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Analysis of the Adjuvant Therapeutic Effect of Epalrestat Tablets in Enhancing the Treatment of Diabetic Complications

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Abstract: *Objective:* To evaluate the adjuvant therapeutic effect of Epalrestat tablets on diabetic complications. *Methods:* 96 patients with diabetic complications who were admitted to the hospital from September 2021 to September 2023 were selected and randomly divided into two groups using a random number table. The observation group was treated with Epalrestat tablets combined with Ginkgo Dipyridolum Injection, while the control group was treated with Ginkgo Dipyridolum Injection only. The total effective rate, blood glucose indicators, oxidative stress indicators, and adverse reaction rates were compared between the two groups. *Results:* The total effective rates of diabetic nephropathy (DN), diabetic foot (DF), and diabetic peripheral neuropathy (DPN) in the observation group were higher than those in the control group ($P < 0.05$). After 12 weeks of treatment, the blood glucose indicators in the observation group were lower than those in the control group, and the oxidative stress indicators were better than those in the control group ($P < 0.05$). The adverse reaction rate in the observation group was lower than that in the control group ($P < 0.05$). *Conclusion:* Epalrestat tablets can assist in improving the clinical efficacy of patients with diabetic complications, lowering their blood glucose levels, reducing oxidative stress damage, and decreasing adverse reactions after medication.

Keywords: Epalrestat tablets; Diabetic complications; Adjuvant therapy

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1. Introduction

The high incidence of diabetes is related to factors such as changes in dietary structure, changes in the living environment, and increased work pressure. It is a metabolic chronic disease characterized by continuous elevation of blood glucose, and its progression can affect renal function, foot function, and peripheral nerves, leading to various complications. At this stage, the main treatment for diabetic complications is symptomatic drug therapy, to improve complication symptoms and reduce their long-term harm. Among them, Ginkgo Dipyridolum Injection is a commonly used therapeutic drug for this disease, which can expand coronary and cerebral blood vessels, and improve vascular wall tension, thereby reducing vascular permeability and correcting ischemia and other manifestations [1]. However, the effectiveness of single-drug treatment with this medication is

not satisfactory, and it needs to be combined with other drugs. Epalrestat tablets are commonly used aldose reductase inhibitors that can inhibit multiple pathways of protein kinase C signaling, increase carbon monoxide production, and thus protect neurovascular function and improve overall efficacy [2]. Based on this, this study selected 96 patients with diabetic complications to evaluate the therapeutic effect of Epalrestat tablets.

2. Materials and methods

2.1. General information

96 patients with diabetic complications admitted to the hospital between September 2021 and September 2023 were selected and randomly divided into two groups using a random number table. The observation group consisted of 48 patients, including 27 males and 21 females, aged between 40 and 78 years old with a mean age of (52.65 ± 4.19) years old. The duration of diabetes ranged from 1 to 10 years with a mean of (5.84 ± 0.97) years. The types of complications included 19 cases of DN, 16 cases of DF, and 13 cases of DPN.

The control group also consisted of 48 patients, including 28 males and 20 females, aged between 41 and 79 years old with a mean age of (52.91 ± 4.32) years old. The duration of diabetes ranged from 2 to 10 years with a mean of (5.91 ± 0.90) years. The types of complications included 18 cases of DN, 16 cases of DF, and 14 cases of DPN. There was no statistically significant difference in basic information between the two groups ($P > 0.05$).

Inclusion criteria: age < 80 years old; normal cardiac, liver, and kidney function; normal mental state; meeting medication indications; informed consent for the study.

Exclusion criteria: patients with malignant tumors or infectious diseases; patients with major organ parenchymal diseases; incomplete clinical data; allergy to study drugs; withdrawal from the study.

2.2. Methods

Both groups of patients followed a low-sugar, low-salt, and low-fat diet, with moderate daily exercise to control blood glucose levels. If the patient's HbAlc level was less than 7%, they were administered vitamin B1 orally at a dose of 20 mg three times a day, combined with adenosine cobalamin at a dose of 0.5 mg three times a day for 12 weeks.

The control group was treated with Ginkgo Dipyridolum Injection at a dose of 20 mL mixed with 250 mL of 0.9% sodium chloride solution, administered via intravenous infusion once daily for 12 weeks.

The observation group was treated with Epalrestat tablets combined with Ginkgo Dipyridolum Injection. The usage and dosage of Ginkgo Dipyridolum Injection were the same as above. Epalrestat tablets were administered orally at a dose of 50 mg three times a day for 12 weeks.

