Alpha-Lipoic Acid Effectiveness in Early Stages of Carpal Tunnel Syndrome: Short Term Follow-up

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Abstract

Carpal Tunnel Syndrome (CTS) is still the most common nerve compression syndrome of the upper extremity. The aim of this paper is to analyze the effectiveness of Alpha-Lipoic Acid (ALA) in early stages of carpal tunnel syndrome. We conducted a double-blind prospective study. A total of 84 patients with instrumental diagnosis of carpal tunnel syndrome at an early stage, based on nerve conduction study, were evaluated. The primary endpoint was the search for improvement of parameters in electrophysiological studies, correlated with the administration of ALA. Secondary endpoints were static 2-points discrimination and the Boston Carpal Tunnel Syndrome Questionnaire (BCTSQ). The statistical analysis has not shown any type of correlation between the evolution of electromyographic measurements and the administration of ALA (p-value > 1.2). On the other side, the statistical analysis showed an improvement regarding the 2-point discrimination and the BCTSQ (p-value < 0.05). Alpha-lipoic acid did not improve nerve conduction velocity, but a statistically significant reduction of symptoms referred by the Boston Carpal Tunnel score, and an improvement of the two-point discrimination test was obtained.

Keywords

1 Carpal Tunnel 1; 2 Alpha-Lipoic Acid 2; 3 Conservative Treatment

Introduction

Carpal Tunnel Syndrome (CTS) is still the most common nerve compression syndrome of the upper extremity, with an incidence rate in 2001 of 1.8/1000 of the population, reaching an incidence of carpal tunnel decompression between 43 and 73 per 100,000 a year in the United Kingdom and approximately 400,000 surgical procedures performed every year in the United States [1].

The pathology itself was first described by Sir James Paget in 1854, while the elective treatment of open section of the retinaculum was described by Learmonth in 1933 and spread by Phalen in the 1950s [2].

Literature is replete with articles with 4416 indexed publications (source PubMed) between 2009 and 2019. A very large number of patients have a mild carpal tunnel syndrome and do not require immediate surgery; therefore, conservative therapeutic strategies can and should be implemented for those cases. Among the conservative therapeutic strategies, we can mention the use of night-time static splints, physiotherapy treatments and the intake of neurotrophic agents.

The aim of this paper is to analyze the effectiveness of Alpha-Lipoic Acid (ALA) in early stages of carpal tunnel syndrome.

Materials and Methods

We conducted a retrospective study. A total of 84 patients with instrumental diagnosis of carpal tunnel syndrome at an early stage, based on nerve conduction study were evaluated.

Boston Carpal Tunnel Syndrome Questionnaire (BCTSQ) and static 2-point discrimination test (using Dellon discriminator) were administered. The patients were treated with 2 different strategies. Both patients' groups were treated conservatively: group A (n-42) included patients treated with a static thermoplastic splint for three months during night-time while group B (n-42) patients were treated with a static thermoplastic splint for three months during night-time in association with ALA administration for 60 days. All patients underwent a follow up at three months with nerve conduction study, static 2-point discrimination test and Boston Carpal Tunnel Syndrome Questionnaire (BCTSQ).

The first author performed all physical examinations and the follow-up.

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All nerve conduction studies were performed in the same care institution.

The inclusion criteria were:

- Early stage carpal tunnel syndrome (Bland's CTS severity index of 1 or 2) [3]
- Little or no impairment with everyday activities
- Age between 18 and 80 years
- Anesthesia or paraesthesia in the median nerve territory
- Positive Phalen, reverse Phalen or Tinel test

The exclusion criteria were:

- Previous surgery on the hand affected by carpal tunnel syndrome
- Previous conservative treatment for carpal tunnel syndrome on the same hand
- Clinical history of polyneuropathy
- Diagnosis of diabetes or metabolic syndrome
- Diagnosis of polymyalgia
- Post traumatic carpal tunnel syndrome
- Rheumatoid arthritis or other rheumatological pathology
- Hypersensitivity to alpha lipoic acid
- Age inferior to 18 and superior to 80

The study was conducted in accordance with the national ethics criteria.

The study was also conducted in accordance with the Helsinki convention and good clinical practice considering that the administration of ALA-R was already used in the preoperative management protocols at our institute, a formal ethical approval was not requested for this study. Written informed consent was obtained from all participants.

Drug components were 800 mg ALA, microcrystalline cellulose, dibasic calcium phosphate, calcium carbonate, silicon dioxide, talc, magnesium stearate, sodium carboxymethylcellulose, glycerol behenate, hydroxypropyl methylcellulose, polyvinylpyrrolidone, shellac, acetylated mono and diglycerides of fatty acids; dye: E171.

A total of 102 patients were screened, but 14 were not eligible and 4 patients declined to participate in the study.

