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ORIGINAL ARTICLE

Platelet-rich plasma in treatment of patients with idiopathic carpal tunnel syndrome

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Abstract

Background Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy in the upper extremity. Treatments for CTS alternate from conservative strategies to surgical decompression of median nerve. Few studies have applied platelet-rich plasma (PRP) for treating idiopathic CTS, with acceptable success rates. Further studies are needed to reach concrete conclusion.
Objective To study the effect of PRP injection in treatment of mild to moderate idiopathic CTS.
Methods This is a randomized controlled trial in a cohort of Egyptian patients suffered from mild to moderate CTS. They were randomly divided into two groups. Group 1: patients received ultrasound guided PRP injection and group 2 patients received ultrasound guided corticosteroid injection. The outcome measures were assessed via Visual Analog Scale, the Boston Carpal Tunnel Syndrome Questionnaire, electrophysiological findings in sensory and motor functions of median nerve and morphological changes of median nerve detected by ultrasound.
Results This study included 150 patients suffered from mild to moderate idiopathic CTS 15 did not provide the written consent and 37 participants were excluded from the study based on the exclusion criteria leaving only 98 patients to participate in the study they were divided into two groups PRP Injection Group (PRP-inj-G) — this group included 49 patients (40 females and 9 males) steroid injection Group (St-inj-G) — included 49 patients (41 females and 8 males). At the beginning of study there was no significant difference between both groups in all parameters. (a) PRP injection had significantly improved the clinical manifestations, the electrodiagnostic examination (EDX) parameters of the median nerve (MN), and the median nerve cross sectional area (m-CSA) at 1 month and 3 months post-injection evaluation in comparison to baseline recordings; (b) local steroid injection had significantly improved the clinical manifestations, the EDX parameters of the MN, and the m-CSA at 1 month and 3 months post-injection evaluation in comparison to baseline recordings and (c) PRP injection was superior to the local steroid injection in the improvement of clinical manifestations as well as the MN motor conduction velocity along the wrist-elbow segment, the sensory latency (SL) and the MN sensory conduction, this superiority was observed in third month follow-up suggesting better outcomes in long-term follow-up.
Conclusion Platelet-rich plasma could be effective treatment of mild to moderate idiopathic CTS and superior to corticosteroid in improving pain, function, and distal sensory latency of median nerve.
Trial registration Clinical Trials.gov Identifier: NCT03863873

Key Points:
- *PRP is effective treatment of mild to moderate CTS.*
- *PRP is superior to corticosteroids in improving pain and function in CTS.*

Keywords Carpal tunnel syndrome · Corticosteroids · Platelet rich plasma

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Abbreviations

APBm	Abductor pollicis brevis muscle
BCTQ	Boston carpal tunnel questionnaire
BCTQ-FSS	Boston carpal tunnel questionnaire functional status scale
BCTQ-SSS	Boston carpal tunnel questionnaire symptom severity scale
CTS	Carpal tunnel syndrome
CMAP	Compound muscle action potential
DML	Distal motor latency
EDX	Electrodiagnosis
GFs	Growth factors
ICTS	Idiopathic carpal tunnel syndrome
Inj.G	Injection group
m.CSA	Median cross sectional area
MN	Median nerve
PRP	Platelet rich plasma
RCT	Randomized controlled trial
SNAP	Sensory nerve action potential
SNCV	Sensory nerve conduction velocity
SL	Sensory latency
VAS	Visual analog scale

Introduction

Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy in the upper extremity. The prevalence of CTS in the general population has been estimated to be 1–5% [1]. Treatments for CTS vary beside conservative approaches (medication, night splint, steroid injections, and physical therapy) in accordance with surgical decompression about the median nerve. Despite the provision of several therapies, their efficacies generally were unfavorable or short-lived [2]. A record showed that round 60% to 70% sufferers along CTS underwent conservative therapy still had symptoms at 18 months follow-up [3]. Moreover, a latest study has proven that wrist splint treatment failure was 69% with 12 months follow-up [4]. Although conservative treatment is encouraged for mild-to-moderate CTS, surgical treatment is generally advocated for severe CTS, considering the fact that failure in surgery ranges out of 7–75% [5]. Therefore, it is necessary to explore and develop a unique non-surgical intervention for CTS. The use of native steroid injections has been mentioned within the literature as early as 1980. A coherence review [6] over that the native corticosteroid injection for severe CTS provided symptomatic profit at 1 month compared with placebo. Platelet-rich plasma (PRP) is autologous fraction of human blood and encompasses a bigger concentration of platelets than baseline levels of blood. The most constituent of PRP is believed to be platelet degradation products, together with multiple growth factors, that have well-defined roles in wound healing and inflammation [7]. Recently, the beneficial outcomes about PRP regarding nerve fiber regeneration were recorded in animal studies [8]. Since 2014, partial research applied PRP for treating medical peripheral neuropathy, with acceptable success rates [9].

Aim of the work

To study the effect of platelet-rich plasma injection in treatment of mild to moderate idiopathic carpal tunnel syndrome in comparison to effect of corticosteroids.

