EREDETI KÖZLEMÉNY

ORIGINAL ARTICLE

Efficacy of intravenous alpha lipoic acid in the treatment of neuropatic pain due to carpal tunnel syndrome

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Background and purpose – In this study, we analyzed the effect of oral and oral + intravenous Alpha-lipoic acid (ALA) treatment on pain level and physical examination findings in patients diagnosed with carpal tunnel syndrome (CTS).
Methods – A total of 115 patients patricipated in the study. Physiotherapy and wrist splint were first applied to all patients diagnosed with CTS in the study. 40 patients were treated with oral ALA after iv. ALA therapy, 35 patients received only oral ALA treatment and 40 patients did not receive any medication. The patients were divided into 3 groups as those who received only splint treatment and physiotherapy, those who received oral ALA treatment, and those who received oral ALA treatment after iv. treatment. All patients were assessed before the treatment, and at the 1st and 3rd months of the treatment. In clinical assessment, visual analog scale (VAS) forms were filled to define the pain severity, the Boston symptom severity scale (BSSS) and Boston functional status scale (BFDS) were filled for evaluating symptoms and functional status.
Results – VAS, BSSS and BFDS scores of the patients who were treated with intravenous and then oral ALA were found to be significantly lower at the end of both the 1st and 3rd months compared to the patients who received only oral ALA or no medication (p=0.001; p<0.001), (p=0.001; p<0.001), (p=0.006; p<0.001).
Conclusion – We think that iv. ALA is effective in the treatment of symptoms associated with CTS.

Keywords: alphalipoic acid, carpal tunnel syndrome, pain

Az intravénás α-liponsav hatékonysága a carpalis alagút szindróma okozta neuropathiás fájdalom kezelésében
Öztürk G, MD; Demiryurek BE, MD

Háttér és cél – Ebben a vizsgálatban elemeztük az orális és az orális + intravénás α-liponsav- (ALA-) kezelés hatását a fájdalom szintjére és a fizikális vizsgálati leletekre carpalis alagút szindrómával (CAS) diagnosztizált betegeknél.
Módszerek – Összesen 115 beteg vett részt a vizsgálatban. A vizsgálatban először fizioterápiát és csuklósínt alkalmaztak minden CTS-sel diagnosztizált betegnél. Negyven beteget kezeltek orális ALA-val az intravénás ALA-terápia után, 35 beteg csak szájon át kapott ALA-kezelést, 40 beteg pedig nem kapott semmilyen gyógyszert. A betegeket három csoportra osztottuk: azokra, akik csak sínkezelésben és fizioterápiában részesültek, azokra, akik orális ALA-kezelésben részesültek, és azokra, akik intravénás ALA-kezelés után orális ALA-kezelésben részesültek. Minden beteget megvizsgáltak a kezelés előtt, valamint a kezelés 1. és 3. hónapjában. A klinikai értékelés során a betegek a fájdalom súlyosságának meghatározására a vizuális analóg skálát (VAS), a tünetek és a funkcionális állapot értékelésére a Boston Tünetsúlyossági Skálát (BSSS) és a Boston Funkcionális Állapot Skálát (BFDS) töltötték ki.
Eredmények – A VAS-, BSSS- és BFDS-pontszámok az intravénás, majd orális ALA-val kezelt betegeknél mind az 1., mind a 3. hónap végén szignifikánsan alacsonyabbnak bizonyultak azokhoz a betegekhez képest, akik csak orális ALA-t kaptak vagy nem kaptak gyógyszert (p = 0,001; p < 0,001), (p = 0,001; p < 0,001), (p = 0,006; p < 0,001).
Következtetés – Úgy gondoljuk, hogy az intravénás ALA hatékony a CTS tüneteinek kezelésében.

