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Analysis of the Efficacy of Finerenone Combined with Irbesartan in the Treatment of Diabetic Nephropathy

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Abstract: *Objective:* To analyze the clinical effect of using finerenone combined with irbesartan in the treatment of diabetic nephropathy. *Methods:* Eighty-five patients with diabetic nephropathy who received inpatient treatment in our hospital from July 2023 to June 2024 were selected and divided into the control group (42 cases) and the observation group (43 cases) according to the differences in drug treatment programs. The control group received oral treatment with finerenone tablets, and the observation group received treatment with finerenone combined with irbesartan. The differences in the blood glucose level, renal function indicators, serological level, and adverse reactions of the two groups were compared and analyzed. *Results:* After treatment, the levels of fasting blood glucose, 2-hour postprandial blood glucose, glycated hemoglobin, blood creatinine, urea nitrogen, blood uric acid, TGF-β1, SFRP-4, GSK-3β, and ICAM-1 in the observation group were significantly lower than those in the control group ($P < 0.05$). In the control group, there was one case each of vertigo, palpitation, rash, vomiting, and angioneurotic edema during treatment, with a total incidence rate of 11.90%; the observation group had one case each of vertigo and vomiting, with a total incidence rate of 4.65% ($P > 0.05$). *Conclusion:* In the clinical treatment of patients with diabetic nephropathy, finerenone combined with irbesartan therapy can significantly improve patients' blood glucose level and serological levels, and alleviate patients' renal function, showing positive clinical application value.

Keywords: Diabetic nephropathy; Irbesartan tablets; Finerenone tablets; Renal function; Blood glucose level; Serum level

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1. Introduction

Diabetic nephropathy (DN) is one of the common microvascular complications in diabetes mellitus, with an incidence rate of about 40% in diabetes mellitus patients, and has become a major cause of end-stage renal disease (ESRD) [1]. With the increasing prevalence of diabetes mellitus worldwide, the incidence of DN has

also increased significantly, posing a serious threat to the quality of life and health of patients. The pathologic features of DN mainly include the thickening of the glomerular basement membrane, proliferation of thylakoid cells, and glomerulosclerosis, which may lead to proteinuria and gradual deterioration of renal function [2]. Existing therapeutic strategies for DN include glycemic control, blood pressure management, and proteinuria reduction. Antihypertensive drugs, especially angiotensin receptor blockers (ARBs) such as irbesartan, have shown significant efficacy in reducing urinary protein levels and delaying the deterioration of renal function [3]. Irbesartan dilates blood vessels and lowers blood pressure by inhibiting the action of angiotensin II, while having a protective effect on the kidneys. However, the use of ARB analogs alone has limited effect in some patients, thus new treatment options are necessary to further improve patient prognosis [4]. Finerenone is a novel non-steroidal mineralocorticoid receptor antagonist (MRA), which has been widely used in chronic kidney disease (CKD) and diabetes-related nephropathy in recent years. It acts by blocking the activation of mineralocorticoid receptors and reducing inflammatory response and fibrotic process [5]. Clinical studies have shown that finerenone can significantly reduce the level of urinary protein and delay the decline of renal function, and its mechanism of action has better selectivity and fewer side effects than traditional MRA drugs such as spironolactone. In order to investigate the effectiveness of finerenone combined with irbesartan regimen in the treatment of diabetic nephropathy, the present study was conducted as a small-sample clinical trial.

2. General information and methods

2.1. General information

Eighty-five patients with diabetic nephropathy who received inpatient treatment in our hospital from July 2023 to June 2024 were selected and divided into a control group (42 cases) and an observation group (43 cases) according to the differences in drug treatment regimens. In the control group, there were 23 males and 19 females, with an average age of 60.4 ± 7.3 years, a disease duration of 3 to 14 years, and a body mass index (BMI) of 21.45 ± 0.62 kg/m^2. In the observation group, there were 22 males and 21 females, with an average age of 61.1 ± 6.8 years, a disease duration of 3 to 16 years, and a BMI of 21.51 ± 0.71 kg/m^2. A comparison of the general data of the two groups of patients found no significant difference ($P > 0.05$). This study has been approved by the Ethics Committee of the hospital for implementation.

Inclusion criteria: (1) Diagnosed with diabetic nephropathy according to the Diagnostic Criteria of Chinese Guidelines for the Prevention and Control of Diabetic Kidney Disease (2021 Edition) [6]; (2) Aged between 18 and 75 years old; (3) Glomerular filtration rate (eGFR) of 30–90 mL/min/1.73m², with moderate renal hypoplasia but not severe renal insufficiency; (4) Patients and their legal guardians were able to understand the content of the study and voluntarily signed an informed consent form.

