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A randomized study camparing oral versus injection triamcinolone in carpal tunnel syndrome

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Abstract

Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy found in clinical practice. Corticosteroids are effective in treating CTS. The purpose of this study was to evaluate the efficacy of oral versus local injection of triamcinolone in relieving symptoms and improving neurophysiological parameters in CTS. This is a randomized controlled trial performed at Hasan Sadikin Hospital, Bandung. Inclusion criteria were idiopathic CTS patients without thenar atrophy and no contraindications to corticosteroids. Subjects were divided into oral or injection groups. The oral group was given 16 mg triamcinolone daily for 2 weeks followed by 8 mg daily for the next 2 weeks and local placebo injection. The injection group was given 15 mg local injection triamcinolone and oral placebo. The outcome was assessed using Global Symptom Score and nerve conduction studies. Fifty subjects were randomized to oral or injection group. The injection group show significant improvement at 2 and 4 weeks while the oral group showed significant improvement only at 2 weeks. Comparing both groups, improvement in neurophysiological parameters were significantly greater in the injection group.
In *conclusion*, local injection triamcinolone show better neurophysiologic outcome and efficacy in relieving symptoms compared to oral triamcinolone in CTS.

INTRODUCTION

Carpal tunnel syndrome (CTS) is the commonest focal compressive neuropathy causing entrapment of the median nerve at the carpal tunnel. Paresthesia, especially nocturnal acroparesthesia, and pain are the most frequent complaints.[1,2] Manktelow *et al,* concluded that CTS is one of the most frequent diseases causing disability, leading to reduction in productivity.[3]

Repetitive motion involving the hand can cause inflammation of the area surrounding the median nerve at carpal tunnel resulting in entrapment and cause injury due to mechanical compression or an ischemic process. CTS may be associated with obesity, hypothyroidism, rheumatoid arthritis, diabetes mellitus and pregnancy.

In 1992, De Krom *et al* found that 3.4% of adult women were known to suffer from CTS.[4] According to Ferry *et al* in their study, the prevalence of CTS was 7 - 16%.[5] In a survey conducted from July 2004 to July 2005 at Hasan Sadikin Hospital, Bandung, there were 485 visits of patients with CTS with mean of 1-2 patients daily and almost 90% were female.

There are several treatment options for patients with CTS, depending on its severity, ranging from physiotherapy, pharmacologic treatment (for e.g. diuretics, pyridoxine, non-steroidal anti-inflammatory drugs (NSAIDs), oral corticosteroids, local injection of corticosteroids) to surgical treatment. Surgery is considered the most effective therapy, but Nancollas *et al* found failure of surgery in 57% of their patients with CTS.[6]

In a systematic review on conservative alternative therapy of CTS, it was found that diuretics, pyridoxine, and NSAIDs were less effective in relieving symptoms, while local injection of corticosteroids seemed to be effective.[7] Low dose of oral corticosteroid therapy in short term was found to be effective in improving symptoms of CTS by Chang *et al*.[8] However, the study conducted by Gerritsen *et al* did not support this.[9]

In assessing the symptoms of CTS there are several methods, one of them is Global Symptom Score (GSS).[10] This score is easy to perform and good since it covers motor and sensory symptom in patients with CTS. Nerve Conduction Studies (NCS) can establish the diagnosis, determine the severity and detect improvement of CTS.

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In a survey conducted in Hasan Sadikin Hospital, Bandung, approximately 72.8% of the patients complained of persistent symptoms with NSAIDs; while, many of them refused to receive surgical treatment. Therefore, it is necessary for the clinician to find a more effective therapy than NSAIDs while avoiding high treatment costs as only few Indonesians have health insurance.

Based on previous studies, it is known that both oral and local injection of corticosteroids were effective.[11,12] Oral corticosteroids are an alternative treatment for CTS in Indonesia in addition to local triamcinolone injection. So far, there are no published reports of studies on comparing of oral and local injection corticosteroids in CTS in Indonesia. The objective of this study was to compare the effectiveness of oral versus local injection of triamcinolone in terms of relief of symptoms and improvement in NCS parameters in CTS patients. This study aims to show that alternative treatments could lead to subjective and objective improvement in CTS and result in better quality of life.

