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The Effect of Oral alpha lipoid acid drug in management of Diabetic Neuropathy by Electrophysiological Assessment

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ABSTRACT

Background: DPN are nerve disorders associated with diabetes, which affect approximately half of all diabetes patients. NCS is frequently used to assess the presence of severity of peripheral nerve involvement in patients with diabetes.

Objective: To Assess the effect of oral alpha lipoic acid supplementation on type 2 diabetic neuropathy patients through Electrophysiological study.

Subjects and methods: The study was carried out over a period of 1 year from May 2017 to June 2018.This study conducted at the out patient Clinic. A total of 62 enrolled patients with type 2 diabetes mellitus were undergo neurological examination then Electrophysiological tests of both upper and lower limbs were assessed firstly prior to the initiation of oral ALA administration baseline NCS and the second was after 3months following initiation of oral treatment with ALA (300 mg twice daily) .

Results: NCS performed with surface Electrode for 62 diabetic patients and only 34 patients treated by alpha lipoic acid the results showed high significant ($p<0.001$) correlation. There is a highly significant($p<0.001$) decrease values in the DML of examined nerves (tibial, peroneal and ulnar nerves) in diabetic patients before treatment by oral ALA and after treatment. On the other hand, There is a highly significant($p<0.001$) increase values in the NCV of examined nerves (tibial, peroneal and ulnar nerves) in diabetic patients before treatment by oral ALA and after treatment.

Conclusion: Oral treatment with ALA over 3 months demonstrates effectiveness of this drug in treating DPN which leads to improving Motor nerve function and great improvement in NCS results.

Key words: Nerve conduction study, Diabetic peripheral neuropathy, Alpha lipoic acid, distal motor latencies, nerve conduction velocities.

INTRODUCTION

DPN are nerve disorders associated with diabetes, which affect approximately half of all diabetes patients. There are many mechanisms by which hyperglycemia causes nerve damage, hyperglycemia also leads to elevated intracellular glucose and cellular toxicity in the endothelial cells of the capillaries associated with peripheral nerves. This damages the blood vessels and ischemia of the nerves which may be responsible for neuropathy[(1)].

Nerve conduction studies are frequently used to assess the presence and severity of peripheral nerves involvement in patients with diabetes. They are sensitive, specific, reproducible, and easily standardized. Studies are most commonly performed on upper and lower limbs on motor nerves. Nerve conduction studies performed with surface or needle electrode, surface technique is more widely used, easier to perform, more comfortable and produce results that are easier to measure. [(2,3)]

Alpha-lipoic acid (ALA)

Possesses beneficial effects both in the prevention and in the treatment of diabetic neuropathy .ALA is an antioxidant in diet that rapidly absorbed then transported to the intracellular compartments, and reduced to dihydrolipoic acid (DHLA) under the action of enzymes. LA, which plays an essential role in mitochondrial bioenergetic reactions, has drawn considerable attention as an antioxidant for use in managing diabetic complications such as retinopathy, neuropathy and other vascular diseases[(2)] .ALA is found in low amounts in vegetables such as spinach, broccoli, tomatoes, and animal tissues with the highest concentration found in the kidneys, heart, and liver[(4)].

Here we try to Assess the effect of oral ALA supplementation on type 2 diabetic neuropathic patients through Electrophysiological study.

MATERIALS AND METHODS

This was observational study conducted at the outpatient clinic .The study was carried out over a period of 1 year from May 2017 to June 2018. A total of 62 enrolled patients with type 2 diabetes mellitus were undergo neurological examination to confirm presence of signs and Symptoms of peripheral nerve dysfunction after exclusion of other diseases cause peripheral neuropathy like chronic renal failure ,liver failure ,hypothyroidism, leprosy, porphyria etc.[(5)]

Electrophysiological tests of both upper and lower limbs were performed with surface electrodes for ulnar, tibial ,and common peroneal nerves which include recording of distal motor latency (DML), compound muscle action potential(CMAP)amplitude, and motor nerve conduction velocity (MNCV). NCS was done before and after of initiation of oral treatment with 300 mg twice per day with ALA by 3 months.