Kulcsszavak: α-liponsav, carpalis alagút szindróma, fájdalom

Carpal tunnel syndrome (CTS) is the most frequently experienced upper extremity trap neuropathy that results from median nerve entrapment at the wrist and lowers the conduction velocity of the median nerve[1]. Its prevalence is 3-6% and it is more frequently seen in women[2, 3]. Among the many CTS risk factors such as pregnancy, obesity, recurrent wrist movements, occupational reasons, and female gender, chronic diseases may also underlie the etiology of CTS including diabetes mellitus (DM), hypothyroidism and rheumatoid arthritis (RA). As a pathophysiological mechanism, compression on the median nerve first disrupts the microcirculation, and subsequently venous pooling happens. As the pressure continues, following intraneural edema leads to myelin loss and fibrosis[2]. Diagnosis is made by physical examination, clinical symptoms and electromyographic (EMG) tests[4–6].

Alpha-lipoic acid (ALA, thioctic acid) was first discovered by *Reed* et al in 1951[7]. ALA has a key role in the pyruvate dehydrogenase enzyme complex (PDC) functioning in mitochondria which is composed of three enzymes: E_1 (pyruvate dehydrogenase), E_2 (dihydrolipoyl transacetylase), and E_3 (dihydrolipoyl dehydrogenase)[8]. The biochemical and metabolic actions of ALA in diseases such as diabetes that cause oxidative stress and neuropathy are well established[9–11]. There exist several investigations in the literature evaluating the efficacy of ALA in the treatment of CTS[12–16]. However, the ALA which was utilized in these studies was in oral form and no study exists assessing the efficacy of intravenous ALA treatment. In this current investigation, it was aimed to determine the effects of oral versus oral+intravenous ALA treatments on CTS pain severity and physical examination findings in patients diagnosed with CTS.

Methods

The study, which was planned cross-sectional, was carried out with patients who were administered to the Neurology department of Acıbadem Kocaeli Hospital and Memorial Sisli Hospital.

Participants

Following detailed physical and EMG examination of all subjects participating in the study, 164 patients between the ages of 18-70 who were diagnosed with right, left or bilateral mild CTS were selected. Among those, 49 patients were excluded because they could not continue ALA treatment and did not attend the outpatient clinic; thus, a total of 115 patients were involved in the study. After the diagnosis of CTS, physiotherapy and wrist splints were applied to all of the patients including those who were not treated with oral or oral+intravenous ALA. 40 patients were treated with oral ALA after iv. ALA therapy, 35 patients received only oral ALA treatment and 40 patients did not receive any medication. The patients were divided into 3 groups as those who received only splint treatment and physiotherapy, those who received oral ALA treatment, and those who received oral ALA treatment after iv treatment. All patients were examined before the treatment and at the 1st and 3rd months of the ALA treatment.

To calculate the sample size, power analysis was employed [Type error (0.05), target power (0.80), difference between means (δ=15.22), standard deviation value (σ=160.9)]. Patients with vitamin D, vitamin B12 and folic acid deficiency in the last 6 months or receiving vitamin therapy, patients with DM, thyroid disease, osteoporosis, rheumatoid arthritis, thoracic outlet syndrome, cervical radiculopathy, wrist fracture, tendon and connective tissue disease, renal failure and chronic pain patients with diseases that cause hereditary or acquired polyneuropathy, those with a history of neurological and psychiatric diseases and previous CTS surgery, and those with a diagnosis of severe CTS and those who receive medical treatment to neuropathic pain were excluded.

Drug administration schedule

Treatments were assigned after a simple randomization procedure using sealed envelopes. All patients were given general advice on how to take the drug. Thirtyfive patients received oral treatment with 600 mg of racemic ALA (mixture of 50/50 of R and S enantiomers) once daily (before food) for 90 days. Forty patients received intravenous racemic ALA 600 mg/50 ml every afternoon after a meal (to prevent hypoglycemia) for 30 days acording to ALA protocol; and after the termination of this 30 day treatment regime, they received oral treatment with 600 mg of racemic ALA (mixture of 50/50 of R and S enantiomers) once daily before food for 60 days[17].

