Single vs. two steroid injections for carpal tunnel syndrome: a randomised clinical trial

S. M. WONG,1 A. C. F. HUI,1 S. K. LO,2 J. H. CHIU,1 W. F. POON,1 L. WONG1
Department of Medicine,1 Prince of Wales Hospital, Shatin, NT, Hong Kong, Institute for International Health,2 University of Sydney, Sydney, Australia

SUMMARY
We investigated the efficacy of a single vs. double steroid injections in the treatment of carpal tunnel syndrome (CTS) in a randomised double-blind controlled trial. Patients with idiopathic CTS were randomised into (i) one group receiving a baseline methylprednisolone acetate injection plus a saline injection 8 weeks later and (ii) a second group receiving methylprednisolone acetate injection at baseline and at 8 weeks. The primary outcome was the Global Symptom Score (GSS). Forty patients were recruited. By 40 weeks, the mean GSS improved from 25.6 to 14.1 in the single-injection group whereas from 26.7 to 12.6 in the reinjection group, but there was no significant difference in GSS between the two groups (p = 0.26). There were also no significant differences in terms of electrophysiological and functional outcomes. The results suggest that an additional steroid injection confers no added benefit to a single injection in terms of symptom relief.

Keywords: Carpal tunnel syndrome; steroid injection; randomised controlled trial

INTRODUCTION
The best available evidence for the nonsurgical treatment of carpal tunnel syndrome (CTS) includes splinting, local steroid injection and oral steroid (1). A review of 17 studies, including randomised trials, on the efficacy of an isolated steroid injection found that the average short-term response rate was 76%, but only 6.5%–33% of patients remain in remission in the long term (2–6). In practice, many physicians offer another injection of steroid to patients who relapse, but there is no trial-based evidence to support the usefulness of repeat injections. We therefore conducted a double-blind, randomised trial to assess the efficacy of a single steroid injection as compared with repeat injections in the treatment of idiopathic CTS.

METHODS
This was a prospective double-blind study in which all patients with CTS were randomised at baseline to receive an initial local steroid injection followed 8 weeks later by either another local injection of steroid or an equal volume of saline solution. The local ethical committee had approved the study, and informed consent was required from all patients. We recruited consecutive patients with newly diagnosed CTS of less than 12 months’ but longer than 3 months’ duration from our medical clinics. Co-interventions such as splinting, oral medications and alternative therapy such as acupuncture were withheld for the duration of the study. To confirm the diagnosis in all patients with sensory symptoms over a median nerve distribution, we performed motor and sensory nerve conduction studies (Viking III, Nicolet, Madison, WI, USA) were performed in median and ulnar nerves using standard techniques of supramaximal stimulation and surface electrodes following professional guidelines on the clinical and electrophysiological diagnosis of CTS (7,8). We used a bandwidth setting of 20 Hz to 3 kHz, sweep speed 1 ms/division and gain 10–20 μV/cm. Skin temperature was maintained at or above 30 °C. Compound muscle action potentials, distal motor latencies (DMLs), nerve conduction velocities and sensory nerve action potentials were measured. Patients were enrolled into the study if they fulfilled the criteria below:

- sensory symptoms over median nerve distribution;
- confirmatory electrophysiological: prolonged median nerve DML > 4 ms or median-ulnar palmer sensory latency difference greater than 0.5 ms (values derived from our local centre);
- failed splinting for 2 months or more.

The following exclusion criteria applied:

- patients with the evidence of severe CTS: clinical examination showing wastage of the thenar muscles or fibrillation

Correspondence to:
Dr Andrew C. F. Hui, Department of Medicine, Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin, Hong Kong
Tel.: + 852 26323131
Fax: + 852 26375396
Email: cfhui@cuhk.edu.hk

© 2005 Blackwell Publishing Ltd Int J Clin Pract, December 2005, 59, 12, 1417–1421
steroid injections for carpal tunnel syndrome