Exclusion criteria: (1) Presence of severe hepatic insufficiency; (2) Patients receiving medications that affect renal function, such as ACEI (angiotensin-converting enzyme inhibitor) or ARB; (3) Pregnant or lactating women; (4) Patients with a previous history of coronary artery disease, heart failure, or myocardial infarction; (5) Patients with a history of allergic reaction to the investigational drugs (finerenone, irbesartan).

2.2. Methodology

After admission, all patients were given correct lifestyle guidance and standardized metabolic therapy. Patients in the control group were given finerenone tablets (BayerAG, specification of 20 mg/tablet, product batch numbers

202103028, 202307027) for oral treatment. The starting dose was half tablet/time, once a day, and the dose was increased to one tablet/time, once a day after four weeks of continuous use. The dose of finerenone tablets in the observation group was the same as that of the control group, and the oral treatment of irbesartan (Yangzijiang Pharmaceutical Group Jiangsu Zilong Pharmaceutical Co., Ltd., specifications of 75 mg/tablet, product batch numbers 202104017, 202305019) was increased from the fifth week. Both groups were treated for three months.

2.3. Observation indicators

(1) The changes in blood glucose levels of the two groups were observed and compared after three months of medication, including fasting blood glucose (FBG), 2-hour postprandial blood glucose (2hPG) levels, and glycated hemoglobin (HbA1c) levels.

(2) The changes in renal function of the two groups of patients were observed and compared, including blood creatinine (SCr), blood urea nitrogen (BUN), and blood uric acid (UA).

(3) Fasting venous blood of 5 mL was centrifuged for 10 minutes to separate the serum. Enzyme-linked immunosorbent assay was used to detect serum glycogen synthase kinase-3β (GSK-3β), secreted frizzled-related protein-4 (SFRP-4), transforming growth factor-β1 (TGF-β1), and intercellular adhesion molecule-1 (ICAM-1) levels.

(4) The occurrence of adverse reactions was observed and recorded such as vertigo, palpitation, rash, vomiting, and angioneurotic edema during the administration of the drug in both groups. Total incidence rate = total incidence cases/total cases × 100%.

2.4. Statistical methods

SPSS24.0 statistical software was applied to analyze and process the relevant data. Measurement data were expressed as mean ± standard deviation (SD) and compared with *t*-test; count data were expressed as [*n* (%)] and compared with χ^2 test. $P < 0.05$ was used to indicate that the difference was statistically significant.

3. Results

3.1. Comparison of blood glucose levels between the two groups after treatment

After treatment, the levels of FBG, 2hPG, and HbA1c of patients in the observation group were significantly lower than those of the control group, and the difference was statistically significant ($P < 0.05$), as shown in **Table 1**.

Table 1. Comparison of blood glucose levels between the two groups after treatment (mean ± SD)

Groups	*n*	FBG (mmol/L)	2hPG (mmol/L)	HbA1c (%)
Control group	42	6.57 ± 1.04	9.08 ± 1.32	7.34 ± 0.49
Observation group	43	5.21 ± 1.01	7.97 ± 1.24	6.12 ± 0.43
t	-	6.116	3.997	12.209
P	-	0.000	0.001	0.000

3.2. Comparison of renal function between the two groups after treatment

After treatment, the levels of SCr, BUN, and UA of patients in the observation group were significantly lower than those of the control group, and the difference was statistically significant ($P < 0.05$), as presented in **Table 2**.

Table 2. Comparison of renal function between the two groups after treatment (mean ± SD)

Groups	*n*	SCr (μmol/L)	BUN (μmol/L)	UA (mmol/L)
Control group	42	86.34 ± 15.29	7.51 ± 1.35	318.35 ± 16.49
Observation group	43	73.79 ± 11.16	6.29 ± 1.14	305.17 ± 17.37
t	-	4.330	4.506	3.586
P	-	0.000	0.000	0.001

3.3. Comparison of serological levels between the two groups after treatment

After treatment, the levels of TGF-β1, SFRP-4, GSK-3β, and ICAM-1 of patients in the observation group were significantly lower than those of the control group, and the difference was statistically significant ($P < 0.05$), as shown in **Table 3**.

Table 3. Comparison of serological levels between the two groups after treatment (mean ± SD)

Groups	*n*	TGF-β (μg/L)	SFRP-4 (pg/mL)	GSK-3β (μg/L)	ICAM-1 (ng/mL)
Control group	42	280.79 ± 18.78	125.62 ± 32.44	35.93 ± 10.25	382.29 ± 49.13
Observation group	43	191.72 ± 11.06	90.71 ± 12.08	29.31 ± 8.22	265.45 ± 37.18
t	-	26.719	6.604	3.289	12.382
P	-	0.000	0.000	0.002	0.000

3.4. Comparison of the occurrence of adverse reactions between the two groups

One case each of vertigo, palpitation, rash, vomiting, and angioneurotic edema occurred during treatment in the control group, with a total incidence rate of 11.90%, while one case each of vertigo and vomiting occurred in the observation group, with an incidence rate of 4.65%. The chi-square test was $P > 0.05$, as illustrated in **Table 4**.