Scales used

In clinical assessment, visual analog scale (VAS) forms were filled to define the pain severity and Boston CTS questionnaire forms were filled for evaluating symptoms and functional status. The VAS, utilized to evaluate the pain severity of patients, is a 10 cm straight line scale with numbers between 0 and 10 (0: no pain, 10: worst possible pain)[18]. Boston symptom severity scale (BSSS) and Boston functional status scale (BFDS) were two parts of the Boston CTS survey. This scale was developed by *Levine* and coworkers in 1993 and the Turkish validity and reliability study of this questionnaire was achieved by *Sezgin* et al.[19–21]. For each item, there are 5 different questions that can be responded quantitatively with a stratified point scale from 1 to 5. The average count is calculated by dividing the total score by the number

of questions; and therefore ranges from 1 to 5. Higher scores demonstrate more severe declines in functional capacity. While there are 11 questions in the symptom severity scale, there are 8 questions in the functional capacity scale[21].

Electrophysiological examinations

Electrophysiological examinations of all groups included in the investigation were performed by the same physician with a Nihon Kohden brand (Tokyo, Japan) EMG device[22]. The research was conducted with superficial electrodes, using standard nerve conduction techniques [(mild CTS: difference between median sensory response distal latency and ulnar sensory response distal latency >1 ms, or 4th finger registered median ulnar nerve difference between peak latencies >0.5 ms[23]. Moderate CTS: In addition to the above, expension of the distal latency of the median motor nerve (>4.0 ms)[23]. Severe CTS: Often low/lack of sensory potential amplitude and decreased motor response amplitude (5.5 ms)][23]. It was evaluated whether there was a relationship between the severity of CTS pain and functionality after ALA use among the patient groups (groups that received only oral ALA treatment, received oral ALA treatment after iv. ALA treatment, and did not receive medication).

Statistical analysis

NCSS (Number Cruncher Statistical System) 2007 (Kaysville, Utah, USA) program, Shapiro-Wilk test and graphical examinations were used for the conformity of the quantitative data to the normal distribution. Bonferroni correction, Kruskal-Wallis test, Dunn-Bonferroni test, and Bonferroni-corrected pairwise evaluations were used.

Table 1. *Demographic features*

		n (%)
Sex	Male	54 (47.0)
	Female	61 (53.0)
Age	*Mean±Std*	44.72±17.48
	Median (Min-Max)	41 (19–86)
Mild/Moderate CTS	Mild	55 (47.8)
	Moderate	60 (52.2)
Unilateral /Bilateral CTS	Unilateral	60 (52.2)
	Bilateral	55 (47.8)
Treatment	No medical treatment	40 (34.8)
	ALA – oral	35 (30.4)
	ALA – iv+oral	40 (34.8)

CTS: carpal tunnel syndrome, ALA: alpha-lipoic acid, iv: intravenous

Results

The demographic features of the study is summed up in **Table 1**. Research was carried out with 115 cases, 47% (n=54) male and 53% (n=61) female, in the Acibadem Kocaeli hospital and Memorial Sisli Hospital between April and September 2021. Age ranges were 19 to 86 years, with a mean of 44.72±17.48 years. Thirty seven patients had hypertension and 12 patients had coronary artery disease and therefore were receiving medical treatment. Eight case had a history of surgical operation because other reason than CTS.

Among the cases, 34.8% (n=40) did not receive pharmacological treatment, 30.4% (n=35) received oral ALA,

Table 2. Comparison of descriptive characteristics by treatment groups

		Treatment groups			*p*
		No medical treatment (n=40)	Oral ALA (n=35)	Oral ALA after i.v. treatment (n=40)	
Sex	Male	19 (47.5)	16 (45.7)	19 (47.5)	[a]*1.000*
	Female	21 (52.5)	19 (54.3)	21 (52.5)	
Age	*Mean±Std.*	44.18±17.57	47.89±17.18	42.5±17.7	[b]*0.404*
	Median (Min-Max)	41 (19–82)	49 (19–82)	37 (19–86)	
Mild / Moderate CTS	Mild	21 (52.5)	17 (48.6)	17 (42.5)	[a]*0.669*
	Moderate	19 (47.5)	18 (51.4)	23 (57.5)	
Unilateral/Bilateral CTS	Unilateral	20 (50.0)	18 (51.4)	22 (55.0)	[a]*0.918*
	Bilateral	20 (50.0)	17 (48.6)	18 (45.0)	

