# EFFECTS OF A-LIPOIC ACID COMBINED WITH METHYLCOBALAMIN ON SERUM SERUM HUMAN INSULIN-LIKE GROWTH FACTOR-1, HUMAN NERVE GROWTH FACTOR, AND MOTOR AND SENSORY NERVE CONDUCTION VELOCITY IN TYPE 2 DIABETIC PERIPHERAL NEUROPATHY

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***ABSTRACT***

***Objective****: To investigate the effects of α-lipoic acid combined with methylcobalamin on serum human insulin-like growth factor-1 (ICF-1), human nerve growth factor (NAF), and motor and sensory nerve conduction velocity in type 2 diabetic peripheral neuropathy.*

***Methods:*** *Eighty patients with type 2 diabetic peripheral neuropathy treated in our hospital's endocrinology department from June 2017 to October 2018 were selected. These patients were divided into a control group (n = 40) and an observation group (n = 40) according to the random number table method. Once a day for 60 days, the control group was treated with methylcobalamin intravenously, and the observation group was treated with α-lipoic acid intravenously on the basis of the control group. Enzyme-linked immunosorbent assay was used to detect IGF-1 and NGF levels, and electromyographic analysers were used to detect motor and sensory nerve transmission speed. The clinical efficacy, adverse reactions, IGF-1, NGF levels, and motor and sensory nerve transmission speed differences of the two groups were compared.*

***Results:*** *After treatment, the total effective rate of the observation group was 97.50 and the control group was 77.50. The total effective rate of the observation group was significantly higher than that of the control group (p<.05). The levels of serum NGF and IGF-1 in the observation group and the control group were significantly higher than before treatment, and the levels of NGF and IGF-1 in the observation group were significantly higher than those in the control group (p<.01). The motor and sensory nerve peroneal and median nerve conduction velocities in the observation group and the control group were significantly higher than before treatment, and the motor and sensory nerve peroneal and median nerve conduction speeds in the observation group were significantly higher than those in the control group (p<.01). The incidence of adverse reactions was 12.50 in the control group and 17.50 in the observation group (p>.05).*

***Conclusions:*** *There is clinical efficacy in combining α-lipoic acid with mecobalamin in the treatment of DPN. This approach could improve nerve conduction speed and nerve growth factor levels, and it has fewer adverse reactions. It is worthy of application and promotion.*

***Keywords:*** *α-lipoic acid, mecobalamin, type 2 diabetic peripheral neuropathy, insulin-like growth factor-1, human nerve growth factor, motor nerve conduction velocity, sensory nerve conduction velocity.*

*DOI: 10.19193/0393-6384_2021_2_150*

***Received*** *March 15, 2020;* ***Accepted*** *October 20, 2020*

## Introduction

Diabetic peripheral neuropathy (DPN) is a common chronic neurological complication of type 2 diabetes. Diabetic neuropathy can affect peripheral and central nerves, but the greater effect is peripheral neuropathy[(1-2)]. DPN is a chronic complication with various causes including oxidative stress, metabolic dysfunction, vascular damage and persistent hyperglycemia[(3)]. Oxidative stress is a common cause and pathway of chronic complications of diabetes. Oxidative stress can destroy nerve growth nutrition factors, induce the occurrence of DPN, and cause nerve damage[(4)]. DPN patients are usually elderly and have had diabetes for more than five years, and it is more common in patients with poor glycemic control. According to research statistics, 60% to 90% of patients with diabetes have varying degrees of peripheral

neuropathy[5]. The most frequent clinical manifestations are paresthesia, pain, and numbness of the affected limb, diabetes can even cause disability or death. Thus, it poses a great threat to the quality of life and health of patients[6]. Choosing the right drug treatment is of great significance for restoring the condition of DPN patients.

Methylcobalamin could effectively increase the speed of nerve transmission and promote nerve block, but monotherapy still fails to achieve the expected results[7]. Studies have shown that α-lipoic acid could effectively improve nerve conduction speed and nerve tissue bleeding, alleviate oxidative stress responses of various diseases, and eliminate a variety of oxygen free radicals[8].

In this study, the observation group was treated with α-lipoic acid and methylcobalamin to explore the clinical efficacy of this approach on human insulin-like growth factor-1 (IGF-1), human nerve growth factor (NGF) levels and motor and sensory nerve conduction velocity.

## Material and method

### *Materials*

Eighty patients with type 2 diabetic peripheral neuropathy treated in our endocrinology department from June 2017 to October 2018 were selected.

*The inclusion criteria were:*

• Patients Meet the diagnostic criteria for diabetic peripheral neuropathy in the guidelines for the prevention and treatment of type 2 diabetes[9];

• Reduced nerve conduction velocity, accompanied by symptoms such as pain in the affected limb;

• Informed consent.

