Original Article

The Efficacy of Dexamethasone Sodium Phosphate Compared to Triamcinolone Acetonide in the Treatment of Carpal Tunnel Syndrome: A Randomized Double-Blind Controlled Trial

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Background: Corticosteroid injections have been used in carpal tunnel syndrome (CTS). However, there have been reported side effects associated with the drugs. Dexamethasone sodium phosphate has been studied to cause fewer side effects and the least neurotoxic agent. However, evidence of the efficacy of dexamethasone sodium phosphate in CTS is still lacking.

Objective: To compare the efficacy of dexamethasone sodium phosphate and triamcinolone acetonide in the treatment of CTS and observe their complications.

Materials and Methods: A prospective randomized double-blind controlled trial study was performed between January and December 2015 at HRH Princess Maha Chakri Sirindhorn Medical Center, Srinakharinwirot University in Nakhon Nayok province. Patients with CTS were randomly assigned into two groups based on the mode of treatment with either dexamethasone sodium phosphate or triamcinolone acetonide. Results of treatment were measured via hand grip power, positive Phalen's test time, Global Symptom Score for Carpal Tunnel Syndrome (GSS), Disability of Arm, Shoulder, and Hand Questionnaire (DASH) score. Negative outcome in patients that required surgery and the complications were also recorded.

Results: Sixty patients with CTS were randomly assigned into two groups [dexamethasone sodium phosphate group (n = 30) and triamcinolone acetonide group (n = 30)]. There was no difference of demographic data between the two groups. The dexamethasone sodium phosphate group improved significantly in positive Phalen's test time (mean difference -5.53; 95% confidence interval -0.56 to -10.50, p=0.029). In other measurement, the dexamethasone sodium phosphate group had better scores and had a lower number of patients who required and underwent surgery, but there was no significant difference between the two groups (p>0.05). No serious complication was detected at the time of follow-up.

Conclusion: In the treatment of CTS by corticosteroid injection, dexamethasone sodium phosphate was effective and improved significantly in positive Phalen's test time, compared to those treated with triamcinolone acetonide, which was widely prescribed. No serious complication was detected in either groups.

Keywords: Carpal tunnel syndrome, Steroid injection, Corticosteroid

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Carpal tunnel syndrome (CTS) caused by median nerve compression can often be found in patients who present with pain, numbness, and paresthesia. It could lead to a lower quality of life and affect daily activities of patients[1,2]. The treatment of CTS can be divided into two groups depending on the requirement of surgery[3,4]. Patients who do not require surgery can receive oral medication, physical therapy, or steroid injections[1-3].

Patients who receive oral medication are usually prescribed with non-steroidal anti-inflammatory drugs (NSAIDs) concurrently with physical therapy[1,2,4]. If the outcome is unsatisfactory then, a steroid injection into the carpal tunnel is indicated[4-7]. The popular corticosteroid compound used is triamcinolone acetonide, which has demonstrated positive treatment outcome[6-8]. However, there have been reported

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side effects associated with the drug including hypopigmentation at the site of injection, subcutaneous fat atrophy, crystallization of the drug in the membrane of the wrist, and post-injection flare. The biggest concern when using triamcinolone acetonide is that it might be injected accidentally into the median nerve. In that case, it would cause axonal and myelin degeneration, which can lead to median nerve palsy and paralysis of the thenar muscles. The paralysis of thenar muscles lead to the loss of function of the pollex, decreasing the utility of the hand, and causing difficulties in further treatment[7-9].

Dexamethasone sodium phosphate has been reported to cause fewer side effects. Furthermore, while a misplaced injection into the nerve causes damage, it is considered reversible[9]. It is also classified as safe for pregnant women[10,11]. Reports have also shown that the efficacy between dexamethasone sodium phosphate and triamcinolone acetonide in the treatment of trigger finger is comparable[12]. The pathophysiology of trigger finger and CTS are caused by inflammation and swelling of the surrounding synovial tissue of the flexor tendon[13,14]. However, there has not been studies that compare the use of dexamethasone sodium phosphate and triamcinolone acetonide in the treatment of CTS.

The purpose of the present research was to compare the treatment outcome of dexamethasone sodium phosphate and triamcinolone acetonide in CTS and to observe the side effects and complications that occur throughout the duration of the treatment.

