Effect of alprostadil on hemorheology, immune function, MDA, SOD and ROS in patients with diabetic nephropathy

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Objective: To investigate the effect of alprostadil on hemorheology, oxidative stress and immune function in patients with diabetic nephropathy. Methods: A total of 90 cases of diabetic nephropathy patients were divided into control group (45 cases) and observation group (45 cases). The control group was treated by conventional therapy, and the observation group was received extra alprostadil. The levels of hemorheology, oxidative stress and immune function indexes were measured and compared. Results: The levels of blood glucose, blood lipid and UAER had a significant improvement in both groups, and the level of UAER in the observation group decreased more significantly than that in the control group after treatment; the levels of hemorheology indexes (high, middle and low shear of blood viscosity, plasma viscosity, deformation index and erythrocyte aggregation index) had a significant improvement after treatment, and the levels of low shear of blood viscosity and erythrocyte aggregation index in the observation group decreased more significantly than that in the control group after treatment. The levels of oxidative stress indexes (MDA, ROS and SOD) had a significant improvement in both groups, and the levels of MDA, ROS and SOD decreased more significantly after treatment. The levels of CD4+, CD4+/CD8+ in the observation group increased significantly after treatment, while the level of CD8+ had no significant improvement. The levels of CD4+, CD8+, CD4+/CD8+ in the control group had no significant differences, while the levels of CD4+, CD4+/CD8+ in the observation group were significantly higher than that in the control group. Conclusions: Alprostadil treatment can obviously improve renal function, hemorheology, oxidative stress and immune function in patients with diabetic nephropathy.

1. Introduction

Diabetic nephropathy (DN) is a common diabetic chronic complication caused by diabetic microangiopathy. End-stage renal disease in diabetes patients has a high incidence and mortality, brings physical and mental destruction to patients, and has a serious impact on quality of life. It is generally recognized that its pathogenesis is related to dysfunction of internal secretion, immune system, hemorheology, fat and oxidative stress. This study compared the indexes of hemorheology, immunologic function and oxidative stress in DN patients before and after treatment, aimed to investigate the effect of alprostadil on hemorheology, oxidative stress and immune function in DN patients.

2. Materials and methods

2.1. General materials

From August 2013 to July 2015, a total of 90 cases of DN patients in our hospital were selected and divided into control group and observation group according to the random number table method, with 45 cases in each group. In the observation group, there were 25 males and 20 females, who were 37-70 (57.42±13.46) years old, the courses of diabetes were 10-18 years, and the average courses were (14.46±3.25) years. In the control group, there were
26 males and 14 females, who were 56-77 (59.12±14.51) years old, the courses of diabetes were 11-18 years, and the average courses were (15.19±3.89) years. Inclusion criteria: all patients were diagnosed with diagnostic criteria of DN, without immune system or immune function disease, with more than 30 years' age. Exclusion criteria: without patients with primary kidney disease or caused by other reasons; without patients with severe heart, lung, and liver dysfunctions; without patients with the recent use of antioxidants. The general data of gender, including age and course, were comparable.

2.2. Research method

Patients in two groups conducted standard dietary intake of diabetes patients, and used the conventional treatments including stabilization of blood sugar. Alprostadil (Beijing ted pharmaceutical co., LTD) was additionally used in the observation group compared with the control group, 10 μg alprostadil was added into 100 mL physiological saline, intravenous drip once a day for three weeks.

2.3. Observational indexes

The fasting venous blood of patients was collected in the early morning before and after treatment, respectively, and was used to measure FPG (fasting plasma glucose), hemoglobin A1c (Hb A1c), triacylglycerol (TG), total cholesterol (TC) and urinary albumin excretion rate (UAER). Hemodynamic indexes of patients in two groups were measured by LBY-N6 blood rheometer (Beijing Precil Instrument Co., Ltd.) before and after treatment, including plasma viscosity, whole blood viscosity (high, medium and low shear), deformation index and aggregation index of hematokrit. 2 mL fasting venous blood of patients was collected in the early morning before and after treatment, respectively, serum was separated by centrifugation and stored at -20 °C for further test. Serum reactive oxygen species (ROS) was measured by colorimetric method, superoxide dismutase (SOD) and malondialdehyde (MDA) was measured by spectrophotometer method. Peripheral blood T-lymphocyte subsets (CD4+, CD8+, CD4+/CD8+) were measured by FC500 flow cytometry with its related reagents, the kits were purchased from Beijing Biosino biological technology co., LTD, and the test was conducted according to use instruction strictly.

