Randomized Double-Blinded Clinical Trial of 5% Dextrose versus Triamcinolone Injection for Carpal Tunnel Syndrome Patients

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Objective: Perineural injection with 5% dextrose (D5W) is a novel strategy in the treatment of carpal tunnel syndrome (CTS). In contrast, perineural injection with corticosteroid has been used for decades for treating CTS, but possible neurotoxicity has been a major concern. No studies investigating the comparative effects have been published so far. The authors performed a prospective, randomized, double-blinded, head-to-head comparative trial to compare these two approaches for patients having mild-to-moderate CTS.
Methods: Fifty-four participants with mild-to-moderate CTS were randomly divided into dextrose and steroid groups. The patients were administered 1 session of perineural injection with 5ml D5W (dextrose group) or 3ml triamcinolone acetonide mixed with 2ml normal saline (steroid group), under ultrasound guidance. A visual analog scale was assigned to assess the primary outcome. The secondary outcomes were assessed using the Boston Carpal Tunnel Syndrome Questionnaire, cross-sectional area of the median nerve, and electrophysiological studies. The assessment was performed prior to injection and 1, 3, 4, and 6 months postinjection.
Results: All patients (27 wrists per group) completed the study. Compared with the steroid group, the dextrose group exhibited a significant reduction in pain and disability through the 4th to the 6th month ($p < 0.01$).
Interpretation: Our study demonstrates that perineural injection of D5W is more beneficial than that of corticosteroid in patients with mild-to-moderate CTS at 4 to 6 months postinjection.

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Carpal tunnel syndrome (CTS), caused by increased pressure in the carpal tunnel with regard to gradual ischemia and damage of the median nerve (MN), is the most common peripheral neuropathy.[1,2] CTS can be treated with nonsurgical (analgesics, wrist splint, corticosteroid injection, physiotherapy, and extracorporeal shockwave) and surgical interventions. Despite the conservative approaches that are thought to be beneficial for most patients with mild-to-moderate CTS,[3] Cochrane only supports their short-term efficacy.[4] Although surgical intervention provides good outcomes, there are possible complications, such as surgical pain, weakness, and pillar pain.[5] Hence, surgical therapy is generally recommended for patients with severe CTS or those with mild-to-moderate CTS who respond unsatisfactorily to conventional approaches.[6] Therefore, there is a need for a promising method to treat CTS without surgical intervention.

Perineural injection of dextrose is a new treatment for peripheral entrapment neuropathy. It was first advocated by Dr John Lyftogt in 2005.[7] Moreover, 5% dextrose (D5W) has been commonly used in such cases, because D5W possesses osmolarity similar to that of normal saline, and no harmful effects have been reported from animal and human studies.[8–11] Additionally, the concentration of D5W is < 10%. At 10%, dextrose induces thickening of transverse carpal ligament in rabbits,

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with cumulative effect of continuous injection because hypertonic dextrose can stimulate inflammation.[5,12] In contrast, it is hypothesized that D5W could decrease neurogenic inflammation. Nevertheless, there are a few cases and small clinical trials investigating perineural injection of D5W for pain relief.[13–16] In 2017, Wu et al[16] revealed that there was at least a 6-month effectiveness of perineural injection of D5W, in a double-blinded randomized controlled trial for mild-to-moderate CTS.

In the past few decades, corticosteroid was the most used injectate for perineural injection under blind or ultrasound-guided technique in patients with CTS, with constructive effect.[17–23] However, Cochrane has demonstrated its short-term (1 month) effect compared to placebo control.[24] Moreover, physicians are concerned regarding the possible adverse effects of corticosteroid, including widespread axonal and myelin degeneration, skin thinning, tendon rupture, soft tissue atrophy, steroid-flare, crystal-induced synovitis, and hot flushes.[19,25] Although both perineural injection with D5W and corticosteroid injection were commonly used in clinical practice for treating CTS, there is no published study investigating their comparative effects so far.

In our clinical practice, we observed greater effectiveness and longer effect of perineural injection of D5W than that of corticosteroid. We hypothesized that perineural injection of D5W may be more effective than corticosteroid for CTS, with respect to pain and disability. Hence, we conducted a randomized, double-blinded, head-to-head comparative trial with perineural injection of D5W or corticosteroid for patients with mild-to-moderate CTS.

