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Research Article

Nucleo CMP Forte™ for the treatment and rehabilitation of patients with carpal tunnel syndrome

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Abstract

Introduction: Carpal Tunnel Syndrome (CTS) is the most common and best well-known cause of peripheral nerve compression. To date, none of the studies have determined the optimal combination of pyrimidine nucleotides and electrical stimulation (ES) in CTS patients. The objective of the study was to evaluate the effectiveness of a novel product containing uridine and cytidine monophosphate (Nucleo CMP Forte™) in combination with ES for the treatment of CTS.

Methods: This open-label, randomized, controlled study involved 60 patients with CTS at the Azerbaijan Medical University (Baku, Azerbaijan) and Research Institute of Medical Rehabilitation between 2017 and 2021 years. Patients were randomized to receive the exploratory treatment (Nucleo CMP Forte™ and ES) or single ES treatment for ten days. The combination treatment included two stages: Nucleo CMP Forte™ and ES for ten days (stage one), and Nucleo CMP Forte™ as monotherapy (stage two) for ten days.

Results: In the exploratory group, the complete restoration of pain sensitivity was achieved by 17.1% of patients and the narrowing of the existing zone of hypesthesia by 74.3%. Positive Tinel test was revealed in 52.4% of patients after the first and 76.2% after the second stage in the exploratory group, versus 43.8% in the control group. Mean values in the Boston Carpal Tunnel Questionnaire significantly decreased in both groups.

Conclusion: Nucleo CMP Forte™ in combination with ES contributes to a more pronounced regression of patients' complaints, clinical manifestations, severity, and neurophysiological indicators in mild-to-moderate CTS.

Introduction

Carpal Tunnel Syndrome (CTS) is a complex disorder with sensitive, motor, and autonomic symptoms [1,2]. It is caused by the compression and traction of the median nerve at the level of the carpal tunnel. The repetitive stress causes chronic inflammation of the connective tissue, increasing the pressure inside the canal of the wrist, and resulting in venous hyperemia and edema which leads to ischemic damage of the nerve. CTS is the most common and well-known cause of peripheral nerve compression, with an incidence ranging from 50 to 150 cases in 100,000 inhabitants [3]. Its diagnosis is based on clinical data, questionnaires, and neurological examinations [4]. When symptoms are mild, provocative maneuvers (such as Tinel's and Phalen's test) may elicit CTS symptoms and require further examinations; however, when symptoms are severe (weakness, sensory deficits, or limitations in daily living activities), studies on nerve conduction are recommended. Electroneuromyography (ENMG) is the gold standard for evaluating the function of the median nerve in patients with clinical manifestations of CTS [4-8]. But the value of electrodiagnostic (EDX) study grades as a prognostic indicator of clinical results after Carpal Tunnel Release (CTR) remains controversial. Neuroimaging, especially ultrasound, provides information about the nerve in the carpal

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tunnel [9-11]. Additionally, magnetic resonance imaging (MRI) allows visualizing surrounding tissues, but its efficacy is limited by difficulties in revealing the entire nerve trunk [12-13] Normally, CTS is manifested by numbness, paresthesia, and pain in the innervation of the median nerve. These symptoms may be accompanied by objective changes in the sensitivity and muscle strength of tissues of the hand [14] In general, there are two approaches to the treatment of CTS [15-17] A conservative approach is based on treating underlying causes to stop the CTS progression. Immobilization is recommended in order to eliminate active movements in the affected hand [18]. The wrist is fixed in a neutral position so the tension in the carpal canal will be minimal. The carpometacarpal and the interphalangeal joints are fixed in slight flexion for the same purpose [19,20]. Non-steroidal anti-inflammatory drugs (NSAIDS) are used to relieve the symptoms [15-17]. Oral diuretics reduce swelling, and corticosteroids (prednisone, hydrocortisone) alleviate the median nerve compression and provide quick temporary relief [15]. Drug therapy does not reduce the CTS severity of sensory and motor symptoms in all cases. Thus, it is necessary the combination with non-drug therapies such as physiotherapy, acupuncture, manual therapy, and physical exercises, a trial of superficial heat for short-term pain relief [15,17,21-24]. Kinesiotherapy, and in particular mechanotherapy, helps in maintaining the trophy of the paretic muscles of the thenar, improving nervous conduction and excitability, and restoring motor function [25]. Muscle hypotrophy is influenced by a light/attentive massage that should be performed daily [26]. Electrical stimulation (ES), causing excitation of nerves and muscle contraction, has been demonstrated to enhance blood and lymph circulation, stimulate metabolic and trophic processes and improve the conductivity of nerve trunks and the electrical excitability of the neuromuscular apparatus [17,21-23]. Nucleotide-based therapies may also be considered an optimal treatment for patients with mild-moderate CTS [13,27]. To date, none of the studies have determined the optimal combination of pyrimidine nucleotides and ES in CTS patients, which could increase the effectiveness of conservative treatment and shorten the time of regression of existing motor and sensory disorders, reduce its severity, prevent disability in patients, and reduce economic costs. Therefore, the objective of the present study was to evaluate the effectiveness of a novel product containing uridine and cytidine monophosphate (Nucleo CMP Forte™) in combination with ES for the treatment of CTS.