Median motor distal latency was obtained by recording over the abductor pollicis brevis muscle with stimulation at the wrist. Median sensory nerve conduction velocity was calculated between the index finger and the wrist. If both of these tests were normal, an orthodromic palmar stimulation was performed. A median-ulnar mixed nerve palm difference of 0.4 ms or greater was considered abnormal.

The statistical analysis was carried out through the SPSS (IBM) software.

For the dichotomous variables the chi-square test and the students' T test were used. For continuous variables, nonparametric tests were carried out.

The primary endpoint was to evaluate the improvement of parameters in electrophysiological studies, correlated with the administration of ALA.

Secondary endpoints were to evaluate static 2-points discrimination and the Boston Carpal Tunnel Syndrome Questionnaire (BCTSQ).

The two-point discrimination test is used to assess if the patient is able to identify two close points on a small area of skin, and how fine the ability to discriminate this are. It is a measure of tactile agnosia, or the inability to recognize these two points despite intact cutaneous sensation and proprioception.

The 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.

Results

A total of 84 patients were enrolled in this study from March 2018 and January 2019. The last follow up of the last patient was conducted in April 2019.

Patients were equally distributed between two groups.

We registered no adverse effect with ALA administration.

We found a drop-out of 4 patients in group A and 7 patients in group B. This dropout rate was calculated during the sample size calculation, thus it did not affect our results.

The demographic characteristics of the sample in question were:

- 61 women and 23 men
- Mean age of 58 (SD +/- 4,2 years)
- Symptoms onset 13 months (DS +/- 7,4 months)

The value of orthodromic sensory conduction velocity from index finger to wrist was in mean 43,2 m/s (SD +/- 4,8) for group A and of 42,6, (SD +/- 2,8) for group B before the treatment. After the treatment the mean was 41,3 (SD +/- 4,5) for group A and 40,2 (SD +/- 3,9) for group B (Table 1).

The measurement of BCTSQ was in mean 35,3 (SD +/- 5,6) for group A and of 33,6 (SD +/- 3,4) for group B before the treatment. After the treatment the mean was 34,4 (SD +/- 4,5) for group A and 25,6 (SD +/- 7,6) for group B.

The Two-point discrimination test was in mean 6,4 (SD +/- 2,2) for group A and of 6,7 (SD +/- 2,5) for group B before the treatment. After the treatment the mean was 6,3 (SD +/- 1,9) for group A and 4,9 (SD +/- 1,3) for group B (Table 2).

The statistical analysis has not shown any type of correlation between the evolution of electromyographic measurements and the administration of ALA (p-value > 1.2).

On the other side, the statistical analysis showed an improvement regarding the 2-point discrimination and the BCTSQ, for both a p-value < 0.05 was found.

	Before	After
Group A	35,3 (SD +/- 5,6)	34,4 (SD +/- 4,5)
Group B	33,6 (SD +/- 3,4)	25,6 (SD +/- 7,6)

Table 1: BCTSQ results.

	Before	After
Group A	6,4 (SD +/- 2,2)	6,3 (SD +/- 1,9)
Group B	6,7 (SD +/- 2,5)	4,9 (SD +/- 1,3)

Table 2: Point discrimination test results.

Discussion

Alpha-lipoic acid is an organophosphoric compound produced by plants, animals and humans, and was first isolated from Reed in 1951 [4].

This molecule has several characteristics, such as its antioxidant property, and it is widely used for the treatment of diabetic polyneuropathy, associated with pain and paraesthesia. Naturally, ALA is localized at the mitochondrial level, where it acts as a cofactor for pyruvate dehydrogenase and alpacetogluarate dehydrogenase.

Despite the significant amount of possible therapeutic effects, ALA has a relatively low efficacy due to its kinetic profile. Some studies suggest that it has a bioavailability of approximately 30%, a short half-life and that it is inactivated by gastric acids and liver metabolism [5]. Furthermore, it seems that bioavailability decreases with advancing age and that there are no substantial differences based on gender.

Several studies have shown that there may be a rationale for using ALA in cases of compressive neuropathy, such as carpal tunnel syndrome, the most frequent compressive neuropathy found in clinical practice [6].

Symptoms are caused by compression of the median nerve below the carpal tunnel. Nerve damage is caused by a reduction in blood flow in the endoneural capillaries that causes an alteration in the blood-neural barrier level; thus causing endoneural edema, venous congestion, an ischemic state that leads to an alteration of the nervous metabolism. Clinically the patient will report acroparesthesias at the level of the innervation area of the median nerve, and in the more advanced stages dexterity movements are impaired, up to the paralysis of the opposing musculature.

Patients with mild and moderate carpal tunnel syndrome may be offered conservative treatments (night splints, corticosteroid infiltrations and physical therapies). Patients with moderate and severe carpal tunnel syndrome who have not benefited from conservative therapies for more than 3-6 months should instead be directed to surgical decompression of the median nerve.