Patients and Methods

Study Design

From December 2016 to April 2018, 60 patients diagnosed with mild-to-moderate CTS were screened and 54 of them (total 60 wrists) were enrolled in this study. All the participants were recruited consecutively from the outpatient clinic of the Department of Physical Medicine and Rehabilitation at the Tri-Service General Hospital. Patients with suspected CTS were referred for this trial by primary care specialists. A single investigator obtained clinical history and performed physical examinations and electrophysiological studies. The subjects were divided into 2 groups (dextrose and steroid groups) that were distributed using block randomization (1:1 ratio) by random numbers generated using Excel (Microsoft, Redmond, WA), which was performed by an independent researcher. The patients were administered 1 session of perineural injection with 5ml D5W (Vitagen Injection 5%, Taiwan Biotech, Taoyuan city, Taiwan, Republic of China)[16] or 3ml (10 mg/ml) triamcinolone acetonide (Shincort, Yung Shin Pharmaceutical Industrial Co, Taichung city, Taiwan, Republic of China) mixed with 2ml normal saline,[21] under ultrasound guidance based on previous studies. If the patients were diagnosed with bilateral CTS, both wrists were assigned to the same group. All participants were instructed to refrain from other conservative therapies for treating the symptoms of CTS from 2 weeks prior to participation throughout the study period, except for acetaminophen (500mg, up to 4g/day) as a rescue agent. A nurse regularly checked whether any of these medications were administered.

Standard Protocol Approvals, Registrations, and Patient Consents

This 6-month follow-up study was permitted and reviewed by the institutional review board of our institute, with the written agreements and informed consent of all the enrolled participants. This trial was officially listed and accepted at www.ClinicalTrials.gov with the registration number NCT02990962.

Inclusion and Exclusion Criteria

Patients, aged 20 to 80 years, diagnosed with mild-to-moderate CTS, with symptoms lasting for a minimum of 3 months, and confirmed by electrophysiological study, were enrolled. The definition of clinical symptoms/signs, and inclusion and exclusion criteria are presented in Table 1.[26,27]

Electrophysiological Study and Grades of CTS

The methods used for diagnosing and grading CTS based on electrophysiological study are presented in Table 2.[28–30] Only patients with mild-to-moderate CTS were eligible for recruitment in this study.

Ultrasound-Guided Perineural Injection with D5W and Corticosteroid

A physician performed the ultrasound-guided injection (MyLab; 25 Gold; Esaote, Genoa, Italy) as reported previously.[27] The MN was identified at the proximal inlet of the carpal tunnel (scaphoid-pisiform plane). Under in-plane ulnar approach, 3ml injectate was injected to hydrodissect the MN from the flexor retinaculum, and the residual 2ml injectate was then injected to hydrodissect the inferior MN away from the flexor tendons. After injection, the operator scanned through the whole carpal tunnel to confirm the delivery of injectate throughout the tunnel.[27] Every patient was observed for half an hour after injection for any complications, such as nerve trauma, ecchymosis, or bleeding, before discharge.

Outcome Measurements

A second investigator, blinded to the randomized allocation and treatment methods, implemented all the outcome

TABLE 1. Inclusion and Exclusion Criteria of CTS

Inclusion criteria of symptoms and signs (subjects diagnosed as CTS if meeting criterion 1 with > 1 of criteria 2, 3, or 4)
1. Nocturnal paresthesia/dysthesia with or without pain over the subjected hand, which could be associated with posture or overuse of the wrist, or relieved with shaking motion of the hand
2. Numbness in the sensory distribution of MN
3. Weakness with atrophic change of the MN-innervated thenar muscles
4. Phalen test (+) and/or Tinel sign (+)
Exclusion criteria (excluded if meeting any 1)
1. History of polyneuropathy, brachial plexopathy, thoracic outlet syndrome, or wrist surgery
2. History of inflammatory arthritis, hypothyroidism, pregnancy, rheumatologic disorders, or having pacemaker
3. Current warfarin use, previous steroid injection for CTS, trauma or neoplasm at injection site, hypersensitivity to corticosteroid, or skin infection (injection site)

CTS = carpal tunnel syndrome; MN = median nerve.

measurements. Evaluations were performed at time points prior to injection and 1, 3, 4, and 6 months postinjection. The prespecified primary and secondary outcomes were the between-group difference in change between baseline and 6th month postinjection. For patients receiving bilateral injections, data from the dominant hand were used for measure outcomes. The investigator also evaluated every participant for symptoms or signs of complications. Deterioration in electrophysiological parameters and ultrasonographic findings were assessed at each follow-up time point.