Materials and methods

Study design

This open-label, randomized, controlled study included patients with CTS at the Azerbaijan Medical University (Baku, Azerbaijan) and the Research Institute of Medical Rehabilitation between 2017 and 2021 years. Patients for the study were selected by randomization according to the inclusion and exclusion criteria. The inclusion criteria to participate in the study were: age between 18 and 70; diagnosis of CTS and median nerve conduction blockade (verified by electroneuromyography, ENMG, and examination). Exclusion criteria included: diabetes mellitus and atherosclerosis of blood vessels; hypersensitivity to pyrimidine nucleotides; compression of C_5, C_6 roots (confirmed by MRI); rheumatoid arthritis in the acute phase (at the time of the study); and contraindications to ENMG (disturbance of skin integrity). Patients were randomized to receive the exploratory combination treatment (Nucleo CMP Forte™ and ES) or single ES treatment for ten days. The combination treatment included two stages. At the first stage of the treatment, patients received an intramuscular injection of Nucleo CMP Forte™ and ES for ten days. In the second stage, patients continued to receive an injection of the Nucleo CMP Forte™ as monotherapy for ten days. Nucleo CMP Forte™ is composed of 3 mg of uridine monophosphate and 5 mg of cytidine monophosphate [19]. The ES treatment of the median nerve in the wrist area was performed with the Amplipulse device by using Russian currents. The second type of current operation was used at a modulation depth of 100%, and a frequency - of 30 Hs.

The presence of conduction blockade along the fibers of the median nerve was verified with the nerve conduction study by using the method of short segments (inching technique). Stimulation was performed at 6 points on the wrist and palm along the nerve with an interval of 1 cm. The difference between latencies of adjacent points (1 cm) had not exceeded 0.5 msec.

Endpoints and variables

Electrical stimulation procedures and injections of the drug were well tolerated by patients, and no side effects were observed. The primary endpoint included effectiveness outcomes with the exploratory and control treatments in terms of spontaneous pain syndrome, the severity of symptoms, functional disorders, assessment of discriminatory sensitivity, Phalen's and Tinel tests, and neurophysiological (ENMG) parameters. Before receiving the treatments, patients underwent a general clinical and neurological examination, and an ENMG study to identify the presence of a conduction blockade, and the degree of compression of the median nerve in the carpal canal. Spontaneous pain syndrome was evaluated using a 10-point Visual Analog Scale (VAS). The severity of symptoms and functional disorders was determined with the Boston Carpal Tunnel Questionnaire (BCTQ). It is composed of the Symptom Severity Scale (SSS) and Functional Status Scale (FSS). The BCTQ-SSS consists of 11 multiple-choice questions, with answers scoring from one to five, depending on severity. The BCTQ-FSS included eight items, and scores vary from one (no difficulty) to five (very difficult). The ENMG study determined the following indicators: speed of conduction of impulses along the motor and sensory fibers of the median and ulnar nerves; parameters of the M-potential and S-potential of the nerves (amplitude, area, latency, duration); conducting an inching test (to determine the level and degree of compression of sensitive fibers in the wrist area); and testing the F-wave along the median and ulnar nerves. The severity of the pain syndrome or the intensification of negative and positive sensory symptoms in the zone of innervation by the median nerve of the thumb, index, and middle fingers were evaluated in sharp flexion of the hand and holding it in this position for more than one minute (Phalen's test). The severity of paresthesia

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(tingling, creeping, numbness, etc.) was also assessed in the wrist and/or fingers of the hand or in response to tapping at the site of the projection of the median nerve in the wrist (Tinel test). Discriminatory sensitivity, i.e. the ability to distinguish between two simultaneously applied stimuli at closely spaced thenar points was determined by Weber's caliper. The legs of the caliper were brought together until the double touch was no longer distinguishable. Hand strength was determined on a 5-point scale when 1-2 fingers of the hand were flexed to form a ringlet. The general condition and the changes in patients' complaints were also assessed.

