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ORIGINAL ARTICLE

# Platelet-rich plasma versus corticosteroid injections for carpal tunnel syndrome

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**ABSTRACT**

**Background:** Platelet-rich plasma therapy has the potential to promote peripheral nerve regeneration through the autologous supply of growth factors. Therefore, this study aimed to compare the effects of platelet-rich plasma injections with the effects of corticosteroid injections in the treatment of carpal tunnel syndrome.

**Methods:** In total, 40 patients with mild carpal tunnel syndrome were equally divided into two groups. Nerve conduction studies were carried out, and the Boston Carpal Tunnel Questionnaire was administered to both groups before treatment. One group of patients received platelet-rich plasma injections, and the patients in the other group received corticosteroid injections into the carpal tunnel. The patients were followed for 6 months. After 3 and 6 months, the nerve conduction studies and the Boston Carpal Tunnel Questionnaire were repeated.

**Results:** Although distal motor latencies did not change in either of the groups during the follow-up period, improvements in sensory nerve conduction were recorded after 3 months in both groups. However, there was no significant difference between the groups in the nerve conduction studies. In the Boston Carpal Tunnel Questionnaire, both the symptom severity score and the functional capacity score of the platelet-rich plasma group were significantly better than those of the corticosteroid group after 3 months, although there were no significant differences after 6 months.

**Conclusions:** Platelet-rich plasma injections may be considered for the temporary symptomatic relief of mild carpal tunnel syndrome.

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Boston questionnaire; carpal tunnel syndrome; nerve healing; platelet-rich plasma; nerve conduction study

## Introduction

Carpal tunnel syndrome (CTS) is the most common peripheral entrapment neuropathy, accounting for ~90% of all entrapment neuropathies [1]. Endoscopic and open carpal tunnel release are the standard treatments for patients with muscle atrophy with or without severe abnormalities on nerve conduction studies (NCS), and for patients whose symptoms do not respond to conservative treatment [1,2]. However, some patients only occasionally experience symptoms and have minimal-to-mild NCS findings. For such patients, there are various treatments that do not involve surgical procedures. Among these treatments, splinting and local injection of corticosteroids are the most commonly used and are the best supported by published evidence [3].

Although there is good evidence that the effects of local corticosteroid injections last longer than 15 months in 50% of patients with mild CTS [4], the remaining patients may still experience worsening of the symptoms. Additionally, local corticosteroid injections are associated with well-known complications such as median nerve injury and degenerative tendon ruptures [5].

Platelet-rich plasma (PRP) is an autologous fraction of human blood and has a greater concentration of platelets than baseline levels of whole blood. The main constituent of PRP is thought to be platelet degradation products, including multiple growth factors, which have well-defined roles in wound healing and inflammation. These growth factors include platelet-derived growth factor, transforming growth factor (TGF), epidermal growth factor, vascular endothelial growth factor (VEGF), and insulin-like growth factor-1, contained within the $\alpha$-granules of platelets [6].

Recently, PRP has received considerable attention for its effects on healing after musculoskeletal injuries [7,8]. PRP has also been shown to reduce nerve injury caused by 10% dextrose in the rabbit median nerve in an experimental model [9]. However, PRP as a treatment modality is still under investigation; its mechanism of action and appropriate dosing and indications remain unclear [10].

In this study, we aimed to compare the effects of local PRP injections with those of local corticosteroid injections in the treatment of idiopathic CTS using NCS and the Boston Carpal Tunnel Questionnaire (BCTQ) as outcome measures.

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## Materials and methods

### Patients and outcome measures

The present study was conducted according to the Helsinki Declaration of 1975. Informed consent was obtained from each patient. We recorded patients' demographics and pre-injection data, including age, sex, and BCTQ and NCS results. Only patients who had numbness, pain, and a tingling sensation in the distribution of the median nerve distal to the wrist and minimal-to-mild NCS findings indicating CTS according to the guidelines of the American Association of Electrodiagnostic Medicine (AAEM) [11] were included. Patients were excluded if they had moderate-to-severe NCS findings, space-occupying lesions within the carpal tunnel, traumatic CTS, pregnancy, diabetes mellitus, rheumatoid arthritis, or had had previous CTS surgery.

