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Original Research

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

Nancy A. Baker, MD, MS [a], Diep Vuong, MD [b], Mark Bussell, DPT [c], Lida Gharibvand, PhD [c], Sarah Lee, MD [d], Bryan Tsao, MD [a]

[a] *Department of Neurology, Loma Linda University (LLU) School of Medicine, Loma Linda, California*
[b] *Department of Physical Medicine & Rehabilitation, Loma Linda University (LLU) School of Medicine, Loma Linda, California*
[c] *LLU School of Allied Health, Loma Linda, California*
[d] *Loma Linda University (LLU) School of Medicine, Loma Linda, California, United States*

KEYWORDS
Carpal tunnel syndrome;
Physical therapy modalities;
Rehabilitation;
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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.

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

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Results: Ten participants completed the trial, 5 each in the treatment and 5 each in the sham groups. The total percentage change in BCTQ and Boston Functional Status Scale scores decreased at baseline, 1 week, and 3 months after intervention. However, there was no difference between control and intraneural facilitation group. Within-group differences showed non-statistically significant differences for all the groups except for the BCTQ questionnaires after 3 months of intraneural facilitation therapy was completed (P=.043) compared with baseline. Between-group differences showed large effects for the BCTQ questionnaires (d=1.933) and wrist to forearm ratio (WFR) 1 week after completion of intervention.

Conclusions: This pilot study suggests that intraneural facilitation might improve symptoms and possibly function but did not improve median nerve cross-sectional area or WFR in CTS at follow-up evaluation 3 months after completion of intervention.

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.[1] Intraneural facilitation has been suggested to improve clinical function in patients with diabetic-associated polyneuropathy, a model for ischemic neuropathy.[1] 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.[2,3] 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,[a] by the same examiner. Sensory and motor nerve conduction studies of the median nerve were done using standard techniques.[4,5] 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.[4,6] 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.[b] The maximum normal limit of terminal motor latency for the median nerve is 4.2 ms. [4,6] 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 <2 years ago, 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.[c] The median nerve was measured in the axial (transverse) plane by continuous tracings just inside the hyperechoic epineural rim of the nerve.[7] The median cross-sectional area (CSA) (mm^2) 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 mm^2 and WFR≥1.4 was considered positive for CTS.[7,8] 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 mm^2 and WFR≥1.4.[7,8]

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 holds 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 pressurized 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