The primary endpoint variable was the Global Symptom Score (GSS). This is a scoring system, which has been used in previous CTS studies, that rates symptoms on a scale of 0 (no symptoms) to 10 (severe) in five categories: pain, numbness, paraesthesia, weakness/clumsiness and nocturnal awakening; the sum of the scores in each category was the GSS (10–12). This was recorded at baseline, 8, 24 and 40 weeks, and any side-effects were recorded by another author (AH) who was blinded to treatment allocation. Patients were excluded from the study at 8 weeks if GSS reached zero at 8 weeks by the same author (AH), and the second injection would not be given. Electrophysiological testing and functional assessment in terms of grip strength were also performed at baseline, 8 and 40 weeks and noted as secondary outcome by two researchers who were not otherwise involved in the management of the patients. As to grip strength measurements, all patients were tested with a JAMAR hydraulic hand dynamometer (Sammons Preston Inc., Bollingbrook, IL, USA); each case was assessed at a seated position with shoulder in the neutral position and elbow in 90° flexion. These trials were repeated on the left hand. Three trials were recorded, and the mean value, in kilograms, was documented.

Based on the data from previous trials (6,12), we expected the double-injection group to show continuous improvement from a mean GSS of 26–13 at 8 weeks and 7 at 40 weeks, the end of the study. This was based on the assumption that a single injection of steroids would yield a 50% improvement on the GSS and that a repeat steroid injection would have an accumulating effect on symptomatic relief in patients with CTS. The single injection plus placebo group will show improvement in GSS from 26 to 13 at 8 weeks and 11 at the end of the study based on the assumption that a placebo response would yield a 20% improvement in the GSS score. We deduced the differences in GSS for the placebo group at 8 weeks after injection was 4.3 (SD = 7.3) and that for the injection group was 11.3 (SD = 7.7). The sample size of 40 was estimated to be able to achieve 80% power and a 0.05 alpha level. Repeated measures ANOVA was used to compare the effectiveness of the two groups, as well as to examine the change from baseline to week 40, with respect to the primary and secondary outcome measures. The overall level of significance was set to 0.05; the sharpened Bonferroni procedure was used to adjust for individual alpha level when multiple testings were performed (13).

RESULTS

Forty-two eligible patients were invited to join the study; two declined on the ground of the fear of needles. Twenty patients were randomised to the double steroid injection group and 20 patients to the single steroid and placebo injection group. Subject demographic and clinical characteristics were comparable (Table 1). None of the patients reached a GSS of zero at week 8 so there was no need to omit the second injection at week 8 (Figure 1).

Table 1 Demographic characteristics of the patients

| Features                  | Single-injection group | Double-injection group |
|---------------------------|------------------------|------------------------|
| Patients, n               | 20                     | 20                     |
| Mean age (SD), years      | 46.4 (5.6)             | 47.3 (9.6)             |
| Sex (female/male)         | 17/3                   | 17/3                   |
| Baseline GSS              | 25.6 (11.6)            | 26.7 (10.1)            |
| Location of CTS           |                        |                        |
| Left                      | 2                      | 2                      |
| Right                     | 3                      | 2                      |
| Bilateral                 | 15                     | 16                     |
| Baseline DML (SD), ms     |                        |                        |
| Left                      | 6.2 (0.2)              | 4.9 (1.5)              |
| Right                     | 4.3 (0.8)              | 4.7 (0.8)              |
| Bilateral (left/right)    | 4.4 (1.0)/4.5 (1.1)    | 4.6 (1.1)/5.6 (2.0)    |

CTS, carpal tunnel syndrome; DML, distal motor latency; GSS, Global Symptom Score.
The mean GSS values from baseline to week 40 are summarised in Table 2. The treatment group improved from 26.7 at baseline to 12.6 at week 40 (an improvement of 53%), whereas the placebo group improved from 25.6 to 14.1 (an improvement of 45%). However, the pattern of change in mean GSS over time was not significantly different between the two groups (p = 0.26). The change in the mean GSS occurred mainly in the first 8 weeks, but then the GSS became steady from week 8 onwards. Although both groups demonstrated symptomatic improvement after treatment, the scores were not significantly different at any of the four time points.

There were no significant differences between two groups in neurophysiological parameters and grip strength (Table 3A,B). Six patients in the double-injection group (30%) along with two patients in the placebo group (10%) reported mild local pain and tenderness of the injected site with radiation over the median nerve distribution following the second injection lasting from 1 to 5 days.