Data analysis

Continuous variables are expressed with the mean and Standard Deviation (SD); whereas categorical ones with absolute and relative frequencies. Comparisons between groups were carried out with statistical analysis. To determine the difference in mean values and establish the effectiveness of treatment, all clinical data, the results of the tests performed (Fallen, Tinnel) and electromyography indicators were analyzed. Mean values of all parameters before and after the first stage of treatment and after the course of treatment in patients of the first group were compared. In patients of the second group, statistical analysis of the parameters was carried out before and after the course of treatment. Statistical significance was established with $p < 0.05$. Statistical procedures were carried out Excel program using the criteria of Student and X^2 of Pearson.

Results

Baseline population characteristics

A total of 60 patients were included in the study (40 in the exploratory group and 20 in the control one). Patients were predominantly women (93.3% of them), with a mean age was 53.1 ± 1.5 years, and duration of the disease between 1-3 years (38.3%; Table 1). Most of the patients (63.3%) showed severe CTS symptoms. The CTS was bilateral in 49 patients (81.7%), and unilateral in 11 (18.3%, eight right-sided and three left-sided). Further information on pain and symptoms is described in the Supplementary material. Phalen's and Tinel tests were positive in 46 (76.7%) and 37 patients (61.7%), respectively. The mean value of the discriminatory sensitivity was 11.2 ± 0.1 mm. Changes in the reflex sphere are shown in Supplementary Table 1. The study of the motor fibers of the median nerve revealed a significantly higher latency of the M-response (4.4 ± 0.1 *vs.* 3.1 ± 0.04 msec; $p < 0.001$) and duration (6.7 ± 0.2 *vs.* 6.2 ± 0.1 msec; $p < 0.05$) in the exploratory group, compared to control (Table 2). A significantly lower amplitude (6.9 ± 0.1 *vs.* 8.8 ± 0.2 mV; $p < 0.001$), area (24.5 ± 0.3 *vs.* 31.4 ± 0.8 mV*msec; $p < 0.001$), and conduction velocity (56.0 ± 0.4 *vs.* 58.6 ± 0.4 m/sec; $p < 0.001$) were also found. Changes in mean values of the amplitude of the S-response and conduction velocity in the study of the sensory fibers of the median nerve were significantly higher in the exploratory group, compared with the control, expressed by an increase in latency and duration ($p < 0.001$), and a decrease in amplitude and ICV ($p < 0.001$; Table 2). The BCTQ at baseline is shown in Supplementary Table 2.

Table 1: Baseline sociodemographic and clinical characteristics of patients.

	Total patients (N = 60)
Gender, n (%)	
Male	4 (6.7)
Females	56 (93.3)
Age, mean years ± SD	53.1 ± 1.5
Duration of the disease, n (%)	
1 year	19 (31.7)
1-3 years	23 (38.3)
>3 years	18 (30.0)
Severity of the CTS symptoms, n (%)	
Mild	15 (25.0)
Moderate	38 (63.3)
Severe	7 (11.7)
Mean BCTQ score ± SD	2.84 ± 0.05
Phalen's test	
Positive, n (%)	49 (81.7)
Duration, mean sec ± SD	20.1 ± 0.2
Positive Tinel test, n (%)	37 (61.7)
Discriminatory sensitivity, mean mm ± SD	11.2 ± 0.1

SD: Standard Deviation; CTS: Carpal Tunnel Syndrome; BCTQ: Boston Carpal Tunnel Questionnaire

