

DOI: 10.5455/medarh.2013.67.7-9

Med Arh. 2013 Feb; 67(1): 7-9

Received: October 28th 2012 | Accepted: January 25th 2013

CONFLICT OF INTEREST: NONE DECLARED

## ORIGINAL PAPER

# Alpha Lipoic Acid and Glycaemic Control in Diabetic Neuropathies at Type 2 Diabetes Treatment

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**Introduction:** Diabetes mellitus is a metabolic, chronic and incurable disease which reduces span and quality of life. Over 50% of diabetic patients have clinical manifestations of diabetic neuropathy. **Aim:** To show a positive influence of alpha lipoic acid on clinically manifested diabetic neuropathy symptoms as well as the effect of alpha lipoic acid in patients glycaemic control. **Material and methods:** Testing has been conducted in Cantonal Hospital "Irfan Ljubijankic MD" in Bihac and included 20 diabetes type 2 patients who were diagnosed with clinically manifested diabetic neuropathy. All the patients' conditions were evaluated by: medical history, clinical parameters, detailed internal examination, laboratory analyses for glycaemic control assessment and mono filament test. They were treated with oral anti-diabetics and insulin as well as with alpha lipoic acid preparation in duration of four months. They were divided into two groups, with good ( $HbA1c < 7\%$ ) and poor ( $HbA1c \geq 7\%$ ) glycaemic control. Medical control has been conducted four months after the research started. **Results:** Twenty patients took part in the research, 7 male and 13 female. The average age of the patients was 58.6 in the first and 55.6 years in the second group. The average patients' disease duration was  $13.4 \pm 6.6$  years in the first and  $11.2 \pm 5.4$  years in the second group. The difference in gender, average age and disease duration in both groups statistically is not significant ( $p \leq 0.05$ ). The number of negative points after the therapy has been reduced for 56.4% in the first and 43.1% for the second group ( $p \leq 0.05$ ). Prior to the treatment, all the patients in both groups had paresthesia. At medical checkup, there were 40% less patients in the first group and 10% in the second one ( $p \leq 0.01$ ). The difference is statistically significant ( $p \leq 0.05$ ) in night pain occurrence between two groups of patients after alpha lipoic acid treatment (40% more patients had night pain in the second group after the treatment). The same number of patients in both groups, 40% had muscle atrophy and difficulty in walking. At medical checkup, 30% in first group and 20% less patients had discomforts ( $p \geq 0.05$ ). Regression of subjective sensations in both groups of patients after alpha lipoic acid treatment has been noted. **Conclusion:** Alfa lipoic acid is an effective drug in the treatment of diabetic distal sensory-motor neuropathy and its therapeutic effect is more effective in patients with good glycaemic control. **Key words:** diabetic neuropathy, alpha lipoic acid, glycaemic control.

organs in the body, including the retina, kidneys, large blood vessels and peripheral nerves. Diabetic neuropathy is frequent and unpleasant complication. Over 50% of people with diabetes have clinical manifestations of diabetic neuropathy. It is characterized by progressive loss of nerve fibers based on chronic hyperglycemia with the important role of genetic and environmental hypersensitivity factors. Hyperglycemia leads to glucose metabolism disorders in cells, leading to increased production of sorbitol, which reduces the level of protective substances mioinositol in the structure of cell membranes. Poor circulation in the blood vessels leads to malnutrition and ischemic neurons. More than 80% of all diabetic neuropathy seems distal, symmetrical sensorimotor neuropathy (1, 2). The loss of sensitivity occurs early and is manifested as tingling in the fingers, tingling, burning, itching, pain in the feet, cramps in the calves, decreased sensation to vibration, pain and temperature. Difficulties occur, usually in the lower extremities during the night. With further progression of the disease motor symptoms and signs in the form of weakness and muscle atrophy occur in feet, lower legs, hands. Clinical diagnosis of distal symmetrical sensorimotor diabetic neuropathy is established on the basis of clinical history and examination, which includes a mandatory mono filament test. The gold standard for diagnosis is elec-

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## 1. INTRODUCTION

Diabetes mellitus is the most common metabolic disease in humans and is a chronic and incurable disease which reduces the quality and duration of life. It is a global problem with social,

health and economic consequences. Today, over 300 million people are living with the disease and the number is increasing every year by about 7 million. The long duration of the illness develops complications and damages vital

tromyoneurography - EMNG (3). The mono filament test was introduced as a medical standard for early diagnosis of diabetic neuropathy. It performs nylon mono filament 5.07 application on nine points in foot perpendicular to the skin. Patient has closed eyes during the performance test and gave us notice when feeling the touch of a filament. Loss of sensory is recorded as a negative point and a high risk of diabetic neuropathy.

