

Research Progress in Drug Therapy of Diabetic Peripheral Neuropathy

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Abstract: Diabetic peripheral neuropathy has a serious impact on the health and quality of life of patients. At present, the disease is mainly treated by aldose reductase inhibitors and other drugs. These drugs can effectively relieve the clinical symptoms of patients, and have good improvement effect on their neurological function, which can delay the development of the disease to a large extent. In clinical treatment, for the treatment of the disease, mainly in the premise of stable control of blood sugar, give patients the corresponding drug adjuvant treatment. In this paper, on the basis of consulting the relevant literature, we analyzed the progress of drug treatment of patients.

1. Introduction

Diabetic peripheral neuropathy (DPN) is a common complication of diabetes. The main clinical manifestations include limb numbness, pain, hyperalgesia, myasthenia, etc. At present, there is no exact research demonstration for the pathological mechanism of this disease in clinical research. It is speculated that it may be related to the patient's long-term severe hyperglycemia and the resulting metabolic disorders. In the clinical treatment, mainly for the pathogenesis of diabetic peripheral neuropathy, as well as related risk factors for treatment, and for its metabolic disorders to correct, improve its microcirculation, and through effective drugs for its nerve repair. This article reviews the progress of drug treatment of diabetic peripheral neuropathy as follows.

2. Application of hypoglycemic drugs

In the clinical treatment of patients with diabetic neuropathy, effective control of blood glucose can delay the development of the disease to a large extent. For such patients, if their blood sugar rises rapidly from hypoglycemia to hyperglycemia, the risk of diabetic peripheral neuropathy will be very high, and other serious diseases may be induced, so it is very important to keep the blood glucose stable in the normal range. Most patients with type 2 diabetes can effectively maintain blood glucose stability through diet control and oral hypoglycemic drugs, without the use of insulin. When patients with poor glycemic control or diagnosed with type 1 diabetes, insulin should be used in the early stage. At this stage, the commonly used hypoglycemic drugs include insulin growth factor preparation, dipeptidyl peptidase preparation and so on. These drugs can play a certain therapeutic effect on patients with diabetic neuropathy.

3. Drugs for correcting metabolic disorders

3.1. Antioxidants

Lipoic acid is one of the most commonly used antioxidants in clinic. It has obvious scavenging effect on oxidative stress products and can regenerate other antioxidants. These drugs can effectively inhibit the oxidative stress in the nerve, increase the blood flow of the nerve, and effectively accelerate the nerve conduction velocity. Zhang Meiqin ^[1] pointed out in the study that lipoic acid drugs can effectively relieve the pain, numbness and other symptoms existing in patients, and the drug effect is very obvious. In addition, other antioxidant drugs can also reduce the activity of polyols, have a good recovery effect on the nerve, effectively improve the neurophysiological function, and can achieve good antioxidant effect^[2].

3.2. Aldose reductase inhibitors

Aldose reductase can catalyze a variety of aldehydes and ketones into alcohols, participate in the metabolism of lipid-derived aldehydes, change various molecules in cells, and participate in the process of oxidative stress. Relevant clinical studies have pointed out that aldose reductase inhibitors have certain control effect on the condition of diabetic neuropathy patients, which can reduce the level of sorbitol in nerve cells, further delay the small F wave, and improve the conduction velocity of tibial nerve and sural nerve^[3-4]. This inhibition of enzyme activity may be effective due to the inhibition of this enzyme. Drugs with this characteristic include epalrestat and hydantoin preparations. Many studies have shown that epalrestat can effectively delay the development of diabetic peripheral neuropathy, and has good improvement effect on motor nerve and sensory nerve conduction function of patients.

3.3. Glycosylation product inhibitors

At present, the effect of this drug on human body is still in the experimental stage, and its representative drugs are amino arc, thiamine pyrophosphate, etc. Deng Huihui ^[5] and other researchers pointed out in related research that glycosylation product inhibitors have potential protective effect on vascular endothelial cells, have obvious improvement effect on blood supply of nerve microvascular, can effectively inhibit the thickening of microvascular basement membrane, effectively reduce the demyelination and axonal degeneration of nerve fibers, and have an obvious improvement effect on nerve conduction velocity. Glycosylation products inhibitors also have the effects of anti-oxidation stress and anti-inflammatory reaction, which is an important reason that they can effectively delay the development of the disease. In addition, glycosylation product inhibitors have a certain inhibitory effect on the synthesis of nitric oxide synthase. To a certain extent, this drug can be used as a preventive drug. For the application of this aspect, we need to continue to pay attention and research in the future.

