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Platelet-rich plasma versus corticosteroid injections for carpal tunnel syndrome: Clinical and electrophysiological study

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ABSTRACT

Aim of the work: To evaluate the effectiveness of platelet rich plasma (PRP) injections in carpal tunnel syndrome (CTS) in comparison to corticosteroids clinically and electrophysiologically.
Patients and methods: The study included 36 patients with idiopathic mild to moderate CTS divided into two groups: group I received PRP and group II received corticosteroid injections into the carpal tunnel. Nerve conduction studies were carried out, visual analogue scale (VAS) and the Boston Carpal Tunnel Questionnaire (BCTQ) were administered to patients of both groups immediately before treatment, one and three months after treatment.
Results: The mean age (36.6 ± 8.8 years vs 38.5 ± 8 years), disease durations (19 ± 11 months vs 14 ± 9 months) and genders were comparable. PRP injection was significantly better than corticosteroids injection as regard VAS, symptom severity scale (SSS), functional status scale (FSS) of BCTQ as well as the distal sensory latency after one and three months of injection. There was no significant difference between both groups in other assessed parameters including distal motor latency, amplitude of compound muscle action potential, motor and sensory conduction velocities of the median nerve. There was a significant correlation between VAS and distal sensory and motor latency of the median nerve in both groups before, 1 and 3 months after injection.
Conclusions: Single local injection of the PRP proved to be an effective treatment choice for CTS. PRP therapy seemed to be superior to steroid, showing more improvement clinically as regard the pain and function and electrophysiologically as regard the distal sensory latency throughout the follow-up period.

1. Introduction

Carpal tunnel syndrome (CTS) is characterized by compression of the median nerve in the carpal tunnel [1]. Pain, tingling, numbness and loss of muscle strength are common symptoms of CTS which affect the performance of daily activities such as feeding, dressing, undressing, hygiene and writing, also it affects work productivity and quality of life [2,3]. In Egyptian females from Zagazig with fibromyalgia, CTS was found as one of the main causes of functional impairment [4].

Nerve conduction study (NCS) is a medical diagnostic test which commonly used in daily clinical practice to confirm clinical diagnosis of CTS [5,6]. In an Egyptian study, there was an insignificant difference between NCS and high resolution ultrasound in diagnosis of idiopathic CTS while US was valuable for exclusion of secondary cases and to detect anatomical variants of the median nerve [7]. Neurophysiological recording was found to support the diagnosis of CTS [8] and was also able to determine subclinical pronator syndrome [9].

The treatment of CTS involves conservative and surgical decompression interventions [10]. Medication, splinting, physical therapy and local injection of corticosteroids are the most commonly used methods to treat patients with mild to moderate symptoms of CTS [11]. Local steroid injection in CTS provides temporary relief of symptoms [12]. Corticosteroid injections are effective by decreasing the swelling in the connective tissue, which relieves pressure on the median nerve [13] and ultrasound-guided injection provides precision, maximizes the effectiveness and reduces complications [3].

Platelet rich plasma (PRP) is a concentrated blood plasma which contains roughly 3–5 times the number of platelets found in whole

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blood which contains a corresponding fold increase in growth factor concentrations [14]; these growth factors play variety of roles in tissue regeneration and healing [15–17]. In the last years, PRP has received considerable attention for its therapeutic effects. PRP has been widely used as a safe and novel treatment in dentistry, orthopedics, ophthalmology, neurosurgery and cosmetic surgery [18,19]. Recently, increasing evidence has revealed the beneficial effects of PRP on axon regeneration and neurological recovery [1]. In a study on Egyptian patients from Zagazig with plantar fasciitis, PRP injection was well tolerated and a safe therapeutic option comparable to steroid injection on follow-up [20]. Furthermore it was reported to be of similar effectiveness in treatment of Egyptian patients with rotator cuff tendinitis [21].

In this study, we aimed to evaluate the effectiveness of PRP injections in comparison to the effect of corticosteroid injections in the treatment of idiopathic CTS clinically and electrophysiologically.