Patients

This randomized controlled clinical trial was carried out between July 2017 and June 2018, on 150 patients with mild to moderate idiopathic carpal tunnel syndrome recruited from rheumatology and rehabilitation outpatient clinic Mansoura University Hospital. Before inclusion in the study, the aim of work and all procedures of the study were explained to all participants. All participants were asked to provide a written consent. From the initial 150 participants invited to participate, 15 did not provide the written consent and 37 participants were excluded from the study based on the exclusion criteria leaving only 98 patients to participate in the study. The institutional research board of Faculty of Medicine, Mansoura University, approved this study (code: MS/17.06.34). The trial was conducted according to the Declaration of Helsinki's principles.

Clinical definition of CTS

In the present study, definition of CTS was made according to the American Academy of Neurology criteria [10].

1. Paresthesia, pain, swelling, or clumsiness of the hand aggravated by sleeping, maintained hand or arm posture, or repetitive hand action that is alleviated by a change in hand posture or by hand shaking.
2. Sensory impairment in the MN innervated territory of the hand.
3. Motor deficit or atrophy of the MN innervated muscles.
4. Positive Phalen's maneuver and/or Tinel's sign.

CTS was defined when criterion 1 + at least one criteria from 2 to 4 were fulfilled. However, in the current study, the patients who fulfilled criterion 3 were not included in the study. The diagnosis of CTS was confirmed by the EDX testing.

Electrophysiological parameters were assessed using (Neurowerk Sigma medizin-Tchnik). Mild to moderate idiopathic CTS with a neurophysiological confirmation were included in this study [11], Mild CTS—prolonged (relative or absolute) sensory latencies with normal motor studies. No evidence for axon loss. Moderate CTS—abnormal median sensory latencies as

noted for mild CTS, and (relative or absolute) prolongation of median motor distal latency. No evidence of axon loss. The cut-off points or normal range of this study were:

Upper limit of the median sensory nerve distal latency is ≤ 3.6 ms at a distance 14 cm away from the active recording. Upper limit of distal motor latency (DML) of the MN is < 4.3 ms at a distance 8 cm away from the thenar muscle belly. Median motor nerve conduction velocity, lower limit of normal 49 m/s. Median sensory nerve conduction velocity, lower limit of normal 49 m/s [12]. Cross sectional area was measured using ultrasound (siemens, Acuson P300) at the proximal inlet of the carpal tunnel using the pisiform bone as a landmark. The average of CSA was calculated using three measurements each [13]. Normal ranges for median nerve area at the distal wrist crease had varied among reports, ranging from 7.2 to 9.8 mm^2, the values for diagnosing CTS range from 9 to 15 mm^2 [14].

Inclusion criteria

Patients with mild-to-moderate idiopathic CTS with clinical manifestations failed to respond to conservative treatment (such as splint, medications, physical therapy) for at least 3 months and they were diagnosed by electrophysiological study and musculoskeletal ultrasound.

Exclusion criteria

Diabetes**,** hypothyroidism, rheumatoid arthritis, previous carpal tunnel decompressive surgery, cervical radiculopathy, polyneuropathy, brachial plexopathy, traumatic nerve injury, thoracic outlet syndrome, previous corticosteroid injection into the carpal tunnel in the preceding 4 weeks, anemia (hemoglobin < 10 g%), coagulopathy, and pregnancy.

Data collection

Baseline clinical data collected by interviewing the participants included demographic characteristics, history of associated medical conditions such as diabetes mellitus, previous corticosteroid injection into carpal tunnel or decompressive surgery of carpal tunnel, and presence of any systemic autoimmune disease.

Clinical examination

All patients were subjected to general systemic examination, local musculoskeletal examination of cervical spine and upper extremity, musculoskeletal and neurological examination to the cervical spine and upper extremity to reveal occurrence of the cervical radiculopathy or any condition that may affect the MN (e.g., plexopathy, signs suggestive of MN entrapment other than CTS, scar that may indicate previous cut wound/surgery of the MN). Wrist examination: presence of local condition of the hand that is associated with CTS (e.g., deformity, local scar of previous operation or trauma, tenosynovitis). Motor and sensory examination of median nerve and provocative clinical tests as Phalen's test and Tinel's test to diagnose carpal tunnel were done.

Laboratory assessment

blood samples were taken from all participants and analyzed for measuring complete blood count, erythrocyte sedimentation rate, random blood glucose, and c reactive protein at Mansoura University Hospital lab.

Randomization

After baseline evaluation, the eligible patients ($n = 98$) were randomly allocated into treatment groups by means of block randomization (size of block = 4, with last block size = 2). The patients in each block were randomized by the use of sealed envelope. Patients were blind to agents used in injection. After inclusion of a patient, a physiatrist drew an envelope and opened it (Fig. 1).

Methods

Intervention

PRP injection group (PRP-inj-G) This group included 49 patients (40 females and 9 males). Their age ranged from 20 to 60 years.

PRP preparation Sixteen milliliters of blood was obtained from each patient using special PRP kits (GD medical pharma, Dutch company). The blood was collected on citrated tubes with a mixing ratio of 9:1 by volume. Tubes underwent first centrifugation at a speed of 3000 rpm (704 g) for 3 min (to separate red blood cells from plasma). Plasma was then removed by syringe and then placed into another sterile tube with no anti-coagulant and then underwent second centrifugation at a speed of 4000 rpm (1252 g) for 15 min. The supernatant platelet poor plasma was then removed leaving 2 ml of PRP pellets in the sediment, and suspend the PRP pellets by gentle shaking of the tube. PRP is activated by adding 200 μl of 0.025 calcium chloride [15].