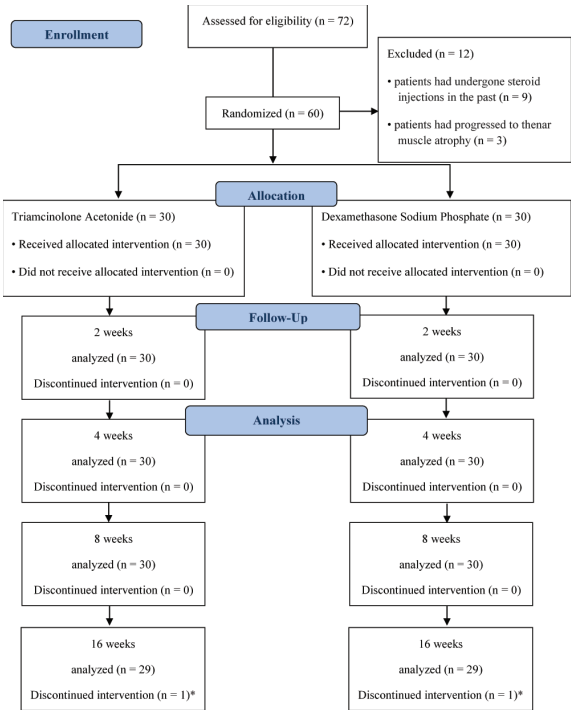
Materials and Methods

The present study received permission from the Ethics Committee of the Faculty of Medicine, Srinakharinwirot University. The research was conducted using a prospective, randomized double blind, control trial comprised of patients who received treatment at the HRH Princess Maha Chakri Sirindhorn Medical Center between January and December 2015. The criterion for selection was patients who had been diagnosed with CTS. The diagnosis and severity of CTS were established through a combination of history, and physical examination (muscle wasting, grip strength, sensation, Phalen's test, and Tinel sign positive). The patients suspected of having CTS would be confirmed with nerve conduction study before being enrolled in the present study[14,15]. Patients who refused to participate, patients with contraindication to medications used in the study, patients with previous steroid injections, pregnant women, patients with thenar muscle atrophy, and other associated pathologies of the hand were excluded. In patient with bilateral CTS, the most symptomatic hand (identified as the main source of symptoms and activity limitations) was treated. The patients were randomly assigned into two groups of 30 by blocked randomization via a computer-generated randomization list (two groups, 1:1 ratio) in varying blocks. Sequentially numbered, opaque, concealed envelopes containing group assignments were prepared.

All patients were briefed on the mode of treatment, benefits of steroid injections, possible side effects, included the treatment of complications that may arise, and had signed an informed consent prior to the beginning of the study. Then the randomization was done by the study nurse, who opened the envelope containing the group assignment.

Patients were separated into two groups; the experimental group would be received injections with dexamethasone sodium phosphate 4 mg/mL (1 mL) combined with 1% lidocaine (1 mL); and the control group would be received injections with triamcinolone acetonide 10 mg/mL (1 mL) combined with 1% lidocaine (1 mL). Both groups had a total of 2 mL of medication being administered by a nurse in a one-time only injection following instructions from a pre-sealed envelope. The nurse prepared the injection in a covered syringe for the orthopedic surgeons immediately after randomization. The orthopedic surgeons then injected the prepared steroid by 24-gauge needle on the ulnar side to the Palmaris longus tendon at the distal wrist crease to prevent the median nerve injuries from direct needle penetration, and advanced slowly1 to 2 centimeters as it transversed the flexor retinaculum in a 45 to 60-degree angle to the forearm. The needle was repositioned if resistance was encountered or patient reported pain or paresthesias in the fingers. Neither the patient nor the practitioner was aware of the medication being administered (double-blind). The follow up appointments were carried out by a physician at 2, 4, 8, and 16 weeks after the initial injection.

Measurement of the results were carried by hand grip power using a hand grip dynamometer, positive Phalen's test time, Global Symptom Score for Carpal Tunnel Syndrome (GSS), scores ranging from 0 to 50 points, with higher scores indicating increased severity of symptoms[16], and the Thai version of Quick Disabilities of the Arm, Shoulder, and Hand (Quick DASH-TH) questionnaire, which was widely accepted and reliable questionnaire with high clinical correlations[17-20]. The comparison between groups was performed during the follow up intervals.