2. Patients and methods

The study included 36 adult patients with idiopathic mild to moderate CTS diagnosed according to American Association of the Electrodiagnostic Medicine (AAEM) criteria [22] recruited from the Rheumatology and Rehabilitation outpatient clinic, Zagazig University Hospitals. After failure of conservative treatment for at least one month, they were enrolled in the study. Patients with thrombocytopenia, local infection, non-steroidal anti-inflammatory drugs (NSAIDs) use (<48 h pre-injection), secondary CTS (malignancy, pregnancy, rheumatological diseases, diabetes), past history of corticosteroid injection in the same wrist and patients with severe CTS were excluded. All patients gave their informed consent prior to their inclusion and the study was reviewed and approved by the Institutional Review Board (IRB) Committee of Zagazig University Hospitals.

Patients were equally divided into two groups; the first group included patients receiving local PRP injection whereas the second received local corticosteroid injection into the carpal tunnel. For all patients, full history was taken and clinical assessment included sensory and motor examination and provocative tests for CTS were done for all patients. Nerve conduction studies (NCS) were carried out. Visual analogue scale (VAS), symptom severity scale (SSS) and functional status scale (FSS) of Boston Carpal Tunnel Questionnaire (BCTQ) were administered to patients immediately before treatment, one and three months after treatment. NCS was performed in NCS and Electromyography (EMG) unit at Rheumatology and Rehabilitation Department, Faculty of Medicine, Zagazig University using (NIHON KOHDEN) electromyography equipment. The normative values taken in the NCS & EMG laboratory for median motor distal latency was $\leq$4.2 ms. and median sensory distal latency $\leq$3.5 ms. [23].

PRP preparation: The whole blood of 10 ml was taken from each patient. The blood is collected on citrated tube with the mixing rate was 9:1 in volume and mixing by inversion. The tubes were centrifuged (first centrifugation). The rotation speed and time was 704g (3000 rpm $\times$ 3 min), which was the minimum for separating red blood cells (RBCs) from plasma. The tubes were then taken out from the centrifuge and arranged on a holder and the plasma was collected by syringes and transferred to another sterile tube without anticoagulant and was centrifuged (second centrifugation). The second centrifugation was performed on plasma tube at 4000 rpm (1252g) for 15 min, which is the fastest speed of the machine and considered to be the realistic time as a daily practice. The supernatant platelet poor plasma (PPP) was removed leaving 2 ml of PRP on sediment (platelet pellet), and suspend the platelet pellets by gently shaking the tube. PRP activated by addition of 200 ul of 0.025 calcium chloride (CaCl2) [24].

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. 2 ml of PRP was injected into the carpal tunnel. Resting was recommended in the injected wrist for 24 h. NSAIDs use was restricted in both groups because of the possibility of platelet function inhibition.

Corticosteroid injection: Single injection of methylprednisolone acetate 40 mg/1.0 ml was injected using the same technique as that described for the PRP injection.

Statistical analysis: All data were collected, tabulated and statistically analyzed using SPSS 20.0 for windows (SPSS Inc., Chicago, IL, USA). Quantitative data were expressed as mean ± SD and median (range), and qualitative data as number and percentage. Continuous data were checked for normality by using Shapiro Walk test. Student's *t*-test was used to compare between two groups of normally distributed variables while Mann Whitney *U* test was used for non-normally distributed. ANOVA test was used to compare between >2 groups of normally distributed variables. Percent of categorical variables were compared using Chi-square test or Fisher's exact test when appropriate. Pearson's correlation coefficient was calculated to assess relationship between various study variables. All tests were two sided. p-value < 0.05 was considered significant.