2.4. Statistical analysis

Measurement data were described as mean ± standard deviation, inter-group comparison was carried out by t test, Enumeration data were compared by χ² test. SPSS20.0 statistical software was adopted for data analysis. Values of P<0.05 were considered to be statistically significant difference.

3. Results

3.1. Comparison of blood glucose, lipids and UAER

The levels of blood glucose, lipids and UAER before treatment in both groups were not statistically significant before treatment (P>0.05). After treatment, the levels of blood glucose, lipids and UAER in both groups significantly improved compared with that before treatment, while the levels of FPG, HbA1C, TG and TC in both groups were not statistically significant (P>0.05). The level of UAER in the observation group after treatment was significantly lower than that in control group (P<0.05) (Table 1).

3.2. Comparison of hemorheology before and after treatment

The levels of hemodynamic indexes, including plasma viscosity, whole blood viscosity (high, medium and low shear), deformation index and aggregation index of hematokrit in both groups were not statistically significant before treatment (P>0.05). After treatment, the levels of hemodynamic indexes, including plasma viscosity, whole blood viscosity (high, medium and low shear), deformation index and aggregation index of hematokrit in both groups significantly improved compared with that before treatment (P<0.05). In the observation group, the level of whole blood viscosity (low shear) was significantly lower than that in control group, and the level of aggregation index of hematokrit was significantly lower than that in control group (P<0.05) (Table 2).

3.3. Comparison of oxidative stress before and after treatment

The levels of oxidative stress factors, including MDA, SOD and ROS in both groups were not statistically significant before treatment (P>0.05). After treatment, the level of MDA in both groups significantly improved compared with that before treatment, the levels of SOD and ROS in both groups significantly decreased compared with that before treatment (P<0.05). In the observation group, the level of MDA was significantly higher than that in control group (P<0.05), the level of SOD was significantly lower than that in control group, the level of ROS was significantly lower than that in control group (Table 3).

3.4. Comparison of immune function before and after treatment

The levels of immune function indexes, including CD4+, CD8+, CD4+/CD8+ in both groups were not statistically significant before treatment (P>0.05). After treatment, the levels of CD4+ and CD4+/CD8+ in the observation group significantly improved compared with that before treatment, while the level of CD8+ in the observation group was not statistically significant (P>0.05). In the control group, the levels of immune function indexes were not statistically significant (P>0.05). In the observation group, the level of CD4+ was significantly higher than that in control group.
mesangial cells, proliferate mesangial matrix and repair the renal alprostadil could improve microcirculation, weaken the glomerular FPG, Hb A1c, TC and TG were not statistically significant, indicating that the level of UAER in the observation group significantly decreased slowing kidney disease (CKD) variable speed. The results indicated reducing urinary protein excretion, improving the kidney function and that DN treated by alprostadil in early stage could receive the effects of DN is considered as a disease of glomerular sclerosis associated with death[1-3]. DN morbidity reaches 20%-40% in diabetic patients, the kidney failure in later period and so on, is the leading cause of diabetic hypertension, proteinuria, progressive renal damage, edema, acute diabetes complications and mainly shows clinical features of sugar metabolic disorder, its pathogenesis is concealed, is a kind of DN is a disease of glomerular sclerosis associated with. 4. Discussion

Comparison of immune function before and after treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>CD4+ (%)</th>
<th>CD8+ (%)</th>
<th>CD4+/CD8+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>45</td>
<td>Before treatment</td>
<td>25.3±4.8</td>
<td>24.4±7.6</td>
<td>1.0±0.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>38.2±5.4*</td>
<td>27.4±7.8</td>
<td>1.4±0.7*</td>
</tr>
<tr>
<td>Control</td>
<td>45</td>
<td>Before treatment</td>
<td>25.1±4.7</td>
<td>24.5±6.8</td>
<td>1.0±0.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>28.5±4.9</td>
<td>27.2±7.3</td>
<td>1.1±0.4</td>
</tr>
</tbody>
</table>

Note: compared with before treatment, *P<0.05; compared with control group, #P<0.05.