4. Application of drugs to improve microcirculation

4.1. Cilostazol

Cilostazol tablets have a significant inhibitory effect on platelet aggregation and activation of phosphodiesterase activity in vascular smooth muscle, thus exerting the effect of vasodilation and antiplatelet. At the same time, it has a certain inhibitory effect on epinephrine in patients, which can effectively reduce the platelet adhesion rate, reduce the blood viscosity, and increase the blood

supply of nerve terminals ^[6]. Cilostazol tablets can effectively increase the blood supply of gastrocnemius muscle tissue, and effectively increase the blood flow of lower limbs of patients, which has a significant effect on improving the clinical symptoms of patients with neuropathy. ^[7] study, Liu Xiaoxia and others used cilostazol tablets combined with epalrestat tablets ^[7] treatment of diabetic peripheral neuropathy. The results showed that the clinical symptoms of patients were significantly relieved, and the nerve conduction velocity was also greatly improved. This shows that cilostazol tablets have a good promoting effect on the nerve recovery and disease rehabilitation of patients with diabetic peripheral neuropathy.

4.2. Prostaglandin analogues

Prostaglandins can directly act on the vascular smooth muscle of patients through the resistance effect of endothelin, play the role of vasodilator, effectively inhibit platelet aggregation, reduce blood viscosity, increase the blood supply of peripheral nerve, and effectively improve the microcirculation of patients. At present, prostaglandin E1 and beraprost sodium are commonly used as representative drugs. ^[8] study, Xu Yanrong et al. (M23) divided the diabetic peripheral neuropathy patients into groups, the control group was treated with basic treatment, and the experimental group was treated with Lipo prostaglandin E1. The results showed that the clinical symptoms of patients ^[8] experimental group were significantly improved, and the nerve conduction velocity was also significantly improved. Prostaglandin drugs have a certain affinity for patients with diabetic peripheral neuropathy, and have the advantages of slow decomposition, small dosage and long-term effect, which are commonly used drugs in patients with diabetic peripheral neuropathy. Relevant studies have indicated that prostaglandins can improve the sciatic nerve of patients with diabetic neuropathy, but its mechanism still needs to be further verified^[9]. However, in China's guidelines for the prevention and treatment of type 2 diabetes, this drug has been included in the indications of the drug, and its safety and effectiveness have been verified through experiments.

4.3. Calcium antagonists

The majority of patients with diabetic peripheral neuropathy will aggravate peripheral neuropathy, which will aggravate peripheral neuropathy. Calcium antagonists can improve the endothelial function of patients, increase the density of capillaries in the nerve, promote the growth of microvessels, increase the blood flow around nerve endings, and improve the condition of ischemia and hypoxia in patients. Moreover, these drugs can activate white blood cells, effectively participate in the anti-inflammatory reaction, effectively alleviate the clinical symptoms of patients, and accelerate their nerve conduction velocity.

5. Application of nerve repair drugs

Diabetic peripheral neuropathy patients, whose nerve injury is accompanied by segmental demyelination and axonal degeneration, the repair of nerve injury is a long process. The commonly used drugs in clinical application include Mecobalamin, cytidine disodium triphosphate, cerebroside and carnosine, nerve growth factor, etc. Mecobalamin can promote fat metabolism. After entering the nerve cells, it can repair the nerve tissue in the axonal damaged area, which can effectively improve the clinical symptoms such as limb numbness and pain. Methionine synthetase is involved in the synthesis of structural proteins and lecithin in neurons, which can effectively promote the regeneration of nerve tissue and provide nutritional support for nerve cells. ¹²ⁿ B is an important coenzyme, and Mecobalamin is a preparation of ¹²ⁿ B cobalt amide. The use of this kind of drugs