**DISCUSSION**

This is the first randomised clinical trial evaluating the efficacy of repeat steroid injections in the treatment of CTS. The

**Table 2** Summarised results in mean Global Symptom Score (GSS) values

| Group            | Time       | Baseline | 8 weeks  | 24 weeks | 40 weeks | p-Value from baseline |
|------------------|------------|----------|----------|----------|----------|-----------------------|
| Single injection | Baseline   | 26.7 ± 10.1† | 15.2 ± 9.9 | 15.9 ± 10.6 | 12.6 ± 9.1 | <0.001                |
| Double injection | Baseline   | 25.6 ± 11.6* | 11.4 ± 7.6 | 13.0 ± 9.7 | 14.1 ± 11.0 | <0.001                |
| p-Value between groups | Baseline | 0.75 | 0.19 | 0.37 | 0.64 |

*Mean GSS for the placebo group at baseline was significantly different from that at 8, 24 and 40 weeks (all p-values < 0.001 after sharpened Bonferroni adjustment). †Mean GSS for the treatment group at baseline was significantly different from that at 8, 24 and 40 weeks (all p-values < 0.001 after sharpened Bonferroni adjustment).
optimal number of injections is uncertain, but traditionally the concern over potential local and systemic side-effects limits the number of steroid injections prescribed (14–16). Increasing evidence suggests that although this form of treatment is generally effective in the short term, most patients require carpal tunnel release with long follow-up (17–19). In one recent study, in which the use of repeat injection was noncontrolled, only 17 of 81 patients (21%) report adequate symptom relief at 18 months (18).

The duration of this study was chosen in view of the fact that some patients with CTS may undergo spontaneous improvement after 10 months (19). The data failed to demonstrate continual improvement in symptoms following an additional steroid injection, based on our original hypothesis. Close examination of the mean GSS data shows that the outcomes of the two groups were not significantly different not because of the lack of statistical power, but because they were fairly similar. The benefit in symptom score occurred mainly after the initial steroid injection with minimal improvement after 8 weeks. Symptoms reached a plateau regardless of whether steroid injection or placebo was then given. One limitation of this study was referral bias, as it was conducted in a regional hospital; whether the results could be duplicated in a primary setting is unclear. However, our criteria should have excluded the cases of long duration or those with clinical or electrophysiologically severe CTS.

In conclusion, the results from this study suggest that additional local steroid injection was no more useful than a single one in terms of symptomatic relief in the long term. In view of this finding and the possibility of axonal injury and irreversible nerve dysfunction, it seems logical to recommend surgical decompression to those CTS patients who remain symptomatic or relapse after an initial steroid injection (20–22).

Table 3A Results of mean grip values in kilograms

| Injection | Baseline | 8 weeks | 40 weeks | p-Value | Baseline | 8 weeks | 40 weeks | p-Value |
|-----------|----------|---------|----------|---------|----------|---------|----------|---------|
| Single    | 20.9 ± 4.7 | 20.4 ± 5.1 | 20.2 ± 6.6 | 0.91 | 22.0 ± 5.3 | 20.9 ± 6.2 | 21.4 ± 6.6 | 0.59 |
| Double    | 22.0 ± 7.0* | 20.6 ± 6.2 | 18.2 ± 6.6* | 0.01 | 22.3 ± 7.3 | 21.9 ± 7.2 | 20.0 ± 7.0 | 0.21 |
| p-Value   | 0.55     | 0.97    | 0.32     |       | 0.86    | 0.68    | 0.50     |       |

*Not significantly different from each other after sharpened Bonferroni adjustment.

Table 3B Results of median nerve distal mean latency values (ms)

| Injection | Baseline | 8 weeks | 40 weeks | p-Value | Baseline | 8 weeks | 40 weeks | p-Value |
|-----------|----------|---------|----------|---------|----------|---------|----------|---------|
| Single    | 4.5 ± 1.1 | 4.4 ± 0.9 | 4.2 ± 1.1 | 0.08 | 4.5 ± 1.0 | 4.5 ± 1.0 | 4.3 ± 1.0 | 0.39 |
| Double    | 4.6 ± 1.1 | 4.3 ± 1.1 | 4.5 ± 1.0 | 0.39 | 5.4 ± 1.9 | 5.0 ± 1.5 | 5.2 ± 1.5 | 0.13 |
| p-Value   | 0.79     | 0.83    | 0.42     |       | 0.08    | 0.24    | 0.03     |       |