Ultrasound-guided injection Proper preparation with antiseptic solution of skin overlaying the point of injection was performed guided by ultrasonography (Siemens Acuson P300 machine). With the palm facing upward and the wrist joint in slight extension, the MN will be recognized at the inlet of the CT [16]. The injection was guided by ultrasound with the use of the ulnar in-plane technique [17]. Ulnar artery was

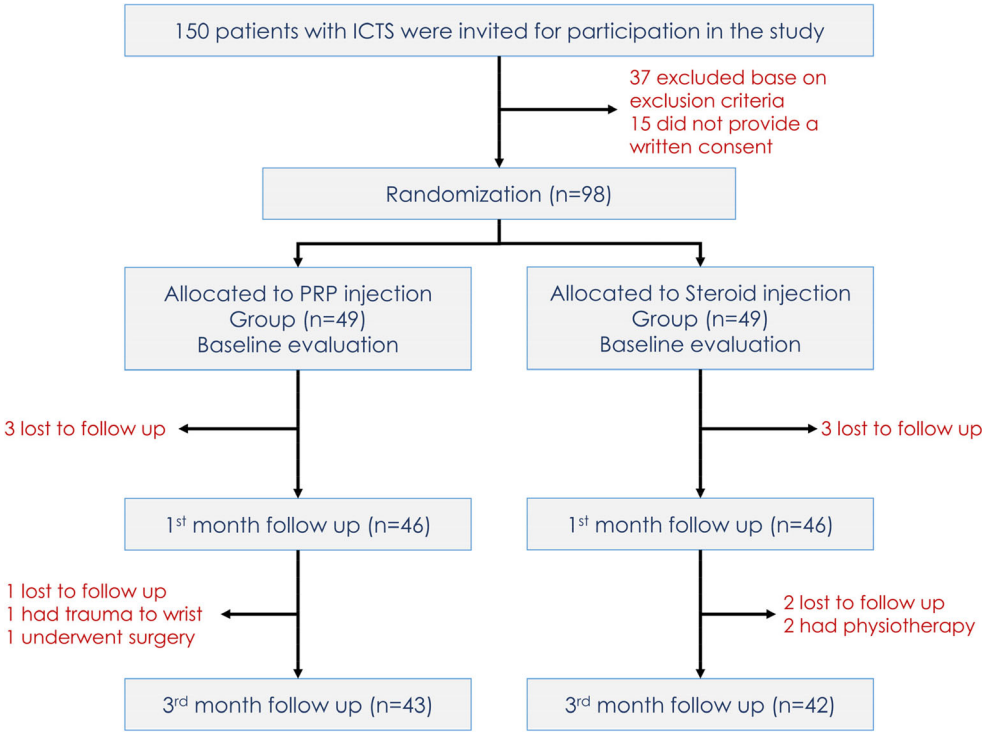

Fig. 1 Flow chart of participants in the study

identified by the means of Doppler imaging, and a 25-gage needle was introduced from the ulnar side of the wrist between CT and MN. Then the entire CT was scanned to confirm that the injection had dispersed through the proximal to the distal area of the CT. All patients were observed for 30 min post-injection for the possibility of dysesthesia or bleeding [16].

PRP injection A 25-gage needle was gently introduced 1 cm proximal to the distal wrist-flexion crease just to the ulnar side of the palmaris longus tendon and 2 ml of PRP was injected into the CT.

Steroid injection group (St-inj-G) included 49 patients (41 females and 8 males) with their age ranging from 20 to 60 years. Single injection of 1 ml of methyl prednisolone acetate 40 mg/ml using a technique similar to that described for the PRP injection.

Post injection care for both groups

- Some patients may have minimal to moderate discomfort after injection. So, to control pain, patients should apply ice on the injection site and also modify activity as tolerated.
- Rest for 1 day.
- Patient immediately returns to work 2days after injection.
- Pain medication in the form of paracetamol only was allowed for the next 3 months if needed. The patients were instructed to stop analgesics 48 h before visit to allow proper symptoms assessment.
- Physical therapy, splinting, or exercise were not allowed.

Outcome measures

The following parameters were assessed as primary composite outcome measures at baseline and after 1 month and after 3 months post-injection in all participants.

Primary outcome measures

1- Pain Visual Analogue Scale

The VAS-pain score is composed of a continuous horizontal line. This line is 100 mm in length. To measure the intensity of pain, the score is anchored by (0 score = no pain) at one end and (100 score = worst imaginable pain) on the other end. The patient places a mark to the VAS line at the point which represents the intensity of his pain [18].

2- Paresthesia, Phalen's, and Tinel's tests

Secondary outcome measures

1. Boston Carpal Tunnel Syndrome Questionnaire:

The Boston CT Questionnaire (BCTQ) is a patient-based outcome measure that was designed specifically for CTS patients. BCTQ has two distinct scales, the Symptom Severity Scale (BCTQ-SSS) containing 11 questions and the Functional Status Scale (BCTQ-FSS) containing eight items.

All questions were rated for degree of difficulty on a five-point scale. Each scale produces a final average score (sum of the scores divided by number of items) with a higher score indicative of greater disability. The BCTQ was used as an outcome measure in clinical trials, and has been reported as a validity and reliable tool for assessment of CTS [19].