3. Results

This study was carried out on 36 adult patients (4 males and 32 females) with idiopathic CTS; 6 mild and 30 moderate. Patients were divided into two groups according to the treatment approach. Group I (corticosteroid group) included 18 patients (16 females and 2 males) with mild to moderate (3 mild, 15 moderate) CTS. Their mean age was 36.6 ± 8.8 years (20–50 years) and the disease duration was 19 ± 11 months (3–39 months). Group II (PRP group) included 18 patients (16 females and 2 males) with mild to moderate (3 mild, 15 moderate) CTS. Their mean age was 38.5 ± 8 years (25–50 years) and disease duration was 14 ± 9 months (3–36 months). Results were comparable between both groups as regard, age, body mass index (BMI) and disease duration (p > 0.05).

There was a significant difference in VAS, SSS, FSS in both groups 1 and 3 months after injection. The improvement was significantly more pronounced in the PRP group (Table 1).

There was a significant difference in distal sensory and motor latency, amplitude of compound muscle action potential (CMAP) and sensory nerve action potential (SNAP), sensory and motor conduction velocity of the median nerve in both groups 1 and 3 months after injection, but the improvement was significantly more pronounced in PRP group as regard the distal sensory latency (Table 2, Fig. 1). There was no significant difference between both groups in other assessed NCS parameters including distal motor latency (DML), amplitude of CMAP, motor conduction velocity, amplitude of SNAP and sensory conduction velocity (SNCV) of the median nerve.

There was a significant correlation between VAS and distal sensory and motor latency of the median nerve in both groups before, 1 and 3 months after injection (Table 3).

4. Discussion

The effect of PRP on healing after musculoskeletal injuries has received considerable attention. The idea of using PRP in the treatment of this peripheral entrapment neuropathy originated from the various studies reporting positive effects of PRP on regeneration of peripheral nerves [25–30].

The current study demonstrated that PRP injections into the carpal tunnel relieved symptoms where the VAS was significantly

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Table 1
Visual analogue scale (VAS), symptom severity scale (SSS) and functional status scale (FSS) in patients with idiopathic carpal tunnel syndrome injected with platelet rich plasma or corticosteroids.

Parameter mean ± SD	Group I Corticosteroid (n = 18)		Group II PRP (n = 18)	p
VAS	Baseline	7.2 ± 1.3	7.05 ± 1.4	0.8
	After 1 mo.	3.5 ± 2.35	2.1 ± 2.6	**0.03**
	After 3 mo	5.2 ± 1.9	3.4 ± 2.09	**0.002**
	P	**0.0001**	**0.0001**	
SSS	Baseline	36.8 ± 7	33.2 ± 6	0.1
	After 1 mo.	22.3 ± 7.4	18.6 ± 10.7	**0.02**
	After 3 mo	28.6 ± 6.8	21.5 ± 10.2	**0.001**
	P	**0.0001**	**0.0001**	
FSS	Baseline	19.6 ± 4.6	18.3 ± 4.4	0.4
	After 1 mo.	13.9 ± 3.8	11.9 ± 5.3	**0.037**
	After 3 mo	16.7 ± 4	13.3 ± 4.8	**0.003**
	P	**0.0001**	**0.0001**	

VAS: Visual analogue scale (VAS), SSS: symptom severity scale, FSS: functional status scale, PRP: platelet rich plasma. Bold values are signficant at $p < 0.05$.

Table 2
Motor and sensory nerve conduction studies in patients with idiopathic carpal tunnel syndrome injected with platelet rich plasma or corticosteroids.