REFERENCES
1. Marshall S. Carpal tunnel syndrome. Clin Evid 2004; 11: 1417–34.
2. Graham RG, Hudson DA, Solomons M, Singer M. A prospective study to assess the outcome of steroid injections and wrist splinting for the treatment of carpal tunnel syndrome. Plast Reconstr Surg 2004; 113: 550–6.
3. Ozdogan H, Yazici H. The efficacy of local steroid injections in idiopathic carpal tunnel syndrome: a double-blind study. Br J Rheumatol 1994; 23: 272–5.
4. Girlanda P, Dattola R, Venuto C et al. Local steroid treatment in idiopathic carpal tunnel syndrome: short- and long-term efficacy. J Neurol 1993; 240: 187–90.
5. Dammers JW, Veering M, Vermeulen M. Injection with methylprednisolone proximal to the carpal tunnel: randomized double blind trial. BMJ 1999; 319: 884–6.
6. Wong SM, Hui ACF, Tang A et al. Local vs systemic corticosteroids in the treatment of carpal tunnel syndrome. Neurology 2001; 56: 1565–7.
7. American Academy of Neurology, American Association of Electrodagnostic Medicine, American Academy of Physical Medicine and Rehabilitation. Practice parameter for carpal tunnel syndrome (summary statement). Neurology 1993; 43: 2404–9.
8. American Academy of Neurology, American Association of Electrodagnostic Medicine, American Academy of Physical Medicine and Rehabilitation. Practice parameter for electrodagnostic studies in carpal tunnel syndrome (summary statement). Neurology 1993; 43: 2404–5.
9. Bland JD. Do nerve conduction studies predict the outcome of carpal tunnel decompression? Muscle Nerve 2001; 24: 935–40.
10. Herskovitz S, Berger AR, Lipton RB. Low-dose, short-term oral prednisone in the treatment of carpal tunnel syndrome. Neurology 1995; 45: 1923–5.
11. Chang MH, Chiang HT, Lee SS, Ger LP, Lo YK. Oral drug of choice in carpal tunnel syndrome. Neurology 1998; 51: 390–3.
12. Hui ACF, Wong SM, Wong KS et al. Oral steroid in the treatment of carpal tunnel syndrome. Ann Rheum Dis 2001; 60: 813–4.
13 Hochberg Y, Benjamini Y. More powerful procedure for multiple significance testing. *Stat Med* 1990; 9: 811–8.
14 Katz JN, Simmons BP. Carpal tunnel syndrome. *N Engl J Med* 2002; 346: 1807–12.
15 Gottlieb NL, Riskin WG. Complications of local corticosteroid injections. *JAMA* 1980; 243: 1547–8.
16 McConnell JR, Bush DC. Intraneural steroid injection as a complication in the management of carpal tunnel syndrome. A report of three cases. *Clin Orthop* 1990; 250: 181–4.
17 Hayward AC, Bradley MJ, Burke FD. Primary care referral protocol for carpal tunnel syndrome. *Postgrad Med J* 2002; 78: 149–52.
18 Hui AC, Wong SM, Tang A et al. Long-term outcome of carpal tunnel syndrome after conservative treatment. *Int J Clin Pract* 2004; 58: 337–9.
19 Armstrong T, Devor W, Borchel L, Contreras R. Intracarpal steroid injection is safe and effective for short-term management of carpal tunnel syndrome. *Muscle Nerve* 2004; 29: 82–8.
20 Padua L, Padua R, Aprile I, Pasquletti P, Tonali P. Multiperspective follow-up of untreated carpal tunnel syndrome: a multicenter study. *Neurology* 2001; 56: 1459–66.
21 Gelberman RH, Rydevik BL, Pess GM, Szabo RM, Lundborg G. Carpal tunnel syndrome. A scientific basis for clinical care. *Orthop Clin North Am* 1988; 19: 115–24.
22 Werner RA, Andary M. Carpal tunnel syndrome: pathophysiology and clinical neurophysiology. Review. *Clin Neurophysiol* 2002; 113: 1373–81.

*Paper received June 2005, accepted August 2005*