2. Electrodiagnostic testing:

The anti-dromic sensory and motor nerve conduction studies of the MN were measured in all patients using Neurowerk Sigma medizin-Tchnik machine. For motor conduction study the MN is stimulated 8 cm proximal to the active electrode over the APBm (abductor pollicis brevis muscle) at elbow [20]. The DML (distal motor latency), conduction velocity along the elbow-wrist segment, and the distal compound muscle action potential (CMAP) amplitude from wrist stimulation were recorded.

For the median sensory conduction study, the active recording electrode was placed on the proximal phalanx at the second digit while the reference electrode was placed 4 cm distal to the active electrode. Stimulation to the MN was applied at 14 cm proximal to the active recording electrode [21]. The SL and the sensory nerve action potential (SNAP) amplitude were recorded.

3. Cross sectional area of the median nerve by ultrasound

US examination of the m-CSA for all patients was performed using a 7–13 MHz linear array probe with a calibrated device (Siemens, Acuson P300 apparatus) on the same day of EDX examination and clinical evaluation. All US examinations were performed with the wrists at the neutral position. The US examiner applied a minimal pressure force to avoid induction of artificial nerve deformation. Three measurements of the m-CSA at the level of most-protuberant portion of the pisiform bone were performed. The mean of the three measurements is calculated [22].

The investigators who assessed the baseline data and outcome measures were blind to treatment procedures, one experienced investigator in USA was responsible for US assessment, another one experienced investigator in NC and EMG was responsible for EDX assessment and another one clinical experienced investigator was responsible for clinical assessment.

Statistical analysis

All statistical analyses were performed using SPSS for windows version 20.0 (SPSS, Chicago, IL). Data were tested for normality of distribution prior to any calculations. All continuous data were normally distributed and were expressed in mean ±standard deviation (SD). Categorical data were expressed in number and percentage. The comparisons were determined using Student's *t* test for two variables or one-way ANOVA test for comparison among than two variables with continuous data. Chi-square test was used for comparison of variables with categorical data. Statistical significance was set at $p < 0.05$.

Results

At entry of the study, this current RCT included 98 patients with mild to moderate ICTS who were randomized into the two treatment groups, 49 patients in each group. From these patients, 43 patients in PRP-inj-G and 42 patients in the St-inj-G completed the 3 months follow-up period and hence only the data of these hands were included in the statistical analyses. Fourteen patients had bilateral ICTS, only the dominant hand underwent the intervention procedure and hence only the data of this hand is included in the statistical analysis.

As shown in Table 1, the two groups were matched for age, sex, BMI, and the inclusion of the dominant hand. The frequency of the presence of paresthesia and the positivity for Phalen's test and Tinel's test did not differ significantly between the two groups. Similarly, the average VAS-pain score, BCTQ-SSS, and the BCTQ-FSS did not differ significantly between the two groups.

Table 2 compares the findings of the motor and sensory EDX examination and the m-CSA by US examination between the hands with mild to moderate ICTS in the two groups at baseline. All motor and sensory EDX parameters as well as the m-CSA were similar in the two groups.

Table 3 demonstrated paresthesia, VAS-pain, positivity for Phalen's test, positivity for Tinel's test, BCTQ-SSS and BCTQ-FSS showed significant improvement. Motor conduction parameters, sensory conduction parameters and m-CSA were significantly improved along the study period in the PRP-inj-G.

Table 4 demonstrated paresthesia, VAS-pain, positivity for Phalen's test, positivity for Tinel's test, BCTQ-SSS, and BCTQ-FSS showed significant improvement, motor conduction parameters, sensory conduction parameters, and m-CSA were significantly improved along the study period in the St-inj-G.

Table 5 compares clinical manifestations, electrodiagnostic, and US findings of the studied ICTS hands between the two groups after 1 month follow up period. The frequency of the presence of paresthesia and the positivity for Phalen's test and Tinel's test had been decreased in the two groups than in the baseline, however, these parameters did not differ significantly between the two groups. Similarly, the average VAS-pain score, BCTQ-SSS, and the BCTQ-FSS also were improved but did not differ significantly between the two groups. All the motor and

Table 1 Comparison of general characteristics, clinical features of patients with CTS in the PRP-inj group and Steroid-inj group

	PRP-inj-G(43)	St-inj-G(42)	Student's *t* test	
	Mean ± SD	Mean ± SD	*t*	*p*
Age (years)	38.3 ± 6.4	40.7 ± 9.4	1.389	0.171
BMI (kg/m^2)	30.9 ± 3.8	30.7 ± 4.4	0.361	0.719
Sex (*n*, %)				
Male	8, 18.6%	6, 14.3%		
Female	35, 81.4%	36, 85.7%	0.288[a]	0.591
Dominant hand (*n*, %)	37, 86.0%	34, 81.0%	0.401[a]	0.527
Symptoms				
Paresthesia	39, 90.7%	37, 88.1%	0.152[a]	0.697
VAS-pain	68.1 ± 6	69.5 ± 4.9	1.178	0.242
Signs				
+ve Phalen's test	42, 97.7%	40, 95.2%	0.370[a]	0.616
+ve Tinel's test	34, 79.1%	36, 85.7%	0.645[a]	0.422
BCTQ				
BCTQ-SSS	3.5 ± 0.4	3.4 ± 0.4	1.102	0.274
BCTQ-FSS	3.5 ± 0.4	3.4 ± 0.5	1.282	0.204

[a] X2 value, Chi square test

BCTQ Boston Carpal Tunnel Questionnaire, *BCTQ-SSS* Boston Carpal Tunnel Questionnaire symptoms severity scale,BCTQ-FSS Boston Carpal Tunnel Questionnaire Functional Status Scale

sensory EDX parameters as well as the m-CSA did not differ significantly between the two groups.

