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Clinical Efficacy of Pentoxifylline Combined with Thioctic Acid in the Treatment of Painful Diabetic Peripheral Neuropathy

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Abstract: *Objective:* To observe the efficacy of pentoxifylline + thioctic acid in the treatment of patients with painful diabetic peripheral neuropathy (PDPN). *Methods:* 70 patients with PDPN admitted from October 2019 to October 2022 were selected and randomly grouped, with pentoxifylline + thioctic acid treatment in Group A and thioctic acid treatment in Group B, and the treatment efficacy was compared. *Results:* The treatment efficacy in Group A was higher than that of Group B, $P < 0.05$; the points of each symptom of PDPN in Group A were lower than that of Group B, $P < 0.05$; the C-reactive protein and electromyography indexes of PDPN patients in Group A were better than that of Group B, $P < 0.05$. *Conclusion:* PDPN patients treated with pentoxifylline + thioctic acid can optimize nerve function, inhibit inflammation progression, and reduce PDPN symptoms, which is an efficient and feasible treatment option.

Keywords: Thioctic acid; Pentoxifylline; Painful diabetic peripheral neuropathy; Efficacy

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1. Introduction

Diabetic patients often experience peripheral neuropathy, which can affect autonomic, sensory, and motor nerves, leading to symptoms such as numbness and pain in the extremities. This can even result in secondary motor impairment and neurological dysfunction, characterized by high disability rates and long disease duration. Some patients with neuropathy exhibit painful diabetic peripheral neuropathy (PDPN). Analyzing the causes, PDPN is associated with metabolic disorders and insufficient vascular oxygen supply. It is also closely related to genetic factors, immune responses, and vitamin deficiencies [1]. At present, the basic clinical treatment of PDPN is to stabilize blood glucose, and at the same time, administer medications that nourish the nerves and restore peripheral circulation to control the progress of PDPN [2]. Thioctic acid is a commonly used therapeutic drug for PDPN, which can inactivate aldose reductase, and also block protein glycosylation-like changes, thus preventing neuropathy caused by high blood glucose; in addition to this, the administration of pentoxifylline can restore local microcirculation [3]. In this paper, we explore the treatment efficacy of pentoxifylline + thioctic

acid with 70 PDPN patients.

2. General information and methods

2.1. General information

A sample of 70 PDPN patients admitted from October 2019 to October 2022 were selected and randomly grouped. There was no difference between the information of PDPN patients in Group A and Group B, $P > 0.05$, as shown in **Table 1**.

Table 1. Analysis of PDPN patients' data

Groups	Gender		Age (year)		Disease duration (years)	
	Male	Female	Interval	Mean	Interval	Mean
Group A ($n = 35$)	21	14	49–67	57.18 ± 2.46	2–13	7.51 ± 2.11
Group B ($n = 35$)	22	13	50–68	57.21 ± 2.49	2–14	7.49 ± 2.18
χ^2/t	0.0603		0.0507		0.0390	
P	0.8060		0.9597		0.9690	

2.2. Inclusion and exclusion criteria

Inclusion criteria: the appearance of neuralgia, such as limb tingling and burning pain; informed consent; electromyography suggests slow conduction.

Exclusion criteria: non-diabetes-induced neuropathy; secondary ketoacidosis; mental abnormalities.

2.3. Treatment methods

The diet of diabetic patients was monitored, they were urged to exercise and regulate fasting blood glucose to 4.4–7.0 mmol/L and postprandial blood glucose < 10 mmol/L.

Group A received pentoxifylline (Inner Mongolia White Medicine Pharmaceutical Co., Ltd.) + thioctic acid (Yabao Pharmaceutical Group Co., Ltd.) treatment: Pentoxifylline was administered via intravenous drip, with a single dose of 0.1 g of the drug placed into 250 ml of normal saline, once a day. Thioctic acid was also administered via intravenous drip, with a single dose of 600 mg of the drug placed into 250 ml of normal saline, once a day. The treatment was administered for a duration of two months.

Thioctic acid treatment in Group B was the same as that in Group A.

2.4. Observation index

(1) Treatment efficacy: PDPN patients with normal tendon reflexes, motor and sensory nerve conduction speed > 5 m/s were recorded as highly effective; tendon reflexes improved, motor and sensory nerve conduction speed ≤ 5 m/s were recorded as effective; tendon reflexes and conduction speed did not change were recorded as ineffective.

(2) Symptom score: The 3-point method was used to assess the symptoms of muscle atrophy, limb pain, sensory loss, limb weakness, limb numbness, etc. The score is positively correlated with the degree of disease in PDPN patients.

(3) Inflammation and electromyography indexes: The level of C-reactive protein (CRP) was measured, as well as motor nerve conduction velocity (MNCV) and other indexes.

2.5. Statistical methods

The data of PDPN patients were processed by SPSS21.0, % was used to record (χ^2 validation) count data of PDPN patients, while mean ± standard deviation (SD) was used to record (*t* validation) measurement data of PDPN patients. There were statistical differences if $P < 0.05$.

3. Results

3.1. Treatment efficacy

The treatment efficacy of PDPN patients in Group A was higher than that in Group B, $P < 0.05$, as shown in **Table 2**.

Table 2. Comparison of efficacy of PDPN patients [*n* (%)]

Groups	Highly effective	Effective	Ineffective	Total effectiveness
Group A (*n* = 35)	26 (74.29)	8 (22.86)	1 (2.86)	97.14
Group B (*n* = 35)	19 (54.29)	10 (28.57)	6 (17.14)	82.86
χ^2	-	-	-	3.9683
P	-	-	-	0.0464

3.2. Symptom scores

After medication, all the symptom scores of PDPN in Group A were lower than those in Group B, $P < 0.05$, as shown in **Table 3**.