[a]Fisher Freeman Halton Test, [b]One-Way ANOVA Test
CTS: carpal tunnel syndrome, ALA: alpha-lipoic acid, iv: intravenous

Table 3. *Comparison of VAS scores*

VAS	Before Tr.	1. month	3. month		Before Tr. – 1. month Δ	Before Tr. – 3. month Δ	1. month – 3. month Δ
	Median (IQR)	*Median (IQR)*	*Median (IQR)*	*p*	*Median (IQR)*	*Median (IQR)*	*Median (IQR)*
No ALA treatment (n=40)	4 (3–7)	5 (3–8)	6 (3–7)	[c]*0.001***	–1 (–1/0)[cc]	–1(–2/0.5)[cc]	0 (–1/0)
Oral ALA (n=35)	4 (3–5)	3 (2–6)	3 (1–4)	[c]*0.001***	–1 (–2/0)[cc]	–2 (–3/–1)[cc]	0 (–1/0)
Oral ALA after iv treatment (n=40)	6 (3–7)	4 (1–5)	2 (1–3)	[c]*0.001***	–2 (–3.5/–1.5)[cc]	–3 (–4/–2)[cc]	0 (–0.5/0)
p	[d]*0.429*	[d]*0.001***	[d]*0.001***		[d]*0.001***	[d]*0.001***	[d]*0.620*

[d]Kruskal Wallis test& Dunn Bonferroni Test
[c]Friedman test & [cc]Dunn Bonferroni Test (p<0,01 significance of changes in comparison to the pretreatment values)
**p<0,01
VAS: Visual Analog Scale, Before Tr.: before treatment, ALA: alpha-lipoic acid

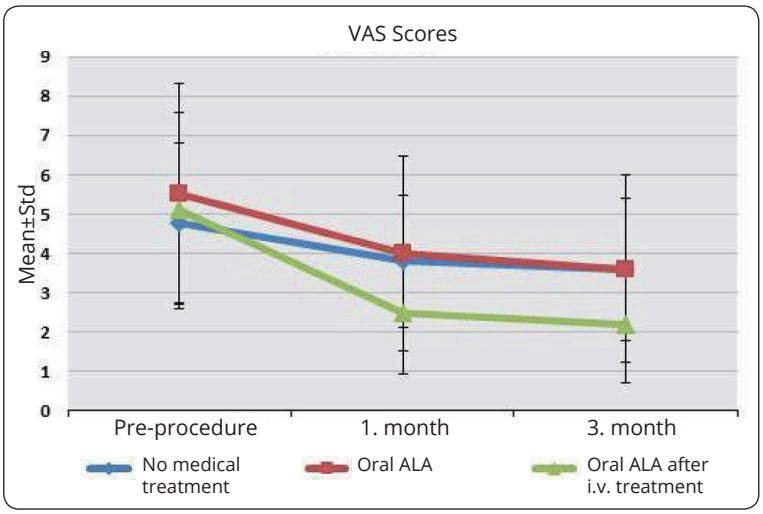

Figure 1. *VAS Scores changes of treatment and non-treatment groups*

and 34.8% (n=40) received oral ALA treatment after iv. treatment. **Table 2** summarizes the comparison of descriptive characteristics by treatment groups. Gender, age, the severity status (mild or moderate CTS) and side (unilateral versus bilateral) of the cases did not differ statistically according to the treatment groups (p>0.05).

Table 3 summarizes the comparison of VAS scores by treatment groups and **Figure 1** depicts these changes. The VAS scores of the subjects who received oral ALA after iv. treatment were significantly lower than those who did not receive medication and those who received oral ALA treatment (p=0.009; p=0.003; p<0.01). A statistically significant difference was found between the 3rd month VAS scores of the treatment groups (p=0.001; p<0.01). The VAS scores of the subjects who received oral ALA after iv. treatment were significantly lower than those who did not receive medication and those who received oral ALA treatment (p=0.004; p=0.006; p<0.01).