Table 6 showed at 3 months follow-up, the frequency of the Phalen's test and Tinel's test positivity and the frequency of the paresthesia in distribution of MN were significantly lower in the PRP-inj-G in comparison to the St-inj-G. The average VAS-pain score was also significantly lower in the PRP-inj-G compared to the St-inj-G. The BCTQ-SSS and BCTQ-FSS were significantly improved in the PRP-inj-G. The motor conduction velocity of the median nerve along the elbow-wrist segment in the PRP-inj-G was significantly higher than the St-Inj-G ($p = 0.002$). In addition, the SL of the median nerve in the PRP-inj-G was significantly lower than the St-Inj-G ($p = 0.046$). The amplitude of the SNAP (sensory nerve action potential) of the median nerve in the PRP-inj-G was significantly higher than the St-Inj-G ($p < 0.001$). On the other hand, DML, distal CMAP amplitude, MN sensory conduction, and the m-CSA did not differ significantly between the two groups at 3 months post-injection evaluation.

Complications of PRP and corticosteroid injection

There were no recorded side effects in all patients. Just increase pain sensation in PRP group in the first 48 h following injections, patients received paracetamol and local ice application.

Discussion

The effects of the PRP injections on the musculoskeletal diseases after injury had gained much attention. The use of PRP as a treatment option in cases with peripheral entrapment neuropathy was based on the data obtained from several studies that revealed positive effects of PRP on peripheral nerve regeneration as PRP was found to hasten functional axon recovery and can limit nerve damage [23]. Conversely, Piskin et al. (2009) [24] found that PRP did not augment the regeneration of the axons of the damaged peripheral nerves in mice. Thus, this study was designed to evaluate the effects of the PRP injection compared to the steroid injection in the patients with mild or moderate ICTS.

Table 2 Comparison of electro-diagnostic and US findings between the PRP-inj-G and Steroid-inj-G at baseline

	PRP-inj-G(43)	St-inj-G(42)	Student's *t* test	
	Mean ± SD	Mean ± SD	*t*	*p*
Motor conduction studies				
Distal motor latency (msec)	4.9 ± 0.9	5.0 ± 0.7	0.508	0.613
Motor conduction (m/s)	56.2 ± 2.3	57.1 ± 3.2	4.373	0.131
Distal CMAP amplitude (mV)	5.8 ± 1.4	6.4 ± 1.7	1.724	0.088
Sensory conduction studies				
Sensory latency (msec)	5.2 ± 0.5	4.9 ± 0.5	2.737	0.068
Sensory conduction (m/s)	32.2 ± 1.9	31.4 ± 2.2	1.775	0.080
SNAP amplitude (μV)	16.3 ± 1.8	17 ± 1.7	1.790	0.077
US examination				
m-CSA (mm^2)	13.6 ± 1.2	13.2 ± 1.3	0.408	0.215

CMAP compound muscle action potential, *SNAP* sensory nerve action potential, *m-CSA* median nerve cross sectional area

Table 3 Change in the clinical data, EDX, and US findings along the study period in the PRP-inj-G(43)

	At baseline	After 1 month	After 3 months	Repeated measure ANOVA test	
	Mean ± SD	Mean ± SD	Mean ± SD	*F*	*p*
Symptoms					
Paresthesia	39, 90.7%	8, 18.6%	4, 9.3%	58.234	< 0.001
VAS-pain	68.1 ± 6.0	24.4 ± 7.3	21.8 ± 6.5	150.217	< 0.001
Signs					
+ve Phalen's test	42, 97.7%	8, 18.6%	4, 9.3%	62.423[a]	< 0.001
+ve Tinel's test	34, 79.1%	6, 14.0%	2, 4.7%	52.225[a]	< 0.001
BCTQ					
BCTQ-SSS	3.5 ± 0.4	2.4 ± 0.6	2.0 ± 0.7	94.739	< 0.001
BCTQ-FSS	3.5 ± 0.4	3.1 ± 0.4	2.1 ± 0.6	111.916	< 0.001
Motor conduction studies					
Distal motor latency (msec)	4.9 ± 0.9	4.5 ± 0.6	4.4 ± 0.6	30.706	< 0.001
Motor conduction (m/s)	56.2 ± 2.3	57.1 ± 1.9	57.4 ± 3.5	34.416	< 0.001
Distal CMAP amplitude (mV)	5.8 ± 1.4	8.6 ± 2.1	8.8 ± 2.2	43.924	< 0.001
Sensory conduction studies					
Sensory latency (msec)	5.2 ± 0.5	4.2 ± 0.8	3.8 ± 0.8	114.136	< 0.001
Sensory conduction (m/s)	32.2 ± 1.9	34.9 ± 2.5	35.7 ± 3.6	40.403	< 0.001
SNAP amplitude (μV)	16.3 ± 1.7	19.1 ± 2.3	18.5 ± 2.2	37.847	< 0.001
US examination					
m-CSA (mm^2)	13.6 ± 1.2	10.9 ± 1.3	10.6 ± 1.4	99.127	< 0.001

[a] X2 value, Chi square test

BCTQ Boston Carpal Tunnel Questionnaire, *BCTQ-SSS* Boston Carpal Tunnel Questionnaire Symptom Severity Scale,BCTQ-FSS Boston carpal Tunnel Questionnaire Functional Status Scale, *CAMP* compound muscle action potential, *SNAP* sensory nerve action potential, *m-CSA* median nerve cross sectional area

The results of the present study had shown that PRP injection had resulted in significant VAS-pain score reduction at 1 month and at 3 months post-injection in comparison to the pain level at the baseline evaluation.