The drug of choice for treating diabetic neuropathy is products of alpha-lipoic acid in combination with symptomatic therapy and physical treatment. Alpha lipoic acid is a powerful antioxidant, the only soluble in fat and water. According to the recommendations for drug treatment the form of the ampoule at a dose of 600 mg 250 ml 0.9% NaCl is applied for a period of 21 days. Because the preparation is photo sensitive, the system is protected by a cover. Therapy is continued perorally in capsules of 600 mg in the morning, before eating, in the long term (minimum three months) and it continues with the maintenance dose of 300 mg in the long term (4, 5). Early detection of diabetic neuropathy, good glycaemic control and avoidance of risk factors (smoking, alcohol, hypertension) can delay or slow the progression of diabetic neuropathy (6).

## 2. AIM

To show a positive effect of alpha lipoic acid on clinical manifestation of symptoms of diabetic neuropathy. To show a positive result of the therapeutic effect of alpha lipoic acid in relation to glycaemic control patients with type 2 diabetes or overt diabetic neuropathy.

## 3. MATERIALS AND METHODS

The study was conducted at the Cantonal Hospital "Irfan Ljubijankić MD" in Bihać, Department of Internal Medicine and the hospitals' diabetic clinic. It included 20 patients, men and women aged 39 to 78 years. The study involved patients with diabetes type 2 who were diagnosed clinically manifest diabetic neuropathy. All patients completed the evaluation of the situation:

- Medical history (onset of illness, duration of illness, treatment of disease),

- Clinical parameters (age, body height, body weight, sex),
- Done detailed review of internist,
- Laboratory analyzes to evaluate glycaemic control (HbA1c, fasting glucose, postprandial glycaemia),
- Monofilament test.

All patients were treated with oral anti diabetic drugs and insulin well as with preparations of alpha lipoic acid for a period of four months. They were divided into two groups. The first group consisted of patients with good glycaemic control (HbA1c <7%) and the second group of patients with poor glycaemic control (HbA1c ≥ 7%). A medical checkup is performed four months after the beginning of the study.

## 4. RESULTS

Twenty (20) patients took part in the research, 7 male and 13 female. Patients' average age is 58.6 years in the first group and 55.6 years in the second group of patients. The average patients' disease duration is 13.4±6.6 years and 11.2±5.4 years for the second one. The difference in gender, average age and average duration of the disease is statistically insignificant for both groups ( $p \geq 0.05$ ).

While performing mono filament test, the number of negative spots in both groups at the beginning and at end of therapy is statistically significant ( $p \leq 0.01$ ), as well as the number of negative spots in both groups of patients after the therapy ( $p \leq 0.05$ ) (Chart 1).

All the patients in both groups had paresthesias prior to the treatment. At medical checkup, 6 patients (60%) had

paresthesias in the first group and 9 patients (90%) in the second one ( $p \leq 0.01$ ). Seven patients from the first group (70%) had night legs pain, and 8 patients (80%) in the second one. At medical checkup, none of the patients from the first group had leg pains (gait disturbance) and 5 patients had leg pains (50%) in the second one. ( $p \geq 0.05$ ). The difference is statistically significant (Chi test,  $p \leq 0.05$ ) in representation of night pain between the two groups of patients after alpha lipoic acid treatment. Muscle atrophy and difficulty in walking affected the same number of patients in both groups, 4 patients each (40%). At medical checkup, 3 patients from the first group (30%) and 2 patients in the second group (20%), had muscle atrophy and difficulty in walking ( $p \geq 0.05$ ) (Chart 2).

Regression of patients' subjective sensations has been noted in both groups of patients after alpha lipoic acid treatment. Therefore, in group with better glycoregulation 60% of patients felt very well, 30% moderately better and 10% felt the same. In the group with bad glycaemic control, 10% of patients felt very well, 50% moderately better, 30% the same and 10% felt worse (Chart 3).

## 5. DISCUSSION

Diabetes mellitus Type 2 as a massive non virulent disease with its acute and chronic complications influences heavily on patients' life quality and represents a serious health and socioeconomic issue. Aim in treating these patients is to establish metabolic homeostasis, prevent occurrence of complications and ensure their treatment once they occur.

In this research, results of four months treatment with alpha lipoic acid preparation done on patients with type 2 diabetes with verified clinically manifested diabetic distal sensorimotor neuropathy have been observed. According to the values of glycolized hemoglobin (HbA1c), measured in the beginning and the

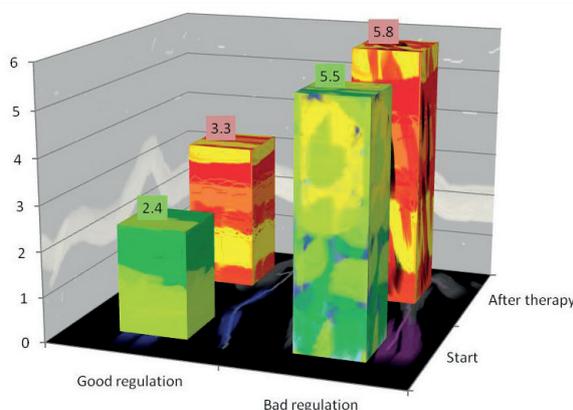


Chart 1. The average number of negative spots while performing monofilament test in both groups of patients at the beginning and at end of alpha lipoic acid treatment.