Effectiveness of the treatments

A significant decrease in the mean VAS for pain was found in the exploratory group between baseline (6.6 ± 0.2) and first (3.8 ± 0.3, $p < 0.01$) and second stages (1.6 ± 0.26, $p < 0.001$; Table 3). Changes in symptoms, complaints, and severity during the treatments are described in the Supplementary material. In the exploratory group, the complete restoration of pain sensitivity was achieved by 17.1% of patients, and the narrowing of the existing zone of hypesthesia by 74.3%. Additional effectiveness results are shown in Supplementary Table 3. The mean duration of the onset of sensory symptoms (Phalen's test) significantly increased from baseline (22.5 ± 0.4 sec) to the first (41.5 ± 1.5 sec) and second stages of treatment (48.3 ± 0.7 sec, $p < 0.001$) in the exploratory group, and from baseline (17.1 ± 0.6 sec) to the end of treatment in the control group (21.2 ± 1.8 sec, $p < 0.05$). Positive Tinel test was revealed in 52.4% of patients after the first and 76.2% after the second stage in the exploratory group, versus 43.8% in the control group. The discrimination distance significantly decreased after the first stage of treatment (from 11.3 ± 0.5 to 10.1 ± 0.2 mm; $p < 0.01$), and to the second stage (9.1 ± 0.2 mm; $p < 0.001$; Table 3). The mean BCTQ-SSS index significantly decreased after the first stage of treatment (from 2.8 ± 0.1 to 1.8 ± 0.1; $p < 0.001$), and to the second (1.5 ± 0.1; $p < 0.001$) in the exploratory group, and from baseline (2.7 ± 0.1) to the end of treatment (1.9 ± 0.2, $p < 0.001$) in the control group. The mean BCTQ-FSS index also significantly decreased after the first stage of treatment (from 2.9 ± 0.1 to 2.2 ± 0.1; $p < 0.001$), and the second (1.3 ± 0.1; $p < 0.001$) in the exploratory group, and from baseline (2.8 ± 0.1) to the end of treatment (2.2 ± 0.2, $p < 0.001$) in the control group. Further information from BCTQ scores during the treatments is shown in Supplementary

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Table 2: Baseline electroneuromyography indicators in the stimulation of motor and sensory fibers, inching indicator and F-wave.

Nerves	Indicators	Before treatment [a]	Control	*p* - value [b]
Stimulation of motor fibers (M ± m)				
N. medianus (*n* = 105) [c]	M-response: Latency period (ms)	4.4 ± 0.1 / 3.2 ± 0.2	3.1 ± 0.04	<0.001 / N.S.
	Residual period (ms)	3.0 ± 0.2 / 2.0 ± 0.3	1.8 ± 0.1	<0.001 / N.S.
	Amplitude (mV)	6.9 ± 0.1 / 7.4 ± 0.4	8.8 ± 0.2	<0.001 / N.S.
	Duration (ms)	6.7 ± 0.2 / 6.0 ± 0.2	6.2 ± 0.1	<0.05 / N.S.
	Area, (mV*ms)	24.5 ± 0.3 / 25.4 ± 0.5	31.4 ± 0.8	<0.001 / N.S.
	ICVeff (m/s)	56.0 ± 0.4 / 56.9 ± 1.1	58.6 ± 0.4	<0.001 / N.S.
N. ulnaris (*n* = 91) [c]	M-response: Latency period (ms)	2.3 ± 0.02 / 2.1 ± 0.04	2.6 ± 0.1	N.S. / N.S.
	Residual period (ms)	1.0 ± 0.02 / 1.0 ± 0.16	1.3 ± 0.06	N.S. / N.S.
	Amplitude (mV)	9.7 ± 0.1 / 9.9 ± 0.6	10.0 ± 0.2	N.S. / N.S.
	Duration (ms)	5.6 ± 0.05 / 9.9 ± 0.2	6.2 ± 0.1	N.S. / N.S.
	Area, (mV* mV)	25.1 ± 0.5 / 25.6 ± 0.4	27.4 ± 0.5	<0.001 / <0.05
	ICVeff (M/S)	60.5 ± 0.4 / 61.6 ± 0.4	61.4 ± 0.5	N.S. / N.S.
Stimulation of sensor fibers (M ± m)				
N. medianus (*n* = 104) [c]	S-response: Latency period (ms)	3.0 ± 0.05 / 2.5 ± 0.2	2.1 ± 0.03	<0.001 / <0.01
	Amplitude (mV)	17.8 ± 0.4 / 25.7 ± 1.2	31.7 ± 1.2	<0.001 / <0.01
	Duration (ms)	3.3 ± 0.1 2.9 ± 0.2	2.8 ± 0.1	N.S. / N.S.
	Area, (mV* ms)	19.4 ± 0.8 19.4 ± 1.2	20.9 ± 0.8	N.S. / N.S.
	ICVaff (m/s)	52.5 ± 0.8 / 58.7 ± 1.5	66.4 ± 0.6	<0.001 / <0.001
N. ulnaris (*n* = 87) [c]	S-response: Latency period (ms)	2.0 ± 0.02 2.0 ± 0.08	2.0 ± 0.04	N.S. / N.S.
	Amplitude (mV)	21.7 ± 0.3 23.4 ± 0.5	24.3 ± 1.1	<0.05 / N.S.
	Duration (ms)	2.8 ± 0.3 2.4 ± 0.2	2.5 ± 0.1	<0.05 / N.S.
	Area, (mV* ms)	19.1 ± 0.3 19.5 ± 0.9	14.8 ± 0.8	N.S. / N.S.
	ICVaff (m/s)	63.8 ± 0.5 62.5 ± 0.7	64.7 ± 0.8	N.S. / N.S.
Baseline inching indicator (M ± m)				
n = 110 [c]	The latency period (ms)	1.14 ± 0.03	<0.5	<0.001
Baseline indicators of F-wave				
N. medianus (*n* = 69) [c]	The minimum latency period (ms)	26.3 ± 0.2 / 25.3 ± 0.4	24.7 ± 0.3	<0.001 / N.S.
	Amplitude (mkV)	278.5 ± 14.4 / 210.0 ± 7.1	207.0 ± 18.4	N.S. / N.S.
	ICV_{max} (m/s)	67.5 ± 1.4 / 60.4 ± 6.4	74.2 ± 4.7	N.S. / N.S.
	Tachydispersion (m/s)	10.9 ± 0.5 / 6.43 ± 0.5	8.6 ± 2.7	N.S. / N.S.
	Latency period F_{min}–M (ms)	22.1 ± 0.2 / 21.9 ± 0.6	21.7 ± 0.3	N.S. / N.S.
	Amplitude F/M (%)	3.3 ± 0.3 / 1.8 ± 0.4	1.9 ± 0.2	N.S. / N.S.
N. ulnaris (*n* = 60) [c]	The minimum latency period (ms)	24.9 ± 0.2 / 27.7 ± 0.5	25.4 ± 0.4	N.S. / N.S.
	Amplitude (mkV)	182.3 ± 12.0 / 217.1 ± 11.1	218 ± 18.3	N.S. / N.S.
	ICV_{max} (m/s)	64.1 ± 2.4 / 62.7 ± 1.2	62.8 ± 3.0	N.S. / N.S.
	Tachydispersion (m/s)	10.2 ± 0.3 / 5.8 ± 0.4	8.4 ± 1.7	N.S. / N.S.
	Latency period F_{min}–M (ms)	22.4 ± 0.2 / 22.4 ± 0.4	22.5 ± 0.7	N.S. / N.S.
	Amplitude F/M (%)	1.4 ± 0.2 / 0.9 ± 0.1	1.4 ± 0.2	N.S. / N.S.

