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Correlation of urodynamic characteristics with insulin resistance and serum damage media in diabetic patients with benign prostatic hyperplasia

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ABSTRACT

Objective: To study the correlation of urodynamic characteristics with insulin resistance and serum damage media in patients with diabetes and benign prostatic hyperplasia (BPH). **Methods:** 45 patients with type 2 diabetes mellitus and BPH treated in our hospital between May 2014 and August 2016 were selected as DM+BPH group, 58 patients with BPH alone were selected as BPH group, and 50 healthy volunteers were selected as control group. Urodynamic tester was used to measure the maximum flow rate (MFR), postvoid residual (PVR) and detrusor pressure at maximum flow rate (Pdet), and serum was collected to determine insulin resistance indexes and oxidative stress indexes. **Results:** MFR and Pdet of DM+BPH group were significantly lower than those of control group (P<0.05) while PVR was significantly higher than that of control group (P<0.05); MFR of BPH group was significantly lower than that of control group (P<0.05) while PVR and Pdet were significantly higher than those of control group (P<0.05); MFR and Pdet of DM+BPH group were significantly lower than those of BPH group (P<0.05) while PVR was significantly higher than that of BPH group (P<0.05); insulin secretion index (HOMA-β), insulin sensitive index (ISI) as well as serum manganese superoxide dismutase (MnSOD), copper-zinc superoxide dismutase (CuZnSOD) and glutathione peroxidase (GPx) levels of DM+BPH group and BPH group were significantly lower than those of control group (P<0.05) while insulin resistance index (HOMA-IR) as well as serum thioredoxin (Trx) and thioredoxin-interacting protein (TXNIP) levels was significantly higher than those of control group (P<0.05); HOMA-β, ISI as well as serum MnSOD, CuZnSOD and GPx levels of DM+BPH group were significantly lower than those of BPH group (P<0.05), positively correlated with MFR and Pdet, and negatively correlated with MFR, and HOMA-IR as well as serum Trx and TXNIP levels was significantly higher than those of BPH group (P<0.05), negatively correlated with MFR and Pdet, and positively correlated with MFR. **Conclusions:** Insulin resistance and oxidative stress injury are the mechanisms that cause the urodynamic changes in patients with diabetes and BPH.

1. Introduction

Benign prostatic hyperplasia (BPH) is common urinary system disease in elderly men, and the hyperplastic prostate tissue will squeeze the urethra and cause voiding dysfunction[1]. In recent years, the incidence of type 2 diabetes mellitus with BPH is rising, and the continuously elevated blood glucose will activate the oxidative stress to cause oxidative peripheral nerve damage[2]. When diabetic neuropathy involves the sympathetic and parasympathetic nerves that control bladder, voiding dysfunction will occur; the combination of type 2 diabetes mellitus and BPH will cause damage to the sympathetic and parasympathetic nerves that control bladder as well as urinary tract compression and urination obstruction, thus leading to the voiding dysfunction. In the following study, in order to define the voiding function in patients with diabetes and BPH, the

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urodynamic features were analyzed, and the insulin resistance and serum damage medium levels associated with urodynamic changes were also analyzed.

2. Materials and methods

2.1. Research subjects

45 patients with type 2 diabetes mellitus and BPH treated in our hospital between May 2014 and August 2016 were selected as the DM+BPH group of the study, 58 patients with BPH alone were selected as BPH group, and the patients with type 2 diabetes mellitus were diagnosed after oral glucose tolerance test and with good blood glucose control and glycosylated hemoglobin content <7%; patients with BPH were with prostate volume >20 mL after ultrasonography. DM+BPH group were 59–67 years old and with prostate volume (23.5±3.5) mL; BPH group were 58–65 years old and with prostate volume (24.2±4.1) mL; 50 healthy volunteers receiving physical examination in our hospital during the same period were selected as control group, and they were 49–62 years old. The three groups of subjects were not significantly different in general information ($P>0.05$). The informed consents were obtained from all the patients.

2.2. Urodynamic testing methods

Laborie urodynamic tester was used to determine urodynamic indexes of three groups of subjects, patients drank plenty of water and urinated after they had strong urge to urinate, and the maximum flow rate (MFR) was tested; then they took lithotomy position, two-way catheter was inserted through the urinary tract to extract and determine postvoid residual (PVR); after that, F1 rectum piezometer tube was inserted through the anus to determine detrusor pressure at maximum flow rate (Pdet).

2.3. Insulin resistance evaluation methods

5 mL of peripheral blood specimen was collected from three groups of subjects and centrifuged to get serum, immunoluminescence kits were used to determine insulin and blood glucose levels, and HOMA model was referred to calculated insulin secretion index (HOMA-β), insulin resistance index (HOMA-IR) and insulin sensitive index (ISI).