For the group that did not receive ALA treatment: A significant difference was found between the VAS scores of the cases without pharmacological treatment (p=0.001; p<0.01). The decreases in the 1st and 3rd month VAS scores compared to the pre-procedure were found to be statistically significant (p<0.01). For the oral ALA treatment group: A significant difference was found between the VAS scores of the cases treated with oral ALA (p=0.001; p<0.01). The decreases in the 1st and 3rd month VAS scores compared to the pre-procedure were found to be statistically significant (p<0.01). The change in VAS scores in the 3rd month compared to the first month was not significant (p>0.05). For oral ALA treatment group after iv. treatment: A significant difference was found between the VAS scores of the cases treated with oral ALA after iv. treatment (p=0.001; p<0.01). The decreases in the 1st and 3rd month VAS scores compared to the pre-procedure were found to be statistically significant (p<0.01). The change in VAS scores in the 3rd month compared to the first month was not significant (p>0.05).

Table 4 summarizes the comparison of Boston Symptom Severity scores by treatment groups and **Figure 2** depicts these changes. A statistically significant difference was found between the first month Boston symptom severity values in the treatment groups (p=0.011; p<0.05). Boston Symptom Severity scores of the patients who received oral ALA after iv. treatment were signifi-

Table 4. *Comparison of Boston Symptom Severity Scores*

Boston Symptom Severity Score	Before Tr.	1. month	3. month		Before Tr. – 1. month Δ	Before Tr. – 3. month Δ	1.month – 3. month Δ
	Mean±Std	*Mean±Std*	*Mean±Std*	*p*	*Mean±SD*	*Mean±Std*	*Mean±Std*
No ALA treatment (n=40)	27.50±11.49	25.35±10.36	24.48±9.99	[e]*0.001***	–2.15±1.72[ee]	–3.03±2.20[ee]	–0.88±0.99
Oral ALA (n=35)	31.57±14.3	27.77±12.58	27.14±12.34	[e]*0.001***	–3.80±2.44[ee]	–4.43±2.74[ee]	–0.63±1.14
Oral ALA after iv treatment (n=40)	28.88±11.87	20.48±8.89	19.55±8.51	[e]*0.001***	–8.40±4.97[ee]	–9.33±5.63[ee]	–0.93±1.58
p	[b]*0.368*	[b]*0.011**	[b]*0.006**		[d]*0.001***	[d]*0.001***	[d]*0.575*

[b]One-Way ANOVA Test & Bonferroni Test
[e]Repeated Measures Test & [ee]Bonferroni Test
[d]Kruskal Wallis Test & Dunn Bonferroni Test
**p<0,01, *p<0,05
Before Tr.: before treatment, Std: standart deviation, ALA: alpha-lipoic acid

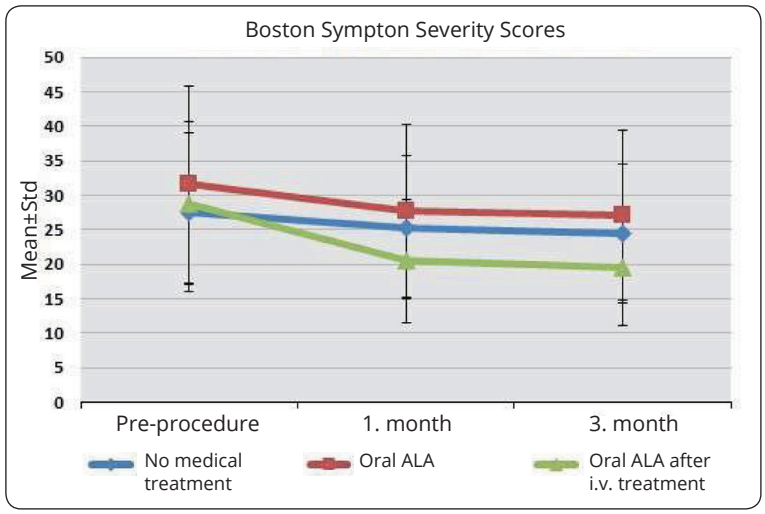

Figure 2. *Boston Symptom Severity scores changes of treatment and non-treatment groups*