Inclusion criteria

We enrolled people with type 2 diabetes mellitus and established DPN regardless of the gender, the definition of DPN will be the "presence of symptoms and signs of peripheral nerve dysfunction in people with diabetes after the exclusion of other causes[(6)].

Diabetic Patients were having peripheral neuropathy diagnosed by history, Symptoms and Neurological examination who had a verbal informed consent prior to the first nerve conduction study assessment(baseline NCS) and the second was 3months following initiation oral treatment with 300 mg twice per day ALA in 2nd visit.

NCS is the most abundant component of the electro diagnostic evaluation, so a simple, noninvasive, objective, and sensitive measurement which is intended as a gold standard test for corroborating the diagnosis of peripheral neuropathy[(7)].

RESULTS

Statistical Analysis

Spss version 16 was used for the Statistical Analysis. Descriptive results were represented as mean with standard deviation (SD) and percentage. The comparisons between the parameters of NCS before and after treatment was done by T-Test. The results of this study revealed that the age of patients (39-72) , they were distributed as in (Figure1).

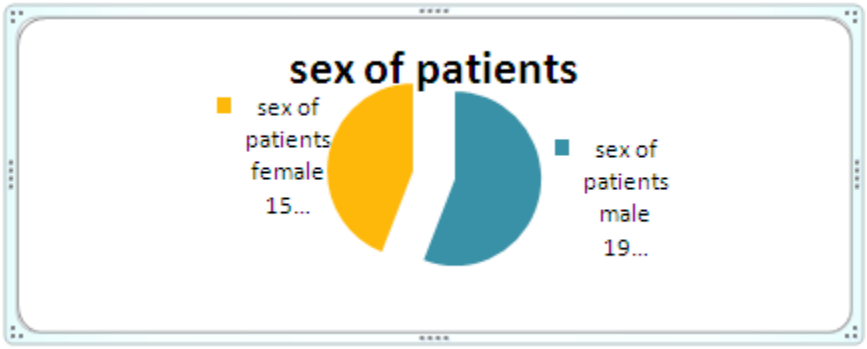

Figure 1: distribution of patient according to sex

In this study ,we found that 50 of diabetic patient complain from symptom and sign of diabetic PNP then NCV performed on 50 patients before treatment then only 34 of them followed and 16 missing .

During the comparison between the two studied groups(before treatment and after treatment) the following results as shown in (table 1) were obtained

There is a highly significant($p<0.001$) decrease values in the distal motor latencies (DML) of examined nerves (tibial, peroneal and ulnar nerves) in diabetic patients before treatment with oral ALA and after treatment as shown in (Table 1 and Figure 2).

Table 1: Comparison between DML before and after treatment by oral ALA drug

Nerve	Number of nerves	Mean of DML Before R	SD	Mean of DML after R	SD	P valu
Tibial	65	7.4	1.5	6.3	1	0.001
Peroneal	68	6.7	1.2	5.6	0.9	0.001
Ulnar	68	3.3	0.7	2.6	0.5	0.001
	Total=201					