2.4. Serum oxidative stress index detection methods

5 mL of peripheral blood specimen was collected from three groups of subjects and centrifuged to get serum, and radioimmunoprecipitation kits were used to detect the levels of manganese superoxide dismutase (MnSOD), copper-zinc superoxide dismutase (CuZnSOD), glutathione peroxidase (GPx) as well as thioredoxin (Trx) and thioredoxin-interacting protein (TXNIP).

2.5. Statistical analysis

SPSS20.0 software was used to input and analyze data, measurement data comparison among three groups was by variance analysis, pair-wise comparison was by *LSD-t* test, correlation analysis was by Pearson test and $P<0.05$ indicated statistical significance in differences.

3. Results

3.1. Urodynamic indexes of three groups of subjects

Analysis of urodynamic indexes MFR, PVR and Pdet among three groups of subjects is as follows: MFR and Pdet of DM+BPH group were significantly lower than those of control group ($P<0.05$) while PVR was significantly higher than that of control group ($P<0.05$); MFR of BPH group was significantly lower than that of control group ($P<0.05$) while PVR and Pdet were significantly higher than those of control group ($P<0.05$); MFR and Pdet of DM+BPH group were significantly lower than those of BPH group ($P<0.05$) while PVR was significantly higher than that of BPH group ($P<0.05$) (Table 1).

Table 1

Comparison of urodynamic indexes among three groups of subjects ($\bar{x}\pm s$).

Groups	n	MFR (mL/s)	PVR (mL)	Pdet (cm H_2O)
DM+BPH group	45	11.77±1.47△▲	133.26±16.71△▲	27.89±3.36△▲
BPH group	58	18.24±2.03△	92.52±10.26△	48.51±6.10△
Control group	50	23.78±3.91	67.25±8.12	37.51±5.63

△: compared with control group, $P<0.05$; ▲: compared with BPH group, $P<0.05$.

3.2. Insulin resistance-related indexes

Analysis of insulin resistance-related indexes HOMA-IR, HOMA-β and ISI among three groups of subjects is as follows: HOMA-β and ISI of DM+BPH group and BPH group were significantly lower than those of control group ($P<0.05$) while HOMA-IR was significantly higher than that of control group ($P<0.05$); HOMA-β and ISI of DM+BPH group were significantly lower than those of BPH group ($P<0.05$) while HOMA-IR was significantly higher than that of BPH group ($P<0.05$) (Table 2).

Table 2

Comparison of insulin resistance-related indexes among three groups of subjects ($\bar{x}\pm s$).

Groups	n	HOMA-IR	HOMA-β	ISI
DM+BPH group	45	3.42±0.45△▲	22.41±3.52△▲	-4.89±0.71△▲
BPH group	58	2.29±0.34△	40.58±5.18△	-4.11±0.57△
Control group	50	1.25±0.15	68.93±8.14	-3.05±0.41

△: compared with control group, $P<0.05$; ▲: compared with BPH group, $P<0.05$.

3.3. Serum oxidative stress indexes

Analysis of serum oxidative stress indexes MnSOD, CuZnSOD, GPx, Trx and TXNIP among three groups of subjects is as follows: serum MnSOD, CuZnSOD and GPx levels of DM+BPH group and BPH group were significantly lower than those of control group (P<0.05) while Trx and TXNIP levels were significantly higher than those of control group (P<0.05); serum MnSOD, CuZnSOD and GPx levels of DM+BPH group were significantly lower than those of BPH group (P<0.05) while Trx and TXNIP levels were significantly higher than those of BPH group (P<0.05) (Table 3).

3.4. Correlation analysis

Pearson test analysis of the correlation between urodynamic indexes and insulin resistance as well as oxidative stress indexes showed that MFR and Pdet were positively correlated with HOMA-β, ISI as well as serum MnSOD, CuZnSOD and GPx levels, and negatively correlated with HOMA-IR as well as serum Trx and TXNIP levels; MFR was negatively correlated with HOMA-β, ISI as well as serum MnSOD, CuZnSOD and GPx levels, and positively correlated with HOMA-IR as well as serum Trx and TXNIP levels.