METHODS

This is a randomized controlled study performed at Hasan Sadikin Hospital, Bandung, Indonesia. The subjects of this study were patients with CTS seen at the Neurology Clinic who met the inclusion and exclusion criteria from November 2006 to March 2007. The subjects were then informed that they would receive two types of treatment, i.e., oral and injection. Inclusion criteria for this study were all patients with CTS who agreed and signed the consent form. Exclusion criteria were thenar muscle atrophy, cervical radiculopathy, polyneuropathy, pregnancy, rheumatoid arthritis, diabetes mellitus, hypothyroidism, and obesity, as well as contraindication to corticosteroids, e.g. presence of peptic ulcer, acute infection, and systemic fungal infection. The patients with CTS who had previously received oral corticosteroid therapy or local injection of corticosteroid within the last 3 months were also excluded.

The diagnostic criteria for CTS used in this study are the Rempel criteria. The Rempel diagnostic criteria of CTS is the combination of clinical symptoms of pain or paresthesia or anesthesia in the distribution of median nerve or the presence of hand weakness, Tinel's or Phalen's test positive and the presence of abnormality in NCS examination.[13] All subjects were assessed using the Global Symptom Score (GSS, Table 1) to assess their intensity of pain, paresthesia, numbness, weakness and night awakening due to pain, using score 0 (no symptoms) to 10 (the most severe symptom).[10]

Subjects were randomized by block permutation into two groups. The oral group received local injection of 1.5cc Nacl 0.9% on affected hand and oral triamcinolone therapy at dose of 16 mg daily for the first two weeks followed by 8 mg daily for the next 2 weeks. The injection group received local injection of 15 mg triamcinolone and oral placebo for 4 weeks. For local injection, the author used a 25-gauge needle and the needle was inserted slightly ulnar to the palmaris longus tendon at a 45-degree angle toward the tip of the middle finger and advanced 1 to 2 cm to traverses the flexor retinaculum. Aspiration was done to avoid intravascular injection.

Clinical examination and treatment were carried out by the first author, while NCS were conducted by the third author, who was blinded to the treatment arm of the patient until completion of the study. The clinical outcome was assessed by the first author using GSS after 2 and 4 weeks of treatment, while NCS was done after 4 weeks (Figure 1). For NCS, the distal latencies, amplitudes and conduction velocities of median

Table 1: Global Symptom Score

Global Symptom Score (*GSS*)

	Symptoms	Score
1.	Pain	
2.	Paresthesia	
3.	Numbness	
4.	Weakness	
5.	Night awakening due to pain	Total Score

Each symptom was given score which ranges from 0 (if there is no symptom) to 10 (the most severe symptom)

