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Effect of mouse nerve growth factor combined with mecobalamine on treatment of diabetic peripheral neuropathy

De−Rong Hu*

Department of Neurology, Central Hospital of Ankang City, Shanxi Province, 725000, China

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ABSTRACT

Objective: To observe the clinical effect of mouse nerve growth fact (NGF) combined with mecobalamine on treatment of diabetic peripheral n-europathy (DPN). **Methods:** A total of 84 cases of patients with DPN treated in ourhospital between April 2012 and June 2015 were selected, and divided into study group and control group randomly (n=42); Control group was only given mecobalamine treatment, while study group was given mouse nerve growth factor combined with mecobalamine treatment for 4 weeks. TThe motor nerve conduction velocity median nerve (MNCV), sensory nerve conduction velocity (SNCV), serum high sensitivity c-reactive protein (hs-CRP) and Toronto clinical scoring system (TCSS) changes of median nerve and nervus peroneus communis before and after treatment were compared. **Results:** There were no significant differences in MNCV, SNCV of mediannerve and nervus peroneus communis before treatment. MNCV and SNCV of both groups after treatment were significantly increased. MNCV, SNCV of mediannerve and nervus peroneus communis in study group was significantly higher than that in control group. hs-CRP and TCSS scoring of both groups before treatment showed no statistic significant difference. hs-CRP scoring of both groups after treatment showed no significant difference. TCSS scoring was significantly lower than that in control group. Adverse reaction total occurrence rate after given drug in study group was 16.67% (7/42), compared with 7.14% (3/42) in control group, difference was significant. **Conclusions:** Mouse NGF combined with mecobalamine could achieve good curative effect. It is of higher safety in the treatment of patients with DPN, and deserves popularization and application.

1. Introduction

Diabetic Peripheral Neuropathy (DPN) is one of the most common chronic complications of diabetes. According to statistics, 60%-90% patients with diabetes might have different degrees of DPN, mainly showing symmetry multiple neuropathy, clinically featured movement, sensory and autonomic nerve dysfunction, refractory ulcer, infection etc, even amputation possible if it is severe[1]. At present, clinically, specific treatment plan is not achievable for DPN yet, neurotrophic drug treatment is the common choice[2]. Mecobalamine is methyl vitamin B12, which has some curative effect on DPN patients through seeping into nerve cells by exogenetic drug-delivery way[3]. Mouse nerve growth factor (NGF) is a kind of nerve growth factor extracted from salivary gland of mouse, which could treat nerve injuries by many reasons[4].A combination of both have better curative effect in DPN treatment. This study aims to analyze prognosis influence of mecobalamine combined with mouse NGF treatment on DPN patients, and to seek for better DPN therapeutic schedule with efficacy and safety.

2. Materials and methods

2.1. Clinical data

A total of 84 patients with DPN treated in our hospital between April 2012 and June 2015 were selected for implementation

*Corresponding author: De-Rong Hu, Department of Neurology, Central Hospital of Ankang City, Shanxi Province, 725000, China.
Tel: 13399157767
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research. Inclusion criteria were as follows[5]: (1) Clinical symptoms for all patients met DPN diagnostic criteria of WHO; (2) Confirmed by neural electrophysiological monitoring results; (3) Age＞50 years old. Exclusion Criteria were as follows: (1) other types of neuropathy; (2) patients with malignant tumor; (3) patients severely allergic to mecobalamine and mouse NGF; (4) incomplete medical records; (5) heart, liver and kidney function dysfunction. According to digital method, they were randomly divided into study group and control group (n=42), including 20 male cases, 22 female cases; age 51-68 years old, average age (61.2±2.4) years old; Disease course was 3-10 years, average disease course was (7.2±2.1) years. Control group included 19 male cases, 23 female cases; age 53-69 years old, average age as (60.8±2.3) years old; disease course was (4-10) years, average disease course was (7.1±1.9) years. The difference was not significant (P>0.05).