Patients who met the inclusion criteria were informed about the options of early surgical intervention vs local injection treatment. Patients who chose to have local injection treatment were distributed into two groups of equal size. In one group, the patients received local PRP injections into the carpal tunnel, whereas the other group received local corticosteroid injections into the carpal tunnel. The patients were followed for 6 months.

Before the injections were given, the BCTQ [12] was administered by an investigator who was blinded to the groups. This questionnaire comprises a symptom severity scale (SSS) and a functional status scale (FSS). Lower scores on the BCTQ indicate lesser symptom severity and better functional status of the patient. Post-injection follow-up visits were held after 3 and 6 months, during which the NCS and BCTQ were repeated.

All NCS were performed by the same investigator, who was blinded to the groups. NCS of the median nerve segment across the wrist were compared with those of another nerve segment that does not pass through the carpal tunnel (the ipsilateral ulnar nerve) to increase accuracy. An antidromic method was used for the sensory NCS, and sensory conduction velocity (SCV) was measured. Median and ulnar motor conduction studies measuring distal motor latency (DML) were also performed.

### PRP preparation

A peripheral venous blood sample of 15 mL was obtained from the upper extremities of the patients, and 1.5 mL of the sample was used for a platelet count. The remaining 13.5 mL was mixed in a 15-ml sterile centrifuge tube containing 1.5 mL of 3.2% sodium citrate and centrifuged at 4000 rpm for 10 minutes in a centrifuge (Digisystem, New Taipei City, Taiwan). After centrifugation, 2.5 mL of PRP was obtained from the middle fraction of the blood sample between the erythrocytes and the plasma (Figure 1). A PRP sample of 0.5 mL was separated for a platelet count.

### Local PRP injection

A 25-gauge needle was slowly inserted 1 cm proximal to the distal wrist-flexion crease just on the ulnar side of the palmaris longus tendon. The injection was stopped if the patient experienced pain or a sensation of pins and needles in the median nerve distribution. Approximately 2 mL of PRP was administered into the carpal tunnel. The patient was discharged after the injection. Limited movement was allowed in the wrist for 24 hours, and resting was recommended in the case of pain. Non-steroidal inflammatory drug use was restricted in both groups because of the possibility of platelet function inhibition. Intermittent icepack compression was recommended to relieve discomfort in the wrist.

Figure 1. A centrifuged blood sample containing platelet-rich plasma between the erythrocytes at the bottom and plasma at the top of the tube.

### Local corticosteroid injection

Triamcinolone acetonide 40 mg/1.0 mL (Kenacort-A, Bristol-Myers Squibb, New York, NY) was injected using the same technique as that described for the PRP injection.

### Statistical analysis

The data were analyzed using SPSS version 22.0 (IBM statistics for Windows version 22, IBM Corporation, New York, NY). Initial analyses revealed that the values of DML, SCV, SSS, and FSS were normally distributed. Paired sample *t*-tests were used to examine changes within the groups. The changes within the groups were then compared with each other using the general linear model repeated ANOVA (Wilks's lambda distribution). Pearson's correlation test and Kendall's tau-b test were used to determine if there were any correlations between the platelet count in the PRP and other variables. Bonferroni correction was used, which required a value of $p < 0.003$ to reflect statistical significance.