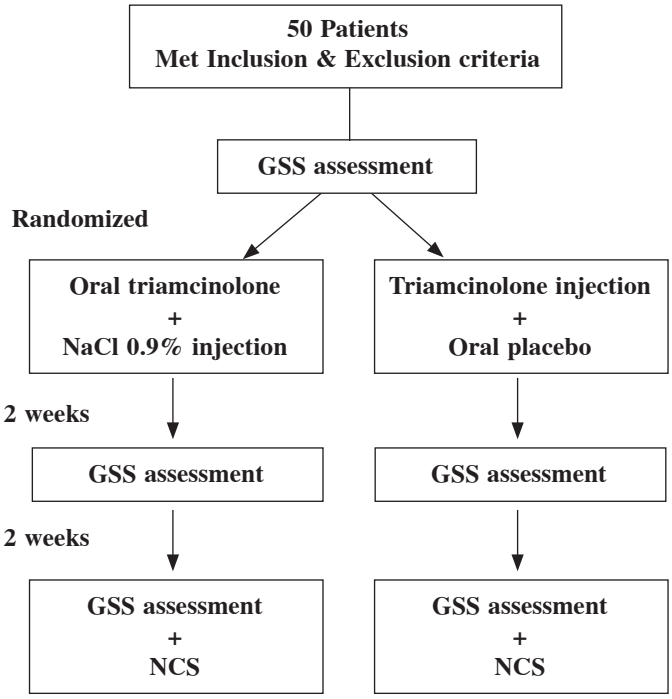

Figure 1. Study flow chart

and ulnar nerves of both hands were assessed. Statistical analysis was carried out using the *t* test or *Mann-Whitney* test using SPSS for Windows version 13.

RESULTS

The subjects were patients with CTS seen at Neurology Clinic at Hasan Sadikin Hospital, Bandung, who met the inclusion and exclusion criteria. There were 50 patients who agreed to participate in the study and signed the written informed consent. Subjects then were randomized into two groups, the oral group and injection group (each 25 subjects).

The mean age of subjects was 53.6 years which range from 46 years to 60 years in injection group. While in oral group, the mean age of subjects was 51.3 years which range from 44 years to 58 years. Females were more than males in both groups (64% in injection group and 72% in oral group). In this study, 84% of the women were housewives. CTS was more in the right hand than the left hand in both groups (72% in injection group and 60% in oral group). The authors chose the hand with the more severe symptoms in bilateral CTS for this study. The one that has been chosen would be injected either with corticosteroid or placebo.

As shown in Table 2, there were no significant differences in age in both groups, onset, baseline mean GSS, baseline mean sensory nerve conduction velocity (SNCV), baseline mean sensory distal latency (SDL), and baseline mean motor distal latency (MDL).

The GSS assessment 2 weeks after treatment (GSS 2-weeks) improved in both the injection and oral groups. Similarly, the GSS 4 weeks after treatment (GSS 4-weeks) also showed improvement in both groups as shown in Figure 2.

Table 3 shows that in the injection group, compared to baseline, mean GSS 2-weeks and mean GSS 4–weeks were significantly less ($p<0.001$ and $p=0.007$ respectively). In the oral group, compared to baseline mean GSS 2-weeks was significantly less ($p=0.003$); however, there was no significant difference between baseline mean GSS and mean GSS 4-weeks ($p=0.214$).

There was no significant difference between both groups for change in mean GSS at 2 weeks and change in mean GSS at 4 weeks (Table 4). There was no difference between the two groups for mean GSS 2-weeks, but mean GSS 4-weeks was significantly lower in the injection group ($p=0.026$) (Table 4).

While change from baseline of SNCV, SDL were not significant for both treatment groups, change from baseline for MDL was significant. Comparing both groups, change in SNCV, SDL

Table 2: Summary of baseline characteristics

Variable	Injection Group n/(Mean/SD)	Oral Group n/(Mean/SD)	P Value	95%CI
Gender				
Female	16 (64%)	18 (72%)	0.544	0.21-2.28
Male	9 (36%)	7 (28%)		
Location of CTS				
Right	18 (72%)	15 (60%)	0.370	0.18-1.91
Left	7 (28%)	10 (40%)		
Mean age (years)	53.6 (7.62)	51,3 (7.56)	0.277	–1.95-6.68
Onset (months)	9.92 (7.11)	7.13 (4.64)	0.057	–0.65-6.24
Baseline mean GSS	21.08 (9.48)	21.17 (5.45)	0.968	–4.53-4.35
Baseline mean SNCV (m/s)	31.44 (5.30)	32.96 (3.86)	0.256	–4.17-1.13
Baseline mean SDL (ms)	4.42 (0.93)	4.12 (0.51)	0.173	–0.13-6.24
Baseline mean MDL (ms)	6.84 (1.72)	6.95 (1.86)	0.829	–1.1-0.91

GSS = Global Symptom Score, SNCV = Sensory Nerve Conduction Velocity, SDL = Sensory Distal Latency, MDL = Motor Distal Latency.

and MDL were significantly greater in the injection group compared to the oral group (p=0.002, p=0.033 and p=0.023 respectively) (Table 5).