2.2. Research method

Control group was only given mecobalamine (produced by Misato Plant of Eisai Co., Ltd., approved by J20070063) treatment, dosage of 500 μg, once a day, intramuscular injection. On this basis, study group was added mouse NGF treatment (produced by Staidson Beijing Pharmaceutical Co., Ltd.; approved by S2000600223), dosage of 1 000 Au, once/d,intramuscular injection. Treatment course of both groups were 4 weeks, one treatment course after treatment, to evaluate curative effect of patients.

2.3. Observation index

EMG was used to monitor motor nerve conduction velocity, MNCV and sensory nerve conduction velocity, SNCV of median nerve and nervus peroneus communis of DPN patients before and after treatment during therapeutic process. Meanwhile, Toronto clinical scoring system (TCSS) was used before and after treatment for evaluation, mainly including symptom score (totally 6 scores) and reflex score (totally 8 scores), and sense score (totally 5 scores) *etc*. The higher the total scoring was, the severer the symptom was. Scatter turbidimetry and Hitachi Automatic Biochemical Analyzer was used to determine hs-CRP levels before and after treatment of both groups.

2.4. Effectiveness evaluation

Significant effectiveness was as follows: Clinical symptoms disappeared, and EMG showed MNCV added value was more than 5 m/s compared with before treatment, or had been restored to normal, TCSS scoring reduced value was more than 5 scores; Effectiveness was as follows: Clinical symptoms released, MNCV added value was less than 5 m/s compared with before treatment, TCSS scoring reduced value was more than 3 scores; Ineffectiveness was as follows: Clinical symptoms had little changes, MNCV had no changes, and TCSS scoring reduced value was less than 3 scores. The total effective rate according was calculated to Significant Effectiveness and Effectiveness ratio.

2.5. Statistical method

SPSS 18.0 statistical software was used for analysis, comparison of effective rate, adverse reaction etc. enumeration data was performed by using χ^2 test, measurement data was expressed as Mean ± SD, and analyzed by t test. P<0.05 showed significant difference.

3. Results

3.1. MNCV and SNCV of both groups before and after treatment

MNCV and SNCV of median nerve and nervus peroneus communis comparison of both groups before treatment showed no significant difference (P>0.05). After treatment, MNCV and SNCV of both groups were significantly increased, but MNCV and SNCV level of median nerve and nervus peroneus communis in study group was significantly higher than that in control group respectively (P<0.05) (Table 1).

3.2 Hs-CRP levels and TCSS scoring of both groups before and after treatment

Hs-CRP and TCSS scoring level comparison of both groups before treatment showed no significant difference (P>0.05). hs-CRP of study group and control group after treatment showed no significant difference (P>0.05), TCSS scoring was significantly lower than control group (P<0.05) (Table 2).

3.3 Adverse reaction after treatment

Adverse reaction total occurrence rate after treatment in study group was 16.67% (7/42), compared with 7.14% (3/42) in control group, and the difference was not significantce (P> 0.05) (Table 3).

Table 1
MNCV and SNCV level of both groups before and after treatment (m/s).

Groups	n	MNCV				SNCV			
		Median nerve		Nervus peroneus communis		median nerve		Nervus peroneus communis	
		Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment
Study group	42	44.52±5.36	62.51±5.84*	38.52±3.27	45.82±3.84*	39.56±3.62	50.58±5.24*	34.56±2.83	43.40±3.27*
Control group	42	45.23±5.17	50.28±4.59*	38.09±4.03	40.27±4.11*	39.19±3.55	42.59±4.28*	34.82±2.91	36.68±3.12*
t	-	0.618	10.671	0.537	6.395	0.473	7.653	0.415	9.636
P	-	0.538	0.000	0.593	0.000	0.638	0.000	0.679	0.000

Note: compared with before treatment,*P< 0.05.

Table 2

hs-CRP and TCSS scoring of both groups before and after treatment.

