EFFECTS OF LIGNET COMBINED WITH MECOBALAMINE ON NERVE CONDUCTION VELOCITY, CLINICAL SYMPTOM AND SIGN SCORE AND CLINICAL EFFICACY IN PATIENTS WITH DIABETIC PERIPHERAL NEUROPATHY

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ABSTRACT

Objective: *To investigate the effects of daglidene combined with mecobalamin on nerve conduction velocity, clinical symptom and sign score and clinical efficacy in patients with diabetic peripheral neuropathy.*

Method: *We randomly selected 88 cases of patients with diabetic peripheral neuropathy from the Department of Secretion in our hospital and randomly divided them into a research group (n = 44) and a control group (n = 44). The control group underwent a cobalt amine solution treatment; the team used a Glenn net joint cobalt amine solution treatment. The two groups were compared before and after treatments along the lines of nerve conduction velocity and clinical symptoms and signs scores.*

Results: *Before treatment, there were no significant differences in MNCV and SNCV of median nerve and common peroneal nerve between the two groups (P>0.05). After treatment, MNCV and SNCV of median nerve and common peroneal nerve in the two groups were significantly higher than they were before treatment, and MNCV and SNCV of median nerve and common peroneal nerve in the study group were significantly higher than in the control group, with a statistically significant difference (P<0.01). Before treatment, there was no significant difference in TCSS scores between the two groups (P>0.05). After treatment, the TCSS scores of the two groups were significantly lower than before treatment, and the TCSS score of the study group was significantly lower than that of the control group, with a statistically significant difference (P<0.01). The total effective rate of the study group was 93.18%; this rate was significantly higher than that of the control group (75.00%) and the difference was statistically significant (P<0.05).*

Conclusion: *Daglidene combined with mecobalamin can improve nerve conduction velocity and clinical symptoms and signs in patients with DPN. This approach also has a strong treatment effect.*

Keywords: *Dagrignet, mecobalamin, diabetes, peripheral neuropathy, nerve conduction velocity, efficacy.*

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Introduction

Diabetes mellitus (DM) is caused by an insulin secretion defect and/or damage to the body's biological functions caused by high blood sugar and metabolic disease[(1)]. Long-term hyperglycaemia in diabetic patients can lead to chronic damage and the dysfunction of tissues such as the eyes, kidneys, heart, blood vessels and nerves[(2)]. Diabetic peripheral neuropathy (DPN) refers to the symptoms associated with peripheral nerve dysfunction in patients with diabetes, and is the most common complication of diabetes[(3)].

Peripheral neuropathy can be bilateral, unilateral, symmetric or asymmetric; among these types bilateral symmetry is the most common. In clinical practice, symmetrical pain and paraesthesia can occur, among which symptoms in the lower extremities are common, including numbness, abdominal distension, pain, sweating, lower extremity joint disease and ulcers, etc. In severe cases, skin damage may occur and amputation may be necessary[(4)]. When a nerve related to movement is injured, muscle strength will undergo different degrees of decline, and in the late stage malnutrition-related muscle atrophy can occur.

Studies have shown that oxidative stress, metabolic disorders, lack of neurotrophic factors and vascular damage can all lead to peripheral neuropathy in diabetic patients. Moreover, the research also reveals that restoring damaged neurotrophic supply and inducing nerve regeneration are the main treatments for DPN[5]. Mecobalamin is a vitamin B12 derivative, which can act directly or indirectly on damaged nerve cells and promote axoplasmic protein synthesis, and is clinically used in the treatment of various types of peripheral neuropathy[6]. As a novel sodium-glucose cotransporter-2 (SGLT) inhibitor, mecobalamin serves as a drug to treat various peripheral nerve injuries[7]. This study was conducted in our hospital to investigate the effects of daglidene combined with mecobalamin on nerve conduction velocity, clinical symptom and sign score and clinical efficacy in patients with diabetic peripheral neuropathy.

Materials and methods

General information

88 patients with diabetic peripheral neuropathy in the Department of Secretion in our hospital were selected.

Our inclusion criteria were as follows

• The main criterion was that patients must meet the clinical diagnostic criteria for diabetes formulated by WHO and the secondary criteria with 2 or more slowdowns;

• Patients for nylon silk examination, foot sensory hypoesthesia or disappear;

• The ankle reflex disappears;

• Abnormal vibration sense;

• Temperature sensation abnormal nerve conduction velocity.

Patients present with primary criteria and 2 or more secondary manifestations.

Exclusion criteria included:

• DPN appears in the patient due to other reasons;

• Primary neurological dysfunction;

• Severe liver and kidney dysfunctions;

• The use of antioxidants and/or other drugs within the last month;

• Malignant tumours;

• Severe arteriovenous vascular disease;

• Cervical spondylosis and serious cerebrovascular disease.

