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ORIGINAL REPORT

TRIAMCINOLONE ACETONIDE VS PROCAINE HYDROCHLORIDE INJECTION IN THE MANAGEMENT OF CARPAL TUNNEL SYNDROME: RANDOMIZED PLACEBO-CONTROLLED TRIAL

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Objective: **The aim of this trial was to compare the efficacy of triamcinolone acetonide and procaine HCl with that of placebo in the treatment of carpal tunnel syndrome.**

Design: **This prospective, randomized placebo-controlled trial included 57 patients (90 median nerves). Ninety median nerves were randomly assigned to 1 of 3 groups: group 1 was injected with 1 ml 0.09% saline, group 2 was injected with 40 mg triamcinolone acetonide, and group 3 was injected with 4 ml 1% procaine HCl. Clinical and electrophysiological evaluations were performed at study onset, and at 2 and 6 months post-treatment.**

Results: **At study onset no significant differences were observed between groups with respect to clinical and electrophysiological parameters. Clinical and electrophysiological evaluations was improved significantly in groups 2 and 3 at post-treatment ($p < 0.05$). No significant changes were observed in group 1 ($p > 0.05$). Moreover, groups 2 and 3 had better scores than group 1 at 2 and 6 months post-treatment($p < 0.05$). There was no difference between groups 2 and 3 in terms of change scores of any terms at post-treatment ($p > 0.05$).**

Conclusion: **Triamcinolone acetonide and procaine HCl injections are effective regarding short- and long-term outcomes compared with placebo injections, and procaine HCl injection was as effective as steroid injection.**

Key words: carpal tunnel syndrome; local anaesthetic; corticosteroid.

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INTRODUCTION

Steroid injection into the carpal tunnel is frequently used and is known to be safe and effective in the treatment of carpal tunnel syndrome (CTS) (1). The aim of steroid injection is to reduce the inflammation and swelling of the flexor tenosynovitis, and reduce the pressure exerted on the median nerve. Steroids are usually mixed with local anaesthetics, such as lidocaine HCl or prilocaine HCl (2–5), which have positive effects that can aid the treatment of CTS by inhibiting the spontaneous discharge ability of excitable cells (6, 7).

Procaine HCl is one of the most common local anaesthetics used in neural therapy and has the highest pKa level; thus the ability of procaine HCl to ionize is the highest among the local anaesthetics. Ionization ability is positively correlated with the efficacy of local anaesthetics (8, 9). Karadaş et al. (10) compared the efficacy of steroid injection and procaine HCl injection in treatment of CTS, and reported that local procaine HCl injection was as effective in reducing the symptoms of CTS and improving electrophysiological findings as steroid injection. That study was the first to compare local steroid injection and high-dose local procaine HCl injection. Results obtained with the steroid and procaine HCl were similar, and both had long-term positive effects on CTS (10). However, there was no placebo group in that study, and they did not use the Boston Carpal Tunnel Questionnaire (BCTQ), which is a patient-reported outcome measure for CTS that has been tested for validity, reliability and responsiveness, the psychometric properties of which have been described extensively (11).

Accordingly, the aim of this first randomized placebo-controlled trial was to compare the efficacy of triamcinolone acetonide and procaine HCl with that of placebo in the treatment of CTS.

MATERIAL AND METHODS

Patients with clinically suspected primary CTS were referred to the electromyography (EMG) laboratory of our hospital. Patients with symptoms of CTS, including nocturnal paraesthesia, pain in the median nerve distribution during activity, or numbness in the median nerve distribution, and positive electrophysiology study results were asked to participate in the study if they were > 18 years old, had symptoms for less than one year, had no evidence of inflammatory arthritis, hypothyroidism, previous wrist trauma, or pregnancy, and had not previously been injected with steroids or local anaesthetics into the carpal tunnel, splinted, or operated on at the carpal tunnel. Patients with median nerve distal motor latency (DML) and sensory nerve conduction velocity (SNCV) longer than the reference values, and median nerve sensory peak latency ≥ 0.4 ms longer than that of the ulnar nerve based on median-vs-ulnar

digit IV antidromic sensory peak latency comparison underwent needle electromyography of the abductor pollicis brevis (APB) muscle. Patients with fibrillation potentials, positive sharp waves, or chronic neuropathic changes (decreased recruitment pattern, long duration or high amplitude of motor unit potentials) during needle electromyography, and patients with both normal motor and sensory conduction values were excluded. Among the patients with bilateral symptoms and positive electrophysiology findings, both hands were included in the study. All the patients provided informed consent and the study was approved by the local Institutional Review Board.