*The exclusion criteria were:*

• Use drugs that affect the identification of effects, such as analgesics and antioxidants before enrolment;

• Those who are allergic to the research drug;

• Malignant tumour;

• Renal insufficiency;

• Pregnancy and lactation;

• Mental illness.

The patients were divided into a control group and an observation group by the random number table method. Of the 40 patients in the observation group, there were 18 females and 22 males, aged 45-76 years, with an average age of (55.11±7.12) years.

The duration of diabetes was 5-14 years (9.62±4.62). Of the 40 patients in the control group, there were 19 females and 21 males, aged 45-75 years, with an average age of (54.86±6.98) years. The duration of diabetes was 6-15 years (9.76±4.74).

There were no significant differences in gender, age, and duration of diabetes between the two groups ($p>.05$).

### *Method*

Both groups were instructed in exercise, diet control, and hypoglycaemia (blood glucose less than 10 mmol/L two hours after a meal and blood glucose less than 8 mmol/L when fasting).

The control group used only methylcobalamin (produced by Fujian Jinshan Biopharmaceutical Co., Ltd., approval number: Sinopharm H20044740, specification: 500 ug) intravenously, 500 μ each time, once a day.

The observation group was intravenously infused with methylcobalamin (Manufactured by Stade Pharmaceutical Factory, Germany, approval number: Sinopharm Standard J20090105, specification: 20 mg) once a day, 500 μg each time, and intravenously infused with alpha-lipoic acid, 600 mg each time, once a day.

All were added with 250 ml of physiological saline (produced by Wuhan Binhu Shuanghe Pharmaceutical Co., Ltd., approval number: Sinopharm standard word H42020475, specification: 250 mL) and diluted. Patients in both groups were treated for 120 days.

### *Observation indicators*

Enzyme-linked immunosorbent assay was used to detect the levels of IGF-1 and NGF before and after treatment, 4 mL of fasting blood was collected, and the serum was separated after centrifugation. The serum was stored in a refrigerator at -70°C and stored under refrigeration.

Nerve conduction velocity was examined with an electromyographic analyser and purchased from Xihuayi Technology Co., Ltd. to measure the motor conduction velocity of the common peroneal and median nerves and the sensory conduction velocity of the sural and median nerves.

### *Statistical significance*

SPSS 19.0 software was selected for analysis and statistics, and other measurement data were expressed by ($\bar{x}\pm s$).

Independent sample t-test was used. Count data were expressed as [n (%)], and comparison was performed using $\chi^2$ test. $p<.05$ was considered statistically significant.

## Results

### *Comparison of clinical efficacy between the two groups*

After treatment, the total effective rate was 97.50% in the observation group and 77.50% in the control group. The total effective rate in the observation group was significantly higher than in the control group, and the difference was statistically significant (p<.01). See Table 1.

| Group | n | Marked effect | Effective | Invalid | Total effective rate |
|---|---|---|---|---|---|
| Control group | 40 | 17 (42.50) | 14 (35.00) | 9 (22.50) | 31 (77.50) |
| Observation group | 40 | 20 (50.00) | 19 (47.50) | 1 (2.50) | 39 (97.50) |
| $\chi^2$ | | | | | 7.314 |
| *p* | | | | | .007 |

**Table 1:** Comparison of clinical efficacy between the two groups (%).

### *Comparison of serum NGF and IGF-1 levels between two groups of patients*

Before treatment, there was no significant difference in serum NGF and IGF-1 levels between the two groups of patients (p>.05).

After treatment, the levels of serum NGF and IGF-1 in the observation group and the control group were significantly higher than before the treatment, and the levels of NGF and IGF-1 in the observation group were significantly higher than those in the control group, and the differences were statistically significant (p<.01). See Table 2.

| Group | n | NGF | | | | IGF-1 | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Before treatment | After treatment | *t* | *p* | Before treatment | After treatment | *t* | *p* |
| Control | 40 | 12.51 ±3.70 | 24.21 ±4.67 | 12.419 | <.01 | 157.43 ±20.29 | 192.04 ±31.31 | 4.936 | <.01 |
| Observation | 40 | 12.99 ±3.95 | 66.30 ±12.92 | 24.955 | <.01 | 156.41 ±31.40 | 251.71 ±41.38 | 11.603 | <.01 |
| *t* | | 0.560 | 19.376 | | | 0.172 | 7.272 | | |
| *p* | | 0.576 | < .01 | | | 0.863 | < .01 | | |

**Table 2:** Comparison of serum NGF and IGF-1 levels.

### *Comparison of motor and sensory nerve conduction velocity between two groups of patients*

Before treatment, there was no significant difference in the conduction velocity of the peroneal and median nerves of the motor and sensory nerves between the two groups (p>.05). After treatment, the transmission speeds of the peroneal and median nerves of the motor and sensory nerves in the observation group and the control group were significantly higher than before treatment, and the transmission speeds of the peroneal and median nerves of the motor and sensory nerves in the observation group were significantly higher than those of the control group. The differences were statistically significant (p<.01). See Table 3.

