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Research Paper

Use of Opera in Carpal tunnel syndrome, a prospective study

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ABSTRACT: *Carpal tunnel syndrome (CTS) is the most common peripheral nerve entrapment syndrome, accounting for 90% of all neuropathies: generally, the patient complains of pain, changes in sensitivity such as numbness, tingling and burning. The aim of our study was to determine the efficacy of a supplement based on alpha lipoic acid (OPERA) in 20 patients with Carpal tunnel syndrome treated at the U.O Neurology, G. Pini Hospital Milan. The diagnosis of CTS was based on electromyography. At the first visit sensory and motor NCS were reported: distal motor latency and speed of sensitive conduction were detected before and at the end of the treatment. To all patients Boston Carpal Tunnel Syndrome Questionnaire was administered. All patients were required to take an OPERA capsule once daily, on an empty stomach for 2 months. At the end of treatment sensory and motor NCS were re-evaluated during electromyography and BCTQ questionnaire analyzed to assess Opera efficacy. Median nerve CMAP distal motor latency, at the end of treatment, improved in 63% of patients with baseline value > 4 m/s. Median nerve SAP velocity conduction (SCV) at the end of treatment improved in 75% of patients in and 55% of them values returned above the normal threshold. Regarding BCTQ, at the end of treatment, SSS score improved in 75% of subjects and FSS in 65%. Conclusions: our study has demonstrated the efficacy of Opera supplementation in Carpal tunnel syndrome. The use of this medication should be taken in consideration as a good practice in this setting of patients. Data from our study are encouraging to be confirmed by further investigations.*

KEYWORDS: *alpha-lipoic acid, boswellia serrata, carpal tunnel syndrome, neuroprotective*

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I. INTRODUCTION

Carpal tunnel syndrome (CTS) is the most common peripheral nerve entrapment syndrome, accounting for 90% of all neuropathies. The clinical symptoms and physical examination findings in patients with this syndrome are recognized widely and various treatments exist, including non-surgical and surgical options. Despite these advantages, there is a paucity of evidence about the best approaches for non-surgical assessment of carpal tunnel syndrome and to guide treatment decisions [1]. Carpal tunnel syndrome is an entrapment neuropathy caused by compression of the median nerve as it travels through the wrist's carpal tunnel. Early symptoms of carpal tunnel syndrome include pain, numbness, and paresthesia. These symptoms typically present, with some variability, in the thumb, index finger, middle finger, and the radial half (thumb side) of the ring finger. Patients often report numbness, tingling, and pain that increase at night. Weakness, clumsiness, and temperature changes also are common complaints. The thumb, digits 2 and 3, and the radial half of digit 4 are typically affected. Patients with carpal tunnel syndrome often will have a positive "flick sign," meaning that symptoms increase when they flick their hand and wrist Pain also can radiate up the affected arm. With further progression, hand weakness, decreased fine motor coordination, clumsiness, and atrophy can occur. In the early presentation of the disease, symptoms most often present at night when lying down and are relieved during the day. With further progression of the disease, symptoms will also be present during the day, especially with certain repetitive activities, such as when drawing, typing, or playing video games. In more advanced disease, symptoms can be constant [2]. Most carpal tunnel syndromes are idiopathic. Other causes include intrinsic factors (which cause pressure within the tunnel), extrinsic factors (which cause pressure from outside the tunnel) and overuse/exertional factors. The most common causes of carpal tunnel syndrome include genetic predisposition, history of repetitive wrist movements such as typing, or machine work as well as obesity, diabetes, autoimmune disorders such as rheumatoid arthritis, and pregnancy [3]. The available literature has