All patients had complete baseline, 2, 4, and 8weeks data for the primary outcomes

* Patients with missing data at other follow-up times because of early surgery were included in the statistical model but the missing data were not replaced

Figure 1. Study flow diagram.

Statistical analysis

The total sample size of 51 patients randomized equally (1:1 randomization) to each treatment arm would provide 80% statistical power to detect a mean difference (MD) in primary end point (hand grip power, positive Phalen's test time, DASH score, and GSS score) at 16 weeks after randomization. The authors assumed a 20% difference in mean DASH score between groups as well as a common standard deviation of 25% (effect size 20/25 0.8), which is similar to previous study[12]. In the protocol, we aimed to enroll 60 patients to compensate for withdrawals. The analysis was performed according to intention to treat principles. The adequacy of randomization was tested by comparing demographic the data between groups at enrollment using the Independent t-test and/or the Mann-Whitney U test for continuous variables and Chi-square and/or Fisher's exact test for categorical variables. For each visit (at 2, 4, 8, and 16 weeks), Multivariable analysis, presented as MD and their 95% confidence intervals (95% CI), adjusted for baseline measurements was assessed differences between groups using analysis of covariance (ANCOVA). For overall MD, generalized estimating equations implemented (GEEs) under generalized linear model was used to compare between the two groups. Survival analysis between the groups were investigated using logrank test. The differences were considered statistically significant at *p*-value lower than 0.05. The data were analyzed using SPSS v.23.0 for Windows.

Results

The present study had seventy-two patients. Twelve patients were excluded and included nine patients because of steroid injections in the past and three patients that progressed to thenar muscle atrophy. Therefore, the present study consisted of sixty patients. They were evaluated and randomly divided into two groups. The triamcinolone acetonide group comprised of 30 patients and the dexamethasone sodium phosphate group also comprised of 30 patients (Figure 1). Patient's demographics data are shown in Table 1. Both groups were similar in terms of gender, age, occupation, dominant hand, side of symptoms, and duration of symptoms (p>0.05).

At the study onset, there was no significant differences observed between the groups with respected to hand grip power, positive Phalen's test time, DASH

Table 1. Demographic data of the patients*

Parameters	Triamcinolone acetonide injection (n = 30)	Dexamethasone sodium phosphate injection (n = 30)
Gender, n (%)		
Male	6 (20.0)	11 (36.7)
Female	24 (80.0)	19 (63.3)
Age (years)		
Mean ± SD	49.3±11.4	48.7±12.2
Median (min-max)	50 (28 to 72)	48.5 (28 to 71)
Occupation, n (%)		
Hand worker	19 (63.3)	21 (70.0)
Others	11 (36.7)	9 (30.0)
Dominant hand, n (%)		
Right	28 (93.3)	28 (93.3)
Left	2 (6.7)	2 (6.7)
Side of symptoms, n (%)		
Right	13 (43.3)	17 (56.7)
Left	17 (56.7)	13 (43.3)
Dominant hand	13 (43.3)	17 (56.7)
Non-dominant hand	17 (56.7)	13 (43.3)
Duration of symptoms (months)		
Mean ± SD	7.3±9.5	4.7±3.9
Median (min-max)	3.5 (1 to 48)	3.5 (1 to 18)