Primary Outcome

Visual Analog Scale. The severity of digital pain or paresthesia or dysesthesia within 1 week before evaluation was recorded using a visual analog scale (VAS), with the score ranging from 10 (tremendous pain) to 0 (no pain).[27,31] A minimum decrease of 1.3 points in VAS or 25% reduction in pain is considered the minimal clinically important difference for pain intensity.[32,33]

Secondary Outcome

Boston Carpal Tunnel Syndrome Questionnaire. The Boston Carpal Tunnel Syndrome Questionnaire (BCTQ) includes 2 subscales (11 questions on symptom severity and 8 questions on functional status) and is the most commonly used measurement for CTS.[34] The scores ranged from 0 to 5 for each question, in which a score of 0 applied to mildest or no difficulty in activity; a score of 5 implied extreme severity and dysfunction. The minimal

TABLE 2. Electrophysiological Study and Grades of Carpal Tunnel Syndrome

Cutoff points or abnormal value
1. Distal sensory latency of MN > 3.6 milliseconds (stimulator 14cm distant from the active electrode at 2nd interphalangeal joints)
2. DML of the MN ≥ 4.3 milliseconds (stimulator 8cm distant from the active electrode at thenar muscle)
Grades
1. Minimal: abnormal segmental or comparative tests only
2. Mild: only abnormal digit/wrist SNCV + normal DML
3. Moderate: abnormal digit/wrist SNCV + abnormal DML
4. Severe: absent digit/wrist SNCV + abnormal DML
5. Extreme: both absent motor and sensory responses

DML = distal motor latency; MN = median nerve; SNCV = digit/wrist sensory nerve conduction velocity.

clinically important difference for BCTQ-severity and BCTQ-function is 8.8 and 4 points, respectively.[35]

Cross-Sectional Area of MN

The cross-sectional area (CSA) was measured using an electronic caliper at the same level as the injection site (scaphoid-pisiform level) at baseline and the 1st, 3rd, and 6th months after injection.[26,27] The measurements were made 3 times, and the values obtained were averaged for analysis.

Electrophysiological Study

Examination of electrophysiological parameters was performed at baseline and the 1st, 3rd, and 6th months after injection, as reported in our previous studies.[16,27,36] To measure the value of antidromic sensory nerve conduction velocity, the physician operated the stimulator 14cm proximal to the active electrode over the 2nd interphalangeal joints. To measure the distal motor latency (DML), the stimulator was placed 8cm proximal to the active electrode on the abductor pollicis brevis muscle. All measurements were made 3 times, and the mean value was used for statistical analysis.

Global Assessment of Treatment

All participants self-reported the therapeutic effect after injection at the 1st, 3rd, and 6th month based on 5 levels: much improved, improved, no change, worse, and much worse. If the patient answered much improved or improved, it would be referred to as an effective outcome response.[16]

Sample Size

With the use of G*Power 3.1.9.2 (UCLA, Los Angeles, CA), a preliminary power analysis was performed by independent t test with comparison of between-group difference in change of VAS between baseline and 6th month postinjection. The result suggested that at least 52 participants were needed to achieve the appropriate power ($[1 - \beta] = 0.80$; $\alpha = 0.05$; because no preliminary data were available, we used a large effect size of 0.80).[37]

Data Analysis

Statistical analysis was performed for all collected data by using SPSS statistics version 22 (IBM, Armonk, NY). Independent t test and chi-squared test or Fisher exact test were used to analyze continuous and categorical demographic data, respectively. Repeated-measures analysis of variance with subsequent post hoc Bonferroni test was used for the intragroup data at different follow-up time points. The independent t test was performed to compare the change from baseline values between groups at each time point. The statistical tests were 2-tailed, and a p value < 0.05 was considered statistically significant. The Bonferroni correction was performed for the intergroup comparisons at different time points. Bonferroni-corrected values of $p < 0.01$ (0.05/5 time points) for the intergroup comparisons were considered statistically significant to avoid inflated type I errors.