indicated a combination of several pathophysiologic mechanisms in CTS. These mechanisms are interacting and include the increased pressure in the tunnel, median nerve microcirculation injury, median nerve connective tissue compression, and synovial tissue hypertrophy. The neuropathy combines phenomena of compression and traction. Nerve compression and traction may cause disorders of the intraneural microcirculation, lesions in the myelin sheath and the axon, as well as alterations in the supporting connective tissue. The entrapment of a peripheral nerve occurs because of its passage through an anatomical compartment that has become too tight, resulting in altered function within the nerve and dysfunction/damage of the nerve from the site of compression. Median nerve entrapment in the carpal tunnel at the wrist is the most common example of this [4]. Electroneuromyography is the basics for carpal tunnel syndrome diagnosis. Electrodiagnostic studies include nerve conduction studies and electromyography. Nerve conduction studies confirm CTS by detecting impaired median nerve conduction across the carpal tunnel, with normal parameters in the other nerves of the upper limbs. Electromyography assesses neurogenic pattern in the muscles innervated by median nerve [5]. Treatment of CTS incidences in patients depends on the severity of the disease. In minor and modest circumstances, a trial of conventional treatment is encouraged on the patients. This includes splinting, corticosteroids, physical therapy, therapeutic ultrasound, and yoga. Over 80% of persons suffering from carpal tunnel syndrome have a positive response to conservative treatments. However, there is an 80% chance of the symptoms recurring in these patients within one year. Doctors should only consider surgery when the condition produces negative responses to conservative therapies [6]. The use of splints is a significant response action for minor to moderate CTS due to its effortlessness, inexpensiveness, and admissibility. Another management option is engaging patients in physical therapy, including carpal bone mobilization, ultrasounds, and nerve glide exercises [7]. Treatment with oral prednisone, at a dosage of 20 mg daily for 10 to 14 days, improves symptoms and function compared with placebo; the improvement lasts up to eight weeks. Oral corticosteroids are less effective than corticosteroid injection. Nonsteroidal anti-inflammatory drugs, diuretics, and vitamin B_6 are not effective therapies [8,9].

OPERA (Gam Farma srl, Milan, Italy) is a dietary supplement where a lipoic acid (240 mg), Boswellia S. (40 mg), MSM (200 mg) and Bromelain (20 mg) are combined in a single hard gelatin capsule. Those capsules are equipped with Actisystemboxes system, a programmable carrier technology capable to deliver biologically active substances selectively at pH value around 7.01, typically detected in the early stages of inflammation of various tissues, such as myelin sheaths of the nerves. In a previous study OPERA was able to improve chemotherapy-induced peripheral neuropathy symptoms in a prospective series of patients treated with neurotoxic drugs, with no significant toxicity. In another study conducted in patients with polyneuropathy Opera significant reduced pain attacks with good tolerability [10,11].

The aim of our prospective study was to determine the efficacy of OPERA supplementation in a series of patients with Carpal tunnel syndrome.

II. MATERIALS AND METHODS

Our clinical study consisted of a convenience sample of 20 subjects treated at the U.O Neurology, G. Pini Hospital Milan. Informed consent was obtained from all individual participants included in the study. Patients aged more than 18 years old, symptoms as upper limbs paresthesia, numbness, and motor impairment, with a diagnosis of mild to moderate CTS as defined by the criteria of Padua et al. [12] were included. Exclusion criteria included other peripheral nerve diseases, medical conditions potentially associated with polyneuropathy as diabetes or oncological treatments, orthopedic conditions affecting the wrist and pregnancy.

The diagnosis of CTS was based on electromyography. At the first visit sensory and motor NCS were reported: median nerve CMAP distal motor latency and SAP velocity conduction (SCV) were detected before and at the end of the treatment.

Distal motor latency has been detected in right arm in 11 subjects, in left arm in 2 subjects and in both in 7 subjects. Considering the normal limit of < 4 m/s for the distal motor latency, at baseline in 12 subjects was < 4 m/s with average value of 3,67 m/s (range 3,13-3,98) in right arm and 3,57 m/s (range 2,96-3,92) in left arm.

In 8 subjects distal motor latency was > 4 m/s with average value of 4,44 m/s (range 4,05 -5,23) in right arm and 4,26 m/s (range 4,25-4,27) in left arm.

SCV has been detected in right arm in 10 subjects, in left arm in 2 subjects and in both in 8 subjects. Considering the normal limit of > 50 m/s, at baseline in all subjects was below the threshold with average value of 44,4 m/s (range 33,8-48) in right arm and 42,1 m/s (range 36,7 -45,5) in left arm.

To all patients Boston Carpal Tunnel Syndrome Questionnaire was administered. Boston Carpal Tunnel Questionnaire (BCTQ) is a disease-specific measure of self-reported symptom severity and functional status. It is frequently used in the reporting of outcomes from trials into interventions for carpal tunnel syndrome [13].

Boston Carpal Tunnel Questionnaire consists of 2 distinct subscales: Symptom severity scale (SSS) and Functional status scale (FSS).

Symptom severity scale investigates the severity of symptoms (pain, numbness, weakness, paresthesia) during the day and night; it is made up of 11 items to which the patient is asked to respond by indicating a quantitative score on an ordinal scale from 1 to 5.