SD = standard deviation; min = minimum;max = maximum

* No significant differences between two groups

Table 2. Clinical outcomes of the patients

Outcomes	Triamcinolone acetonide		Dexamethasone sodium phosphate		MD	95% CI	*p*-value
	Mean	SD	Mean	SD			
Hand grip (kilogram)							
0 week	20.27	6.91	22.13	8.90	N/A	N/A	N/A
2 weeks	20.01	7.03	21.94	9.39	0.17	-0.84 to 1.19	0.732
4 weeks	21.02	7.30	22.87	9.29	0.14	-0.96 to 1.25	0.794
8 weeks	21.29	7.29	23.76	9.36	-0.37	-1.94 to 1.21	0.643
16 weeks	2.059	7.14	22.89	8.01	-0.31	-1.76 to 1.15	0.674
Overall	N/A	N/A	N/A	N/A	-0.09	-1.05 to 0.87	0.856
Positive Phalen's test time (second)							
0 week	19.83	10.38	24.83	12.69	N/A	N/A	N/A
2 weeks	20.83	9.57	27.33	13.44	-2.03	-4.92 to 0.86	0.165
4 weeks	34.33	12.91	39.00	13.67	-1.04	-6.36 to 4.28	0.697
8 weeks	42.33	16.95	52.00	11.42	-5.88	-12.40 to 0.65	0.076
16 weeks	53.00	12.77	57.67	5.53	-4.06	-9.46 to 1.32	0.136
Overall	N/A	N/A	N/A	N/A	-5.53	-0.56 to -10.50	0.029*
DASH score							
0 week	55.13	25.35	56.28	23.26	N/A	N/A	N/A
2 weeks	52.33	23.84	48.96	25.24	3.08	-2.93 to 9.10	0.309
4 weeks	33.47	23.17	29.60	23.06	3.95	-3.46 to 11.35	0.290
8 weeks	27.08	23.56	16.91	19.05	8.56	-0.67 to 17.80	0.069
16 weeks	20.10	24.04	9.94	15.83	7.50	-2.94 to 17.94	0.155
Overall	N/A	N/A	N/A	N/A	6.44	-3.52 to 16.41	0.205
GSS score							
0 week	30.90	8.73	29.00	9.40	N/A	N/A	N/A
2 weeks	26.83	8.99	24.27	10.86	0.90	-2.74 to 4.53	0.623
4 weeks	14.60	10.03	12.23	9.64	1.35	-2.76 to 5.46	0.512
8 weeks	9.97	10.68	5.79	7.62	2.47	-2.01 to 6.96	0.274
16 weeks	6.30	8.99	2.46	4.03	2.93	-0.86 to 6.72	0.127
Overall	N/A	N/A	N/A	N/A	2.88	-1.19 to 6.94	0.166

SD = standard deviation; MD = mean difference; CI = confidence interval; N/A = not applicable

* Statistical significance

score, and GSS score. For positive Phalen's test time at 2, 4, 8, and 16 weeks, there was not significant difference observed between the groups. However, the overall positive Phalen's test time improved significantly in the dexamethasone sodium phosphate group compare to triamcinolone acetonide group (MD -5.53; 95% CI -0.56 to -10.50, p=0.029) (Table 2).

In the other clinical measurements, there was not statistically significant difference observed between the two groups with respect to hand grip power, DASH score, GSS score at 2, 4, 8, 16 weeks post-treatment, and overall outcomes (p>0.05). Dexamethasone sodium phosphate group had better scores than triamcinolone acetonide group at week 2 to 16 post treatment (Table 2).

Minor side effects were observed in one patient of the triamcinolone acetonide group. The patient had localized redness and swelling around injection site, but the conditions recovered spontaneously at the time of follow up. There was no serious complication detected.

There was a higher number of patients who required and underwent surgery in the triamcinolone acetonide group (n = 6) compared to dexamethasone sodium phosphate group (n = 3). Most patients required surgery in both groups had symptoms relapsed after 16 weeks post-treatment but there was no significant difference between the two groups (p=0.288) (Figure 2).

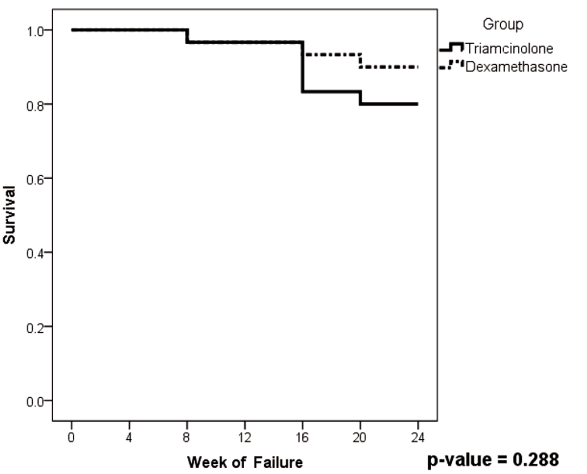


Figure 2. Survival analysis of triamcinolone acetonide and dexamethasone sodium phosphate group.