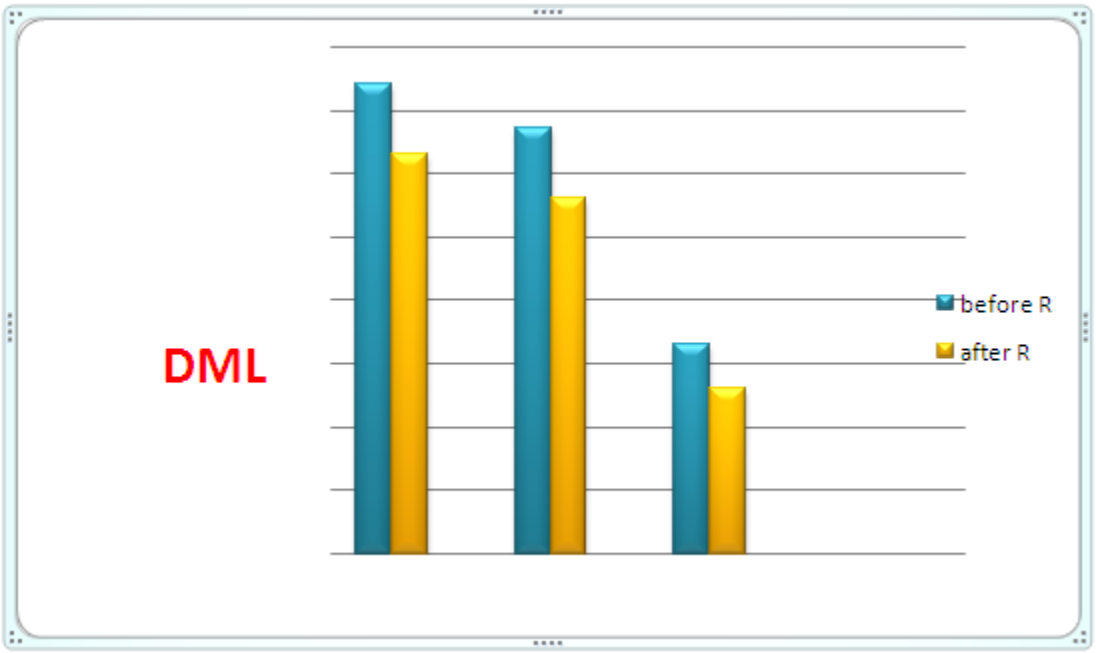

Figure (2) effect of oral ALP drug on DML of examined nerves

On the other hand, there is a highly significant($p<0.001$) increase values in the nerve conduction velocities (NCV) of examined nerves (tibial, peroneal and ulnar nerves) in diabetic patient before treatment with oral ALA and after treatment as shown in (Table 2).

Table 2: Comparison between NCV before and after treatment with oral ALA drug

Nerve	Number of nerves	Mean of NCV Before R	SD	Mean of NCV after R	SD	P valu
Tibial	65	33.1	2.9	34.4	2.6	0.001
Peroneal	68	35	1.8	36	1.5	0.001
Ulnar	68	47.2	1.7	48.6	0.2	0.001
	Total=201					

DISCUSSION

In this study , we can confirm that oral alpha lipoic acid in dose 300 mg twice per day for 3months has important role in improvement of diabetic peripheral poly neuropathy symptom and sign and the results of electrophysiological studies as shown in (table 1 and 2) , this results agree with Zielger et al(2006)(8) demonstrate that oral treatment with ALA over 5 weeks improved the positive sensory symptoms scored by the TSS in diabetic patients. This overall effect was not dose dependent, a significant improvement in TSS was noted as soon as after 1 week with ALA1800mg and after 2 weeks with ALA600 and ALA1200, among the individual TSS symptoms, improvement in pain but not paresthesia and numbness was observed. The mechanisms of the rapid improvement in both neuropathic symptoms and deficits may be related to an improvement in nerve blood flow mediated by the antioxidant action of ALA[(8)].

Also Tingting Han et al(2012) found in their study that treatment with ALA(300–600 mg/day for 2–4 weeks) is safe and that the treatment can significantly improve both nerve conduction velocity and positive neuropathic symptoms[(9).]

while Singh U et al (2008) reviewed significant improvement in symptoms and signs of neuropathy, there is little evidence that ALA has a meaningful effect on nerve conduction. One potential explanation is thatALA preferentially treats small fiber neuropathy, which is not measurable by electro diagnostic studies.[(10)]

Ziegler D et al (2011) demonstrated the effect of chronic ALA administration in 4 years and found that ALA is associated with neuropathic improvements but not nerve conduction, hence no difference in the composite endpoint was found compared to placebo. This trial also concluded that long term treatment of ALA was well-tolerated[(11)].

CONCLUSIONS

Oral treatment with ALA over 3months demonstrates effectiveness in treating DPN which leads to improving Motor nerve function and analyzing the effects of ALA have shown significant reduction of DML and increased of NCV of ulnar, tibial ,and common peroneal nerves.

RECOMMENDATION

We recommend that inter venous (I.V) therapy by ALA is necessary to strengthen existing data and provide greater insight into the efficacy of (I.V) ALA and to assess the side effects of this drug.

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