Functional status scale (FSS) investigates functionality and consists of 8 items to each of which the patient is invited to respond with a quantitative score on an ordinal scale from 1 to 5.

In both subscales, a higher score corresponds to a greater severity of symptoms or a greater inability to perform a certain task with the wrist/hand district.

At baseline Symptom severity scale average value was 2,1 (range 1,5-3,4) and Functional status scale average value was 1,7 (range 1-2,9).

All patients were required to take an OPERA capsule once daily, on an empty stomach for 2 months. At the end of treatment sensory and motor NCS were re-evaluated during electromyography and BCTQ questionnaire analyzed to assess Opera efficacy.

III.RESULTS AND DISCUSSION

Distal motor latency at the end of treatment with Opera in the 12 subjects with normal value at baseline has had average value of 3,52 m/s (range 2,67-3,92) in right arm and 3,44 m/s (range 3,04-3,70) in left arm.

Distal motor latency at the end of treatment in the 8 subjects with baseline value > 4 ms the average value has become 4,16 m/s (range 3,7 -5,15) in right arm and 4,29 m/s (range 4,04-4,55) in left arm: in 5 of the 8 patients **(63%)** there was an improvement bringing their value back to normal threshold.

	BEFORE TREATMENT	**AFTER TREATMENT**
1	4,10 right	3,85 right
2	3,94* right	3,63 right
3	3,85* right	3,92 right
4	4,08 right – 4,04 left	3,94 right – 3,88 left
5	4,25 left	4,55 left
6	4,15 right	3,70 right
7	4,55 right	4,,27 right
8	4,05 right	4,00 right
9	3,95* right	3,80 right
10	3,65* left	3,58 left
11	3,44* right – 2,96* left	3,17 right – 3,04 left
12	3,69* right	3,94 right
13	5,23 right – 4,27 left	5,15 right – 4,04 left
14	3,98* right	3,42 right
15	3,77* right – 3,56* left	3,81 right – 3,58 left
16	3,98* right – 4,19 left	3,77 right –3,52 left
17	3,21* right – 3,92 left	2,67 right – 3,33 left
18	3,44* right – 3,79 left	3,40 right – 3,70 left
19	4,58 right	4,00 right
20	3,13* right	3,13 right

**Normal CMAP distal motor latency detected in the first EMG*

SCV at the end of treatment improved in 15 subjects (**75%)** and in 11 subjects **(55%)** the value returned above the normal threshold: the average value has been 50,2 m/s (range 37,1-75,4) in right arm and 48,9 m/s (range 40 -71,6) in left arm.

	BEFORE TREATMENT	**AFTER TREATMENT**
1	47,1 right – 42,8 left	42,9 right – 41,1 left
2	48 right	75,4 right
3	43,2 right	47,5 right
4	45,5 right – 43,2 left	43,6 right – 40,8 left
5	41,5 left	40,0 left
6	47,5 right	57,1 right
7	43,9 right	47,0 right
8	44,2 right	47,5 right
9	42,9 right	56,8 right
10	40,8 left	51,6 left
11	44,0 right – 43,3 left	60,0 right – 71,6 left
12	45,5 right	41,1 right
13	33,8 right – 43,8 left	37,1 right – 42,4 left
14	48,5 right	59,3 right
15	43,2 right – 42,6 left	44,6 right – 49,9 left
16	43,8 right – 41,1 left	48,0 right – 53,7 left
17	47,4 right – 36,7 left	50,5 right – 46,3 left

18	42,4 right – 45,5 left	46,1 right – 50,9 left
19	40,8 right	48 right
20	48 right	50,3 right

Regarding BCTQ, at the end of treatment SSS score improved in 15 subjects **(75%)** and FSS in 13 **(65%) :** SSS average value has become 1,7 (range 1-2,5) and FSS average value 1,3 (range 1-2,4).

	SYMPTOM SEVERITY SCALE		**FUNCTIONAL STATE SCALE**	
	BEFORE	**AFTER**	**BEFORE**	**AFTER**
1	1,9/5	2/5	1,4/5	1,4/5
2	2/5	1,2/5	1,9/5	1,1/5
3	3,1/5	2,1/5	1,5/5	1,7/5
4	3,4/5	2,4/5	2,1/5	1,7/5
5	2,2/5	2,2/5	2,5/5	2,4/5
6	2,4/5	1,8/5	2,1/5	1,1/5
7	2/5	1,4/5	1,1/5	1,1/5
8	2/5	2,2/5	1,1/5	1/5
9	2,5/5	1,5/5	1,5/5	1/5
10	1,5/5	1/5	1,4/5	1/5
11	1,7/5	1/5	2,1/5	1/5
12	2/5	2,1/5	1,5/5	1,9/5
13	1,8/5	1,6/5	2/5	1/5
14	1,9/5	1,3/5	1,6/5	1/5
15	3,3/5	2,5/5	2,9/5	2,4/5
16	2/5	2,3/5	1/5	1,1/5
17	2/5	1,7/5	1,6/5	1,1/5
18	1,5/5	1,1/5	1,4/5	1,1/5
19	2/5	1,9/5	1,2/5	1,2/5
20	1,8/5	1,7/5	1,4/5	1,4/5