(P<0.05), the level of CD4+/CD8+ was significantly higher than that in control group (P<0.05) (Table 4).

4. Discussion

DN is considered as a disease of glomerular sclerosis associated with urinary protein content than normal which were caused by diabetes sugar metabolic disorder, its pathogenesis is concealed, is a kind of serious diabetes complications and mainly shows clinical features of hypertension, proteinuria, progressive renal damage, edema, acute kidney failure in later period and so on, is the leading cause of diabetic death[1-3]. DN morbidity reaches 20%-40% in diabetic patients, the survival rate of patients with end-stage renal disease is less than 20% in 5 years. The pharmacological effects of alprostadil which is derived by arachidonic acid are widely, alprostadil shows good protection effects of renal function, inhibition of platelet aggregation by expanding heart, aggregation of erythrocyte. Deformation and aggregation of erythrocyte play an important role in hemorheology, deformation of erythrocyte means erythrocyte changes the original shape under the action of external force, and it is a requirement to keep good deformation capacity for erythrocyte by maintaining normal perfusion of capillaries and microcirculation[8,9]. Aggregation degree of erythrocyte represents the blood viscosity, erythrocyte presents different state of aggregation under the action of van der Waals force and surface negative charge, stronger cell aggregation degree represents higher blood viscosity[10]. The increase of blood sugar and glycated hemoglobin in diabetic could result in increased blood viscosity, impaired red blood cells and stranded in the renal microvascular, which could increase blood flow resistance, reduce the blood flow, microvascular perfusion dysfunction and worsen kidney damage. The results indicated that the levels of hemodynamic indexes in both groups significantly improved after treatment (P<0.05), and the levels of whole blood viscosity (low shear), aggregation index of hematokrit in the observation group significantly improved compared with that in the control group (P<0.05), indicating alprostadil could obviously improve hemorheology in DN patients.

Oxidative stress has close ties with inflammatory response after acute intracerebral hemorrhage, oxidative stress could be involved...
in the pathogenesis of acute cerebral hemorrhage by a variety of mechanisms. Unusually high level of ROS in kidney tissue of DN patients could cause the body peroxidation and increase the burden on kidney. The production of MDA is caused by lipid peroxidation of polyunsaturated fatty acids by oxygen radical in the cell membrane, therefore, higher level of MDA is along with higher oxygen free radical level, as well as more serious body tissue injury. SOD is an important indicator of removing oxygen free radicals in the body and preventing the oxygen free radical damage. ROS is produced by mitochondria, a small amount of ROS produced by kidney will not cause damage to the body under normal circumstances, but a lot of ROS can cause abnormalities of renal medulla blood and kidney peroxidation damage. The results indicated that the levels of MDA, ROS and SOD in the observation group significantly improved after treatment (P<0.05). The reason may be that alprostadil enhanced the intracellular adenylate cyclase activity, hemodynamic force was improved by local vessel expansion and enhanced permeability, weaken the oxidative stress by inhibiting the generation of ROS, so that the kidney tissue cells were protected.

Cellular immunity plays a very important role in the body’s immune, the measurement of peripheral blood T-lymphocyte subsets is an important way to monitor the immune function. Immune adhesion function of erythrocyte declined in DN patients, the accumulation of circulating immune complex was caused on vascular walls at the same time. Researches showed that compromised immune system was closely related to the disorders of immune adhesion control system of erythrocyte in DN patients. CD4+ is a kind of important immune cells in the body’s immune system, and mainly expressed in T helper cells. CD8+ is mainly expressed in T cells for inhibition of cell destruction, is beneficial to synthesis and secretion of antibody, and refraining proliferation of T cells. CD4+/CD8+ is abnormal. The results indicated that the levels of CD4+, CD4+/CD8+ in the observation group were significantly higher that in the control group (P<0.05), indicating alprostadil can repair the immune function of DN patients.

In conclusion, alprostadil treatment can obviously improve renal function, hemorheology, oxidative stress and immune function in patients with diabetic nephropathy, and it is worthy of wide clinical application.

References