**Table 1.** Comparison of the results of median nerve conduction studies between groups given platelet-rich plasma and corticosteroid injections.

| | Groups | | | | |
|---|---|---|---|---|---|
| | PRP ($n = 20$) | | Corticosteroid ($n = 20$) | | PRP vs Corticosteroid |
| | Mean (SD) | $p^a$ | Mean (SD) | $p^a$ | $p^b$ |
| DML (ms) | | | | | |
| Pre-injection | 3.56 (±0.12) | | 3.55 (±0.13) | | .971 |
| Post-injection 3rd month | 3.56 (±0.11) | .821 | 3.55 (±0.10) | .577 | .596 |
| Post-injection 6th month | 3.59 (±0.09) | .142 | 3.57 (±0.11) | .215 | .635 |
| SCV (m/s) | | | | | |
| Pre-injection | 35.44 (±3.02) | | 35.81 (±2.44) | | .852 |
| Post-injection 3rd month | 37.84 (±2.44) | *.001* | 37.28 (±2.62) | *.001* | .196 |
| Post-injection 6th month | 36.74 (±2.72) | .756 | 35.96 (±2.28) | .941 | .341 |

[a]Compared with baseline.
[b]The difference between the two groups.
Significant values are shown in italics.
PRP: platelet-rich plasma; SD: standard deviation; DML: distal motor latency; SCV: sensory conduction velocity.

**Table 2.** Comparison of the results of the Boston carpal tunnel questionnaire between groups given platelet-rich plasma and corticosteroid injections.

| | Groups | | | | PRP vs Corticosteroid |
|---|---|---|---|---|---|
| | PRP ($n = 20$) | | Corticosteroid ($n = 20$) | | |
| | Mean (SD) | $p^a$ | Mean (SD) | $p^a$ | $p^b$ |
| Symptom severity scale | | | | | |
| Pre-injection | 2.97 (±0.50) | | 2.96 (±0.43) | | .431 |
| Post-injection 3rd month | 1.32 (±0.22) | *<.001* | 2.13 (±0.37) | *<.001* | *<.001* |
| Post-injection 6th month | 2.41 (±0.36) | .724 | 2.56 (±0.42) | .607 | .645 |
| Functional status scale | | | | | |
| Pre-injection | 2.06 (±0.61) | | 1.94 (±0.48) | | .537 |
| Post-injection 3rd month | 1.12 (±0.37) | *<.001* | 1.69 (±0.35) | *<.001* | *<.001* |
| Post-injection 6th month | 1.91 (±0.18) | .601 | 1.89 (±0.33) | .521 | .861 |

[a]Compared with baseline.
[b]The difference between the two groups.
Significant values are shown in italics.
PRP: platelet-rich plasma; SD: standard deviation.

## Results

A total of 40 patients were included in the study, with 20 in each group (four males and 16 females in each group). The mean ages of the patients were 48.8 (±5.8) years in the PRP group and 48.5 (±6.1) years in the corticosteroid group.

Results for DML and SCV are shown in Table 1. Overall, we were not able to demonstrate any significant differences in NCS values between the two treatment groups at any time point. While DML remained unchanged from pre-injection values to the 3 and 6 months follow-up, SCV showed significant improvement at 3 months for both groups. However, the improved SCV values were not maintained at 6 months.

Results for BCTQ are shown in Table 2. Both treatment groups demonstrated a significant improvement of SSS and FSS at 3 months. The improvement was more pronounced for the group who received PRP injection. For both treatment groups the improved BCTQ results were not maintained at 6 months.

The mean platelet count of the PRP was $1.532 \times 10^6$ ($\pm 3.42 \times 10^5$) and that of whole blood was $2.39 \times 10^5$ ($\pm 5.34 \times 10^4$). We were not able to show a significant correlation between the mean platelet count in the PRP and outcomes. In the PRP group, the SCV decreased in two patients after 3 months. These patients had the lowest platelet concentrations in their injections.

There were no complications or local or systemic side-effects from either type of injection.

## Discussion

Over the past few years, PRP therapy has grown in popularity as a treatment adjunct in various musculoskeletal and ophthalmic diseases as well as in aesthetic surgery [13]. PRP may have the potential to promote peripheral nerve regeneration through the autologous supply of growth factors [14–16]. Zheng et al. [17] showed that PRP considerably stimulated Schwann cell proliferation and increased the expression and secretion of nerve growth factor and glial cell line-derived neurotrophic factor.