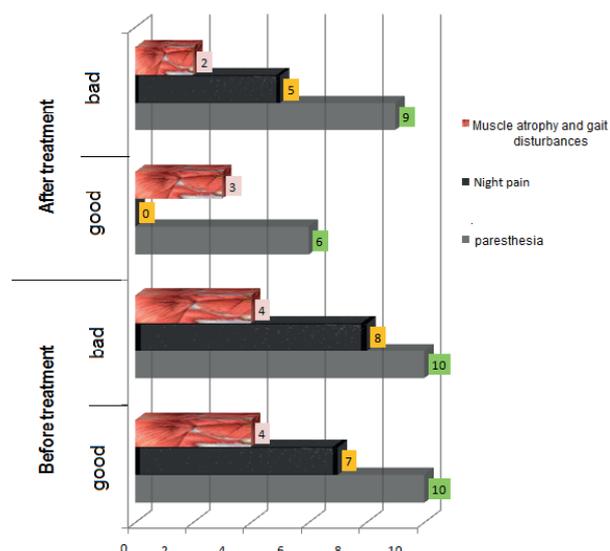


Chart 2. Patients' symptoms in both groups before and after treatment.

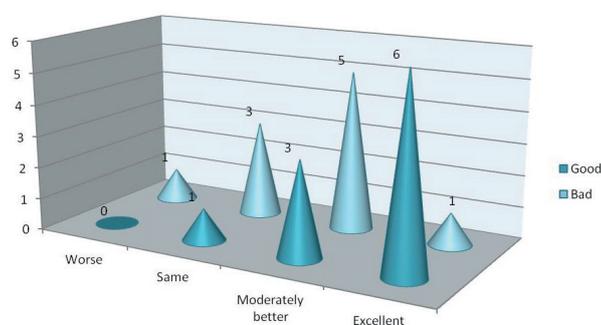


Chart 3. Patients' subjective sensation after treatment

end of research, patients were divided into two groups. The first group consists out of patients with good glycoregulation ( $HbA1c < 7\%$ ) and the second is with the patients with bad glycoregulation ( $HbA1c \geq 7\%$ ).

In both groups of patients there was improvement in symptoms of clinically manifested diabetic distal sensorimotor neuropathy by treatment with alpha lipoic acid preparation infusion in duration of three weeks and then by oral therapy with capsule until the medical checkup. Number of patients with paresthesia, night pains, muscle atrophy and difficulty in walking has been decreased in both groups, but better results were achieved in the group with better glycaemic control. Number of negative spots at mono filament test conducted on patients from both groups shows statistically significant difference with all patients and especially in group of patients with good glycaemic regulation. Also, after the treatment with alpha lipoic acid prep-

aration, the patients show in their subjective sensation a content by results achieved in both groups. As expected, better treatment results were achieved in group of patients who had better glycoregulation.

Clinical study ALADIN I, multi-centric, randomized, double blind, placebo controlled study showed statistically significant effect of applying alpha lipoic acid preparation in infusion on polyneuropathic symptoms in correlation to placebo as well as good drug tolerance in dosage of 600 mg. In the clinical study ALADIN III, multi-centric, randomized, double blind, placebo controlled study which lasted for seven months showed decrease of diabetic neuropathy's symptoms during application of infusion therapy with alpha lipoic acid and continua-

tion of therapy with oral preparations. In clinical studies SYDNEY I and SYDNEY II the examinees, whose glycoregulation with glycolized hemoglobin was observed (7, 8), were included.

Meta-analysis of clinical studies ALADIN I and II, SYDNEY I and NATHAN II with 1258 patients showed improvements of diabetic neuropathy's clinical symptoms in comparison to placebo with alpha lipoic acid in TSS (Total Symptom Score), which showed that alpha lipoic acid improves micro circulation and favorably effects on patients' blood vessel vasodilatation. Patients were treated with infusion therapy for 3 (three) weeks with 600 mg of alpha lipoic acid in 250 ml NaCl once a day and continued with oral therapy in same dosage. Such therapy did not lead to the significant side effects. (9, 10, 11).

## 6. CONCLUSION

Research results show that alpha lipoic acid is an efficient medicament in curing diabetic distal sensorimo-

tor neuropathy and leads to significant improvement of the clinical patients' symptoms and subjective sensation and therefore effects on better quality of life. Therapeutic effect is more efficient at patients with good glycaemic control. The patients showed good medication tolerance in infusion and oral treatment which lasted for 4 (four) months. The results achieved are in accordance with the actual research and literature.

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