At the level of the central nervous system, ALA appears to have neuroprotective and antioxidant effects, as shown in several preclinical and clinical studies. It has been demonstrated that the positive effects of ALA can also be attributed to the activation of catalase and superoxide dismutase [7]. These same mechanisms can be considered in the effect that ALA has in the treatment of carpal canal syndrome, since most of the etiopathogenic mechanisms seem to be due to the damage from ischemia/reperfusion.

Some authors have shown an improvement in electrophysiological parameters in patients undergoing surgical nerve decompressions, when ALA was administered in combination with other antioxidants such as VitB and curcumin during the perioperative period [8,9].

Following surgical decompression of the median nerve, the administration of ALA does not improve the recovery of the conduction speed or the Boston Carpal Tunnel Score, but it enhances the function on the pillar pain and two-point discrimination [10].

Therefore, it is not yet completely clear and explained why alpha-lipoic acid is beneficial in case of peripheral neuropathy. In the case of our study, we found a benefit of subjective perception in the face of a failure to improve electrophysiological parameters. Subsequent studies may be useful for studying this peculiarity.

This study focused on patients suffering from early carpal tunnel. This is because we wanted to standardize the sample in question to try to reduce the dispersion of the data. Subsequent studies will serve to define the role of alpha lipoic acid in advanced studies of carpal tunnel syndrome and the use of this molecule as an adjuvant and neoadjuvant therapy in the case of surgery.

The goal of the orthopaedic surgeon should be always to avoid a surgical procedure when possible. Nevertheless, a high percentage of patient will undergo a surgical procedure for carpal tunnel decompression after a conservative treatment. However, our goal is to postpone the surgery as long as possible. The association of night thermoplastic splint and ALA so ministration has shown a better improvement of symptoms and satisfaction of the patient, when compared with the simple use of the splint; though no significant differences have been detected.

Conclusion

Alpha-lipoic acid did not improve nerve conduction velocity but a statistically significant reduction of symptoms referred by the Boston Carpal Tunnel score, and an improvement of the two-point discrimination test was obtained.

References

1. Atroshi JM, Melhorn I, Talmage JB. Prevalence of carpal tunnel syndrome in a general population. *Orthopedics*. 2013;36(7):497-8.
2. Phalen GS. The carpal tunnel syndrome. *Instructional Course Lectures*. 1957;14:142-8.
3. Bland JD. A neurophysiological grading scale for carpal tunnel syndrome. *Muscle and Nerve: Official J AM Assoc Electrodiagnostic Med* 2000;23(8):1280-3.
4. Reed LJ, DeBusk BG, Gunsalus IC, Hornberger CS. Crystalline α -lipoic acid: a catalytic agent associated with pyruvate dehydrogenase. *Sci*. 1951;114(2952):93-4.
5. Ikuta N, Okamoto H, Furune T, Uekaji Y, Terao K, Uchida R, Iwamoto K, Miyajima A, Hirota T, Sakamoto N. Bioavailability of an R- α -lipoic acid/ γ -cyclodextrin complex in healthy volunteers. *Int J Mol Sci*. 2016;17(6):949.
6. Passiatore M, Perna A, De-Vitis R, Taccardo G. The use of Alfa-Lipoic Acid-R (ALA-R) in patients with mild-moderate carpal tunnel syndrome: A randomised controlled open label prospective study. *Malaysian Ortho J*. 2020;14(1):1.
7. Farr SA, Poon HF, Dogrukol-Ak D, Drake J, Banks WA, Eyerman E, et al. The antioxidants α -lipoic acid and N-acetylcysteine reverse memory impairment and brain oxidative stress in aged SAMP8 mice. *J Neurochem*. 2003;84(5):1173-83.
8. Boyaci MG, Eser O, Kocogullari CU, Karavelioglu E, Tokyol C, Can Y. Neuroprotective effect of alpha-lipoic acid and methylprednisolone on the spinal cord ischemia/reperfusion injury in rabbits. *Br J Neurosurg*. 2015;29(1):46-51.
9. Monroy Guizar EA, Garcia Benavides L, Ambriz Plascencia AR, Pascoe Gonzalez S, Totsuka Sutto SE, Cardona Munoz EG, et al. Effect of alpha-lipoic acid on clinical and neurophysiologic recovery of carpal tunnel syndrome: a double-blind, randomized clinical trial. *J Medicinal Food*. 2018;21(5):521-6.
10. Boriani F, Granchi D, Roatti G, Merlini L, Sabattini T, Baldini N. Alpha-lipoic acid after median nerve decompression at the carpal tunnel: a randomized controlled trial. *J Hand Surg*. 2017;42(4):236-42.