

Effect of anti-oxidant (α -lipoic acid) treatment on improvement of diabetic neuropathic pain

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Objective: To compare the mean change in total symptom score (TSS) or neuropathic symptom score (NSS) in diabetic patients taking α -lipoic acid and in controls taking usual treatments.

Methodology: This randomized control trial study comprised of 110 patients who were divided into equal treatment group and control group. The mean change in TSS was determined in both groups. Data analysis was performed by using SPSS version 20.

Results: Mean age of patients with treatment group was 46.09 ± 11.86 years and in control group 47.67 ± 10.66 years. Male to female ratio was 1.03:1. The mean change in TSS in treatment

group was 2.38 ± 1.99 and in control group was 0.53 ± 1.32 ($p < 0.001$). The comparison of mean TSS score was significantly reduced for other variables (HbA1c, numbness, burning and paresthesia) in post-treatment group than the pretreatment group ($p < 0.001$).

Conclusion: The mean change in TSS improved in diabetic patients taking α -lipoic acid and it showed significantly better effect and reduced the diabetic neuropathic pain in treated patients than controls. (Rawal Med J 202;46:33-36).

Keywords: Diabetes mellitus, complication, neuropathy.

INTRODUCTION

Diabetes mellitus is a devastating disease which results in various complications including diabetic neuropathies. In diabetic neuropathy (DNP), injuries to micro-vessels and large vessels involve the damage supply to the vasa nervorum. It can result in mono-neuropathy, multiplex mono-neuropathy, polyneuropathy (painful), autonomic neuropathy, thoraco-abdominal neuropathy and diabetic amyotrophic involving the damage of which may be associated with diabetic neuropathy include cranial nerves.¹ They are considered one of the commonest diabetic complications which affects up to 50% of the diabetic patients.² Various factors can progress DPN including uncontrolled diabetes, long duration, older age, high lipid levels/dyslipidemia and hypertension.³ Oxidative stress impedes neuropathy.⁴ DPN is associated with loss of sensory and motor sensation which lead to unbearable neuropathic pain.⁵

DPN affects quality of life with considerable morbidity and higher rate of mortality.⁶ α -lipoic acid is a naturally occurring anti-oxidant compound, which is required as cofactor for various metabolic

processes.⁷ In an animal model, various biological activities of α -lipoic acid including reduced oxidative stress, enhance the blood flow to nerves and also boost to nerve conduction have been reported.⁸ It is obtained from food in variable quantities and is used as a pharmacological agent administered in oxidative-stress associated disorders like neurodegenerative disorders, diabetes, ischemic heart diseases, cataract and in mushroom and heavy metal poisoning.^{9,10} Number of clinical reports have described the effect of α -lipoic acid in neuropathic pain and improvement in neuropathic pain symptoms.¹¹⁻¹⁴ A meta-analysis found the dose of 300-600mg/day or intravenously for some weeks was safe, tolerable and improved the pain symptoms significantly.¹⁵ The objective of this study was to investigate the effect of 600 mg of alpha-lipoic acid (α -lipoic acid) on neuropathic pains symptoms (TSS) in diabetic versus controls.

METHODOLOGY

This randomize control trial was conducted at Sir Ganga Ram Hospital, Lahore, Pakistan. The patients of type 1 and type 2 diabetes of both gender,

age between 20-70 years and with diabetics for at least one year with TSS score ≥ 4.0 points at presentation were included in the study. The patients with complex anomalies like malignancy, causes of neuropathic pain without diabetic complications, active cardiovascular disease, patients taking different groups of drugs (analgesic, anti-depressant, or anti-epileptic), or any other pain killer medications and child-bearing female patients not using any effective birth control method and under surveillance of a board-certified gynecologist were excluded from the study. One hundred and ten cases were taken after written informed consent. Ethical approval was obtained from medical ethical committee of Sir Ganga Ram Hospital.

The patients were randomized into study (A) and control (B) groups on by lottery method Monofilament¹⁶ and HbA1c level of patients was measured before the intervention and after six months at the end of treatment. A 5.07 gauge monofilament was used as standard for enrolment of the patients. Total Symptom Score (TSS) is the sum of 4 symptoms reported in neuropathy on a categorical severity scale of 0 to 3 [0=none; 1=mild; 2=moderate; 3=severe].

One tablet of 600 mg of alpha lipoic acid (α -lipoic acid) was given orally to the treatment group daily for 6 months. The standard treatment included oral hypoglycemic or insulin and diabetic care per hospital protocol. Change in TSS was recorded at base line and after 5 weeks of treatment with α -lipoic acid.

Statistical Analysis: Statistical analysis was performed using SPSS version 23. For post-stratification of the data, independent sample t-test was used. $p \leq 0.05$ was considered as significant.

RESULTS

Study included 110 patients; 51% were male and 49% female. The patients with type I diabetes were 29, in which 20 were from treatment group and 9 were from control group. On the other hand, patients with type II diabetes were 81 including 35 patients with treatment and 46 patients were from control groups (Table 1). The mean age of the patients with treatment group was 46.09 ± 11.86 years whereas in control group was 47.67 ± 10.66 years. Change in

TSS score was significantly associated ($p < 0.001$) between the patients, respectively (Table 2).