In 2015, Malahias and co-workers was the first who used the US-guided injection of 1 to 2 mL of PRP in patients who had mild CTS. The study included 14 patients (but no controls) and revealed favorable short-term results (3 months post injection) [25]. In line with the findings of the present study, the study by Malahias et al. (2015) [25] reported that single PRP injection in 14 patients who had mild ICTS for more than 3 months duration had significantly improved the VAS pain 1 month and 3 months after injection. Malahias et al. (2015) also reported that, 1 month after the single injection of PRP, pain had almost disappeared in eight patients and it was noticeably alleviated in three patients and after 3 months the pain was not greatly alleviated only in three patients.

In agreement with our findings, Atwa et al. (2018) [26] injected PRP in the 36 wrists with mild to moderate ICTS and found that pain score on VAS was significantly decreased and BCTQ scores were improved at 1 and 3 months post-injection in comparison to the baseline.

In accordance, Wu et al. (2017) [16] designed a RCT to evaluate the effects of PRP after 6 months in 60 patients with 20.0% of the patients had minimal or mild and 80.0% had moderate CTS and compared the results of the PRP to the effect of night splinting. They found that PRP injection resulted in a significant improvement of the VAS score and in the BCTQ score at 3 months and persisted for at least 6 months in comparison to the group treated with night splinting. Therefore, the study of Wu et al. (2017) [16] showed that the tendency for improvement of the VAS, the BCTQ (both symptom and function scores), and the m-CSA in comparison to the baseline values or in comparison to the controls (used night splinting) seems to remain after a long follow-up duration.

The findings of the current study are also in consistency with Uzun et al. (2017) [27] who followed the patients for 6 months and found that after 3 and 6 months, BCTQ was significantly improved after PRP injection into the CT of 20 patients with CTS.

Recently, Uzun et al. (2017) [27] designed a clinical trial to compare the effect of single injection of PRP compared to single corticosteroid injection in patients with minimal or mild CTS. Although the study revealed that PRP injection resulted in a significant improvement of BCTQ (both the symptom

Table 4 Change in the clinical data, EDX, and US findings along the follow-up period in the St-inj-G(42)

	At baseline	After 1 month	After 3 months	Repeated measure ANOVA test	
	Mean ± SD	Mean ± SD	Mean ± SD	*F*	*p*
Symptoms					
Paresthesia	37, 88.1%	9, 21.4%	11, 26.2%	50.537[a]	< 0.001
VAS-pain	69.5 ± 4.9	25.9 ± 8.3	25.2 ± 7.1	116.422	< 0.001
Signs					
+ve Phalen's test	40, 95.2%	9, 21.4%	11, 26.2%	56.417	< 0.001
+ve Tinel's test	36, 85.7%	6, 14.3%	8, 19%	54.405	< 0.001
BCTQ					
BCTQ-SSS	3.4 ± 0.4	2.5 ± 0.5	2.4 ± 0.7	89.111	< 0.001
BCTQ-FSS	3.4 ± 0.5	3.0 ± 0.4	2.5 ± 0.6	71.821	< 0.001
Motor conduction studies					
Distal motor latency (msec)	5.0 ± 0.7	4.6 ± 0.6	4.5 ± 0.8	20.623	< 0.001
Motor conduction (m/s)	57.1 ± 3.2	59.7 ± 3.6	59.9 ± 3.7	40.914	< 0.001
Distal CMAP amplitude (mV)	6.4 ± 1.7	9.3 ± 3	9.5 ± 3	47.543	< 0.001
Sensory conduction studies					
Sensory latency (msec)	4.9 ± 0.5	4.1 ± 0.6	4.1 ± 0.7	73.000	< 0.001
Sensory conduction (m/s)	31.4 ± 2.2	34.2 ± 2.5	34.3 ± 2.8	65.500	< 0.001
SNAP amplitude (μV)	17 ± 1.7	19.7 ± 2.3	19.2 ± 2.2	46.112	< 0.001
US examination					
m-CSA (mm^2)	13.2 ± 1.3	11.2 ± 1.6	10.9 ± 1.7	74.143	< 0.001

[a] X2 value, Chi square test

BCTQ Boston carpal tunnel Questionnaire, *BCTQ-SSS* Boston Carpal Tunnel Questionnaire Symptom Severity Scale;BCTQ-FSS Boston Carpal Tunnel Questionnaire Functional Status scale, *CAMP* compound muscle action potential, *SNAP* sensory nerve action potential, *m-CSA* median nerve cross sectional area

domain score and that function domain score) at 3 month post-injection evaluation in comparison to the corticosteroid injection group, the difference was insignificant after 6 months. Furthermore, no significant difference between the two groups regarding the EDX parameters was detected. The same study reported that PRP provides better, but temporary, symptomatic relief, since such improvement was not observed after 6 months. Uzun et al. (2017) [27] suggested that the temporary efficacy of PRP can be attributed to the dosing, the frequency of administration, or simply to the temporary modification of the micro-environment.