2.3. Observation indicators

(1) Blood glucose indicators: Fasting blood glucose (FBG), HbAlc, and 2-hour postprandial blood glucose (2hPG) were measured before and after treatment.

(2) Oxidative stress indicators: Venous blood was drawn before and after treatment, and superoxide dismutase (SOD), malondialdehyde (MDA), and reactive oxygen species (ROS) were measured using enzyme-linked immunosorbent assay.

(3) Adverse reactions: Adverse reactions such as nausea and vomiting, diarrhea and abdominal pain, dizziness, loss of appetite, and skin irritation were observed.

2.4. Evaluation criteria for therapeutic effect

(1) DN: Significant effect: asymptomatic or mild symptoms, no abnormality in Cr-C, and a decrease in

UAE of more than 30%; Initial effect: moderate symptoms, mild abnormality in Cr-C, and a decrease in UAE of 10% to 30%; No effect: severe symptoms, severe abnormality in Cr-C, and a decrease in UAE of less than 10%.

(2) DF: Significant effect: healing of ulcer surface or healing degree > 80%, specific decrease in Wagner grade ≥ 2; Initial effect: healing degree of ulcer surface between 50% and 80%, specific decrease in Wagner grade by 1; No effect: healing degree of ulcer surface < 50%, no change in Wagner grade.

(3) DPN: Significant effect: no pain in limbs, normal motor and sensory functions; Initial effect: mild pain in limbs, improvement in motor and sensory functions; No effect: no change in limb pain, motor and sensory functions.

2.5. Statistical analysis

Data processing was performed using SPSS 28.0 software. Measurement data were expressed as mean ± standard deviation (SD) and compared and tested using *t*-values. Count data were expressed as (*n*/%) and compared and tested using chi-square (χ^2) values. Statistical significance was defined as $P < 0.05$.

3. Results

3.1. Comparison of total effective rates between the two groups

The total effective rates of DN, DF, and DPN in the observation group were higher than those in the control group ($P < 0.05$). See **Table 1–3** for details.

Table 1. Comparison of total effective rates of DN between the two groups (*n*/%)

Subgroups	*n*	Remarkable results	Initial effect	No effect	Overall effective
Observation group	19	10	8	1	94.74 (18/19)
Control group	18	7	5	6	66.67 (12/18)
χ^2					4.748
P					0.029

Table 2. Comparison of the overall DF effectiveness rate between the two groups of patients (*n*/%)

Subgroups	*n*	Remarkable results	Initial effect	No effect	Overall effective
Observation group	16	8	6	2	87.50 (14/16)
Control group	16	5	3	8	50.00 (8/16)
χ^2					5.236
P					0.022

Table 3. Comparison of the overall DPN efficiency of the two groups of patients (*n*/%)

Subgroups	*n*	Remarkable results	Initial effect	No effect	Overall effective
Observation group	13	7	5	1	92.31 (12/13)
Control group	14	4	4	6	57.14 (8/14)
χ^2					4.340
P					0.037

3.2. Comparison of blood glucose indexes between the two groups of patients

Before treatment, there is no difference in the comparison of blood glucose indicators between the two groups ($P > 0.05$). After 12 weeks of treatment, the blood glucose index of the observation group was lower than that of the control group ($P < 0.05$) (**Table 4**).

Table 4. Comparison of blood glucose indexes between the two groups of patients (mean ± SD)

Subgroups	*n*	FBG (mmol/L)		HbAlc (%)		2hPG (mmol/L)	
		Before treatment	After treatment	b	After treatment	Before treatment	After treatment
Observation group	48	6.35 ± 1.91	4.31 ± 0.58	11.48 ± 2.03	7.10 ± 1.27	12.37 ± 2.07	7.30 ± 1.25
Control group	48	6.38 ± 1.99	5.24 ± 0.67	11.41 ± 2.09	8.49 ± 1.34	12.31 ± 2.04	9.31 ± 1.29
t		0.075	7.271	0.166	5.216	0.143	7.753
P		0.940	0.000	0.868	0.000	0.887	0.000

3.3. Comparison of oxidative stress indicators between the two groups of patients

Before treatment, there was no difference in the comparison of oxidative stress indicators between the two groups ($P > 0.05$). After 12 weeks of treatment, the oxidative stress indicators of the observation group were better than those of the control group ($P < 0.05$) (**Table 5**).

