

# The effect of botulinum toxin type A injection in decreasing intratunnel tendon tension in carpal tunnel syndrome: a randomized controlled trial for efficacy and safety

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Received 14 April 2019

Accepted 9 July 2019

Egyptian Rheumatology & Rehabilitation  
2019, 46:299–303

## Aim

To evaluate the efficacy of botulinum toxin A on relieving the clinical symptoms caused by median nerve compression in patients with carpal tunnel syndrome.

## Patients and methods

An imbalanced randomization (3 : 1) placebo-controlled parallel group study for efficacy and safety was conducted in Tanta University, Egypt. Group I received Botox injection. Group II received the same amount of normal saline as Botox injection and at the same injection points as group I. All patients were subjected to clinical assessment and electrophysiological assessment of the median nerve before and after 12 weeks.

## Results

Highly significant improvements were noted in group I regarding clinical symptoms and electrophysiological study of the median nerve, whereas group II showed significant improvement in clinical symptoms but no improvement in the electrophysiological study, with significant difference between the two groups.

## Conclusion

Botox injection can be used safely as a treatment option in moderate carpal tunnel syndrome.

## Keywords:

Botox injection, carpal tunnel syndrome, electrophysiology, intracarpal pressure, tendon tension

Egypt Rheumatol Rehabil 46:299–303

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1110-161X

## Introduction

Carpal tunnel is an osteofibrous canal situated in the volar wrist. The boundaries are the carpal bones and the flexor retinaculum. In addition to the medial nerve, the carpal tunnel contains nine tendons: the flexor pollicis longus, the four flexor digitorum superficialis, and the four flexor digitorum profundus [1].

The flexor pollicis longus has its own synovial sheath, whereas the flexor digitorum superficialis and profundus have a common synovial sheath [2].

The flexor carpi radialis tendon, the flexor carpi ulnaris tendon, and the palmaris longus tendon travel outside the carpal tunnel but in close contact with it. The flexor carpi radialis tendon inserts into the scaphoid and the base of the second metacarpal bone after passing through the canal formed by the splitting of the flexor retinaculum. Flexor carpi ulnaris tendon inserts into the pisiform, whereas the palmaris longus tendon continues with the palmar fascia or inserts into the flexor retinaculum [2].

The carpal tunnel creates an enclosed space for the passage of the median nerve, but this is the same feature that can lead to carpal tunnel syndrome (CTS). CTS is the most common type of upper limb entrapments, which accounts for 90% of all entrapment neuropathies [3].

Its mechanism is compression of the median nerve inside the canal. There are a variety of contributing factors [4,5]. Swelling of the structures within the canal or deposition of fluid, which may occur in diabetes, obesity, pregnancy, hypothyroidism, and also congenital narrow diameter of the carpal tunnel may be a predisposing factor. Occupational causes involve use of the hand and arm, such as heavy manual work, work with vibrating tools, or highly repetitive tasks [6,7].

Repetitive microtrauma to the nerve, which is more often the causative agent, owing to a number of poor

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postures, cause an abnormal increase in the tunnel pressure, for example, maximally flexing and/or extending the hand at the wrist joint. Another common postural microtrauma is extending the hand at the wrist joint while flexing the fingers at the metacarpophalangeal and interphalangeal joints. Extending the wrist joint not only increases tunnel pressure, but also, creates tension within the flexors tendons that go through further increase when these muscles contract [3,8].

Long-standing Increase in carpal tunnel pressure leads to median nerve compression with constant numbness, of the thumb, index, and middle fingers and the radial side of the ring finger and atrophy of the thenar muscles can occur with longstanding compression [9,10].

Diagnosis of CTS can be done using the electrodiagnostic testing (electromyography and nerve conduction velocity), which detects the degree of focal slowing across the canal [11]. Moreover, the use of high-resolution ultrasound imaging shows enlargement of the median nerve at the distal wrist crease in symptomatic patients [12].

Conservative treatments of CTS include use of night splints and corticosteroid injection and/or surgery to cut the transverse carpal ligament and relieve the pressure inside the canal [13].

Botulinum toxin type A (BOTOX, Botox Allergan, Inc pharmaceutical) is a neurotoxic protein produced by the bacterium *Clostridium botulinum* and related species. It is also produced commercially for medical, cosmetic, and research use [14].

When injected in small amounts, it can effectively weaken the muscle for a period of 3–4 months. It has been shown to relieve primary headaches, myofascial pain, dystonias, chronic musculoskeletal pain, and various neuropathic pains, including CTS [15].

The aim of the study was to use Botox injection that can relieve the flexor tendons tension created by highly repetitive movements and subsequently the intratunnel pressure without affecting hand function.

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## **Patients and methods**

### **Objectives**

The objective is to evaluate the efficacy of botulinum toxin A on relieving the clinical symptoms caused by nerve compression in patients with CTS through decreasing the tendon tension caused by repetitive

movements and subsequently decreasing the intracarpal pressure.

### **Design**

This was an imbalanced randomization (3 : 1) placebo-controlled parallel group study for efficacy and safety.