cantly lower than those who received oral ALA treatment (p=0.011; p<0.05). A statistically significant difference was found between the medication groups in the Boston symptom severity values at the third month (p=0.001; p<0.01). Boston symptom severity scores of the subjects who received oral ALA after iv. treatment were significantly lower than those who received oral ALA treatment (p=0.006; p<0.01).

For the group that did not receive ALA treatment: A significant difference was found between the Boston Symptom Severity scores of the cases without ALA treatment (p=0.001; p<0.01). The decreases in the 1st and 3rd month Boston Symptom Severity scores compared to the pre-procedure were statistically significant (p<0.01). For the group that received oral ALA treatment: A significant difference was found between the Boston Symptom Severity scores of the cases treated with oral ALA (p=0.001; p<0.01). The decreases in Boston Symptom Severity scores at the 1st and 3rd months compared to the pre-procedure were found to be statistically significant (p<0.01). For the group that received oral ALA after iv. treatment: A significant difference was found between the Boston Symptom Severity scores of the cases treated with oral ALA after iv. treatment (p=0.001; p<0.01).

The rate of change in Boston symptom severity scores of patients who received oral ALA after iv. treatment was significantly higher than those who did not receive treatment and those who received oral ALA treatment (p=0.001; p=0.001; p<0.01). The rates of change in Boston symptom severity scores in those receiving oral ALA treatment were significantly higher than those without medication (p=0.046; p<0.05).

Table 5 summarizes comparison of Boston Functional Status scores by treatment groups and **Figure 3** depicts these changes. For the group without medication: A statistically significant difference was found between the pre-procedure, first month and third month Boston functional status scores of the cases without medication (p=0.002; p<0.01). The mean decrease of 0.40±0.93 units in the third month Boston functional status scores of the cases compared to the pre-procedure was found to be statistically significant (p=0.048; p<0.01). For the oral ALA treatment group: A statistically significant difference was found between the pre-procedure, first month, and third month Boston functional status scores of the patients treated with oral ALA (p=0.001; p<0.01).

Table 5. *Comparison of Boston Functional Status Scores by Treatment Groups*

Boston Functional Status		Total	Treatment Groups			*p*
			No ALA treatment (n=40)	Oral ALA (n=35)	Oral ALA after i.v. treatment (n=40)	
Before tr.	*Mean±Std*	9.10±1.64	9.18±1.69	9.00±1.46	9.13±1.76	[d]*0.960*
	Median (Min-Max)	8 (8–15)	8 (8–14)	8 (8–13)	8 (8–15)	
1. month	*Mean±Std*	8.83±1.22	9.03±1.48	8.63±0.88	8.80±1.20	[d]*0.918*
	Median (Min-Max)	8 (8–12)	8 (8–12)	8 (8–12)	8 (8–12)	
3.month	*Mean±Std*	8.43±1.75	8.78±1.25	8.54±0.85	8.00±2.54	[d]*0.561*
	Median (Min-Max)	8 (0–12)	8 (8–12)	8 (8–12)	8 (0–12)	
	p		[e]*0.002***	[e]*0.001***	[e]*0.001***	
Change Δ						
Before tr. – 1. month	*Mean±Std*		–0.15±0.53	–0.37±0.84	–0.33±0.86	[d]*0.308*
	P		[ee]1.000	[ee]0.769	[ee]1.000	
Before tr. – 3. month	*Mean±Std*		–0.40±0.93	–0.46±1.01	–1.13±3.06	[d]*0.877*
	P		[ee]*0.048**	[ee]*0.037**	[ee]*0.042**	
1. month – 3. month	*Mean±Std*		–0.25±0.67	–0.09±0.28	–0.8±2.85	[d]*0.539*
	P		[ee]*0.985*	[ee]*0.856*	[ee]*1.000*	