Our study demonstrated that PRP injections into the carpal tunnel in patients with mild CTS relieved symptoms, as shown by the improvement in the BCTQ scores 3 months after the injections. Sanchez et al. [18] treated a patient with common peroneal nerve palsy using plasma-rich growth factors. They implied that the benefit could have been due to structural changes through the 'shifting' of the histological properties of extraneural and intraneural tissues from 'stiff scar tissue or fibrosis' to 'benign soft scar tissue'. This shifting effect may explain how local PRP injections could relieve the symptoms of idiopathic CTS.

The BCTQ for CTS [12] was the primary clinical outcome measure in this study. The significant decrease in the SSS and FSS score when compared with the baseline and the difference between the scores of the PRP group and the corticosteroid group after 3 months suggest that PRP provides better, but temporary, symptomatic relief, since such significance was not observed after 6 months. Recently, Park and Kwon [9] found that, compared with saline injections, PRP injections into the carpal tunnel of rabbits with dextrose-induced median nerve injury considerably reduced swelling of the median nerve, suggesting improved healing and the potential for better nerve recovery, as shown by histological examination. The temporary efficacy of PRP could be related to dosing, the frequency of administration, or simply to the temporary modification of the microenvironment.

The ideal concentration of platelets in PRP remains controversial. Qualitative and quantitative platelet changes may affect the regenerative power of PRP. Clinically effective PRP has been defined as having at least 4-times the normal platelet concentration [19]; however, the efficacy of PRP has been demonstrated with less-concentrated preparations [20]. In our study, the mean platelet count of PRP was 6.4-times higher than that of the whole blood. However, we were not able to show a significant correlation between the mean platelet count in the PRP and the results of the BCTQ.

The lack of significant long-term changes in NCS results, symptomatic, and functional improvement preclude the promotion of local PRP injections as a definitive treatment for the underlying pathology of CTS. We believe that PRP has modulatory effects on idiopathic CTS that cannot be explained merely by the effects of the one specific growth factor that it contains. Platelets can release TGF-β and VEGF, both of which have been shown to increase in CTS. These growth factors may be responsible for the subsynovial connective tissue fibrosis and neoangiogenesis that are commonly observed in CTS patients [21,22].

Patients with electrodiagnostically mild CTS are candidates for local corticosteroid injections. However, this treatment method limits tenocyte function by reducing collagen and proteoglycan synthesis, thereby reducing the mechanical strength of the tendon [23]. There is also a risk of median nerve injury, which may result from neurotoxicity of the injected corticosteroids [5]. In that sense, PRP could be a safer, reproducible alternative for temporary symptomatic relief in mild CTS.

As PRP is prepared from the patient's own blood, any concern about immunogenic reactions or disease transfer is eliminated [24]. However, the preparation of PRP is time consuming and requires special medical devices. Patients should be informed of the possibility of temporarily worsening symptoms after the injection due to the stimulation of the body's natural response to inflammatory mediators. Although adverse effects are uncommon and were not encountered in our study, infection and neurovascular injury are possible, and the treatment may not relieve symptoms [24].

The small sample size was a major limitation of this study. Other issues were the non-randomisation and the single-blinded study design. Due to time and resource issues, the choice of treatment was made by the participant after discussion with the clinician. This factor may clearly result in allocation bias, although there were no differences in any of the baseline measures between the two groups. The fact that both groups received an 'active' treatment that required an injection may also have limited any systematic bias between the groups. Another limitation of our study design was the lack of variance in the PRP dose; whether a higher injection volume, platelet concentration, or injection frequency would affect the clinical efficacy is unknown.

## Conclusions

According to the results of our study, we recommend that local PRP injections be considered an option for the temporary symptomatic relief of mild CTS. A larger, randomised study is required to determine if PRP has advantages over corticosteroid injections.

## Disclosure statement

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