Carpal tunnel syndrome (CTS) is the most common peripheral nerve entrapment syndrome worldwide, accounting for 90% of all neuropathies. In the initial phase of carpal tunnel syndrome, various symptoms may be present involving the first three fingers of the hand. Generally, the patient complains of pain, changes in sensitivity such as numbness, tingling and burning. The symptoms occur mainly at night, causing frequent awakenings and the need to shake and shake the hand to make them go away. In the morning, generally, a feeling of awkwardness and stiffness in the hand persists which tends to improve over the course of the day. In the subsequent phases, the symptoms become progressively more disabling and occur more and more often even during the day, during manual activities, especially if repetitive. In the terminal phases of the process, there can be a complete loss of thermal and pain sensitivity. Electromyography and nerve conduction studies are the basis for carpal tunnel syndrome diagnosis. In the initial stages, conservative treatment is taken into consideration, based on the topical application of a local anti-inflammatory, the use of a wrist brace, physical therapies, in particular YAG laser therapy and the use of nutritional supplements such as L- acetyl-carnitine, alpha-lipoic acid [14] and B vitamins. In the case of particularly disabling symptoms that have arisen in the short term, it is possible to perform an infiltration with corticosteroids, preferably under ultrasound control, inside the carpal canal. In case of failure of conservative therapy or if the deficit is severe already at the first visit, it is recommended to perform surgery.

The aim of our study was to determine the efficacy of a supplement based on alpha lipoic acid (OPERA) in 20 patients with Carpal tunnel syndrome treated at the U.O Neurology, G. Pini Hospital Milan. The diagnosis of CTS was based on electromyography. At the first visit sensory and motor NCS were reported: distal motor latency and speed of sensitive conduction were detected before and at the end of the treatment. To all patients Boston Carpal Tunnel Syndrome Questionnaire was administered. All patients were required to take an OPERA capsule once daily, on an empty stomach for 2 months. At the end of treatment sensory and motor NCS were re-evaluated during electromyography and BCTQ questionnaire analyzed to assess Opera efficacy.

Median CMAP distal motor latency at the end of treatment in the 8 subjects with baseline value > 4 m/s the average value has become 4,16 m/s (range 3,7 -5,15) in right arm and 4,29 m/s (range 4,04-4,55) in left arm: in 5 of the 8 patients (**63%)** there was an improvement bringing their value back to normal threshold.

SCV at the end of treatment improved in 15 subjects (**75%)** and in 11 subjects **(55%)** the value returned above the normal threshold: the average value has been 50,2 m/s (range 37,1-75,4) in right arm and 48,9 m/s (range 40 -71,6) in left arm.

Regarding BCTQ, at the end of treatment SSS score improved in 15 subjects **(75%)** and FSS in 13 **(65%):** SSS average value has become 1,7 (range 1-2,5) and FSS average value 1,3 (range 1-2,4).

IV. CONCLUSION

Our study has demonstrated the efficacy of Opera supplementation in patients with mild to moderate Carpal tunnel syndrome.

Electromyography performed after treatment has shown an improvement of distal motor latency of median CMAP in 8 subjects, an increase in SCV in 15 subjects and a return to normal values in 11 subjects. Regarding Boston Carpal Tunnel Questionnaire, there has been an improvement both in symptom severity scale for 75% of subjects and functional severity scale in 65% of subjects.

The use of this medication demonstrated a neuroprotective action and should be taken in consideration as a good practice in this setting of subjects, not only for patients with initial CTS, to prevent the worsening of symptoms, but also for advanced CTS, to help decrease the severity of subjective symptoms in combination with surgery.

Due to the limited number of subjects examined, it is necessary to continue to evaluate CTS patients on a larger scale and in a longer period, to assess the best treatment protocol for every severity grade. However, data from our study are encouraging to be confirmed by further investigations.

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