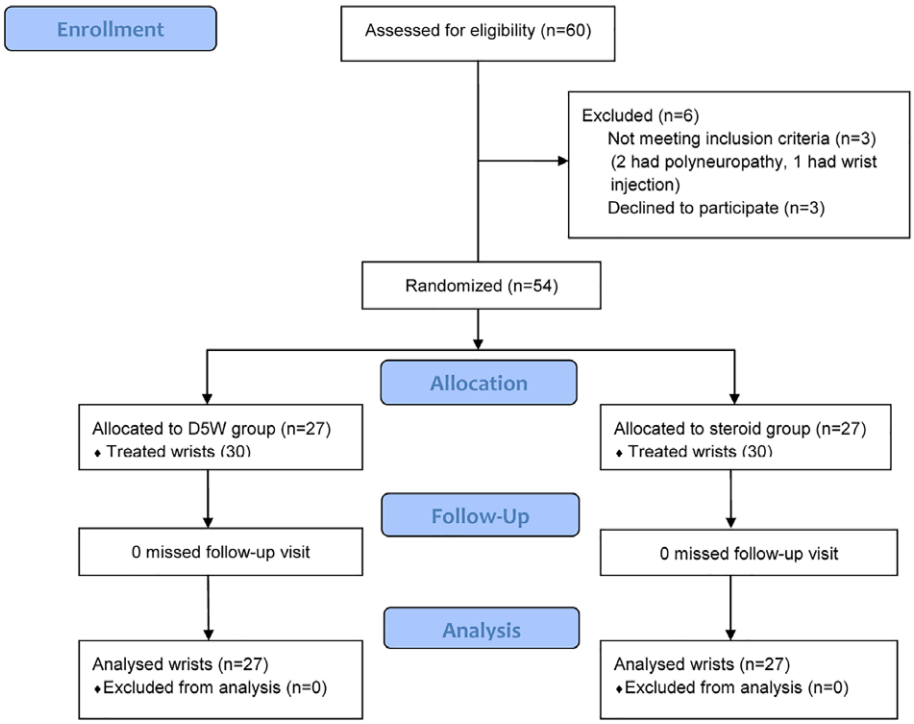

FIGURE 1: Study flow diagram. D5W = 5% dextrose. [Color figure can be viewed at wieyonlinelibrary.com]

Results

A total of 54 participants finished the study, with 27 treated wrists per group (Fig 1). The baseline demographics and clinical characteristics of the study participants are summarized in Table 3, which shows no significant difference between the two groups. The mean durations of symptom onset were 46.8 ± 8.9 and 45.6 ± 9.4 months in the dextrose and steroid groups, respectively. There were 77.8% and 81.5% participants with moderate CTS in the dextrose and steroid groups, respectively. Table 4 documents VAS and BCTQ measurements made before and after injection. All VAS and BCTQ for both the groups showed noteworthy improvement at all the follow-up time points compared to baseline (all $p < 0.05$ except the 6th-month BCTQ-severity and BCTQ-function of the steroid group).

Although there was greater improvement in the VAS and BCTQ scores for the dextrose group than for the steroid group within the initial 3 months, there was no significant difference (see Table 4 and Fig 2). The

TABLE 3. Baseline Demographic and Clinical Characteristics of Study Participants

Characteristic	D5W Group, n = 27	Steroid Group, n = 27	p[a]
Gender, n (%)			0.735
Female	22 (81.5)	21 (77.8)	
Male	5 (18.5)	6 (22.2)	
Age, yr ± SE (range)	58.6 ± 2.2 (31–84)	54.3 ± 2.0 (40–78)	0.159
BH, cm ± SE (range)	157.9 ± 1.3 (147–176)	159.0 ± 1.5 (140–174)	0.575
BW, kg ± SE (range)	67.8 ± 2.6 (44–100)	66.0 ± 2.4 (42–92)	0.603
DM, n (%)	4 (14.8)	5 (18.5)	0.715
Hypertension, n (%)	14 (51.9)	9 (33.3)	0.169
Handedness, n (%)			1.000
Right	27 (100)	26 (96.3)	
Left	0 (0)	1 (3.7)	
Lesion site, n (%)			0.776
Left	10 (37.0)	9 (33.3)	
Right	17 (63.0)	18 (66.7)	
Padua classification (%)			0.735
Moderate	21 (77.8)	22 (81.5)	
Mild	6 (22.2)	5 (18.5)	
Duration, mo ± SE (range)	46.8 ± 8.9 (3–180)	45.6 ± 9.4 (3–180)	0.925
VAS ± SE	6.3 ± 0.3	6.2 ± 0.2	0.743
BCTQs ± SE	28.2 ± 1.2	27.6 ± 1.4	0.723
BCTQf ± SE	20.7 ± 1.1	19.7 ± 0.8	0.435
SNCV, m/s ± SE	32.3 ± 1.1	32.7 ± 1.3	0.837
DML, ms ± SE	5.2 ± 0.3	5.4 ± 0.3	0.698
CSA, mm^2 ± SE	12.7 ± 0.5	13.0 ± 0.6	0.613

[a]Independent t test, chi-squared test, or Fisher exact test.