N.S; Not Statistically Significant

[a]In the numerator: indicators of the affected side; in the denominator: indicators of the intact side

[b]The significance of the difference (p) was calculated in relation to the control

[c]n: Number of patients examined

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Table 4. The ENMG studies revealed a significant increase in the amplitude and area of the M-potential along the median nerve after the first ($p < 0.01$) and second ($p < 0.001$) stages of treatment in the exploratory group (Table 4). Efferent fibers ICV significantly increased from baseline (55.9 ± 0.5) to the first stage (57.9 ± 0.4 m/sec; $p < 0.01$) and second stage of treatment (59.4 ± 0.8 m/sec; $p < 0.001$). In the control group, a significant improvement in the amplitude ($p < 0.05$) and area ($p < 0.01$) of the M-potential recorded from the median nerve was reported after the treatment. After the second stage of treatment, there was a decrease in the latency of the sensory response (from 2.9 ± 0.1 to 2.4 ± 0.1 msec; $p < 0.001$), and an increase in the afferent fiber's excitation conduction velocity (from 54.8 ± 1.0 to 60.1 ± 1.1 m/sec; $p < 0.001$). In patients from the exploratory group, the mean difference between latencies of nearby points normalized decreased after the first stage of treatment (from 1.1 ± 0.1 to 0.5 ± 0.0 msec; p <0.001), and second (0.4 ± 0.0 msec; $p < 0.001$). In the control group, the mean value significantly reduced by the end of treatment (from 1.2 ± 0.1 to 0.8 ± 0.1 msec; $p < 0.001$).