can effectively enhance the repair ability of injured nerves. Chen Ruihua^[10] and others have confirmed in clinical research that Mecobalamin has a very obvious effect on the prevention and treatment of diabetic peripheral neuropathy, especially for the damage of peripheral sensory nerve. At present, this kind of drug has become a routine drug for patients with diabetic peripheral neuropathy. Cytidine disodium triphosphate is a kind of nucleotide derivative, which can effectively enhance the biological activity of nerve cells, promote the regeneration and self-healing of nerve cells, and enhance the damage resistance of nerve cells. The nerve repair drugs used by patients generally have good damage repair effect and have obvious improvement effect on nerve function. At present, neurotrophic factor drugs have not yet entered the clinical practice. Among many nutritional factors, recombinant nerve growth factor is expected to enter clinical application, and three phase clinical trials have been completed.

6. Symptomatic treatment

According to the epidemiological survey, diabetes patients are more likely to have depression than normal people, which makes the treatment of the disease more difficult. Traditional anticonvulsant drugs and new generation of anticonvulsant drugs have certain therapeutic effect on diabetic neuropathy, and can improve the pain and sleep disorders of patients. Tricyclic antidepressants can inhibit synapses, inhibit the reuptake of neurotransmitters, inhibit the pain receptors to a certain extent, and effectively improve the threshold of pain. We can also reduce the sensitivity of related indicators to achieve a certain analgesic effect, so as to alleviate the clinical symptoms of patients. Fu Shaojian^[11] pointed out in the study that duloxetine hydrochloride enteric coated capsules for the treatment of diabetic peripheral neuropathy patients, after a period of treatment, the degree of pain of patients will be significantly reduced, which shows that the drug for diabetic peripheral neuropathy patients with pain symptoms, has obvious relief effect. Some antiarrhythmic drugs, such as lidocaine, mexiletine, etc., can effectively prevent Na⁺ from entering cells, weaken the ability of cell depolarization, and relieve body pain. Some patients with mild or limited pain can also be treated with spray or patch. Patients with severe pain can also be treated with adjuvant drugs.

7. Application of traditional Chinese Medicine

Traditional Chinese medicine treatment of diabetic peripheral neuropathy, has a long history, in the traditional Chinese medicine treatment, mainly through the adjustment of the way of administration, as well as the use of a variety of treatment methods, to implement treatment for patients. Including traditional Chinese medicine compound, Chinese medicine single prescription, Chinese medicine extract treatment, acupuncture, Chinese medicine fumigation treatment, etc., through the traditional Chinese medicine dialectical treatment, can effectively alleviate the clinical symptoms of such patients, and combine it with western medicine, can achieve body superposition effect, can further promote clinical efficacy. Some researchers used modified Taohong Siwu Decoction in the treatment of diabetic peripheral neuropathy, the effect is very ideal. Huang Huirong^[12] and other researchers divided patients with diabetic peripheral neuropathy into control group and observation group. The control group only received moxibustion treatment, while the observation group received acupuncture treatment. The results showed that the clinical total effective rate of the observation group was also higher than that of the control group, and the treatment effect was more ideal. There are also researchers using Xiaoke cold Tongle fumigation treatment of such patients, not only effectively alleviate the clinical symptoms of patients, for its nerve damage also played a very good repair effect, effectively reduce the degree of microvascular lesions, more importantly, this treatment is high safety, operation is relatively simple.

8. Conclusion

At present, there is no exact research demonstration on the pathogenesis of diabetic peripheral neuropathy. It is speculated that the occurrence of this disease is related to many factors. At present, the clinical treatment of this disease is more difficult. In the process of treatment, we need to start from many aspects, and strictly control the blood glucose of patients is an important premise to delay the development of the disease. In addition, for different patients, we should give them appropriate drugs according to their condition and constitution, and formulate individualized treatment plan for them to ensure the clinical treatment effect. Generally, after the blood glucose of patients is controlled stably, antioxidant stress drugs, microcirculation drugs and metabolic disorder drugs can be provided for patients for adjuvant treatment. In the future, with the in-depth study of the etiology and pathological mechanism of this disease, it is believed that more effective drugs can be developed to treat this disease.

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