Parameter mean ± SD	Group I Corticosteroid (n = 18)		Group II PRP (n = 18)	p
Motor NCS	Distal motor latency			
	Baseline	5 ± 0.76	4.8 ± 0.5	0.3
	After 1 mo.	4.5 ± 0.68	4.3 ± 0.65	0.3
	After 3 mo	4.7 ± 0.7	4.5 ± 0.67	0.2
	P	**0.0001**	**0.0001**	
	Amplitude of CMAP			
	Baseline	5.9 ± 1.8	6.2 ± 2.4	0.5
	After 1 mo.	8.7 ± 5.6	11.2 ± 7.8	0.26
	After 3 mo	8.8 ± 5.5	11.5 ± 8	0.3
	P	**0.009**	**0.002**	
	Motor conduction velocity			
	Baseline	54 ± 4.3	56 ± 4.8	0.15
	After 1 mo.	56.6 ± 4	58 ± 4.5	0.2
	After 3 mo	54 ± 3.4	55.1 ± 2.7	0.28
	P	**0.01**	**0.01**	
Sensory NCS	Distal motor latency			
	Baseline	4.6 ± 0.4	4.5 ± 0.5	0.7
	After 1 mo.	4.3 ± 0.4	3.9 ± 0.5	**0.006**
	After 3 mo	4.5 ± 0.5	4 ± 0.56	**0.024**
	p	**0.01**	**0.0001**	
	Amplitude of SMAP			
	Baseline	16.4 ± 8	14.8 ± 7	0.48
	After 1 mo.	20.7 ± 7.3	20.3 ± 6.2	0.9
	After 3 mo	17.6 ± 6.1	19 ± 4.9	0.5
	p	**0.009**	**0.002**	
	Sensory conduction velocity			
	Baseline	39.7 ± 5.8	40.9 ± 5.8	0.5
	After 1 mo.	45.6 ± 6.6	49 ± 7.7	0.1
	After 3 mo	48.7 ± 6	49 ± 5.6	0.78
	p	**0.0001**	**0.0001**	

PRP: platelet rich plasma, NCS: nerve conduction study, CMAP: compound muscle action potential, SNAP: sensory nerve action potential. Bold values are significant at $p < 0.05$.

reduced 1 and 3 months after injection when compared with the baseline. These results go ahead with Nikolaou et al. [31], who demonstrated that single injection of PRP in 32 patients with mild to moderate CTS showed significant improvement in the VAS 1 and 3 months after injection. The present findings were in agreement with Malahias et al. [32] who found significant improvement in VAS after 1 and 3 months of PRP injection in the treatment of CTS.

The scores of symptom severity scale and functional status scale of Boston carpal tunnel questionnaire in PRP group were significantly reduced 1 and 3 months after injection. These results agreed with Uzun et al. [33] who showed significant improvement in BCTQ 3 months after PRP injection in 20 patients with mild CTS. They reported that the benefit may be due to structural changes through the shifting of extraneural and intraneural tissues from stiff scar tissue to benign soft scar tissue. This shifting effect may explain how local PRP injections could relieve the symptoms of idiopathic CTS. In accordance, Wu et al. [34] found significant reduction in the VAS and BCTQ scores after 1 and 3 months of PRP injection in CTS. The results of this work are in partial agreement with Raeissadat et al. [35], who showed significant improvement in the VAS and BCTQ after 10 weeks of single local injection of PRP with using wrist splint in treatment of 21 patients with mild and moderate idiopathic CTS.

In the patients receiving corticosteroids there was a highly significant improvement in VAS, SSS and FSS at 1 and 3 months after injection. These findings were in agreement with Agarwal et al. [36], who found that local methyl-prednisolone acetate injection in the management of mild CTS showed significant improvement in SSS, FSS of BCTQ 3 months after injection. The findings matched with Peters-Veluthamaningal et al. [37] who explained that

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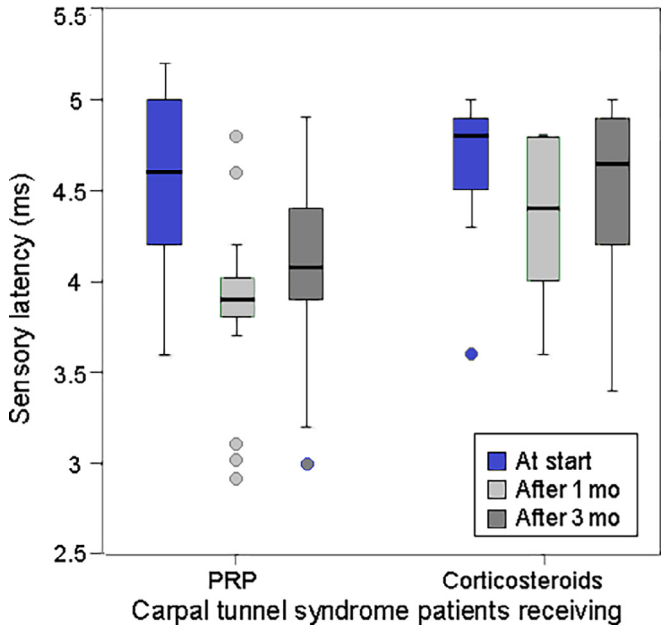

Fig. 1. Sensory latency in carpal tunnel syndrome patients receiving platelet rich plasma or corticosteroids at baseline, after 1 and 3 months treatment.