BCTQ = Boston Carpal Tunnel Syndrome Questionnaire (f = function, s = severity); BH = body height; BW = body weight; CSA = cross-sectional area; D5W = 5% dextrose; DM = diabetes mellitus; DML = distal motor latency; SE = standard error; SNCV = sensory nerve conduction velocity; VAS = visual analog scale.

TABLE 4. The Outcome Variables (VAS and BCTQ) before and after Treatment in Both Groups

	Dextrose Group, n = 27, Mean ± SE	Mean Difference (95% CI)	p^a	Steroid Group, n = 27, Mean ± SE	Mean Difference (95% CI)	p^a
VAS baseline	6.3 ± 0.3			6.2 ± 0.2		
Month 1	4.2 ± 0.3	−2.1 (−1.4 to −2.8)	<0.001	4.2 ± 0.4	−2.1 (−1.0 to −3.2)	<0.001
Month 3	3.3 ± 0.2	−3.1 (−2.2 to −3.9)	<0.001	3.6 ± 0.3	−2.6 (−1.7 to −3.5)	<0.001
Month 4	2.8 ± 0.3	−3.6 (−2.6 to −4.5)	<0.001	3.9 ± 0.3	−2.3 (−1.4 to −3.3)	<0.001
Month 6	2.0 ± 0.3	−4.3 (−3.2 to −5.4)	<0.001	4.5 ± 0.4	−1.7 (−0.7 to −2.7)	<0.001
BCTQs baseline	28.2 ± 1.2			27.6 ± 1.4		
Month 1	19.8 ± 0.9	−8.4 (−4.5 to −12.4)	<0.001	22.5 ± 1.7	−5.0 (−0.6 to −9.4)	0.016
Month 3	16.4 ± 0.7	−11.9 (−8.2 to −15.6)	<0.001	19.8 ± 1.2	−7.8 (−3.5 to −12.0)	<0.001
Month 4	15.9 ± 0.6	−12.3 (−8.4 to −16.2)	<0.001	21.2 ± 1.3	−6.4 (−1.8 to −10.9)	0.002
Month 6	14.7 ± 0.6	−13.5 (−9.3 to −17.6)	<0.001	23.7 ± 1.6	−3.9 (0.6 to −8.3)	0.128
BCTQf baseline	20.7 ± 1.1			19.7 ± 0.8		
Month 1	15.0 ± 0.8	−5.7 (−2.6 to −8.9)	<0.001	16.1 ± 1.0	−3.6 (−0.7 to −6.5)	0.008
Month 3	12.9 ± 0.5	−7.9 (−4.9 to −10.8)	<0.001	15.0 ± 0.8	−4.7 (−2.1 to −7.2)	<0.001
Month 4	12.2 ± 0.6	−8.5 (−5.8 to −11.3)	<0.001	15.9 ± 0.8	−3.7 (−1.1 to −6.4)	0.002
Month 6	11.4 ± 0.4	−9.4 (−5.7 to −13.0)	<0.001	16.6 ± 0.8	−3.0 (1.0 to −6.2)	0.063

[a]Repeated-measures analysis of variance with subsequent post hoc Bonferroni test for the intragroup data.
BCTQ = Boston Carpal Tunnel Syndrome Questionnaire (f = function, s = severity); CI = confidence interval; SE = standard error; VAS = visual analog scale.

improvement of the VAS and BCTQ scores in the steroid group reversed through the 3rd to the 6th month, and there was a significant difference between the two groups (dextrose > steroid) in all the measurements at 4th (1.3-point, 5.9-point, and 4.8-point improvement in VAS, BCTQ-severity, and BCTQ-function scores, respectively) and 6th (2.6-point, 9.6-point, and 6.4-point improvement in VAS, BCTQ-severity, and BCTQ-function scores, respectively) months postinjection (all $p < 0.01$; see Table 4 and Fig 2). All electrophysiological parameters and CSA improved in the dextrose group compared to the baseline, except the DML at the 1st and 6th months ($p = 0.184$ and 0.307, respectively; Table 5). The improvement of electrophysiological parameters and CSA in the steroid group reversed through the 3rd to the 6th months, showing nonsignificant difference in sensory nerve conduction velocity and DML at the 6th month. Although a larger difference was observed between the two groups (dextrose > steroid) at the 6th month of follow-up, there was no noteworthy difference in the electrophysiological findings and CSA (see Table 5).