DISCUSSION

In this study, the authors used the same drug for oral and injection treatment to avoid the pharmacological differences in the medications used. The authors chose triamcinolone, because it is considered a corticosteroid with moderate effect, commonly used in Indonesia and the injectable preparation used acetonide which has the tendency of lipid solubility; so that triamcinolone effect can be sustained longer at the injection site than any other corticosteroid.[14]

The dosage for oral treatment used in this study was based on the study of Chang *et al* using prednisone with dose of 20 mg per day for 2 weeks and continued with the dose of 10 mg per day for next two weeks which has been proved to be effective.[15] Since the dose of 5 mg prednisone is equivalent with 4 mg triamcinolone[16], in this study the author used triamcinolone of 16 mg per day for two weeks and continued with 8 mg per

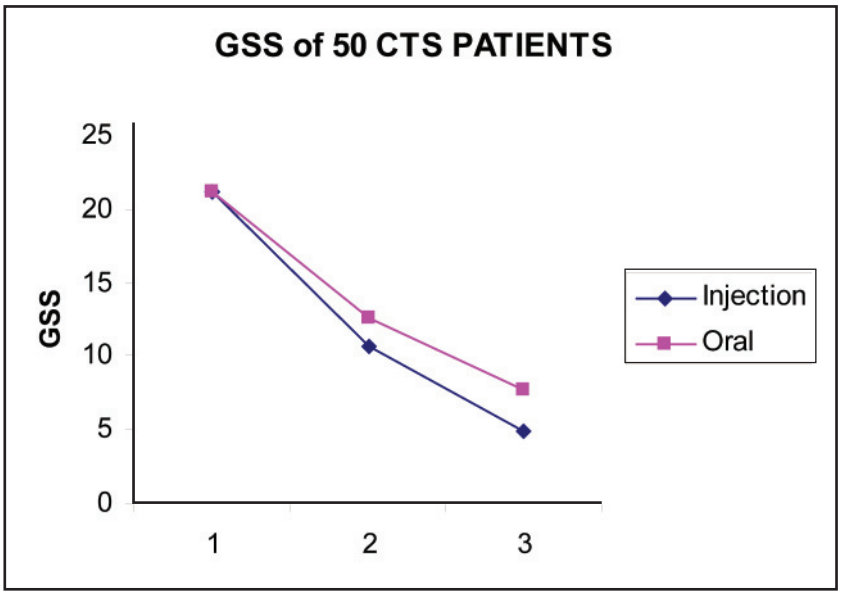

Figure 2. GSS outcome in 50 subjects.

Tabel 3: Outcome assessment of baseline, 2 weeks and 4 weeks

Variable	Mean (SD)									
	Injection Group					Oral Group				
	Baseline	2 weeks	4 weeks	P Value 2 weeks	P Value 4 weeks	Baseline	2 weeks	4 weeks	P Value 2 weeks	P Value 4 weeks
GSS	21.08 (9.48)	10.62 (7.72)	4.88 (4.64)	<0.001	0.007	21.17 (5.45)	12.58 (4.01)	7.67 (3.84)	0.003	0.214
SNCV (m/s)	31.44 (5.30)	–	40.15 (8.23)	–	0.966	32.96 (3.86)	–	34.41 (6.32)	–	0.263
SDL (ms)	4.42 (0.93)	–	3.39 (0.54)	–	0.547	4.12 (0.51)	–	3.86 (1.33)	–	0.459
MDL (ms)	6.84 (1.72)	–	5.42 (1.14)	–	<0.001	6.95 (1.86)	–	6.17 (1.76)	–	<0.001

GSS = Global Symptom Score, SNCV = Sensory Nerve Conduction Velocity, SDL = Sensory Distal Latency, MDL = Motor Distal Latency.

