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Original Article

Efficacy of beraprost sodium in the treatment of diabetic nephropathy in elderly patients

Jing Xia[1], Shanmei Shen[2]

[1]Department of Endocrinology, Affiliated Hospital of Nanjing University of Traditional Chinese Medicine, Jiangyin, Jiangsu Province, China; [2]Department of Endocrinology, Nanjing Drum Tower Hospital, Nanjing, Jiangsu Province, China

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Abstract: Objective: The goal of this study was to investigate the efficacy of beraprost sodium in the treatment of diabetic nephropathy in elderly patients. Methods: A total of 100 elderly patients with diabetic nephropathy were enrolled and randomly divided into the treatment group and the control group, with 50 cases in each group. Patients in the control group received the routine treatment, and patients in the treatment group were given additional beraprost sodium (20 μg/tablet, 2 tablets, tid) on the basis of the routine treatment. All patients were treated for 15 days and the therapeutic efficacy was then evaluated, including urinary protein, blood urea nitrogen (BUN), serum creatinine (Scr), serum cystatin C (Cys-C) and adverse reactions. Results: Urinary protein, BUN, Scr and Cys-C in the treatment group were all lower than those in the control group ($P<0.05$). The therapeutic efficacy of the treatment group was 90%, which was higher than that of the control group (58%) ($P<0.05$). There was no significant difference between the two groups, with respect to the incidence of adverse reactions ($P>0.05$). Conclusion: Beraprost sodium is effective and safe in the treatment of diabetic nephropathy in elderly patients.

Keywords: Beraprost sodium, elderly patients, diabetes, diabetic nephropathy

Introduction

Diabetes often leads to microangiopathy, especially in the kidney [1]. Diabetic nephropathy (DN) is a common complication of diabetes mellitus, which can gradually develop into uremia, which is major death cause of DN patients [2]. The pathogenesis of diabetic nephropathy is complex, involving genetic, metabolic disorders and other factors. Thus far, there has been a lack of rapid and effective treatment of DN. In clinical practice, symptomatic treatment is often used to alleviate clinical symptoms as well as the active treatment of primary disease. It is necessary to receive renal transplantation for patients at end-stage diabetic nephropathy [3]. Long-term medication therapy and the high cost of kidney transplantation have been a great pain and economic burden to patients [4].

With the aging of population, the incidence of diabetes is gradually increasing year by year, and diabetic nephropathy is doing great harm to elderly population. Thus, there is an urgent need for clinicians to explore effective strategies in the treatment of diabetic nephropathy and the protection of renal function.

Prostaglandins can dilate blood vessels, antagonize renin-angiotensin II vasoconstriction, inhibit platelet aggregation, increase renal blood flow, and significantly reduce urinary protein. They are often used to protect renal function [5-7]. Beraprost sodium is an oral prostacyclin with a stable structure and long half-life. It can activate adenylate cyclase, inhibit Ca^{2+} influx, reduce thromboxane A2 production, relax blood vessels, and improve the condition of the disease [8]. In the current study, the therapeutic efficacy of beraprost sodium was analyzed in the treatment of diabetic nephropathy.

Materials and methods

Patients enrolled

A total of 100 elderly patients with diabetic nephropathy who were treated at Affiliated Hospital of Nanjing University of Traditional Chinese Medicine from May 2010 to May 2013

Table 1. Inclusion criteria

Index	Criteria
Age (year)	≥70.0
Urion protein (g/d)	>0.50
BUN (mmol/L)	>7.10
Scr (μmol/L)	>186.00
Duration of diabetes (year)	≥5.0
Differential diagnosis and exclusion	Exclude patients with liminate nephritic syndrome, glome rulonephritis, mental retardation and bleeding tendency

Note: BUN: blood urea nitrogen, Scr: serum creatinine.

Table 2. General information of the enrolled patients

	The treatment group (n=50)	The control group (n=50)	P
Age (year)	79.2±7.4	80.1±7.9	0.698
Age range (year)	70.0-83.0	71.0-86.0	0.710
Gender (male/female, n)	31/19	32/18	0.836
Diabetes duration (year)	11.3±4.6	11.9±5.1	0.611
Diabetes duration range (year)	5.0-14.0	5.0-16.0	0.391
Urinary protein (g/d)	2.24±0.97	2.23±0.91	0.844
BUN (mmol/L)	12.81±2.69	12.80±2.71	0.941
Scr (μmol/L)	235.61±50.31	240.11±49.54	0.829
Cys-C (mg/L)	1.87±0.15	1.86±0.16	0.613
Concomitant diseases (n)			
Hypertension	31	27	0.418
Hyperlipemia	26	29	0.547

Note: BUN: blood urea nitrogen, Scr: serum creatinine, Cys-C: serum cystatin C.

were enrolled in this study. The inclusion criteria for patients in this study are shown in **Table 1**. All the patients were randomly divided into the treatment group and the control group, with 50 cases in each group. This study was approved by the Ethics Committee of the Affiliated Hospital of Nanjing University of Traditional Chinese Medicine, and signed consent was obtained from each patient before the study started.