In total, 74% (20/27) versus 81% (22/27) and 85% (23/27) versus 70% (19/27) patients (dextrose vs steroid) exhibited improved scores in the 1st month ($p = 0.513$) and 3rd month of follow-up, respectively ($p = 0.190$). Moreover, the global assessment showed improvement in 88% (24/27) versus 37% (10/27) of the patients (dextrose vs steroid) at the 6th month of follow-up ($p < 0.001$; data not shown). There were no side effects or complications for any patient. All patients denied the administration of extra medications or other treatments throughout the study.

Discussion

This study is the first prospective, randomized, double-blinded, controlled study conducted to compare the effectiveness of ultrasound-guided perineural injection of D5W and corticosteroid for treating mild-to-moderate CTS. Although significant improvement was observed at most follow-up time points, in both the groups, for all the parameters measured, the intergroup difference was not significant until the 4th month. The dextrose group exhibited significant reduction in pain and disability, compared to the steroid group at 4 and 6 months postinjection. These findings reveal similar short-term effect (up to

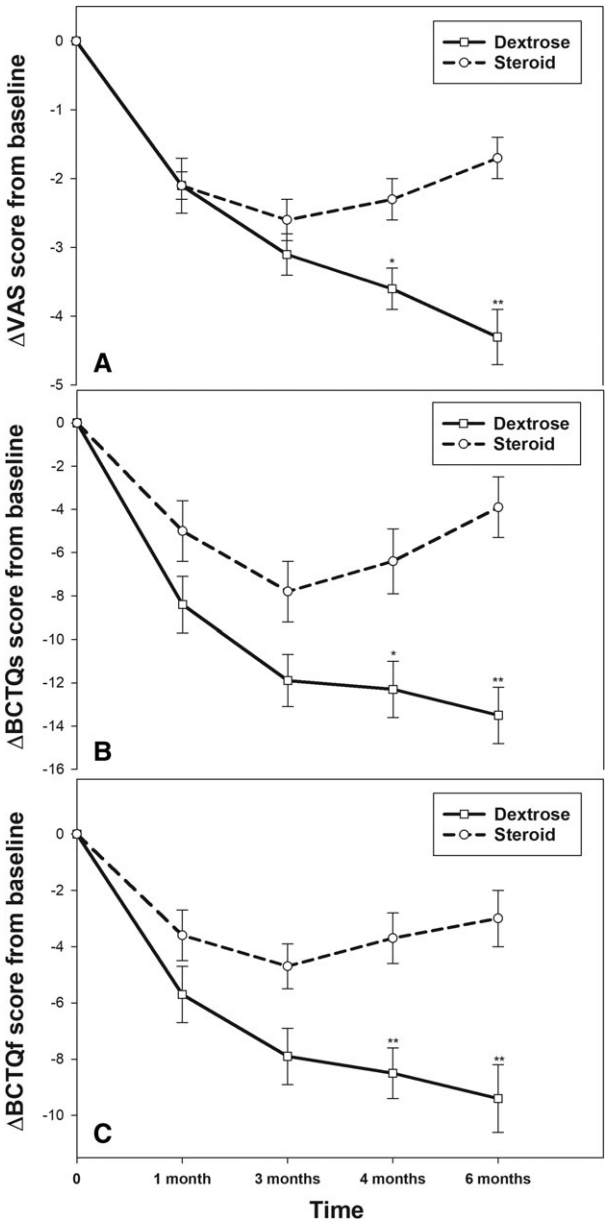

FIGURE 2: Mean change in (A) visual analog scale (VAS) and (B, C) Boston Carpal Tunnel Syndrome Questionnaire (BCTQ) scores (B, severity [s]; C, function [f]) at baseline and postinjection between the dextrose and steroid groups (mean ± standard error). The differences in all the parameters became more marked with longer follow-up (dextrose > steroid), with the differences being significant until the 4th month of follow-up (*$p < 0.01$, **$p < 0.001$; independent *t* test was used). Bonferroni-corrected values of $p < 0.01$ (0.05/5 time points) for the intergroup comparisons were considered statistically significant.

3 months) between the two groups. However, D5W seems be better than corticosteroid with respect to the long-term effectiveness against mild-to-moderate CTS.