All patients were informed and signed informed consent forms. The patients in the study group were randomly divided into a study group and a control group. There were 44 patients in the study group, including 24 males and 20 females, with an average age of (57.23±10.45) years, an average BMI of (20.56±1.56) Kg/m^2, and an average course of disease of (2.15±0.85) years. In the control group, there were 44 patients, including 23 males and 21 females, with an average age of (56.45±11.12) years, an average BMI of (21.02±1.12) Kg/m^2, and an average course of disease of (2.14±0.56) years.

There were no significant differences in age, gender, BMI and other general information between the two groups (P>0.05), as Table 1 makes clear.

Group	Age (year)	Gender (n)		BMI (Kg/m^2)	Average course of disease (years)
		M	W		
Research group (n=44)	57.23±10.45	24	20	20.56±1.56	2.15±0.85
Control group (n=44)	56.45±11.12	23	21	21.02±1.12	2.14±0.56
t/χ^2	0.339	0.046		1.589	0.065
P	0.735	0.831		0.116	0.948

Table 1: Comparison of general data between the two groups of subjects ($\bar{x}\pm s$).

Methods

Patients in both groups were given basic treatment for diabetes, such as hypoglycaemia, regulating water, electricity balance and nutritional support. The control group was treated with mecobalamin alone: patients were orally given 0.5 mg mecobalamin tablets (Nanjing Haoling Pharmaceutical Co., LTD., Yangzijiang Pharmaceutical Group; National Drug Approval: H20052325) 3 times a day over a 4-week cycle.

The study group adopted the regimen of daglidene combined with mecobalamin: a 10 mg tablet of daglidene (AstraZeneca Pharmaceutical Co., LTD., National Drug Approval: J20170040, 10mg/tablet) was given orally, once a day, 5 mg at a time and mecobalamin tablets were given orally, 3 times a day, 0.5 mg at a time over a 4-week cycle.

Observation indexes

Nerve conduction velocity

The conduction velocities of the median nerve and the common peroneal nerve before and after treatment were detected by NDI-092 electromyography, and the MNCV and SNCV of the two groups before and after treatment were compared.

Clinical symptom and sign scoring

The Toronto Clinical Scoring System (TCSS) was used to score neurological symptoms in each group before and after treatment. The TCSS rating scale was used by the same doctor to score the

patients' needle-like sensation, pain, walking instability, lower limb numbness and similar upper limb symptoms, and the changes of the two groups of patients were recorded and compared.

Treatment effect

The clinical symptoms of the two groups of patients before and after treatment were analysed, and the treatment effect of the two programs was evaluated.

Significant effect

Blood glucose level remained at the normal level (FPG 3.6-6.2 mmol/L, 2 hPG < 7.25mmol/L), neuropathy symptoms such as the Achilles tendon reaction disappeared, peripheral nerve sensation was normal and MNCV and SNCV levels increased by more than 2 m/s.

Effective

Hyperglycaemia significantly improved after treatment, neuropathy symptoms such as the Achilles tendon reaction largely disappeared and MNCV and SNCV levels increased by more than 1 m/s.

Invalid

No differences were observed in hyperglycaemia, neuropathy and nerve conduction velocity before and after treatment. Among them, the total effective is obvious effect + effective.

Statistical methods

The data of this study were analysed using the SPSS10.0 software package. The comparison of all measured data was ($\bar{x}\pm s$), and a t-test was used between the groups.

Counting data were expressed as percentages, and a test was used for comparison between groups. Grade data were compared using a Ridit test. P<0.05 was considered statistically significant.

Results

Comparison of nerve conduction velocity between the two groups before and after treatment

Before treatment, MNCV and SNCV of median nerve and common peroneal nerve showed no significant difference between the two groups (P>0.05). After treatment, MNCV and SNCV of median nerve and common peroneal nerve in the two groups were significantly higher than before treatment, and MNCV and SNCV of median nerve and common peroneal nerve in the study group were significantly higher than that in the control group, with a statistically significant difference (P<0.01). These results are shown in Tables 2 and 3.

Group	Median nerve (m/s)		Peroneal nerve (m/s)	
	Before treatment	After treatment	Before treatment	After treatment
Research group (n=44)	50.28±1.56	58.21±2.01	39.52±2.14	44.51±2.48
Control group (n=44)	50.56±1.38	54.34±2.18	40.02±2.06	42.17±2.24
t	0.892	8.657	1.117	4.697
P	0.375	<0.001	0.267	<0.001

Table 2: Comparison of MNCV between the two groups before and after treatment ($\bar{x}\pm s$).