[e]Friedman Test & [ee]Wilcoxon Signed Rank Corrected Pairwise Comparisons
[d]Kruskal Wallis Test & Dunn Bonferroni Test
**p<0,01, *p<0,05
Before Tr.: before treatment, ALA: alpha-lipoic acid

Discussion

In our clinical investigation, the pain and symptom severity scores of the patients who were treated with intravenous and then oral ALA were found to be significantly lower at the end of both the 1st and 3rd months compared to the patients who received only oral ALA or no medication. At the same time, in the group of patients who were treated only with oral ALA, pain and symptom severity scores were determined to be significantly lower at the end of both the first and third months compared to the patients who did not receive ALA. Our study is the first to evaluate the efficacy of iv. ALA treatment in CTS symptoms and neuropathic pain.

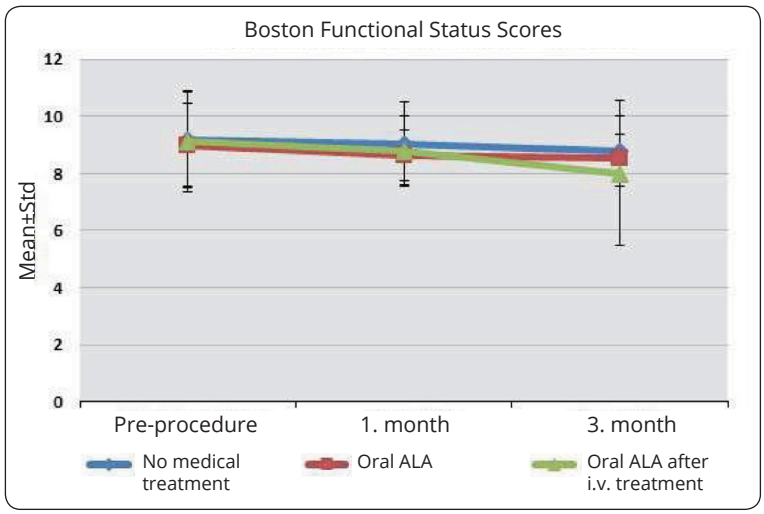

Figure 3. *Boston Functional Status scores changes of treatment and non-treatment groups*

In the nervous system, ALA exerts neuroprotective and antioxidant effects as shown in both experimental and clinical investigations. A study evaluated the actions of ALA in a model of compressive sciatic nerve injury in rats revealed that ALA reduces oxidative stress by increasing the activities of the antioxidant enzymes catalase and superoxide dismutase, and lowers the concentration of malondialdehyde, a lipid peroxidation product[24]. Similar mechanisms may explain the therapeutic effect of ALA in CTS, where an ischemia/reperfusion process triggers the pathology[25, 26]. Several researchers have declared positive results in many studies evaluating the efficacy of ALA treatment in CTS. However, in these studies, ALA was employed in combi-

nation with other antioxidants instead of monotherapy[12–14]. In a study determining the effect of ALA on pain and functionality in CTS, 134 mild and moderate CTS patients were given 600 mg/day oral ALA or placebo for 60 days. As a result, while pain decreased significantly in the group treated with ALA, no change was determined in the functionality scores compared to placebo. However, researchers stated that there was a prolongation of the time to the need to send the patients to surgical treatment thanks to ALA treatment[27]. In a similar study performed by *Luchetti* et al., the efficacy of oral ALA and placebo was compared for 1 month before surgery and 2 months after surgery in patients with CTS; it has been declared that there was a significant lowering in pain intensity in patients treated with ALA before and after surgery compared to the placebo group[15].

