boston Functional Status Scale between-treatment group and control group was examined by the linear mixed model. The changes from pretreatment to post treatment was assessed by Wilcoxon signed-rank test in both groups. Also, because of small sample size, Cohen’s $d$, which is an appropriate measure of difference, was used. Cohen’s $d$ classifies effect sizes as small ($d=0.2$), medium ($d=0.5$), and large ($d\geq0.8$).11

All analyses were performed at an $\alpha$ level of 0.05. Data were analyzed using R software, specifically the nlme package.d

**Results**

Fourteen participants were enrolled between April and December 2018. Each eligible participant was randomly assigned to the treatment or control group by using the random number generator function in a commercially available software program (Excel).6 Four participants withdrew from the study because of limitations with travel, not meeting inclusion criteria, or meeting exclusion criteria, with the remaining 10 participants randomized into treatment and control groups (fig 1). US data for 1 control participant was missing post intervention and was excluded from the analysis. Nine were female, with average age of 51.3 years and average duration of symptoms 28.5 months. Nine were right-handed, and of these 5 had more severe symptoms on the dominant side. Four had bilateral symptoms, and all had more severe symptoms on the nondominant side. Table 1 compares BCTQ and Boston Functional Status Scale scores and US results at baseline and at 1 week and 3 months after intervention. The average of total scores of BCTQ and Boston Functional Status Scale were higher in treatment than control group at baseline.

Linear mixed model showed the total percentage change in BCTQ and Boston Functional Status Scale scores at baseline and at 1 week and 3 months after intervention (fig 2). However, there was no difference between control and intraneural facilitation group. Because the sample size was too small, Cohen’s $d$ was used as measure of difference for the between the groups. Cohen’s $d$ showed large effects for

| Table 1 | Descriptive scores at baseline and after intervention |
|---------|-----------------------------------------------------|
| Variable | Intraneur. Facilitation | Control |
|         | Baseline | 1 wk | 3 mo | Baseline | 1 wk | 3 mo |
| BCTQ | 41.2±5.3 | 37.2±5.1 | 28.6±7.0 | 28.3±8.0 | .043 | NA |
| BFSS | 25.2±1.3 | 19.0±5.1 | 16.2±5.2 | 19.8±9.6 | .066 | NA |
| CSA (mm$^2$) | 14.2±4.8 | 12.4±3.9 | 12.4±3.9 | 12.3±3.4 | .180 | NA |
| WFR (mm) | 2.4±0.9 | 1.8±0.5 | 1.8±0.5 | 2.7±1.0 | .727 | NA |

**NOTE.** Values are presented as mean ± SD.

Abbreviations: BFSS, Boston Functional Status Scale; NA, not available.
the BCTQ questionnaires ($d = 1.933$), and WFR 1 week after completion of intervention.

Wilcoxon signed-rank was applied to all pairwise within differences and showed nonstatistically significant differences for all the groups except for the BCTQs after 3 months of intraneural facilitation therapy was completed ($P = .043$) compared with baseline (see table 1).

**Discussion**

This prospective, controlled, and double-blinded pilot study shows that for both intraneural facilitation and control group, there was an improvement for clinical symptoms in patients with CTS for up to 3 months. There was no difference between control and intraneural facilitation group, which might be because of a small sample size. However, Cohen’s $d$ showed large effects for the BCTQ and WFR for the between-group differences. Intraneural facilitation can possibly improve functional outcomes as early as 1 week and also up to 3 months after treatment. The demographics and duration of symptoms in our small cohort is in consistent with prior series. Despite randomization, participants in the treatment group had higher baseline BCTQ and Boston Functional Status Scale scores or higher levels of pain, more severe symptoms, and poorer functional status than the control group (see table 1). However, while the percentage reduction in BCTQ and Boston Functional Status Scale scores was greater between the treatment and control group, both had similar degrees of changes within their respective cohort (fig 2).

**Study limitations**

Our study limitations are primarily related to the small sample size and bias toward milder forms of CTS because participants with more severe symptoms, including those with clinical symptoms that warranted more aggressive therapy (steroid injections and CTS release surgery), were excluded. It is possible that the sham intervention created an unintentional physiological effect because of the proximity of structures to the median nerve that received exercises and stretches. Last, the brief period between treatment and outcomes (1 week) could underestimate treatment effect and suggests that the enhanced physiological microvascular changes, symptom, and US improvement after intraneural facilitation may take more than 1 week to occur.

**Conclusions**

In summary, we conclude that this pilot study supports a larger prospective, randomized-controlled study to confirm the short- and long-term effects of intraneural facilitation as a viable treatment option for CTS.

**Suppliers**

a. Viking Quest EMG machine; Nicolet Biomedical.
b. Silver surface strip electrodes; Nikolet Viasys Healthcare.
c. LOGIQ e; General Electric Healthcare.
d. R software, nlme package. R Foundation for Statistical Computing.
e. Excel; Microsoft.

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