Table 3. Comparison of PDPN symptom scores before and after medication (mean ± SD, points)

Groups	Muscle atrophy		Limb pain		Reduced sensation		Limb weakness		Limb numbness	
	Before	After	Before	After	Before	After	Before	After	Before	After
Group A (*n* = 35)	2.47 ± 1.21	0.84 ± 0.32	2.61 ± 1.15	0.64 ± 0.26	2.54 ± 0.36	0.61 ± 0.22	2.66 ± 1.14	0.59 ± 0.31	2.58 ± 1.19	0.52 ± 0.25
Group B (*n* = 35)	2.49 ± 1.19	1.36 ± 0.44	2.63 ± 1.13	1.41 ± 0.36	2.53 ± 0.39	1.36 ± 0.31	2.68 ± 1.12	1.41 ± 0.43	2.54 ± 1.21	1.43 ± 0.52
t	0.0697	5.6545	0.0734	10.2582	0.1115	11.6724	0.0740	9.1516	0.1394	9.3308
P	0.9446	0.0000	0.9417	0.0000	0.9116	0.0000	0.9412	0.0000	0.8895	0.0000

3.3. CRP and electromyography

After medication, CRP indexes and electromyography indexes of PDPN patients in Group A were better than those in Group B, $P < 0.05$, as presented in **Table 4.**

Table 4. Comparison of CRP and electromyography indexes (mean ± SD, points)

Groups	CRP (mg/L)		Peroneal nerve MNCV (m/s)		Median nerve MNCV (m/s)	
	Before	After	Before	After	Before	After
Group A (*n* = 35)	17.54 ± 2.11	10.21 ± 0.96	38.42 ± 1.88	48.16 ± 2.43	42.94 ± 2.21	52.06 ± 2.48
Group B (*n* = 35)	17.52 ± 2.13	12.44 ± 1.88	38.43 ± 1.91	41.94 ± 2.26	42.96 ± 2.25	48.36 ± 2.36
t	0.0395	6.2498	0.0221	11.0887	0.0375	6.3940
P	0.9686	0.0000	0.9825	0.0000	0.9702	0.0000

4. Discussion

PDPN accounts for a significant proportion of neuropathic pain cases, and severe pain can greatly reduce patients' quality of life. Clinical practice analysis indicates that the mechanisms of pain in PDPN patients are related to the following factors: (1) In the body, both unmyelinated and myelinated fibers can conduct pain. If these fibers regenerate or become damaged, they can trigger nerve impulses. Additionally, under the influence of hyperglycemia, patients' sensitivity to pain can be increased [4]. (2) Under prolonged hyperglycemia stimulation, the body can generate advanced glycation end-products, which exacerbate stress damage. This can lead to macrophages engulfing adjacent nerve myelin, resulting in segmental demyelination. Consequently, this increases the content of nuclear factors, induces inflammatory responses, and heightens pain sensitivity [5]. Currently, the clinical treatment of PDPN is mostly based on drug regimens, and drugs such as thioctic acid and pentoxifylline are commonly used.

Thioctic acid is an antioxidant drug that can remove free radicals from the body, inhibit oxidative stress, and reduce the degree of damage to the vascular endothelium in patients with PDPN, thus correcting the metabolic disorders that cause endothelial dysfunction [6]. In addition, thioctic acid can remove oxygen mediators from the body of PDPN patients, inhibit oxidative stress response, accelerate nerve conduction, activate Na^+-K^+-ATPase, restore local blood flow, and correct PDPN lesions [7]. The active components of pentoxifylline include theophylline activity, as well as theobromine and caffeine activities, which can block the conversion of cyclic adenosine monophosphate (cAMP) to monophosphate adenosine. This process helps to dilate blood vessels and restore local blood flow in patients with PDPN. Additionally, pentoxifylline can enhance erythrocyte deformability, inhibit platelet aggregation, and prevent the interaction between cells and platelet activation factors, thereby reducing granulocyte reactivity and alleviating hypercoagulable blood states. [8].

Based on the results in this paper, the treatment efficacy of PDPN patients in Group A was higher than that in Group B, $P < 0.05$. It suggests that thioctic acid + pentoxifylline treatment can enhance the treatment efficacy of PDPN. The reason is that thioctic acid belongs to the antioxidant class of drugs, has high activity, and can bind a variety of free radicals and reactive oxygen species, which is conducive to reducing the content of free radicals in the body of patients with PDPN. It can also stimulate the body to generate antioxidants, reduce the degree of oxidative stress, and then optimize vascular function; combined with pentoxifylline, they can further improve the local blood transport, enhance the red blood cell deformation ability, and promote the activation of the platelet factor. It can also inactivate platelet-activating factor, thereby diluting the blood and enhancing the effect of PDPN control [9]. Another set of data showed that the PDPN symptom scores of Group A were lower than those of Group B, with $P < 0.05$; CRP levels and electromyography indexes of PDPN patients in Group A were better than those in Group B, with $P < 0.05$. It was suggested that thioctic acid + pentoxifylline treatment could inhibit inflammation and reduce PDPN disease. Analyzing the reason, the coordinated action of thioctic acid and pentoxifylline can repair the damaged nervous system, correct the metabolic disorders of PDPN patients, and restore the physiological metabolic process of nerve cells [10]. In addition, the combination of the two drugs can also improve endothelial function and restore the physiological functions of limb nerves and blood vessels.

5. Conclusion

In conclusion, the treatment of PDPN patients with thioctic acid + pentoxifylline can inhibit inflammation and reduce PDPN symptoms, which is an efficient and feasible treatment option.

Disclosure statement

The authors declare no conflict of interest.

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