The study patients were randomly assigned to 1 of 3 groups: group 1 was injected with 1 ml 0.09% saline, group 2 was injected with 40 mg triamcinolone acetonide, and group 3 was injected with 4 ml 1% procaine HCl. The same investigator (unaware of the electrophysiological findings and clinical data) performed all the injections. A 25 G needle was inserted 1 cm proximal to the distal wrist-flexion crease, between the palmaris longus and the flexor carpi radialis tendons. The needle was introduced slowly and the injection was stopped if the patient experienced pain or the sensation of pins and needles in the median nerve distribution. Following appropriate needle placement, the injections were administered. Each patient was injected only once.

All the nerve conduction studies were performed by the same investigator, who was unaware of the treatment groups. All the patients completed the BCTQ and visual analogue scale (VAS) of pain. BCTQ has two components to assess symptom severity and functional disability. The BCTQ symptom severity scale has 11 and the BCTQ functional status scale has 8 questions and both use a 5-point scale. Each scale generates a final score (sum of individual item scores divided by the number of items), which ranges from 1 to 5. Higher scores correlate with more severe symptoms and functional impairment, respectively.

A Medelec Synergy (Viasys, Ireland, 2008) electromyograph was used for nerve conduction studies, which were performed at baseline, 2 months post-injection, and 6 months post-injection. DML (ms), compound muscle action potential (CMAP) amplitude (mV, recorded in the APB muscle), compound sensory action potential (CSAP) amplitude (μV), and SNCV (m/s) recordings from digit II were evaluated. Skin temperature was maintained above 31ºC. Median and ulnar nerves were stimulated at the wrist using identical distances from the active electrode, as described by Buschbacher (12). Another investigator collected all the electrophysiological and clinical data and kept them in a locker. Medications, splinting or any other complementary or alternative treatments were not allowed during the study.

Table I. *Patient demographics*

Parameters	Group 1 NaCl injection	Group 2 TCA injection	Group 3 Procaine HCl injection
Patients (*n*)	19	20	18
Age, years, mean (SD)	48.40 (12.13)	46.40 (11.60)	46.83 (5.97)
Sex (female/male), *n*	17/2	17/3	16/2
Location of CTS, *n*			
Right	5	6	3
Left	3	4	3
Bilateral	11	10	12
Total	30	30	30
Duration of symptoms, months, mean (SD)	9.86 (3.39)	9.46 (3.50)	10.20 (2.12)

SD: standard deviation; CTS: carpal tunnel syndrome; NaCl: sodium chloride; TCA: triamcinolone acetonide; HCl: hydrochloride.

Data were analysed using SPSS v.15.0 for Windows. Descriptive statistics are given as mean standard deviation (SD) and quantities. Kolmogorov-Smirnov Test was used to determine whether data followed a normal distribution. Parameters at baseline, and 2 and 6 months post-treatment were compared using the Wilcoxon signed-rank test. Differences between the groups were investigated using the Mann-Whitney *U* test. The study has a power of 80%. The level of significance was set at $p < 0.05$.

RESULTS

A total of 160 median nerves of 102 patients were evaluated and the study included 57 patients (90 median nerves) randomly divided into 3 groups. Group 1 comprised 19 patients (30 median nerves), group 2 comprised 20 patients (30 median nerves), and group 3 comprised 18 patients (30 median nerves). Patient demographics are shown in Table I. Groups were similar in terms of age, gender, and duration of symptoms