Table 3
Correlation of the visual analogue scale with the sensory and motor latencies at start, after 1 and 3 months in carpal tunnel syndrome patients receiving corticosteroids or platelet rich plasma.

Corresponding Variables r(p)		VAS in CTS patients (n = 36)			
		Steroids (n = 18)		PRP (n = 18)	
At start	SL	0.28	(0.26)	0.35	(0.15)
	ML	0.03	(0.92)	0.66	**(0.006)**
After 1 mo	SL	0.15	(0.55)	0.72	**(0.001)**
	ML	0.23	(0.34)	0.75	**(0.0001)**
After 3 mo	SL	0.32	(0.2)	0.65	**(0.003)**
	ML	0.17	(0.5)	0.75	**(0.0001)**

VAS: visual analogue scale, CTS: carpal tunnel syndrome, PRP: platelet rich plasma, SL: sensory latency, ML: motor latency. Bold values are significant at $p < 0.05$.

corticosteroid injection in the carpal tunnel significantly reduced the BCTQ scores 1 and 3 months after injection. In harmony, another Egyptian study [38] reported a significant reduction in the VAS and BCTQ scores 1 month after injection of corticosteroids in 30 patients with mild to moderate CTS.

In the present work, PRP injection was significantly better than corticosteroids as regard VAS, SSS and FSS of BCTQ scores at 1 and 3 months after injection. These results were in agreement with Uzun et al. [33], who showed that PRP was significantly better than corticosteroids injection as regard SSS and FSS after 3 months of injection.

In the PRP group there was a significant improvement in latency, amplitude and velocity of both SNAP and CMAP of the median nerve after 1 and 3 months of injection. In agreement, Wu et al. [34], found that PRP injection in 30 patients with mild to moderate CTS significantly improved the DML and SNCV after 1 and 3 months of injection.

In partial accordance, another study [35] found a significant reduction in latency of median SNAP, but not CMAP, 10 weeks after single local injection of PRP in patients with mild and moderate idiopathic CTS. The incompatibility may be contributed to the difference in dose and duration of follow up as they injected 1 ml PRP with follow up after 10 weeks while in the present work 2 ml PRP was injected with follow up of patients after 1 and 3 months.

In patients receiving corticosteroids, there was a significant improvement in median NCS parameters including latency, amplitude and velocity of both sensory and motor NCS of the median nerve 1 and 3 months after injection. In another study [36] a significant improvement in the values of the nerve conduction parameters including distal motor and sensory latencies at the wrist 3 months after local corticosteroids injection in the management of mild CTS was shown. Similarly in a study on Egyptian patients with mild to moderate CTS [38] an improvement in the electrophysiological parameters including latency, amplitude and velocity of both SNAP and CMAP 1 month after local steroid injection was found.

Only the distal sensory latency significantly improved in the PRP injection group after 1 and 3 months compared to those injected by corticosteroids. In disagreement, others reported no significant difference between both PRP and corticosteroid groups in the parameters of median NCS [33]. This discrepancy could be explained by the difference in sample size and grade of CTS. Among the limitations of this study is the small number of males in both groups, so comparing findings according to the gender was not possible, the small sample size and short follow up period.

In conclusion, single local injection of the PRP proved to be an effective treatment choice therapy for CTS. PRP therapy seemed to be superior to steroid, showing more improvement clinically as regard the pain and function and electrophysiologically as regard the distal sensory latency throughout follow up period.

Conflict of interest

None.

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