Groups	*n*	hs-CRP (mg/L)		TCSS scoring (scores)	
		Before treatment	After treatment	Before treatment	After treatment
Study group	42	4.95±2.23	2.86±1.73*	11.41±2.59	6.48±3.16*
Control group	42	4.86±2.18	3.24±1.55	11.28±2.85	9.14±3.22*
t	-	0.187	1.060	0.219	3.821
P	-	0.852	0.292	0.827	0.000

Note: compared with before treatment,*$P< 0.05$.

Table 3

Adverse reaction of both groups after treatment.

Groups	*n*	Injection spot ache	Blood pressure drop	Dyspnea	Rash	Total occurrence rate
	42	2 (4.76)	2 (4.76)	2 (4.76)	1 (2.38)	7 (16.67)
Study group	42	1 (2.38)	1 (2.38)	1 (2.38)	0 (0.00)	3 (7.14)
χ^2	-					1.816
P	-					0.178

4. Discussion

DPN is the common chronic complications, morbidity rate reaches up to 60%-90%[8] among diabetic patients. At present, undefined DPN pathogenesis brings difficulties for clinical treatment. It is reported that the pathogenesis of DPN mainly includes the microvascular lesion, oxidative stress injury and lack of NGF etc[9]. Clinically, there is no strict standard for DPN treatment. So far, mecobalamine treatment has been the common choice[10]. In recent years, most researches found that whether it is animal model or DPN patients, all existed NGF lack, which made the role of NGF become more and more important during DPN treatment[11,12].

NGF is a kind of nerve growth factor extracted from salivary gland of mouse, which is the earliest found and clearest researched B-class NGF, in other words, a kind of neurotrophic factor. It could promote central and peripheral nerve growth, development, differentiation and regeneration. It is used to treat nerve injuries by multiple reasons[13]. Mecobalamine is methyl vitamin B12, also Methionine synthetase coenzyme, which could successfully seep into nerve cells for function by exogenous drug delivery, combination of both could play better therapeutical effect. In this study, results shows that significant effectiveness rate and total effectiveness rate in study group are significantly higher than that in control group, which indicated that mouse NGF combined with mecobalamine treatment has better curative effect for DPN patients. Comparing the nerve conduction velocity of both groups before and after treatment, we found that after treatment, MNCV and SNCV levels were all significantly increased in both groups, but MNCV and SNCV level of median nerve and nervus peroneus communis in study group was significantly higher than that in control group, which proved that mouse NGF combined with mecobalamine treatment could effectively increase conduction velocity of sensory nerveand motor nerve of DPN patients, and had important clinical significance for DPN treatment. The possible mechanism is that mouse NGF could help maintain the survival and development of the sympathetic and sensory neurons, and meanwhile mecobalamine could promote nerve myelin formation and axon regeneration, combination of both could play cooperation role and increase nerve conduction velocity[15].

Comparing the serum hs-CRP level and TCSS scoring of both groups before and after treatment, we found that hs-CRP comparison in study group and control group showed no significant difference, TCSS scoring in study group was significantly lower than that in control group. Among them, hs-CRP is a sensitive indicator reflecting the body's inflammatory response, while TCSS could reflect the degree of peripheral neuropathy. This study showed that inflammatory response level of both groups after treatment was all reduced, peripheral neuropathy clinical manifestation of patients was reduced. Because of more significant increase in nerve conduction velocity in study group, peripheral neuropathy clinical manifestation are significantly reduced in study group, and curative effect is better[16]. In terms of adverse drug reaction, there is no significant difference in the adverse reaction total occurrence rate after treatment. Combination treatment is of higher safety, because mouse NGF drug use in study group has higher homologous with human NGF structure. Therefore, combination treatment would not increase the adverse reaction in study group.

In conclusion, mouse NGF combined with mecobalamine could achieve good curative effect. It is of higher safety in the treatment of patients with DPN, and deserves popularization and application.

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