Table II. *Electrophysiological findings of patients*

	Group 1		Group 2		Group 3		Group 1 vs group 2	Group 1 vs group 3	Group 2 vs group 3
	Mean (SD)	p^a	Mean (SD)	p^a	Mean (SD)	p^a	p^a	p^a	p^a
DML (ms)									
Baseline	4.24 (1.13)		4.11 (0.99)		4.08 (1.11)		0.871	0.717	0.801
2 months post-treatment	4.25 (0.93)	0.922	3.52 (0.66)	**<0.001**	3.76 (0.81)	**0.004**	**<0.001**	**0.044**	0.066
6 months post-treatment	4.05 (0.87)	0.242	3.68 (0.77)	**<0.001**	3.90 (0.96)	**0.042**	0.213	0.842	0.072
CMAP amplitude (mV)									
Baseline	8.27 (2.48)		8.87 (2.49)		8.48 (1.96)		0.214	0.568	0.286
2 months post-treatment	8.33 (2.19)	0.829	9.30 (1.77)	0.393	8.80 (1.77)	0.303	0.300	0.524	0.941
6 months post-treatment	8.47 (2.50)	0.553	9.11 (2.07)	0.837	8.63 (1.70)	0.600	0.574	0.672	0.495
CSAP Amplitude (μV)									
Baseline	23.33 (9.51)		23.85 (11.79)		21.56 (9.37)		0.877	0.344	0.589
2 months post-treatment	22.89 (5.97)	0.813	29.27 (11.32)	**0.001**	24.45 (7.77)	0.014	**0.001**	**0.023**	0.065
6 months post-treatment	23.22 (7.13)	0.658	26.54 (10.03)	**0.014**	23.16 (7.60)	0.019	**0.030**	0.135	0.574
SNCV (m/s)									
Baseline	40.76 (4.82)		41.45 (6.20)		41.67 (6.75)		0.367	0.225	0.830
2 months post-treatment	40.34 (3.21)	0.530	45.50 (6.24)	**0.001**	45.01 (4.90)	0.007	**0.001**	**0.005**	0.695
6 months post-treatment	40.10 (3.69)	0.773	44.25 (5.88)	**0.002**	44.30 (4.32)	0.022	**0.002**	0.057	0.589

[a]Compared with baseline. Significant values are shown in bold.
DML: distal motor latency; CMAP: compound muscle action potential; CSAP: compound sensory action potential; SNCV: sensory nerve conduction velocity.

Table III. *Clinical findings of patients*

	Group 1		Group 2		Group 3		Group 1 vs group 2	Group 1 vs group 3	Group 2 vs group 3
	Mean (SD)	p^a	Mean (SD)	p^a	Mean (SD)	p^a	p^a	p^a	p^a
BCTQ Symptom Score									
Baseline	2.72 (0.59)		2.73 (0.72)		2.63 (0.75)		0.888	0.414	0.645
2 months post-treatment	2.69 (0.40)	0.888	2.43 (0.66)	**0.001**	2.46 (0.63)	**<0.001**	**0.036**	0.107	0.145
6 months post-treatment	2.68 (0.46)	0.712	2.46 (0.61)	**0.001**	2.47 (0.60)	**0.001**	0.065	0.193	0.208
BCTQ Functional Score									
Baseline	2.82 (0.60)		2.77 (0.93)		2.79 (0.97)		0.297	0.374	0.823
2 months post-treatment	2.79 (0.44)	0.494	2.62 (0.90)	**0.003**	2.67 (0.81)	**0.014**	0.178	0.362	0.566
6 months post-treatment	2.80 (0.43)	0.657	2.64 (0.87)	**0.006**	2.67 (0.79)	**0.018**	0.208	0.267	0.791
VAS									
Baseline	6.11 (0.80)		6.01 (0.83)		**5.90 (1.78)**		0.864	0.701	0.982
2 months post-treatment	5.95 (0.71)	0.123	4.10 (1.46)	**<0.001**	**4.71 (1.76)**	**0.001**	**<0.001**	**<0.001**	0.147
6 months post-treatment	6.08 (0.65)	0.779	4.76 (1.04)	**<0.001**	**5.05 (1.76)**	**0.006**	**<0.001**	**0.008**	0.298

[a]Compared with baseline. Significant values are shown in bold.
BCTQ: Boston Carpal Tunnel Questionnaire; VAS: visual analogue scale.

($p > 0.05$). Side-effects were not observed in any of the groups at the end of the study.

At the study onset significant differences were not observed between the groups with respect to DML, CMAP amplitude, CSAP amplitude, SNCV, BCTQ, BCTQ symptom score, BCTQ functional score and VAS (Tables II and III); however, DML, CSAP amplitude, SNCV, BCTQ symptom score, BCTQ functional score and VAS scores improved significantly in groups 2 and 3 at 2 months post-treatment (all $p < 0.05$), and these improvements persisted at 6 months post-treatment (all $p < 0.05$) (Tables II and III). No significant changes were observed in group 1 at 2 and 6 months post-treatment (all $p > 0.05$).

Significant differences were not observed between groups 2 and 3 with respect to electrophysiological and clinical findings at baseline and change scores at 2 months post-treatment, or 6 months post-treatment (all $p > 0.05$). Although groups 2 and 3 had better scores than group 1 in terms of DML, CSAP amplitude, SNCV, BCTQ symptom severity scale, BCTQ functional status scale and VAS at 2 and 6 months post-treatment (all $p < 0.05$), only changes scores in DML, CSAP and SNCV in groups 2 and 3 were better than group 1 at 2 months post-treatment (all $p < 0.05$) (Tables II and III).