Treatment

Patients in the control group were given a routine treatment, including a diabetic diet (low sodium and low fat, and a high-quality protein of 0.8 g/kg), controlling of blood lipids, captopril to maintain blood pressure in 100-135/75-90 mmHg, biguanides and/or insulin to reduce blood sugar to a normal level. EPO treatment for patients with anemia symptoms, if necessary, iron was employed.

Patients in the treatment group were given beraprost sodium treatment on the basis of the routine treatment. Beiprost sodium tablets (20 μg/tablet, three times per day, two tablets each time).

Patients in both groups received the treatment with 15 days as a period. Urinary protein, BUN, Scr and serum cystatin C (Cys-C) levels were closely monitored before and after the treatment, and the adverse reactions were closely monitored and recorded, including headache, dizziness, gastrointestinal reaction, rash, gastrointestinal bleeding and urinary system bleeding.

Evaluation criteria

Therapeutic efficacy was divided into three grades: marked effect, improved effect and ineffectiveness. Marked effect: urinary protein, BUN, Scr and Cys-C returned to normal level, clinical symptoms disappeared; improved effect: urinary protein, BUN, Scr and Cys-C decreased, but was still higher than the normal level, and clinical symptoms were relieved; ineffectiveness: urinary protein, BUN, Scr and Cys-C did not change or increase and the patient's condition was aggravated or resulted in death. Marked and improved effects were considered as effective.

Statistical analysis

All the data were analyzed using SPSS17.0 statistical software. The measurement data are

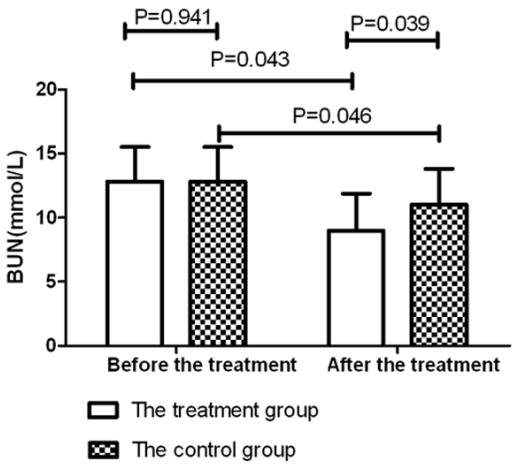

Figure 1. Comparison of BUN before and after treatment. BUN: blood urea nitrogen.

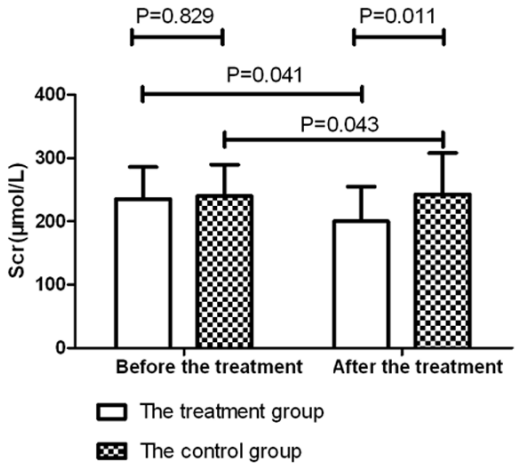

Figure 2. Comparison of Scr before and after treatment. Scr: serum creatinine.

expressed with (mean ± SD), the independent t-test was used to evaluate the inter-group difference at the same time point, and the paired t-test was used to evaluate the intra-group difference before and after the measurement. The counting data was expressed using percentage, and χ^2 test or fisher's exact test were used to determine signficance. P<0.05 was considered statistically different.

Results

General information

As shown in **Table 2**, there were no significant differences with respect to the general information between the two groups (P>0.05).

Comparison of BUN and Scr before and after treatment

As shown in **Figure 1**, there was no significant difference in BUN between the two groups before the treatment (t=0.703, P=0.941). After treatment, the BUN in both groups were significantly lower than those before treatment (the treatment group: t=2.109, P=0.043; the control group: t=2.810, P=0.046). Furthermore, the BUN of the treatment group was lower than that of the control group (t=3.804, P=0.039).

As shown in **Figure 2**, there was no significant difference in Scr between the two groups before the treatment (t=0.451, P=0.829). After treatment, the Scr in both groups were significantly lower than those before treatment (the treatment group: t=2.619, P=0.041; the control group: t=3.109, P=0.043). Furthermore, the Scr of the treatment group was lower than that of the control group (t=4.095, P=0.011).

Comparison of urinary protein and Cys-C before and after treatment

As shown in **Table 3**, before treatment, there was no significant difference in urinary protein between the two groups (t=0.729, P=0.844). After treatment, the urinary protein in both groups were significantly lower than those before treatment (the treatment group: t=3.016, P=0.044; the control group: t=3.210, P=0.049). Furthermore, urinary protein in the treatment group was lower than that in the control group, the difference was statistically significant (t=2.845, P=0.040).

As shown in **Table 4**, before treatment, there was no significant difference in Cys-C between the two groups (t=0.711, P=0.613). After treatment, the Cys-C in both groups were significantly lower than those before treatment (the treatment group: t=3.991, P=0.045; the control group: t=3.619, P=0.047). Furthermore, the Cys-C in the treatment group was lower than that in the control group, the difference was statistically significant (t=3.843, P=0.022).