Tabel 4: The Comparison of outcome in both groups.

Variable	Mean (SD)			
	Injection Group	Oral Group	P Value	95% CI
GSS				
Δ Baseline GSS-2 weeks	10.46 (5.64)	8.58 (4,53)	0.203	–1.05-4.80
Δ Baseline GSS-4 weeks	16.19 (8.10)	13.50 (5.77)	0.186	–1.34-6.72
Δ SNCV(m/det)	8.71 (8.90)	1.45 (6.13)	0.002	–11.66-(–2.86)
Δ SDL (mdet)	1.03 (1.03)	0.26 (1.37)	0.033	–0.08-1.45
Δ MDL (mdet)	1.42 (1.13)	0.78 (0.75)	0.023	0.09-1.18

GSS = Global Symptom Score, SNCV = Sensory Nerve Conduction Velocity, SDL = Sensory Distal Latency, MDL = Motor Distal Latency.

Table 5: Comparison of GSS in both groups

Variable	Mean (SD)			
	Injection Group	Oral Group	P Value	95%CI
GSS				
GSS 2 weeks	10.62 (7.72)	12.58 (4.01)	0.260	–5.45-1.51
GSS 4 weeks	4.88 (4.64)	7.67 (3.84)	0.026	–5.21-(–0.34)

GSS = Global Symptom Score

day for the next two weeks. For the injection, although the recommended dose of local injection of triamcinolone for CTS based on literature is 20 mg[17], the authors used 15 mg triamcinolone which is equals to 15 mg methylprednisolone which has been shown to be effective.[18,19]

This study was different from a previous study conducted by Wong *et al* which compared the effectiveness of methylprednisolone injection and oral prednisone using only clinical outcomes.[18] Neurophysiological outcomes were also assessed in this study. This is supported by Schrijver *et al* who suggested that NCS could provide information on therapeutic effect and it would be better to examine NCS together with clinical symptoms in the assessment of patients who received treatment for CTS.[20]

The mean age of subjects in this study was in line with reviews of some literature suggesting that the incidence of CTS was in the range of 40-60 years old.[21] The higher prevalence of females in this study was in concordance with the literature disclosing that the ratio of female to male was 6:1. It is presumed that hormones play an important role on in development of CTS.[22]

The data indicates that local injection of triamcinolone provides better improvement of clinical symptoms than oral triamcinolone. This was consistent with the study conducted by Wong *et al* which suggested that corticosteroid injection provided better relief of clinical symptoms than oral treatment.[18] According to the literature, in oral steroid administration, only 10% of the drug will bind to receptors leading to a therapeutic effect, while local injection of steroid will bind directly to receptors within the cytoplasm of the cell.[14] The binding of steroids to receptors results in the inhibition of inflammatory mediator production through induction of lipocortin synthesis leading to inhibition of phospholipase A2, ultimately, inhibiting the inflammation process. Inflammatory mediators have been identified to play an important role in producing symptoms in CTS. Triamcinolone injection used in this study was triamcinolone acetonide. It has greater sustained effect compare to other corticosteroid.[14]

Therapy with oral and injection triamcinolone resulted in improvement in the SNCV, SDL, and MDL; however, improvement in the injection group was significantly better compared to the oral group. This is in accordance with the study with longer observation by Chang (2002) which indicate significant difference in SNCV after 12-month observation.[8] Hui *et al* also obtained results which showed significant differences in SNCV at 20 weeks after corticosteroid injection.[23] Other studies have also demonstrated that improvement of clinical symptoms and NCS with local injection of corticosteroid.[24-26]

In conclusion, this study shows that although oral administration of triamcinolone improved clinical symptoms and NCS parameters in CTS, local injection of triamcinolone had better efficacy in relieving symptoms and improving NCS parameters of SNCV, SDL and MDL. However, in cases of patients refusing injection of triamcinolone, oral administration can be considered an alternative.

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