### **Patients**

This study was carried out on 40 patients diagnosed with moderate carpal tunnel syndrome [16] where the sensory potential is still preserved with delay in conduction velocities and the motor slowing, (distal motor latency to abductor pollicis brevis (APB) < 6.5 ms. Patients were collected from those attending the neurosurgery outpatient clinic Tanta University, Egypt for surgical intervention. They were assigned to our study in an attempt to postpone or skip surgery.

### *Inclusion criteria*

Patients with moderate CTS were diagnosed by an electrophysiological study [16].

### *Exclusion criteria*

Patients with a history of previous wrist or elbow trauma or surgery, previous local injection, pregnancy or breastfeeding, neuromuscular junction disorders, causes of neuropathy, for example, diabetes, and any patients with hemorrhagic blood diseases were excluded.

### *Treatment groups*

The sample size was determined according to a population size of ~150 patients per month aged from 30 to 50 years. Patients were simply randomized according to their priority of attendance into two groups according to allocation ratio of 3 : 1 (three for the treatment group and one for the control group). Patients, practitioners, and analysts were aware of the intervention.

Group I ( $n=30$ ): patients of this group received Botox injection in motor points of flexor digitorum profundus (10 IU), flexor digitorum superficialis (10 IU), and flexor pollicis longus (5 IU).

Group II ( $n=10$ ): patients of this group received the same amount of normal saline at the same points of injections as group I.

Both groups were given at-home stretching program for flexors of the forearm.

### *Assessment*

All patients were subjected to the following assessments before as well as after 12 weeks to allow

the reversal of median nerve pathology before the effect of Botox fades.

- (1) Clinical assessment by Levine questionnaire testing functional and symptom severity for CTS [17].
- (2) Electrophysiological study of the median nerve: Motor and sensory distal latencies and amplitudes, and sensory and motor nerve conduction velocities.

#### Ethics, consent, and permission

The study was approved by Local Research Ethics Committee of Faculty of Medicine, Tanta University, with approval code 31082/04/2018. Written consents for publication were obtained from all patients.

Benefits to the patients include improvement of clinical symptoms and hand function and avoidance of the complications of surgical intervention.

Risk to the patients include pain or infection at the site of injection and temporary weakness of the hand grip.

Measures taken to overcome the risk: Proper injection and sterilization technique. Any unexpected risk or adverse effect will be reported.

#### Statistical analysis

All statistical calculations and analysis were done using a computer program (SPSS, version 16, SPSS 16 Inc., Chicago, IL). Mean, SD, Student *t*-test, and probability testing were used in the analysis. A difference was considered to be statistically significant when the *P* value was less than 0.05. *P* values less than 0.01 were considered highly significant. *P* values more than 0.05 were considered statistically nonsignificant.

## Results

Recruitment of the patients was done from those attending neurosurgery outpatient clinics, Tanta University Hospitals.

The study examined 40 patients with moderate CTS diagnosed by electrophysiological studies of the median nerve at wrist. The mean age of patients in group I was 33.5±5.1, with mean disease duration of 2.2±1.5 years, and in group II, the mean age was 33±4.7 years, and disease duration was 2.5±0.5 years, with no significant difference between the two groups (Table 1). The injection was well tolerated. The only adverse reaction reported by all patients in group I was

**Table 1 Comparison between the two groups regarding age and disease duration**

	Group I	Group II	<i>P</i> value
Age	33.5±5.1	33±4.7	>0.05
Disease duration	2.2±1.5	2.5±0.5	>0.05

**Table 2 Comparison of electrophysiological studies of the median nerve before and after treatment and between the two groups**

	Group I (n=30)	Group II (n=10)	<i>P</i> value ( <i>P</i> <sub>3</sub> )
Distal motor latency			
Before	5.95±0.40	5.89±0.49	<i>P</i> <sub>3</sub> >0.05
After	4.92±0.38	5.82±0.42	<i>P</i> <sub>3</sub> <0.01
<i>P</i> value	<i>P</i> <sub>1</sub> <0.01	<i>P</i> <sub>2</sub> >0.05	
Sensory nerve conduction velocity			
Before	25.57±2.62	26.57±2.44	<i>P</i> <sub>3</sub> >0.05
After	35.07±1.32	25.42±2.37	<i>P</i> <sub>3</sub> <0.01
<i>P</i> value	<i>P</i> <sub>1</sub> <0.01	<i>P</i> <sub>2</sub> >0.05	

*P*<sub>1</sub>, comparison between before and after in group I. *P*<sub>2</sub>, comparison between before and after in group II. *P*<sub>3</sub>, comparison between group I and group II.