Discussion

Corticosteroid injections for the treatment of CTS have been used for more than a half of century and have been reported to be effective medicine[5-7]. In CTS, the synovial tissue of flexor tendon shows inflammation and edema. Corticosteroid drugs can reduce inflammation. Therefore, corticosteroid drugs can be used to reduce those inflammations[13,14]. In clinical practice, there is no indication that any corticosteroid should be used as a standard treatment in CTS.

Presently, triamcinolone acetonide is commonly used worldwide as a standard treatment in CTS. However, the characteristics of this drug are water-insoluble, white sediment, and crystallize at the injection site. Therefore, if a physician injects triamcinolone acetonide directly into the nerves, it could cause permanent nerve injury. The characteristics of dexamethasone sodium phosphate are clear, water soluble, and no crystallization. Therefore, if it was injected accidentally into nerve, the nerve injury could recover spontaneously[9]. Furthermore, the use of local dexamethasone injection has no systemic side effect such as changing the blood sugar level of the patients[21,22]. Mackinnon experimented neurotoxicity of the different steroids in an animal study and reported that hydrocortisone and triamcinolone caused widespread axonal and myelin degeneration, and dexamethasone was the least neurotoxic agent[9]. There is limited number of studies on the efficacy of dexamethasone for the treatment of CTS. Niempoog et al examined dexamethasone acetate injections for the treatment of CTS in pregnancy and their results showed the treatment was effective in controlling the symptoms of CTS[10]. Moghtaderi reported pain intensity and electrophysiological parameters were significantly improved after dexamethasone acetate injection in pregnant women with CTS[11].

The present prospective, randomized, double-blind, controlled, clinical study showed that there are noticeable improvements in clinical findings after local steroid injection and the results obtained with triamcinolone acetonide and dexamethasone sodium phosphate were effective. The results of the present study indicate that dexamethasone sodium phosphate is effective and improved significantly in positive Phalen's test time compare to triamcinolone acetonide. Furthermore, there was no serious complication related to the injections observed. However, minor side effects were observed in one patient of the triamcinolone acetonide group. The patient had post-injection flare (localized redness and swelling around injection site). This is a common side effect caused by the crystallization of corticosteroid esters in the injection site, which according to the pharmacological characteristics, is unlikely to be found in the dexamethasone sodium phosphate group[9]. Theoretically, it seems that dexamethasone sodium phosphate injection has fewer complications than other corticosteroids injection. Therefore, the use of dexamethasone sodium phosphate in CTS could be used as an alternative method for treatment of CTS, with the least complications.

The limitation of present study is the CTS patients were also deliberately not being diagnosed by nerve conduction study in all cases. Patients were included and excluded on the basis of clinical findings because nerve conduction study may result in false-negative in cases of true disease. The authors used a combination of clinical findings, along with nerve conduction study to study only a group of patients when CTS was suspected to confirm the diagnosis, and the Phalen's test used in the present study has evidence that there are variations in these values, which may be attributed to substantial inconsistencies in the method of examination and interpretation of the results. Another limitation is the short time of follow up after injection of CTS patients and the lack of information at 20 and 24 weeks' follow-up in clinical parameters.

Conclusion

The treatment of CTS by corticosteroid injection with dexamethasone sodium phosphate is effective and improve significantly in positive Phalen's test time compare to those treated with triamcinolone acetonide, which is widely prescribed currently. Therefore, it can be used as a substitute for there is no serious complication detected in either group.

What is already known on this topic?

Corticosteroid injections have been used in CTS. The popular corticosteroid compound used presently is triamcinolone acetonide. However, there have been reported side effects associated with the drug especially it would cause axonal and myelin degeneration, which could lead to median nerve palsy. Dexamethasone sodium phosphate has been reported to cause fewer side effects. However, there has not been studies conducted in the randomized control trial to prove the efficacy of dexamethasone sodium phosphate compare to triamcinolone acetonide in the treatment of CTS.

What this study adds?

Dexamethasone sodium phosphate is effective and improves significantly in positive Phalen's test time compare to those treated with triamcinolone acetonide. No serious complication associated with dexamethasone sodium phosphate were detected.

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Potential conflicts of interest

The authors declare no conflict of interest.

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