Discussion

Our study aimed at evaluating the effectiveness of the use of ES and Nucleo CMP Forte™ in the complex treatment and rehabilitation of CTS. In patients with mild-moderate CTS, nucleotide-based medications (like Nucleo CMP Forte™), might be considered as a treatment option. Literature evaluating the efficacy of Nucleo CMP Forte™ is scarce [23]. Povedano, et al. [23] in an exploratory, open-label, prospective study analyzed the efficacy of Nucleo CMP Forte™ for improving the symptoms and electromyographic parameters of 40 patients with electromyography-confirmed, mild-moderate CTS. The authors reported a significant decrease in pain symptoms and an improvement in the quality of life after six months. No significant differences were observed in electromyographic findings. Case reports, like Park, et al. [27] have also documented improvements in CTS symptoms with ultrasound-guided polydeoxyribonucleotide injections. Some studies have evidenced that ES in injured peripheral nerves accelerates axonal regeneration [28,29]. Furthermore, ES is able to accelerate axon outgrowth and target muscle reinnervation, promoting functional recovery, in CTS patients with severe axonal degeneration [28]. Gordon, et al. [28] demonstrated that sensory nerve conduction values significantly improved after ES in CTS patients after surgery. Several studies have also revealed that ES is effective in reducing the peripheral nerve causes of pain. Deer, et al. [29] in a prospective study reported the reduction of neuropathic pain in patients who received active ES with an implantable peripheral nerve stimulation (StimRouter) device.

In our present study, results support the effect of the proposed treatment method for decreasing pain syndrome and regression of sensitive, autonomic, and motor disorders. Results also evidence an improvement in BCTQ indicators, i.e. symptom severity and function state scales. Moreover, a pronounced positive dynamic of ENMG indicators was observed, i.e. an increase in the amplitude and area of the motor response, an increase in conduction velocity of both efferent and afferent fibers (ICV motor and sensory fibers), and a significant decrease in the difference between the latencies of nearby points during inching technique. The ES has been extensively shown to affect remyelination in animal models and humans [28]. Therefore, these results may be explained by the intensification of myelination processes and structural and functional restoration of the median nerve under the influence of treatment.

The main limitation of the study was the relatively low number of patients (40 in the exploratory group and 20 in the control one), limiting sub-analyses of variables and thus the conclusions. Besides this, positive dynamics of both clinical data and ENMG indicators, especially, ICV efferent and afferent, after the use of Nucleo CMP Forte™ of the exploratory group highlight the critical importance of this product in the results of the exploratory treatment.

In conclusion, Nucleo CMP Forte™ in combination with ES contributes to a more pronounced regression of patients' complaints, clinical manifestations, severity, and neurophysiological indicators in mild-to-moderate CTS.

Table 3: Effectiveness results during the treatments.

		Exploratory group		Control group	
	Baseline	First stage	Second stage	Baseline	After treatment
Spontaneous pain syndrome					
Mean VAS score ± SD	6.6 ± 0.2	3.8 ± 0.3[a]	1.6 ± 0.2[b]	6.5 ± 0.3	4.6 ± 0.4
Phalen's test					
Duration of the onset of sensory symptoms, mean s (SD)	22.5 ± 0.4	41.5 ± 1.5[b]	48.3 ± 0.7[b]	17.1 ± 0.6	21.2 ± 1.8[c]
Discriminatory sensitivity					
Mean distance, mm (SD)	11.3 ± 0.5	10.1 ± 0.2[a]	9.1 ± 0.2[b]	17.1 ± 0.6	21.2 ± 1.8
BCTQ					
SSS, mean index	2.8 ± 0.1	1.8 ± 0.1[b]	1.5 ± 0.1[b]	2.7 ± 0.1	1.9 ± 0.2[b]
FSS, mean index	2.9 ± 0.1	2.2 ± 0.1[b]	1.3 ± 0.1[b]	2.8 ± 0.1	2.2 ± 0.2[c]

BCTQ, Boston carpal tunnel questionnaire; SSS, symptom severity scale; FSS, function state scale.
Statistical significance: [a]$p < 0.01$; [b]$p < 0.001$; [c]$p < 0.05$

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Table 4: Electroneuromyography indicators in the stimulation of motor and sensory fibers, and F-wave during the treatments.