Group	Median nerve (m/s)		Peroneal nerve (m/s)	
	Before treatment	After treatment	Before treatment	After treatment
Research group (n=44)	39.88±0.89	44.53±1.12	29.53±1.23	33.56±1.81
Control group (n=44)	40.14±1.04	42.16±1.08	30.15±1.41	31.25±1.84
t	1.260	10.104	1.134	5.937
P	0.211	<0.001	0.260	<0.001

Table 3: Comparison of SNCV between the two groups before and after treatment ($\bar{x}\pm s$).

Comparison of TCSS scores between the two groups before and after treatment

Before treatment, there was no significant difference in TCSS score between the two groups (P>0.05). After treatment, the TCSS score of the two groups was significantly lower than before treatment, and the TCSS score of the study group was significantly lower than that of the control group, with a statistically significant difference (P<0.01). Table 4 details these results.

Group	Before treatment	After treatment
Research group (n=44)	9.26±3.16	6.48±2.35
Control group (n=44)	9.21±3.14	8.54±2.11
t	0.075	4.326
P	0.941	<0.001

Table 4: Comparison of TCSS scores between the two groups before and after treatment ($\bar{x}\pm s$).

Comparison of efficacy between the two groups after treatment

After treatment, the total effective rate of the study group was 93.18%, which was significantly higher than that of the control group (P<0.05). These results are shown in Table 5.

Group	Excellent	Valid	Invalid	Total effective rate
Research group (n=44)	23 (52.27%)	18 (40.91%)	3 (6.82%)	41 (93.18%)
Control group (n=44)	17 (38.64%)	16 (36.36%)	11 (25.00%)	33 (75.00%)
χ^2				5.436
P				0.020

Table 5: Comparison of efficacy between the two groups after treatment (case, %).

Conclusion

The occurrence of DPN is closely related to the symptoms of vascular ischemia and hypoxia in diabetic patients, and the continuous high expression of blood glucose in patients can damage the body's microvessels, leading to the thickening of the walls of the small arteries of the neurotrophoblasts, platelet aggregation and the weakening of the nutritional function of microvessels[8]. A cobalt amine, which mainly exists in the blood and marrow fluid, can significantly improve nerve conduction.

With a methyl conversion reaction promoting nucleic acid and protein-fat metabolism, a cobalt amine is a kind of methionine synthetase coenzyme that can transform homocysteine into methionine, participate in the process of DNA nucleoside synthesis of thymine bases, aid in the synthesis of nucleic acid and protein, facilitate axon regeneration and the formation of myelin sheath, prevent the axonal degeneration and repair damaged nerve tissue[9, 10].

In the early treatment of DPN patients, the repair effect of damaged axons is significant, but with the extension of the treatment cycle of DPN patients, the treatment effect of damaged nerves is not ideal[11]. SGLT is a key carrier involved in glucose reuptake by glomerular epithelial cells.

Studies have shown that more than 90% of glucose reuptake by glomerular epithelial cells is mediated by SGLT. SGLT-2 inhibitors have a significant inhibitory effect on the reabsorption of glucose by the kidney, expelling excess glucose from the body and thus lowering blood glucose[12].

The SGLT-2 inhibitor is specifically distributed in the kidneys, and does not affect other tissues and organs. Moreover, it has the advantages of rarely occurring with hypoglycaemia and not increasing weight in diabetic patients[13].

Currently, a total of 6 SGLT-2 inhibitors have been listed in the world, among which dagley has been approved by the State Food and Drug Administration to be listed in China[14].

In this study, MNCV and SNCV of median nerve and common peroneal nerve showed no significant differences between the two groups before treatment (P>0.05). MNCV and SNCV of median nerve and common peroneal nerve in the two groups after treatment were significantly higher than those before treatment, and MNCV and SNCV of median nerve and common peroneal nerve in the study group were significantly higher than those in the control group, with a statistically significant difference (P<0.01). It was suggested that the MNCV and SNCV of DPN patients could be significantly reduced by the specific regulation of blood glucose by a combination of daglidene and mecobalamin.

TCSS score is a non-traumatic method for the diagnosis and evaluation of DPN patients. It has a high sensitivity and specificity for diagnosis and is widely used in clinical practice. After treatment, the TCSS score of the two groups was significantly lower than before treatment, and the TCSS score of the study group was significantly lower than that of the control group, with a statistically significant difference (P<0.01). As already noted, it was suggested that daglidene combined with mecobalamin was effective in the treatment of DPN patients with reduced clinical symptoms and significantly improved prognosis. After treatment, the total effective rate of the study group was 93.18%; this rate was significantly higher than that of the control group (75.00%). This indicates that daglidene combined with mecobalamin positively contributes to the treatment of DPN patients. Most notably, this study found that this approach relieves neurological symptoms and improves quality of life, a finding similar to the research results of Sun et al.[15].

In sum, daglidene combined with mecobalamin can improve nerve conduction velocity and clinical symptoms and signs in patients with DPN. The strategy has a good therapeutic effect, prolongs the life cycle of patients and can be widely used in clinical practice.

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