DISCUSSION

The present placebo-controlled, randomized, clinical study shows that there were noticeable and long-lasting improvements in electrophysiological and clinical findings after local steroid injection and local procaine HCl injection, and the results obtained with the steroid and procaine HCl were similar. However, changes in electrophysiological and clinical findings were not found in patients who received placebo injections. The results of this study indicate that steroid and procaine HCl injections are effective regarding short- and long-term outcomes compared with placebo injections. Most importantly, complications related to the injections were not observed.

Corticosteroid injections into the carpal tunnel have been used for more than 40 years and are reported to be effective in the treatment of CTS (8, 9, 13, 14). Steroids are usually mixed with local anaesthetics before injection in order to reduce pain during injection or to ensure accurate localization. Local anaesthetics are used in small quantities for these purposes. Local anaesthetics decrease and prevent the large transient increase in the permeability of excitable membranes to sodium ions (Na+) that is normally produced by slight depolarization of the membrane. This action of local anaesthetics is due to their direct interaction with voltage-gated Na+ channels. As the anaesthetic action progressively develops in a nerve, the threshold for electrical excitability gradually increases, the rate of the increase in the action potential declines, and the safety factor for conduction decreases. These factors decrease the probability of propagation of the action potential. Thus, local anaesthetics stabilize the sodium channel (6). Sodium channel alterations have been reported following damage or insult to peripheral nerves, as well as injury to fibres in close proximity (15). The change in neuronal excitability (spontaneous and ectopic discharge) contributes to and maintains the condition (10, 16–19). Procaine HCl, the most effective local anaesthetic due to its high pKa level (the highest among local anaesthetics), pharmacologically blocks these channels and the processes underlying this change may be the most efficient mode of treatment (6, 7, 10, 19).

There is a limited number of studies on the efficacy of local anaesthetics in the treatment of CTS. Nalamamachu et al. (19) compared the efficacy of a local 5% lidocaine patch applied daily with that of a single injection of 0.5 ml 1% lidocaine plus 40 mg methylprednisolone acetate, and reported that the lidocaine patch effectively reduced the pain associated with CTS. Armstrong et al. (20) administered 6 mg betamethasone and 1 ml 1% lidocaine to 43 patients, and 1 ml saline placebo plus 1 ml 1% lidocaine to 38 patients, and reported that the patients that received the steroid had significant improvement in median nerve conduction parameters and in treatment satisfaction. In both studies lidocaine was administered in small doses. We used 4 ml 1% procaine HCl. Procaine HCl has a higher ionization level due its high level of pKa. Thus, procaine HCl is hypothesized to be

more effective than lidocaine HCl. Karadaş et al. compared the efficacy of 40 mg triamcinolone acetonide injection and 4 ml 1% procaine HCl injection in the treatment of CTS, and reported that local procaine HCl injection was as effective in reducing the symptoms of CTS and improving electrophysiological findings as steroid injection. The authors mentioned that patients who received both steroid and procaine HCl had better symptomatology scores than those who received either the steroid or procaine HCl alone (10). However, there was no placebo group in that study and they have not used the Boston Carpal Tunnel Questionnaire, which is widely used for patients with CTS. The results of the present study are compatible with the results of Karadaş et al. (10) and Moghtaderi et al. (21), who compared EMLA cream (AstraZeneca Pty Ltd, North Ryde, Australia) (2.5% lidocaine plus 2.5% prilocaine) with steroid injection in the treatment of CTS, and reported that EMLA cream was as effective as the steroid injection in reducing the pain associated with CTS (21); however, their study did not include long-term follow-up or electrodiagnostic evaluation.

The present study does have some limitations; primarily the small patient group with female predominance, and the lack of 12 months' follow-up, as well as the lack of double-blind design. A potential bias would have ensued due to the fact that the physician who performed the injections was not blinded. Nevertheless, the results appear to be significant.

In conclusion, steroid and procaine HCl injections are effective in CTS regarding short- and long-term outcomes compared with placebo injections, and local procaine HCl injection was as effective in reducing the symptoms of CTS and improving electrophysiological findings as steroid injection. Procaine HCl can be used in CTS patients in whom steroid use is contraindicated, such as those with diabetes mellitus.

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