**Table 3 Comparison of the Levine questionnaire regarding symptom severity and functional severity before and after treatment and between the two groups**

	Group I (n=30)	Group II (n=10)	<i>P</i> value
Symptoms severity scale			
Before	41.6±2.5	40.9±0.49	<i>P</i> <sub>3</sub> >0.05
After	12.9±1.07	37.86±2.42	<i>P</i> <sub>3</sub> <0.001
<i>P</i> value	<i>P</i> <sub>1</sub> <0.01	<i>P</i> <sub>2</sub> <0.05	
Functional severity scale			
Before	31.8±1.37	32.57±2.44	<i>P</i> <sub>3</sub> >0.05
After	9.6±1.4	28±3.06	<i>P</i> <sub>3</sub> <0.001
<i>P</i> value	<i>P</i> <sub>1</sub> <0.01	<i>P</i> <sub>2</sub> <0.05	

*P*<sub>1</sub>, comparison between before and after in group I. *P*<sub>2</sub>, comparison between before and after in group II. *P*<sub>3</sub>, comparison between group I and group II.

tingling sensation in the palm, which lasted less than 48 h after injection. In the following tables, assessment of all patients before and after the intervention (Table 2) is illustrated, with comparison of the two groups regarding the symptoms, hand function, and electrophysiological study (Table 3). The distal motor latencies and sensory nerve conduction velocities were chosen for assessment of median nerve improvement as they were the most affected parameters by the compression.

## Discussion

CTS is a compression of the median nerve as it travels through the carpal tunnel. The main symptoms are pain, numbness, and tingling, in the distribution of the median nerve [18]. Symptoms start gradually during the night and may extend up the arm [19]. Normal

pressure of the carpal tunnel is in the range of 2–10 mm. Wrist flexion increases this pressure eight-fold, whereas extension increases it 10-folds [3]. Repetitive flexion and extension of the wrist significantly increase the fluid pressure in the tunnel through thickening of the tendons within the carpal tunnel [20]. The median nerve can usually move up to 9.6 mm to allow wrist flexion and to a lesser extent extension [3]. In long-term compression of the median nerve, this movement leads to injury and scarring of the median nerve, and it becomes locked into a fixed position [21].

Bright *et al.* [22] reported that the FDP tendon tension was 1 N in the resting position and ranged from 10 to 25 N for full active finger range of motion. Schuind *et al.* [23] reported that the average FDP tendon force values were up to 1 N for passive finger flexion, 3 N for passive wrist extension, and 20 N for active finger flexion.

In addition for using highly repetitive flexion movements, these forces will lead to compression of the median nerve. Injecting Botox into muscles that pass through the carpal tunnel can decrease the tension created by these muscle tendons on the median nerve which will allow the regeneration of the nerve. We used a dose for each muscle that is less than quarter the dose used for these muscles.

Our injections were far from the tunnel, and we aimed for decreasing the tendon tension that is caused by the repetitive movements of forearm flexors and subsequently decreasing the pressure on the median nerve.

The injections were well tolerated by all patients. Tingling sensation following Botox injections was reported that faded in 48 h without treatment. Our explanation for that could be owing to extravasation of Botox from the muscles to the adjacent proximal nerve; otherwise, no serious adverse effects were reported, with no reports of decreased hand function. There was no significant difference between the two groups regarding the age of the patients and the disease duration (Table 1). Our results showed significant improvement in distal motor latencies and sensory nerve conduction velocities after 12 weeks of injection in group I and insignificant improvement in group II (Table 2) and highly significant improvement in clinical assessment measured by the Levine questionnaire at the 12th week after injection in group I and significant improvement in group II also was noted, with significant differences between the two

groups (Table 3), which proves that the effect of tendon tension has decreased inside the tunnel after Botox injection. This allowed the partial regeneration of sensory and motor fibers of the median nerve and the alleviation of patient's clinical symptoms.

The improvement in clinical symptoms in group II, though significant in comparison with group I (Table 3), can be explained by the inhibitory effect of intramuscular injection on muscle contraction. Myofascial trigger point is a hyperirritable spot in the skeletal muscle that is associated with a hypersensitive palpable nodule in a taut band and may result in characteristic referred pain, tenderness, motor dysfunction, and autonomic phenomena [24]. This is in contrast with the study reported by Tsai *et al.* [25], which evaluated intracarpal injection of 60 U of botulinum toxin A injected in patients with primary CTS, and the clinical trial sponsored by Sucher [26], which evaluated BOTOX 40U divided into two injection sites of 20U each into Opponens Pollicis and the abductor pollicis brevis, and also the study by Francisco *et al.* [27], which evaluated injection of 30 U of Botox intracarpally guided by ultrasound.

These studies evaluated the anti-inflammatory and the analgesic effect of botulinum toxin A on the neural structure.

There is little mentioned in the literature on the effect of Botox injection in CTS and in the explanation of its mechanism of action on peripheral nerves, but it has proven its efficacy in myofascial pain syndromes, dystonias, tension headaches, and in CTS. Long-term studies are needed to determine the frequency of treatments as the effect only lasts between 3 and 6 months and patients might need two or more injections until complete recovery of the nerve, as this procedure might replace the need for surgery in cases of moderate CTS.

#### **Financial support and sponsorship**

Nil.

#### **Conflicts of interest**

There are no conflicts of interest.

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