Comparison of therapeutic efficacy

As shown in **Table 5**, the therapeutic efficacy of the treatment group was higher than that of the control group, the difference was statistically significant (P<0.001).

Table 3. Comparison of urinary protein before and after treatment (mean ± SD)

Group	The treatment group (n=50)	The control group (n=50)	t	P
Urinary protein (g/d)				
Before the treatment	2.24±0.97	2.23±0.91	0.729	0.844
After the treatment	1.19±0.69	1.70±0.89	2.845	0.040
t	3.016	3.210		
P	0.044	0.049		

Table 4. Comparison of Cys-C before and after treatment (mean ± SD)

Group	The treatment group (n=50)	The control group (n=50)	t	P
Cys-C (mg/L)				
Before the treatment	1.87±0.15	1.86±0.16	0.711	0.613
After the treatment	1.01±0.17	1.54±0.13	3.843	0.022
t	3.991	3.619		
P	0.045	0.047		

Note: Cys-C: serum cystatin C.

Table 5. Comparison of therapeutic efficacy [n (%)]

Group	The treatment group (n=50)	The control group (n=50)
Marked	12 (24)	1 (2)
Improved	33 (66)	28 (56)
Ineffective	5 (10)	21 (42)
χ^2	13.305	
P	<0.001	

Table 6. Comparison of the adverse reactions between the two groups [n (%)]

	The treatment group (n=50)	The control group (n=50)	P
Headache	0	1	1.000
Dizziness	3	2	1.000
Gastrointestinal reaction	2	1	1.000
Rash	1	0	1.000
Gastrointestinal bleeding	0	0	
Urinary system bleeding	0	0	
Total	6	4	0.505

Comparison of the adverse reactions

As shown in **Table 6**, there was no significant difference between the two groups, with respect to the incidence of adverse reactions (P>0.05).

Discussion

In recent years, the incidence of diabetic nephropathy has been increasing, throwing a huge burden to patients and society [9]. For the elderly patients with diabetic nephropathy, it should be strengthened in the treatment to delay the progress, improve the prognosis and reduce the mortality of the disease. Diabetic nephropathy is a disease of glomerular damage caused by glucose metabolism, hemodynamics and other factors. It is characterized by persistent proteinuria [10-13]. The early symptoms of diabetic nephropathy are not always obvious since renal compensatory function may meet the needs of the body. So early diagnosis of diabetic nephropathy can be difficult and delayed diagnosis may lead to the development into renal failure, which can cause the poor prognosis, even directly endanger the lives of patients. Therefore, early diagnosis and treatment is very important [14]. Because of the lack of effective treatment, how to protect renal function in the treatment of the diseases has become the key to the treatment.

Beraprost sodium can regulate vascular tension, and plays an important role in maintaining blood flow in various tissues [6]. Pharmacological studies have shown that beraprost sodium has anti-platelet effects. Oral administration of beraprost sodium in patients with peripheral circulation disorders and healthy adults can inhibit platelet aggregation and platelet adhesion [8, 9]. In the current study,

after the treatment, the urinary protein, BUN, Scr and Cys-C of the treatment group were lower than those of the control group, and the therapeutic efficacy of the treatment group was 90%, which was higher than that of the control group (58%), and there was no significant difference between the two groups with respect to the incidence of adverse reactions. The reasons may be as follows: (1) Beraprost sodium can reduce TNF-alpha (one of the pathogenic factors of diabetic nephropathy) or reduce the incidence of diabetic nephropathy [15-17]. (2) Beraprost sodium can down-regulate vascular endothelial NO synthase, inhibit macrophage infiltration, improve glomerular filtration rate, and reduce the incidence of proteinuria [18]. (3) Beraprost sodium has an antiplatelet effect, increase renal blood flow and relieve the disease. The results of this study were similar to some previous studies [19-21], which also showed that beraprost sodium treatment can reduce the levels of the urinary protein, BUN, Scr and Cys-C more effectively. While the therapeutic efficacy in these reports were over 90%, which was higher than that of the current study. These slight difference may be caused by the number of subjects selected and the different level of medical treatment between different regions.

There are some limitations in the current study, including 1) the small sample size, 2) single-center study, 3) lack of long-term follow-up. All these may cause the statistical bias of the study. In the further research work, optimization of the study design, expansion of the sample size, and development of a multiple-center study, will provide more insight for the optimization of the therapeutic strategies in the treatment of diabetic nephropathy.

In conclusion, on the basis of routine treatment, the use of sodium pralidol is effective and safe in the treatment of elderly patients with diabetic nephropathy, which is worthy of clinical promotion.

Disclosure of conflict of interest

None.

Address correspondence to: Jing Xia, Department of Endocrinology, Affiliated Hospital of Nanjing University of Traditional Chinese Medicine, No.130 Renmin Middle Road, Jiangyin 214400, Jiangsu Province, China. Tel: +86-0510-86700000; E-mail: xiajing568yt@163.com

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