In another clinical investigation, oral ALA and placebo treatment were employed for 1 month before surgery and for 2 months after surgery in patients with CTS, but the change in pain intensity was determined intermittently for 4 months, keeping the time longer than the above mentioned study. It was reported that there was a more significant improvement in pain in the group receiving ALA even at the fourth month compared to placebo[16]. In our study, in parallel to the scientific literature, a significant improvement in pain severity was encountered by patients who received oral ALA as well as by patients who received oral ALA after intravenous compared to patients who did not use ALA.

Although its efficacy in the treatment of neuropathy is established, the therapeutic effect of ALA is relatively low due to its pharmacokinetic profile. The data show that ALA has a short half-life and bioavailability (approximately 30%) due to its profound degradation in the liver, with decreased solubility in the stomach as well as instability. Nonetheless, the utilization of several innovative formulations has greatly improved the bioavailability of ALA. The R enantiomer of ALA shows improved pharmacokinetic parameters, including higher bioavailability, compared to the S enantiomer. Indeed, the employment of amphiphilic matrices has the ability to increase the bioavailability and intestinal absorption of ALA[28]. Also, liquid formulations of ALA can achieve higher plasma concentrations and bioavailability compared to the solidified dosage form. Therefore, improved formulations can enhance both ALA absorption and bioavailability, leading to an enhancement in the therapeutic efficacy[29].

There exist no study in the current literature comparing the efficacy of iv. and oral ALA treatments in the treatment of neuropathy and pain due to CTS. However, in two meta-analyses evaluating the improvement of pain symptoms after oral and iv. administration of ALA treatment in diabetic neuropathy, it was determined that iv. ALA could improve neuropathy symptoms when administered for three weeks, but the symptom relief with oral ALA was not clinically significant[30–32]. In a another trial, oral ALA (600, 1200, or 1800 mg daily) versus placebo was studied in 181 patients with diabetes and symptomatic distal symmetric polyneuropathy[33]. Furthermore a meta-analysis reported in an initial trial, daily iv. ALA for three weeks was associated with reduced pain, paresthesia, and numbness compared with placebo infusions[34]. In our study, the lowering in pain intensity was significantly higher in patients who received iv. ALA than in patients who received oral ALA and in patients who did not receive ALA treatment. We ascribe these findings to the higher bioavailability of ALA in the iv. form.

In the treatment of CTS nonsurgical interventions include splinting, glucocorticoids, physical and occupational therapy techniques (eg, carpal bone mobilization and nerve-gliding exercises), yoga, and therapeutic ultrasound. Up to two-thirds of patients with mild to moderate CTS symptoms have successful outcomes with nonsurgical therapy. However patients with moderate to severe CTS and axonal loss on electrodiagnostic testing and those whose symptoms persist or worsen despite initial nonsurgical therapy are typically referred for surgical decompression[35]. We think that ALA, which is neuroprotective and antioxidant, may be an additional treatment to conventional treatments, since pain relief is partial in non-surgical treatments and there are long treatment processes.

Our study has several limitations. At first, the conducted study is cross-sectional in nature and the follow-up interval is relatively short; thus, it can not be said whether CTS patients' symptoms relapse after longer periods. The efficacy of ALA on pain in patients with moderate and severe CTS could not be evaluated as the patients would not have access to other medical and surgical treatments during the study. We also do not currently determine whether a second period of ALA treatment could relieve the symptoms again. Further studies shall be conducted and longer follow-ups should be considered to evaluate the maintenance of beneficial effects, and to assess the possibility to rechallenge with the same oral + iv. ALA regimen in the treatment of CTS.

In sum, intravenous ALA application is safe and efficient in alleviating the symptoms of CTS. No major side effects were observed. Patients' compliance rates were high, probably because the treatment was administered only once a day. A full-dose administration of intravenous ALA for one month led to more favorable results in terms of pain relief than without medication and with oral ALA-only treatment. We think that intravenous ALA can be evaluated as treatment of neuropathic pain in patients diagnosed with CTS. However, we think that other future studies are required to evaluate the efficacy of the treatment in long term.

CONFLICT OF INTEREST STATEMENT – There are no conflicts of interest.

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