Table 5. Comparison of oxidative stress indicators between the two groups of patients (mean ± SD)

Subgroups	*n*	SOD (μg/mL)		MDA (mmol/mL)		ROS (μmol/L)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	48	53.69 ± 4.61	86.95 ± 6.19	15.67 ± 2.06	33.18 ± 2.41	822.16 ± 19.75	315.93 ± 22.07
Control group	48	53.54 ± 4.68	70.18 ± 6.10	15.60 ± 2.04	24.86 ± 2.13	820.53 ± 19.79	257.61 ± 21.19
t		0.158	13.369	0.167	17.922	0.404	13.206
P		0.875	0.000	0.868	0.000	0.687	0.000

3.4. Comparison of the adverse reaction rate of patients in the two groups

The adverse reaction rate of patients in the observation group was lower than that of the control group ($P < 0.05$) (**Table 6**).

Table 6. Comparison of the adverse reaction rate of patients in the two groups (*n*/%)

Subgroups	*n*	Nausea and vomiting	Diarrhea and abdominal pain	Dizziness	loss of appetite	Skin allergy	Incidence
Observation group	48	1	0	0	1	0	4.17 (2/48)
Control group	48	2	2	1	2	1	16.67 (8/48)
χ^2							4.019
P							0.045

4. Discussion

There are various types of diabetic complications, such as diabetic nephropathy (DN) and diabetic foot (DF), which increase the difficulty of diabetes treatment, exacerbate disease-related pain, elevate the disability rate, and affect patients' treatment prognosis. Currently, Ginkgo Dipyridolum Injection is a fundamental medication for diabetic complications, capable of stabilizing blood glucose levels and inhibiting the progression of complications [3,4]. Ginkgo Dipyridolum, a compound preparation containing drug components like ginkgo and dipyridolum, can dilate blood vessels, block the reuptake process of adenosine by epithelial cells or platelets, reduce phosphodiesterase content, and prevent the massive generation of Thromboxane A2. Therefore, it has fewer side effects and can prevent diabetic cardiovascular and cerebrovascular complications. However, long-term and high-dose administration of Ginkgo Dipyridamolum can lead to adverse reactions, necessitating the combination of auxiliary drugs that are both effective and safe [5].

Epalrestat serves as an adjuvant therapeutic drug for diabetic complications. Its mechanism for the prevention and treatment of this disease involves reducing the efficiency of rapid conversion of glucose into aldose reductase during the polyol metabolism process, enabling sorbitol to fully exert its protective effect on neuronal function, preventing the accumulation of neurons, and thereby improving diabetic peripheral neuropathy symptoms and preventing peripheral nerve disorders [6]. This drug inhibits the pathogenesis of multiple diabetic complications and can act on various substance generation processes such as protein kinase C, polyol pathway, and advanced glycation end products, thus delaying the onset of diabetic complications and achieving better therapeutic effects [7].

The results showed that the total effective rates of DN, DF, and diabetic peripheral neuropathy (DPN) in the observation group were higher than those in the control group ($P < 0.05$). The reason is that Epalrestat can alleviate symptoms such as paresthesia and limb numbness, effectively stabilize blood glucose levels, prolong the half-life of Ginkgo Dipyridolum Injection, increase its plasma concentration, and thereby fully exert the drug's efficacy and enhance the effectiveness of treatment [8]. The blood glucose level in the observation group after treatment was lower than that in the control group ($P < 0.05$). This is because Epalrestat can indirectly inhibit insulin resistance and reduce the degree of neuropathy, assisting patients in effectively lowering blood glucose. Additionally, this drug can reduce the absorption efficiency of carbohydrates by small intestinal tissue, thus lowering postprandial blood glucose levels [9]. The oxidative stress indicators in the observation group after treatment were better than those in the control group ($P < 0.05$). The reason is that Epalrestat selectively inhibits aldose reductase, reaches peak plasma concentration within 1 hour of administration, and can reduce the intracellular sorbitol accumulation rate in neurons through the polyol pathway. This prevents inflammatory factors from continuously damaging renal tissue or nerve blood vessels, thereby reducing oxidative stress reactions [10]. The adverse reaction rate in the observation group was lower than that in the control group ($P < 0.05$). This is because Epalrestat can enhance the utilization of drug components in Ginkgo Dipyridolum Injection, reduce the accumulation of toxic components in the body, and exhibit synergistic mechanisms with the two drugs, leading to increased efficacy and reduced toxicity. Therefore, there are fewer adverse reactions after administration [11].

5. Conclusion

In summary, Epalrestat can be used as a commonly employed adjuvant drug for diabetic complications, exhibiting good efficacy. It can assist in controlling blood glucose, reduce the body's oxidative stress response, and possess high drug safety, highlighting its significant therapeutic advantages.

Disclosure statement

The authors declare no conflict of interest.

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