The mean pre-treatment and post-treatment HbA1c was 8.45 ± 1.36 and 6.81 ± 0.64 , respectively. The comparison of mean pre-treatment paresthesia (1.72 ± 0.93), burning (1.65 ± 0.81) and numbness (0.67 ± 0.66) and post-treatment paresthesia (1.28 ± 0.86), burning (1.08 ± 0.66) and numbness (0.57 ± 0.64) was statistically significant between groups ($p < 0.001$) shown in (Table 3).

Table 1. Demographic variables.

Variable groups		Study Groups		Total
		Treatment	Control	
Type of diabetes	I	20(18%)	9(8%)	26%
	II	35(32%)	46(42%)	74%
Gender	Male	22(20%)	34(31%)	51%
	Female	33(30%)	21(19%)	49%
Total		55	55	110

Table 2. Descriptive statistics of variables.

Parameter	Study Groups		p-value
	Treatment N= 55 Mean $\pm$ SD	Control N= 55 Mean $\pm$ SD	
Age (years)	46.09 ± 11.86	47.67 ± 10.66	0.09
Change in TSS	2.38 ± 1.99	0.53 ± 1.32	$<0.001^*$
Duration of diabetes	11.22 ± 5.37	10.05 ± 5.83	0.279

Table 3. Pre-treatment and post-treatment comparison of different variables.

Parameters	Pre-treatment (n=110) Mean $\pm$ SD	Post-treatment (n=110) Mean $\pm$ SD	p-value
HbA1c (%)	8.45 ± 1.36	6.81 ± 0.64	$<0.001^*$
TSS	5.41 ± 2.69	3.95 ± 2.23	$<0.001^*$
Numbness	0.67 ± 0.66	0.57 ± 0.64	$<0.011^*$
Burning	1.65 ± 0.81	1.08 ± 0.66	$<0.001^*$
Paresthesia	1.72 ± 0.93	1.28 ± 0.86	$<0.001^*$

Table 4. Comparison of change in TSS with different variables.

Variable groups	Gender	Study Groups		p-value
		Treatment	Control	
Gender groups	Male	2.23 ± 1.99	0.62 ± 1.37	$<0.001^*$
	Female	2.48 ± 2.002	0.38 ± 1.24	$<0.001^*$
Age groups (years)	≤ 50	2.30 ± 2.11	0.51 ± 1.31	$<0.001^*$
	> 50	2.56 ± 1.76	0.55 ± 1.36	$<0.001^*$
Duration of diabetes (years)	≤ 12	2.13 ± 2.17	0.52 ± 1.33	$<0.001^*$
	> 12	2.94 ± 1.39	0.54 ± 1.33	$<0.001^*$

In patients with age ≤ 50 years and age > 50 the mean change in TSS improved in treatment group as compared to control group ($p < 0.001$). In patients with duration of diabetes ≤ 12 years, the mean change in TSS in treatment group was 2.13 ± 2.17 , whereas in control group was 0.52 ± 1.33 ($p < 0.001$). Similarly, duration of diabetes > 12 years significantly associated ($p < 0.001$) with the mean change in TSS in treatment group (2.94 ± 1.39), whereas, it was 0.54 ± 1.33 in control group (Table 4).

DISCUSSION

α -lipoic acid is obtained from the foods showing various pharmacological uses like antioxidant properties, improves the symptoms of glycemic control and polyneuropathies and also efficiently alleviates toxicities linked to heavy metal poisoning.¹⁷ Our results are comparable to the previous reports which showed that significant improvement of mean TSS of the α -lipoic acid taking group from baseline measurements with average of 5.7 points in patients and average of 1.8 points in the placebo group ($p < 0.001$).^{10,18}

In another study, it has been documented that TSS did not differ significantly at baseline among the treatment groups and on average decreased by 4.9 points (51%) with α -lipoic acid 600 mg. After 5 weeks, a significant fall occurred in TSS in treatment group (9.44 ± 1.86 to 4.59 ± 1.17) as compared to control group (9.27 ± 1.56 to 6.35 ± 1.62).¹⁹ Previously conducted meta-analysis supports this and was concluded that after 5 weeks of treatment showed a significant fall in TSS (7.99 ± 1.35 to 4.24 ± 1.45) in study group as compared to control group (8.18 ± 1.75 to 6.24 ± 1.70).¹⁹

Similarly, the mean change in α -lipoic acid group was 4.35 ± 3.03 and 2.92 ± 3.18 in control.²⁰ Another study by Hector Garcia-Alcala et al also documented the comparable results to the present study with α -lipoic acid treatment in initial phase (4 weeks) and continued phase (16 weeks) efficiently reduced the symptoms of neuropathic pain, although α -lipoic acid removal as therapy was connected with a higher dose of analgesic treatment.^{21,22} A previous study explored the

intravenous administration of α -lipoic acid (600 mg/day) which relieved the diabetic neuropathic pain and was considered safe after treatment of 3 weeks while cardiac autonomic dysfunctions and neuropathic pain can improve with 800 mg/day of oral intake for several weeks (3-5 weeks).²³

CONCLUSION

Administration of α -lipoic acid in diabetic patients with neuropathic pain improved the mean change in TSS and showed significant impact on relieving the symptoms of neuropathy pain and enhanced the quality of life.

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Conflict of Interest: None declared

Rec. Date: Jan 25, 2020 Revision Rec. Date: Aug 24, 2020 Accept

Date: Dec 28, 2020

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