Despite the increasing popularity of perineural injection of D5W, no evidence-based studies had been reported until the trial reported by Wu et al in 2017,[16] demonstrating the outstanding effect of perineurally injected D5W compared to normal saline, which persisted for at least 6 months in patients with mild-to-moderate CTS.[16] Although the definite mechanism underlying the effectiveness of D5W is not clear, it is hypothesized that dextrose could decrease neurogenic inflammation by inhibiting transient receptor potential vanilloid receptor-1 (TRPV1). The inhibition of TRPV1 could block neurotransmitters, including calcitonin gene-related peptide and substance P, restricting neurogenic inflammation.[38–43]

The method of perineural corticosteroid injection for treating CTS is supposed to reduce perineural inflammation and surrounding soft-tissue swelling.[44] Although Cochrane reported that the therapeutic effect of perineural injection of corticosteroid for CTS did not extend beyond 1 month compared to placebo control,[24] the beneficial effectiveness of previous controlled trials varies. Using ultrasound-guided injection, Lee et al[21] demonstrated 3-month improvement in symptoms, function, and electrophysiological parameters. Makhlouf et al[22] revealed that the therapeutic effect extended up to 6 months. Recently, Wang et al[23] showed improvement in symptoms, functional recovery, and restored nerve function at 12-week follow-up. The discrepancy of the duration of success in the aforementioned studies may arise from differences in assistive guidance, injectate volume, and severity of symptoms. In the current study, the results show considerable improvements in the steroid group compared to baseline up to 6 months, and these findings were compatible with those of recent studies.

The therapeutic effect of perineural injection of D5W and corticosteroid may have been overestimated in our study, because the injection placebo effect and spontaneous remissions of CTS should also be considered. Certainly, Kirwan[45] showed approximately 30% pain relief due to placebo effect within the first few weeks of intra-articular injection in patients with knee osteoarthritis. Moreover, Padua et al[46] reported that 34% of untreated patients with CTS may improve spontaneously after 10 to 15 months of follow-up. Regardless of the injection, placebo effect and spontaneous remission can be ignored in our study, due to the same guidance method and injectate volume being used throughout the randomized, double-blind, and controlled trial. However, the ideal study design would be addition of a sham group to reveal the therapeutic effects of perineurally injected D5W and corticosteroid.

Although there was greater improvement in the VAS and BCTQ scores between groups (dextrose > steroid group) within the initial 3 months, the differences were nonsignificant (see Table 4 and Fig 2). In contrast, the improvements in most electrophysiological parameters and CSA were more enhanced in the steroid than in the

TABLE 5. Comparison of Changes of Electrophysiological Study and CSA between Groups

	Dextrose Group, n = 27, Mean ± SE	Mean Difference (95% CI)	p^a	Steroid Group, n = 27, Mean ± SE	Mean Difference (95% CI)	p^a	Between-Group Difference (95% CI)	p^b
SNCV baseline	32.3 ± 1.1			32.7 ± 1.3				
Month 1	34.2 ± 1.2	1.9 (0.2 to 3.7)	0.024	34.7 ± 1.4	2.1 (1.2 to 2.9)	<0.001	0.1 (−1.2 to 1.5)	0.850
Month 3	34.6 ± 1.2	2.3 (0.6 to 4.0)	0.004	35.4 ± 1.4	2.8 (1.5 to 4.0)	<0.001	0.5 (−1.0 to 2.0)	0.512
Month 6	34.9 ± 1.3	2.6 (0.3 to 5.0)	0.023	33.9 ± 1.3	1.3 (0.6 to 3.1)	0.345	−1.4 (−3.5 to 0.8)	0.203
DML baseline	5.2 ± 0.3			5.4 ± 0.3				
Month 1	5.0 ± 0.3	−0.2 (−0.6 to 0.1)	0.184	5.0 ± 0.2	−0.4 (−0.6 to −0.2)	<0.001	−0.2 (−0.4 to 0.1)	0.253
Month 3	4.8 ± 0.2	−0.4 (−0.7 to 0)	0.030	4.9 ± 0.2	−0.5 (−0.9 to −0.1)	0.022	−0.1 (−0.4 to 0.3)	0.792
Month 6	4.8 ± 0.2	−0.4 (−1.1 to 0.2)	0.307	5.0 ± 0.3	−0.4 (−0.9 to 0.2)	0.356	0.1 (−0.5 to 0.6)	0.828
CSA baseline	12.7 ± 0.5			13.0 ± 0.6				
Month 1	11.3 ± 0.5	−1.4 (−2.0 to −0.8)	<0.001	11.2 ± 0.5	−1.8 (−2.4 to −1.2)	<0.001	−0.4 (−1.0 to 0.2)	0.170
Month 3	10.8 ± 0.4	−1.9 (−2.6 to −1.1)	<0.001	10.8 ± 0.5	−2.3 (−3.0 to −1.5)	<0.001	−0.4 (−1.1 to 0.4)	0.346
Month 6	10.5 ± 0.5	−2.1 (−2.9 to −1.3)	<0.001	11.4 ± 0.6	−1.6 (−2.7 to −0.5)	0.003	0.5 (−0.5 to 1.5)	0.298