Uzun et al. (2017) [27] reported that the benefits of the PRP can be attributed to the diminished scar reaction through shifting of the histological properties of extra-neural tissue and intra-neural tissue from stiff scar tissue or fibrosis to a more benign soft scar tissue during the axonal regeneration.

The results of this work partially agree with Raeissadat et al. (2018) [28], who randomized 41 women with mild to moderate ICTS into two groups; a control group used wrist splinting only and a PRP group that received wrist splinting along with a single local injection of PRP and found that VAS pain and BCTQ significantly decreased in both groups after 10 weeks from treatment.

Our findings are in consistency with the findings of the study by Atwa et al. (2018) [26] who reported significant improvements of the pain and of the BCTQ in CTS patients after local steroid injection. These findings also agree with the findings of Agarwal and co-workers (2005) [29], who reported that intra-carpal single methylprednisolone acetate injection in the patients who had mild CTS had significantly improved the SSS and FSS domains of BCTQ after 3 months following injection. The results of this study matched also with the findings of Peters-Veluthamaningal et al. (2010) [30] who observed that intra-carpal injection of corticosteroid (1 ml of tri-amcinolon acetonide 10 mg/ml) in the CT significantly improved the scores of the BCTQ domains after 1 and 3 months post-injection, however, outcomes of the BCTQ had deteriorated after 12 months. In consistency, El-Badawy (2015) [31] observed a significant reduction of the pain score on the VAS scale and BCTQ score 1 month following intra-carpal corticosteroid injection in 30 wrists with mild or moderate CTS.

The results of this study revealed that single PRP injection was significantly superior to intra-carpal corticosteroid injection as regards the improvement of the VAS pain score and the scores of the BCTQ symptoms and function domains at

Table 5 Comparison of clinical, electrodiagnostic, and US findings between the PRP-inj-G and Steroid-inj-G at 1 month follow-up

	PRP-inj-G(43)	St-inj-G(42)	Student's *t* test	
	Mean ± SD	Mean ± SD	*t*	*p*
Symptoms				
Paresthesia	8, 18.6%	9, 21.4%	0.106[a]	0.745
VAS-pain	24.4 ± 7.3	25.9 ± 8.3	0.337	0.737
Signs				
+ve Phalen's test	8, 18.6%	9, 21.4%	0.106[a]	0.745
+ve Tinel's test	6, 14.0%	6, 14.3%	0.002[a]	0.965
BCTQ				
BCTQ-SSS	2.4 ± 0.6	2.5 ± 0.5	0.268	0.790
BCTQ-FSS	3.1 ± 0.4	3.0 ± 0.4	1.283	0.203
Motor conduction studies				
Distal motor latency (msec)	4.5 ± 0.6	4.6 ± 0.6	0.955	0.342
Motor conduction (m/s)	57.1 ± 1.9	59.7 ± 3.6	3.586	0.082
Distal CMAP amplitude (mV)	8.6 ± 2.1	9.3 ± 3	1.086	0.281
Sensory conduction studies				
Sensory latency (msec)	4.2 ± 0.8	4.1 ± 0.6	0.621	0.537
Sensory conduction (m/s)	34.9 ± 2.5	34.2 ± 2.5	1.276	0.205
SNAP amplitude (μV)	19.1 ± 2.3	19.7 ± 2.3	1.186	0.239
US examination				
m-CSA (mm^2)	10.9 ± 1.3	11.2 ± 1.6	0.821	0.414

[a] X2 value, Chi square test

BCTQ Boston Carpal Tunnel Questionnaire, *BCTQ-SSS* Boston Carpal Tunnel Questionnaire Symptom Severity Scale,BCTQ-FSS Boston Carpal Tunnel Questionnaire Functional Status Scale, *CAMP* compound muscle action potential, *SNAP* sensory nerve action potential, *m-CSA* median nerve cross sectional area

4 weeks and 12 weeks post-injection. These observations agree with the findings of Atwa et al. (2018) [26] and Uzun et al. (2017) [27] as both studies reported that single PRP injection was significantly superior to the intra-carpal corticosteroid injection as regards these clinical parameters at 1 month and 3 months evaluations following the injection.

Consistent to our findings, Wu and colleagues (2017) [16] reported that PRP injection in 30 wrists with mild or moderate CTS had resulted in significant improvement of the DML and the SNCV at 4 weeks and 12 weeks following the injection compared to the baseline. In addition, Atwa et al. (2018) [26] observed that single PRP injection resulted in a significant difference in DML and distal SL, CMAP amplitude, SNAP amplitude, sensory and motor conduction velocities of MN in patients treated with PRP injection and in patients treated with corticosteroid injection 4 weeks and 12 weeks post-injection, and these improvements were significantly more prominent in SL of the PRP injection group. Atwa et al. (2018) [26] also reported insignificant differences between the two groups in other evaluated EDX measurements such as DML, CMAP and SNAP amplitudes, and motor and sensory conduction velocities of MN. Most of the findings of the Atwa et al. (2018) [26] study were similar to the result of this study.