Table 4. Comparison of adverse reactions between the two groups [*n* (%)]

Groups	*n*	Vertigo	Palpitation	Rash	Vomiting	Angioneurotic edema	Occurrence rate
Control group	42	1	1	1	1	1	5 (11.90)
Observation group	43	1	0	0	1	0	2 (4.65)
χ^2	-	-	-	-	-	-	1.321
P	-	-	-	-	-	-	0.250

4. Discussion

Diabetic nephropathy is one of the common and serious complications in patients with diabetes mellitus, and it is the primary cause of ESRD. Once patients develop ESRD, they often need to undergo long-term dialysis treatment or renal transplantation, which not only greatly increases the medical burden, but also significantly reduces patients' quality of life. The pathogenesis of DN is complex and diverse, involving multiple metabolic signals and abnormal regulation of molecular signaling pathways. With the in-depth study of DN, it is now believed that

blood glucose levels, serum metabolites, intrarenal inflammatory response, and fibrosis all play a role in the onset and progression of DN [7]. Hyperglycemia is one of the main characteristics of diabetic patients, and a persistent hyperglycemic state stimulates inflammatory responses and fibrosis in the kidney by increasing the production of advanced glycation end products (AGEs), leading to glomerulosclerosis and tubulointerstitial lesions [8]. At the same time, hyperglycemia activates several intracellular signaling pathways such as protein kinase C (PKC) and transforming growth factor beta (TGF-β), which exacerbate the process of kidney injury. Under hyperglycemia, the production of angiotensin II increases, leading to intraglomerular hyperperfusion and a high-pressure environment, accelerating the decline of glomerular filtration rate and the damage of renal structure, which not only increases the burden on the kidneys by narrowing the blood vessels, but also promotes the release of inflammatory factors, exacerbating the process of renal fibrosis and sclerosis.

In addition to glycemic and hemodynamic factors, oxidative stress is also an important mechanism in the pathogenesis of DN. Hyperglycemia damages the microvascular structure and cells of the kidney by increasing the production of reactive oxygen species (ROS), leading to the gradual decline of renal function. Meanwhile, in the diabetic state, the expression of inflammatory factors in the kidney is increased, such as monocyte chemotactic protein-1 (MCP-1) and tumor necrosis factor-alpha (TNF-α), which further aggravate the damage of glomerular and tubulointerstitial. Diabetic patients are often associated with hyperlipidemia, and fat deposition in renal tubular epithelial cells can trigger renal lipotoxicity, leading to tubulointerstitial injury and fibrosis. The complex interaction of multiple factors leads to the pathogenesis of DN, which is difficult to reverse, and therefore a multi-targeted comprehensive treatment strategy is necessary. The use of finerenone or irbesartan alone in the treatment of diabetic nephropathy has limitations despite its efficacy [9]. Finerenone, as a non-steroidal MRA, is effective in reducing renal inflammation and fibrosis, thereby lowering urinary protein levels and delaying the decline of renal function. However, finerenone alone may have a limited effect on blood pressure regulation in DN patients with hypertension, limiting its clinical application to some extent. Irbesartan, as an ARB, can effectively delay the decline of renal function by vasodilating blood vessels, lowering blood pressure, and reducing glomerular hyperperfusion. However, the use of irbesartan alone cannot effectively inhibit fibrosis and inflammation in the kidney, making its efficacy less significant in some patients.

In this study, by comparing the clinical efficacy of the control group, who received oral finerenone tablets alone, and the observation group, who received a combination of finerenone and irbesartan, it was found that the patients in the observation group had a significant advantage in several clinical indicators. Glucose metabolic indexes such as FBG, 2hPG, HbA1c, and renal function indexes such as SCr, BUN, and UA of patients in the observation group were significantly lower than those of the control group, suggesting that the combined treatment had a stronger effect on glycemic control and renal function protection. The levels of inflammation- and fibrosis-related factors such as TGF-β1, SFRP-4, GSK-3β, and ICAM-1 in the observation group were also significantly lower than those in the control group, indicating that the combined treatment showed more obvious effects in reducing inflammatory responses and delaying renal fibrosis. The reason for this result lies in the complementary mechanism of action of finerenone and irbesartan, i.e., finerenone mainly works by inhibiting inflammation and fibrosis, while irbesartan works by lowering blood pressure and improving renal hemodynamics, and the two act synergistically to ameliorate the pathological process of diabetic nephropathy in a more comprehensive way [10].

5. Conclusion

In conclusion, the application of irbesartan combined with finerenone tablets in the treatment of diabetic nephropathy can obtain significant clinical effects. It can not only greatly improve patients' blood glucose levels and renal function status, but also further reduce patients' inflammatory reactions, which is worthy of popularization and application in the clinical field.

Disclosure statement

The authors declare no conflict of interest.

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