Nerves	Indicators	Before treatment	After the first stage	After the second stage	Control
Stimulation of motor fibers					
N. medianus (*n* = 69)	M-response: Latency period (ms)	4.3 ± 0.1^{e} / 3.6 ± 0.3	4.0 ± 0.1^{c} / 3.4 ± 0.3	4.1 ± 0.2 / 3.7 ± 0.4	3.1 ± 0.04
	Residual period (ms)	2.8 ± 0.1^{e} / 2.0 ± 0.2	2.6 ± 0.1 / 1.8 ± 0.2	2.7 ± 0.1 / 1.7 ± 0.1	1.8 ± 0.1
	Amplitude (mV)	7.2 ± 0.1^{e} / 7.6 ± 0.5	8.3 ± 0.2^{b} / 8.1 ± 0.6	8.7 ± 0.3^{b} / 8.5 ± 0.9	8.8 ± 0.2
	Duration (ms)	6.6 ± 0.3 / 6.0 ± 0.3	6.2 ± 0.1 / 5.9 ± 0.3	6.5 ± 0.1 / 6.4 ± 0.7	6.2 ± 0.1
	Area (mV* ms)	25.1 ± 0.5^{e} / 25.7 ± 1.3	28.2 ± 0.7^{b} / 25.6 ± 0.7	43.0 ± 0.3^{b} / 32.6 ± 0.2^{b}	31.4 ± 0.8
	ICVeff (m/s)	55.9 ± 0.5^{e} / 56.8 ± 1.5	57.9 ± 0.4^{a} / 57.2 ± 0.9	59.4 ± 0.8^{b} / 60.4 ± 1.6	58.6 ± 0.4
N. ulnaris (*n* = 55)	M-response: Latency period (ms)	2.3 ± 0.03 / 2.1 ± 0.06	2.3 ± 0.04 / 2.2 ± 0.1	2.4 ± 0.09 / 2.3 ± 0.2	2.6 ± 0.1
	Residual period (ms)	1.1 ± 0.03 / 1.1 ± 0.2	1.1 ± 0.04 / 1.0 ± 0.1	1.3 ± 0.09 / 1.3 ± 0.3	1.3 ± 0.06
	Amplitude (mV)	10.0 ± 0.14 / 10.2 ± 0.89	10.7 ± 0.2^{c} / 10.9 ± 0.3	11.2 ± 0.3^{a} / 12.0 ± 1.3	10.0 ± 0.2
	Duration (ms)	5.6 ± 0.08^{e} / 5.8 ± 0.3	5.5 ± 0.14 / 5.7 ± 0.2	5.8 ± 0.2 / 5.7 ± 0.4	6.2 ± 0.1
	Area, (mV*ms)	26.0 ± 0.4^{f} / 26.7 ± 0.6	27.4 ± 0.4^{c} / 27.8 ± 0.9	30.7 ± 0.9^{b} / 36.5 ± 1.4	27.4 ± 0.5
	ICVeff (m/s)	62.5 ± 0.6 / 61.2 ± 0.5	62.9 ± 0.4 / 62.9 ± 0.9	64.6 ± 0.8^{c} / 66.1 ± 0.9^{b}	61.4 ± 0.5
Stimulation of sensor fibers					
N. medianus (*n* = 68)	Latency period (ms)	2.9 ± 0.1^{e} / 2.6 ± 0.2^{f}	2.6 ± 0.05^{a} / 2.3 ± 0.1	2.4 ± 0.1^{b} / 2.3 ± 0.1	2.1 ± 0.03
	Amplitude (mV)	18.1 ± 0.7^{e} / 22.6 ± 0.6^{d}	20.1 ± 0.7^{c} / 23.1 ± 0.5	20.7 ± 0.3^{b} / 22.0 ± 1.2	31.7 ± 1.2
	Duration (ms)	3.4 ± 0.2^{d} / 3.1 ± 0.3	3.2 ± 0.1 / 3.1 ± 0.4	3.7 ± 0.2 / 2.9 ± 0.4	2.8 ± 0.1
	Area, (mV*ms)	18.4 ± 1.0 / 18.2 ± 1.4	18.9 ± 1.0 / 18.5 ± 1.2	25.1 ± 2.2^{c} / 17.4 ± 1.9	20.9 ± 0.8
	ICVaff (m/s)	54.8 ± 1.0^{e} / 57.7 ± 1.1^{d}	58.4 ± 0.6^{c} / 62.3 ± 0.6^{b}	60.9 ± 1.1^{b} / 60.9 ± 1.0^{a}	66.4 ± 0.6
N. ulnaris (*n* = 51)	The latency period (ms)	2.0 ± 0.03 / 2.0 ± 0.1	1.9 ± 0.04 / 1.9 ± 0.2	2.2 ± 0.08 / 1.8 ± 0.2	2.0 ± 0.04