4. Discussion

Diabetic peripheral neuropathy is a common complication of type 2 diabetes mellitus, and when neuropathy involves the sympathetic and parasympathetic nerves that control bladder, neurogenic bladder will occur and affect the micturition function[3,4]. In recent years, the incidence of type 2 diabetes mellitus and BPH is rising, and the peripheral nerve complications can also cause the symptoms of urinary tract obstruction and neurogenic bladder, which in turn lead to the changes in urodynamics[5,6]. In order to define the urination condition in patients with type 2 diabetes mellitus and BPH, urodynamic parameters MFR, PVR and Pdet were analyzed in the study. Urodynamics measure the urination function-related parameters MFR, PVR and Pdet based on the principle of hydromechanics and electrophysiology. MFR and Pdet of DM+BPH group were significantly lower than those of control group (P<0.05) while PVR was significantly higher than that of control group (P<0.05); MFR of BPH group was significantly lower than that of control group (P<0.05) while PVR and Pdet were significantly higher than those of control group (P<0.05). This means that the change trend of MFR and PVR is consistent in DM+BPH group and BPH group, and in the process of illness development, different levels of urinary retention and urinary flow rate decrease will appear under the influence of enlarged prostate obstruction and neuropathy. However, Pdet change trend is different between DM+BPH group and BPH group, the decreased Pdet in patients with DM+BPH is associated with the sympathetic and parasympathetic nerve lesions caused by diabetes, the detrusor loses innervation and decreased muscle strength occurs; the elevated Pdet in patients with BPH is related to urinary tract obstruction caused by prostatic hyperplasia, and compensatory bladder detrusor hyperplasia and hypertrophy occur and lead to enhanced muscle contractility[7,8].

The most prominent pathological features of patients with type 2 diabetes are insulin resistance and relatively insufficient isletβcell secretion function, and accompanied by the abnormal activation of inflammation and oxidative stress reaction in the body. In order to define the degree of insulin resistance in the development of type 2 diabetes combined with BPH, insulin resistance- and sensitivity-related indexes of three groups of subjects were analyzed in the study, and the results showed that HOMA-β and ISI of DM+BPH group and BPH group were significantly lower than those of control group (P<0.05) while HOMA-IR was significantly higher than that of control group (P<0.05); HOMA-βand ISI of DM+BPH group were significantly lower than those of BPH group (P<0.05) while HOMA-IR was significantly higher than that of BPH group (P<0.05). HOMA-β is the index that reflects islet β cell secretion function, and its level decrease indicates relatively insufficient

Table 3

Comparison of serum oxidative stress indexes among three groups of subjects (U/L, $\bar{x}\pm s$).

Groups	n	Antioxidant enzymes			Thioredoxin	
		MnSOD	CuZnSOD	GPx	Trx	TXNIP
DM+BPH group	45	14.58±1.75△▲	23.51±3.42△▲	10.33±1.52△▲	17.68±2.31△▲	22.31±3.51△▲
BPH group	58	26.18±3.51△	37.68±4.61△	17.86±2.03△	9.45±1.03△	16.24±1.93△
Control group	50	37.49±5.14	57.29±6.81	32.52±4.18	6.02±0.77	10.42±1.45

△: compared with control group, $P<0.05$; ▲: compared with BPH group, $P<0.05$.

secretion of β cells; ISI is the index that reflects insulin sensitivity, and its level decrease indicates that peripheral tissue is not sensitive to insulin; HOMA-IR is the index that reflects the degree of insulin resistance, and its level increase indicates that peripheral tissue resistance to insulin increases. Combined with the results of correlation analysis, it is believed that the aggravated degree of insulin resistance is associated with the occurrence of type 2 diabetes mellitus combined with BPH as well as the urodynamic change[9,10].

Studies about the pathogenesis of diabetic complications in recent years show that the excessive generation of oxygen free radicals and the excessive activation of oxidative stress on the basis of insulin resistance are the important ways to cause diabetic neuropathy. There are a variety of antioxidant enzymes such as SOD and GPx in cells, and they can maintain the balance of cellular REDOX status. The CuZnSOD and MnSOD in SOD family, also known as SOD1 and SOD2, can rapidly disproportionate the superoxide anions into hydrogen peroxide or molecular oxygen[11,12]; the GPx-1 in GPx family can further remove hydrogen peroxide. In the process of excessive activation of oxidative stress and massive generation of superoxide anions and other oxygen free radicals, CuZnSOD, MnSOD and GPx-1 will be constantly consumed, which leads to the intracellular REDOX state imbalance and causes damage[13,14]. In addition to antioxidant enzymes SOD and GPx, thioredoxin family also plays an important role in the antioxidant process. Trx is a kind of small molecule protein with antioxidant properties, and in the process of oxidative stress, it is released from cells into serum and scavenges free radicals; TXNIP can antagonize the antioxidant effect of Trx[15,16]. In the study, analysis of the levels of the antioxidant enzymes showed that serum MnSOD, CuZnSOD and GPx levels of DM+BPH group and BPH group were significantly lower than those of control group (P<0.05) while Trx and TXNIP levels were significantly higher than those of control group (P<0.05); serum MnSOD, CuZnSOD and GPx levels of DM+BPH group were significantly lower than those of BPH group (P<0.05) while Trx and TXNIP levels were significantly higher than those of BPH group (P<0.05). This means that there is REDOX disorder in patients with diabetes and BPH, characterized by excessive activation of oxidative stress reaction and massive consumption of antioxidant enzymes.

To sum up, there are significant urodynamic changes in patients with type 2 diabetes mellitus and BPH, and the insulin resistance increase and oxidative stress injury are the molecular mechanisms that cause the urodynamic changes.

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