| Time | Motor nerve conduction velocity | | Sensory nerve conduction velocity | |
|---|---|---|---|---|
| | Common peroneal nerve | Median nerve | Common peroneal nerve | Median nerve |
| Before treatment | | | | |
| Control group | 39.98±4.12 | 42.13±5.63 | 31.77±4.75 | 39.12±4.12 |
| Observation group | 40.21±3.11 | 41.66±6.86 | 32.20±3.63 | 39.56±3.63 |
| *t* | 0.281 | 0.335 | 0.454 | 0.506 |
| *p* | .779 | .738 | .650 | .614 |
| After treatment | | | | |
| Control group | 45.53±3.69[a] | 49.29±4.93[a] | 36.58±5.74[a] | 45.49±5.93[a] |
| Observation group | 53.61±4.80[a] | 60.99±5.33[a] | 46.99±3.12[a] | 53.70±4.42[a] |
| *t* | 8.440 | 10.191 | 10.077 | 7.020 |
| *p* | < .01 | < .01 | < .01 | < .01 |

**Table 3:** Comparison of motor and sensory nerve conduction velocity.
*Note: [a]Compared with the same group before treatment, p<.05.*

### *Comparison of adverse reactions between two groups of patients*

After treatment, the incidence of adverse reactions was 12.50%, in the control group and 17.50% in the observation group, but the difference was not statistically significant (p>.05). See Table 4.

| Group | n | Dizziness | Rash | Heat | Total |
|---|---|---|---|---|---|
| Control group | 40 | 1 | 1 | 3 | 5 (12.50) |
| Observation group | 40 | 3 | 2 | 2 | 7 (17.50) |
| $\chi^2$ | | | | | 0.392 |
| *p* | | | | | .531 |

**Table 4:** Comparison of adverse reactions between two groups of patients [n (%)].

## Discussion

The most serious complication of diabetes is DPN. In the absence of other interference factors, the signs and symptoms of peripheral nerve dysfunction appear in patients with diabetes, and its pathogenesis and aetiology have not yet been clarified[10]. Immune factors, neurotrophic factor deficiency, cy-

tokine abnormalities, vascular injury, and metabolic disorders are the main causes of the disease[11]. Patients in early stages may have sensory disturbances such as fever, tactile inductance, symmetry pain, numbness and insect crawling. Generally, the symptoms in lower limbs are more serious. In the later stages, patients may experience symptoms such as malnutrition, weakened function and stinging limbs. If not treated in time, diabetes will increase the disability rate of patients and reduce their quality of life[12]. Alpha-lipoic acid is a strong anti-oxidant stress drug. Its mechanism of action is to mitigate the numbness and pain of patients by increasing the speed of nerve conduction[13]. α-lipoic acid could reduce the products of oxidative stress, improve the hypoxia and ischemia of nerve tissues, and thus increase the speed of nerve conduction. Methylcobalamin can increase nerve conduction speed, improve Wang's cells and neuronal cell metabolism, promote protein and nucleic acid synthesis and promote lecithin synthesis, so it is commonly used for the treatment of diabetic neuropathy[14]. The results of this study show that the clinical efficacy of combining α-lipoic acid with mecobalamin in the treatment of DPN is significantly higher than that of either drug alone. This suggests that this combination of drugs has complementary effects and can more effectively improve DPN. There were no significant differences in adverse reactions between the two groups, suggesting that the combination of drugs has a certain safety and does not increase side effects.

IGF-1 has the function of repairing and promoting growth factors, and it plays an important role in DPN volatilization. IGF-1 gene expression in neural tissues is reduced in the early stages of the disease. Therefore, it has a certain significance in peripheral nerves. Studies have shown that the decrease in IGF-1 levels is most closely related to DPN. The protective effect of IGF-1 and the weakening of peripheral nerve support can lead to DPN. Maintaining IGF-1 can improve DPN and increase nerve conduction speed[15]. NGF has certain effects on the function of sympathetic and sensory nerves in the pathogenesis of DPN. In addition, NGF has a certain regulatory function on blood prosperous cells, thereby maintaining nerve function[16]. NGF levels are lower in the blood and tissues of DPN patients. This NGF deficiency can make nerves more sensitive to other damage factors of the disease and cause nutritional disorders of the nerves. The results of this study show that the serum levels of NGF and IGF-1 in the observation group significantly increased after treatment, suggesting that α-lipoic acid combined with methylcobalamin in the treatment of DPN can increase NGF and IGF-1 levels.

In summary, α-lipoic acid combined with mecobalamin has a good clinical effect on DPN, improves nerve conduction velocity and nerve growth factor levels and has fewer adverse reactions. Therefore, it is worthy of application and promotion.

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