	Amplitude (mV)	19.6 ± 0.6^{e} / 21.5 ± 0.8	26.6 ± 0.4^{b} / 22.4 ± 0.8^{a}	29.7 ± 0.6^{b} / 38.0 ± 1.6^{b}	24.3 ± 1.1
	Duration (ms)	2.9 ± 0.1^{d} / 2.5 ± 0.3	3.0 ± 0.2 / 2.3 ± 0.2	3.9 ± 0.4^{c} / 3.2 ± 0.6	2.5 ± 0.1
	Area, (mV*ms)	17.1 ± 0.5 / 19.1 ± 1.3	24.3 ± 0.4^{b} / 20.6 ± 1.4	29.4 ± 0.4^{b} / 44.1 ± 2.7^{b}	14.8 ± 0.8
	ICVaff (m/s)	64.2 ± 0.8 / 62.43 ± 1.8	64.6 ± 0.8 / 69.3 ± 0.6^{b}	63.8 ± 2.5 / 78.7 ± 1.2^{b}	64.7 ± 0.8
Indicators of F-wave					
N. medianus (*n* = 46)	The minimum latency period (ms)	26.1 ± 0.3^{d} / 25.1 ± 0.5	26.6 ± 0.3 / 23.7 ± 1.1	26.8 ± 0.4 / 26.1 ± 07	24.7 ± 0.3
	Amplitude (mkV)	278.5 ± 14.1 / 210.3 ± 7.1	239.6 ± 7.5 / 302.0 ± 18.2^{b}	200.0 ± 5.8 / 184.3 ± 9.5	207.0 ± 18.4
	ICV $_{max}$ (m/s)	67.5 ± 1.3 / 60.4 ± 6.3	64.5 ± 1.3 / 69.6 ± 3.0	65.2 ± 1.0 / 69.1 ± 1.1	74.2 ± 4.7
	Tachydispersion (m/s)	10.9 ± 0.5 / 6.4 ± 0.5	11.6 ± 0.5 / 11.4 ± 1.4	6.9 ± 0.3 / 6.9 ± 0.5	8.6 ± 2.7
	Latency period F_{min}–M (ms)	22.0 ± 0.3 / 21.7 ± 0.7	22.6 ± 0.3 / 20.3 ± 0.8	22.7 ± 0.3^{c} / 22.3 ± 0.5	21.7 ± 0.3
	Amplitude F/M (%)	3.2 ± 0. 3^{e} / 1.8 ± 0.4	2.4 ± 0.3^{c} / 2.4 ± 0.3	2.0 ± 0.4^{a} / 1.5 ± 0.5	1.9 ± 0.2
N. ulnaris (*n* = 37)	The minimum latency period (ms)	24.6 ± 0.3 / 24.4 ± 0.5	24.1 ± 0.3 / 23.8 ± 0.6	24.5 ± 1.0 / 25.4 ± 0.7	25.4 ± 0.4
	Amplitude (mkV)	182.2 ± 12.0 / 145.0 ± 12.6	246.0 ± 3.3^{b} / 242.2 ± 10.4^{b}	234.7 ± 6.0^{b} / 169.7 ± 9.8	218 ± 18.3
	ICV $_{max}$ (m/s)	64.1 ± 2.4 / 62.7 ± 1.2	62.7 ± 1.8 / 66.6 ± 1.3	63.9 ± 1.6 / 64.1 ± 2.1	62.8 ± 3.0
	Tachydispersion (m/s)	10.2 ± 0.3 / 5.8 ± 0.4	9.7 ± 0.4 / 8.4 ± 0.6^{c}	8.0 ± 0.8^{a} / 8.3 ± 0.3^{c}	8.4 ± 1.7
	Latency period F_{min}–M (ms)	22.0 ± 0.3 / 21.9 ± 0.4	21.7 ± 0.3 / 22.1 ± 0.7	22.9 ± 0.4 / 23.2 ± 0.6	22.5 ± 0.7
	Amplitude F/M (%)	1.4 ± 0.2 / 0.9 ± 0.1	1.6 ± 0.2 / 1.4 ± 0.1^{c}	1.4 ± 0.1 / 1.4 ± 0.1^{c}	1.4 ± 0.2

In the numerator: are indicators of the affected side; in the denominator: indicators of the intact side

The significance of the difference (p-value) is calculated in relation to the initial state: $^{a}p < 0.01$; $^{b}p < 0.001$; $^{c}p < 0.05$; and to the control: $^{d}p < 0.01$; $^{e}p < 0.001$; $^{f}p < 0.05$

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