In contrast, Raeissadat et al. (2018) [28] reported no significant improvement in the DML nor in SL of the MN after 10 weeks from a single local PRP injection in the patients who had mild or moderate ICTS. The discrepancy can be attributed to the differences in the dose of the injected PRP and the duration of the follow-up period because they injected 1 ml of PRP and followed-up the patients for only 10 weeks while in this study, 2 ml of PRP was injected and the patients were re-assessed after 1 and 3 months. Unfortunately, the ideal concentration of platelets in PRP remains controversial and there is no widely agreed RPR dosing and it is reasonable that qualitative and quantitative platelet changes may affect the regenerative power of PRP.

Our observations were in line with that of Atwa and coworkers (2018) [26]. In the study by Agarwal et al. (2005) [29], a significant improvements in the MN conduction parameters including DML and SL at 3 months following intra-carpal corticosteroid injection in patients with CTS was reported. Likewise, in a clinical trial included 30 Egyptian patients who had mild or moderate CTS, El-Badawy (2015) [31] reported an improvement in the EDX parameters including DML, SL, CMAP, and SNAP amplitudes and in conduction velocity 1 month following intra-carpal steroid injection.

Table 6 Comparison of clinical, electrodiagnostic, and US findings between the PRP-inj-G and Steroid-inj-G at 3 months follow-up

	PRP-inj-G(43)	St-inj-G(42)	Student's t test	
	Mean ± SD	Mean ± SD	*t*	*p*
Symptoms				
Paresthesia	4, 9.3%	11, 26.2%	4.170[a]	0.041
VAS-pain	21.8 ± 6.5	25.2 ± 7.1	2.100	0.040
Signs				
+ve Phalen's test	4, 9.3%	11, 26.2%	4.170*	0.041
+ve Tinel's test	2, 4.7%	8, 19%	4.242[a]	0.039
BCTQ				
BCTQ-SSS	2.0 ± 0.7	2.4 ± 0.7	2.752	0.007
BCTQ-FSS	2.1 ± 0.6	2.5 ± 0.6	1.385	0.002
Motor conduction studies				
Distal motor latency (msec)	4.4 ± 0.6	4.5 ± 0.8	0.587	0.559
Motor conduction (m/s)	57.4 ± 3.5	59.9 ± 3.7	3.203	0.002
Distal CMAP amplitude (mV)	8.8 ± 2.2	9.5 ± 3	1.016	0.313
Sensory conduction studies				
Sensory latency (msec)	3.8 ± 0.8	4.1 ± 0.7	2.123	0.037
Sensory conduction (m/s)	55.7 ± 3.6	54.3 ± 2.8	1.998	0.049
SNAP amplitude (μV)	18.5 ± 2.2	19.2 ± 2.2	1.570	0.120
US examination				
m-CSA (mm^2)	10.6 ± 1.4	10.9 ± 1.7	0.959	0.340

[a] X2 value, Chi square test

BCTQ Boston Carpal Tunnel Questionnaire, *BCTQ-SSS* Boston Carpal Tunnel Questionnaire Symptom Severity Scale,BCTQ-FSS Boston Carpal Tunnel Questionnaire Functional Status Scale, *CAMP* compound muscle action potential, *SNAP* sensory nerve action potential, *m-CSA*, median nerve cross sectional area

In the study by Atwa et al. (2018) [26], only the SL was significantly lower in the group injected with PRP 1 month and 3 months following injection in comparison to the corticosteroids injection group. In discrepancy, Uzun et al. (2017) [27] found no significant differences between the PRP injection group and corticosteroid injection group regarding the EDX parameters of MN. This inconsistency can be attributed to the differences in the sample size and severity of the CTS of included patients.

Our findings are compatible with that of Uzun et al. (2017) [27] in that the improvement in symptoms was not correlated with the improvement of EDX measurements. This lack of association between the symptoms improvement and the EDX testing improvement was not surprising since routine EDX testing mainly evaluate the large myelinated rather than the small sensory fibers that can be involved in production of many CTS symptoms [32]. It seems that the EDX testing had a limited role in prediction of the therapeutic outcomes in CTS following surgery or conservative interventions [33].

The actual mechanisms may underlie the effects of PRP in healing of neuropathy are not fully understood and probably are multifactorial. PRP preparations contain various GF which had been proposed to play a favorable role in the process of regeneration of the damaged peripheral nerve fibers. Moreover it is hypothesized that PRP can enhance angiogenesis, neurogenesis, and nerve regeneration by the direct effects of these GFs on MN [34]. It had been also suggested that PRP may reduce the inflammation and swelling of the flexor tenosynovitis that may cause lessening of intra-carpal pressure that is exerted on MN [33].

Interestingly, none of the patients in the PRP-inj-G had an adverse effect due to PRP. The results of the present study had confirmed the positive effects of PRP as a treatment option in cases with mild or moderate ICTS with an acceptable safety profiles.

Despite this is the second study in Egyptian patients searching the efficacy of platelet rich plasma in treatment of carpal tunnel syndrome, short time of follow-up could be considered as the most important limitation.

Conclusion

Single local injection of the PRP proved to be an effective and superior to corticosteroid therapy for treatment of mild to moderate CTS.

Recommendation

Further studies on the effect of PRP on CTS treatment with longer follow-up period to evaluate the long-term efficacy of PRP in the management of CTS.

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Dr. Mohammad k. Senna assessed EDX outcomes, Dr. Reham M. assessed US outcome and Dr. Alaa assessed clinical outcomes.

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Compliance with ethical standards

Disclosures None.

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