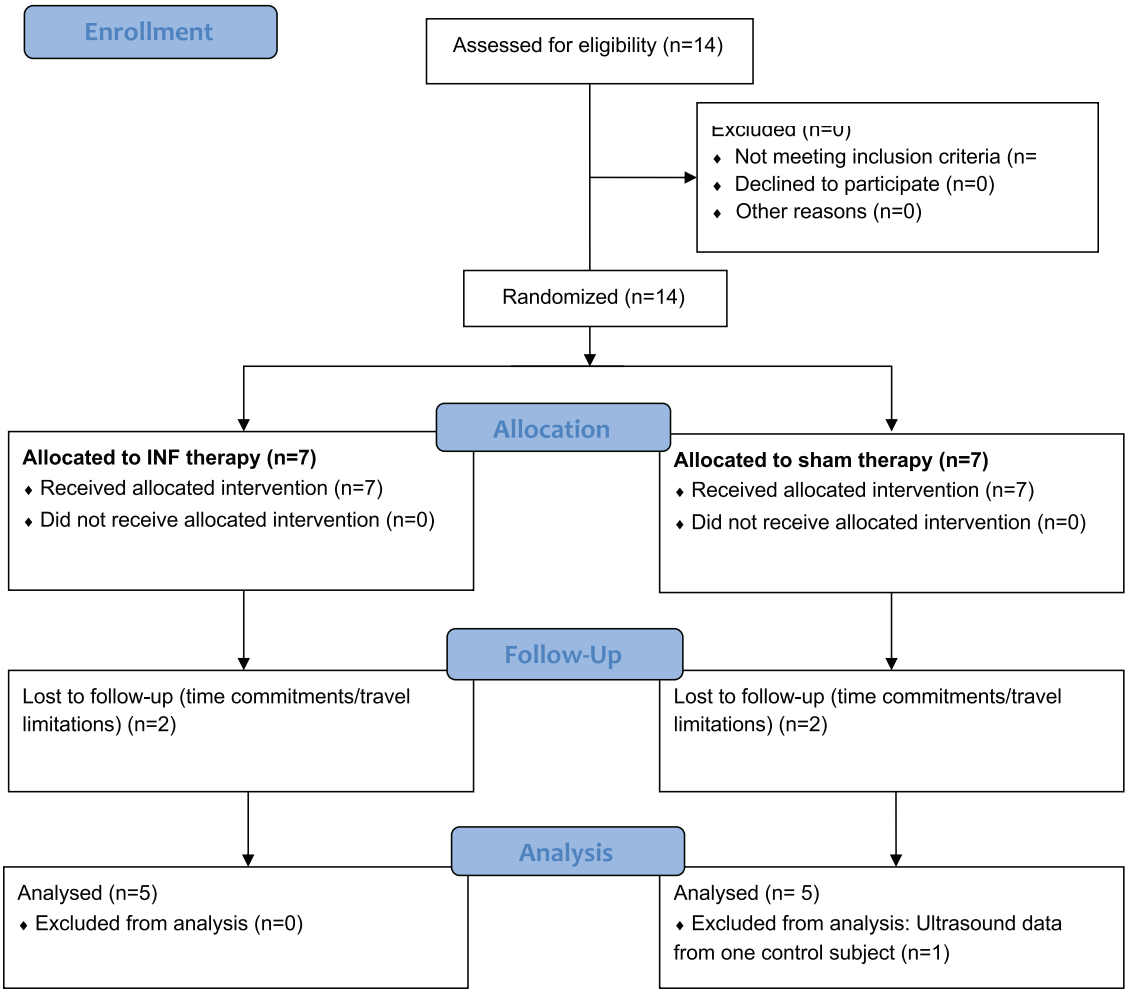

Fig 1 Consolidated Standards of Reporting Trials flow diagram. Abbreviation: INF, intraneural facilitation.

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 ($d \geq 0.8$).[11]

All analyses were performed at an α 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).[e] 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	Intraneural Facilitation					Control						
	Baseline	1 wk	*P* Value*	3 mo	*P* Value*	Baseline	1 wk	*P* Value*	3 mo	*P*	Value*	Cohen's *d*† Baseline	Cohen's *d*† 1 wk	Cohen's *d*† 3 mo
BCTQ‡	41.2±5.3	37.2±5.1	.144	28.6±7.0	.043	37.0±10.5	28.3±8.0	.066	27.2±13.4	.138		0.729	1.933	0.189
BFSS§	25.2±1.3	19.0±5.2	.080	16.2±5.2	.066	21.2±8.2	19.8±9.6	.655	16.2±6.9	.080		0.966	0.150	0
CSA (mm^2)	14.2±4.8	12.4±3.9	.180	NA	NA	16.0±3.4	12.3±1.5	.109	NA	NA		0.657	0.053	
WFR (mm)	2.4±0.9	1.8±0.5	.225	NA	NA	3.6±1.4	2.7±1.0	.465	NA	NA		1.486	1.643	

NOTE. Values are presented as mean ± SD.

Abbreviations: BFSS, Boston Functional Status Scale; NA, not available.

* *P* values were calculated for within-group differences.

† Cohen's *d* calculated for between-group differences $d = \frac{\bar{y}_1 - \bar{y}_2}{\sqrt{\frac{s_1^2}{n_1} + \frac{s_2^2}{n_2}}}$.

‡ Sum of the questions with total score between 11 and 55.$\sqrt{\frac{s_1^2}{n_1} + \frac{s_2^2}{n_2}}$.

§ Sum of the questions with total score between 8 and 40.

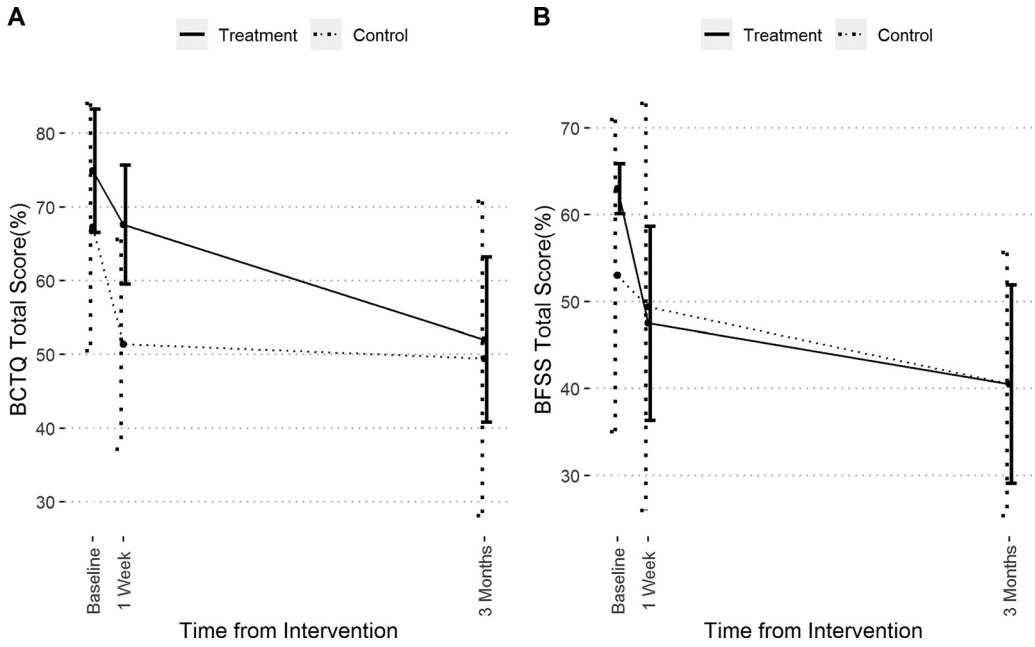

Fig 2 (A) BCTQ total score (%); (B) BFSS total score (%). Abbreviation: BFSS, Boston Functional Status Scale.

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.[3,12] 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.

Corresponding author

Nancy Baker, MD, MS, Loma Linda University (LLU) School of Medicine, Faculty Medical Offices, 11370 Anderson St, Suite B100, Loma Linda, CA 92354. *E-mail addresses:* NANBaker@llu.edu, nancy.baker0@icloud.com.

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