Bonferroni-corrected values of $p < 0.01$ (0.05/5 time points) for the intergroup comparisons were considered statistically significant.

[a]Repeated-measures analysis of variance with subsequent post hoc Bonferroni test for the intragroup data.

[b]Independent *t* test (change from baseline [mean difference] between groups).

CI = confidence interval; CSA = cross-sectional area; DML = distal motor latency; SE = standard error; SNCV = sensory nerve conduction velocity.

dextrose group in the initial 3 months (see Table 5). The absence of a significant intergroup difference within the initial 3 months may be because the corticosteroid injection had already exerted considerable effect. However, the benefit of corticosteroid injection is short term, and the improvement in all parameters of the steroid group reversed through the 3rd to the 6th month, in contrast with the persistent improvement in the dextrose group, reaching a significant difference in the VAS and BCTQ scores between the two groups (dextrose > steroid; see Tables 4–5 and Fig 2). Furthermore, the difference in the changes in VAS and BCTQ scores between the groups obviously exceed the minimal clinically important difference at the 6th month (see Table 4 and Fig 2). Therefore, its clinical significance was evident. Although a trend of improved electrophysiological parameters and CSA between the groups (dextrose > steroid) at the 6th month of follow-up was observed (see Table 5), the difference did not reach statistical significance. Further studies with extended follow-up duration are needed to determine the intergroup differences.

Cochrane found that 2 perineural injections of corticosteroid did not provide further clinical benefit, compared to a single injection.[24] Nevertheless, the many possible adverse effects of corticosteroid such as axonal and myelin degeneration would limit its clinical utility and repetitive injection.[19,25] Peters-Veluthamaningal et al[19] reported that 14 of 36 participants (38.8%) exhibited steroid-flair side effects after injection of triamcinolone acetonide. In contrast, no such side effect of D5W has been published so far.[8–11] We have also noted no associated complications or deterioration in electrophysiological parameters and ultrasonographic findings in the current and previous studies.[16] Consequently, we advocate the replacement of corticosteroid with D5W as the first choice for perineural injection for patients with mild-to-moderate CTS. Although the accumulative effect of perineural injection of dextrose is still unknown, we observed greater effectiveness with repetitive injection in our clinical practice. Further studies are needed to investigate this phenomenon.

This study has a few limitations that were not addressed. First, the mechanism of the therapeutic effect

of D5W was not investigated in this study. Second, our study does not address the exact effect of needle placebo effect and spontaneous remission, due to the lack of a sham group. Third, the observed potential biases might arise if a subject is rating both of his/her own hands, particularly for subjective measures such as VAS and BCTQ, where the patient's perception of one hand can be easily influenced by that of the other. Therefore, the potential bias of selecting the dominant hand in our study should be considered. Nevertheless, almost all similar published studies select the individual (only one hand included per participant) for outcome analysis by using either the dominant hand or the most symptomatic side. Likewise, the 4 dominant hands from 6 patients in our study were also on the symptomatic side (equal to 2 hands in each group). Moreover, both the hands were injected for only 3 patients in each group. Therefore, we believe that the selection bias was minimal and did not impact the statistical results. Finally, the ideal dosage and sessions of perineural injection of D5W remain unclear, which needs further study.

Our study demonstrates that single perineural D5W injection leads to significant reduction in pain and disability, compared to corticosteroid, from the 4th month post-injection. Considering the side effects of corticosteroid, we deem D5W to be a better choice for perineural injection, for patients with mild-to-moderate CTS.

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Author Contributions

Study concept and design: Y.-T.W. and L.-C.C. Data acquisition and analysis: T.-Y.H., M.-J.K., Y.-P.S., and T.-Y.L. Drafting the text and figures: all authors.

Potential Conflicts of Interest

Nothing to report.

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