

Relationship Between Postprandial Blood Glucose, Fasting Insulin, and Glycated Hemoglobin Levels and Early Diabetic Nephropathy in Patients with Type 2 Diabetes Mellitus

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Abstract: *Objective:* To investigate the relationship between postprandial blood glucose (PBG), fasting insulin (FINS), and glycated hemoglobin (HbA1c) levels and early diabetic nephropathy in patients with type 2 diabetes. *Methods:* 96 cases of type 2 diabetes mellitus treated in our hospital from May 2021 to May 2022 were selected as the research subjects. The patients were divided into two groups according to the urinary albumin excretion rate (UAER), with 53 cases in the type 2 diabetes group (UAER < 30 µg/min) and 43 cases in the early diabetic nephropathy group (30 µg/min ≤ UAER < 300 µg/min). PBG, FINS, and HbA1c levels were detected in 87 healthy patients. *Results:* The levels of PBG, FINS, and HbA1c in the early diabetic nephropathy group were higher than those in the control group ($P < 0.01$) and the type 2 diabetes group ($P < 0.01$). *Conclusion:* PBG, FINS, and HbA1c are factors affecting the occurrence of diabetic nephropathy in patients with type 2 diabetes; thus, controlling the levels of PBG, FINS, and HbA1c can effectively prevent the occurrence of diabetic nephropathy in type 2 diabetes mellitus.

Keywords: Type 2 diabetes mellitus; Diabetic nephropathy; Postprandial blood glucose

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1. Introduction

Diabetes is a common chronic disease in China, which seriously affects people's health and threatens lives. Type 2 diabetes, which is mainly caused by pancreatic islet cells, accounts for more than 90% of the incidence of diabetes in China. Type 2 diabetes develops as a result of the compensatory mechanism of islet cells, where more insulin is secreted to reduce the effect of insulin resistance. Hence, there will be increased insulin levels in the blood. When fasting, the blood sugar level is normal, but it will be higher than normal two hours after a meal. At this time, if it is not controlled, the islet cells will eventually lose their compensatory function. Diabetic nephropathy (DN), which is most common microvascular complication of diabetes, accounts for 35% of diabetic complications. DN has become one of the main diseases affecting the health of people in China. It has a complex pathogenesis and is the main cause of end-stage renal disease (ESRD). At present, more than one-third of diabetic patients in China die of renal failure and uremia, and it is believed that DN is caused by the combination of genetic factors, environmental

factors, and immune dysfunction. Postprandial blood glucose (PBG), fasting insulin (FINS), and glycated hemoglobin (HbA1c) are the main components of the extracellular matrix (ECM). They participate in various biological processes in the human body [1-5]. Previous studies have shown that PBG and FINS are associated with the occurrence of early DN, while HbA1c is involved in the pathogenesis of early DN and is related to kidney damage. However, the mechanism of how PBG, FINS, and HbA1c leads to renal injury in early DN is still unclear.

2. Materials and methods

2.1. General information

A total of 96 cases of type 2 diabetes mellitus treated in our hospital from May 2021 to May 2022 were selected as the research subjects. According to the urinary albumin excretion rate (UAER), the patients were divided into two groups, with 53 cases in the type 2 diabetes group (UAER < 30 µg/min) and 43 cases in the early diabetic nephropathy group (30 µg/min ≤ UAER < 300 µg/min). The levels of PBG, FINS, and HbA1c were detected in 87 healthy subjects.

2.2. Methods

5 mL of fasting venous blood was drawn from all subjects, and HbA1c level was detected by high performance liquid chromatography (HPLC) using Lifotronic H9 HBA1c Analyzer and its kit. Roche e602, an automatic electrochemiluminescence immunoassay analyzer, and its accessories were used. FINS levels were measured using reagents, while PBG levels were measured by Roche cobas 8000 modular analyzer, an automatic biochemical analyzer, and its supporting reagents. All operations were carried out according to the instructions of the reagents or instruments.

2.3. Observation indicators

2.3.1. Postprandial blood glucose

In medicine, PBG is used as one of the criteria used to diagnose diabetes. Generally, the 2-hour postprandial blood glucose in a normal person is less than 7.8 mmol/L. Elevated blood glucose observed 2 hours after a meal is common in patients with type 2 diabetes.

2.3.2. Fasting insulin

FINS refers to the amount of insulin produced by the pancreas in the fasting state of the human body. Insulin is the only substance that can lower blood sugar in the human body. In a fasting state, insulin is secreted at a constant rate without the stimulation of food and glucose in the blood. Food, after consumption, is converted into glucose and absorbed into the blood. As a result, the pancreas is stimulated, and a large amount of insulin is secreted within a short period of time to control postprandial blood sugar. Glycogen is continuously synthesized by the liver at night; only when basal insulin counteracts the output of liver glycogen can there be normal fasting blood sugar.

2.3.3. Glycated hemoglobin

HbA1c is produced by hemoglobin in the blood and sugar (mainly glucose) in the blood. Since the non-enzymatic reaction of HbA1c is continuous, slow, and irreversible, its level depends on whether a person is fasting, whether insulin is injected, whether hypoglycemic drugs are taken, *etc.* It is generally believed that in the last 8–12 weeks, HbA1c can be used as a good indicator and monitoring method for diabetes. HbA1c is expressed as the percentage of hemoglobin in adults.

2.4. Statistical analysis

All the data in this study were processed by SPSS 22.0. The measurement data were expressed as mean \pm standard deviation and tested by t-test, while the enumeration data were tested by chi-squared test.

3. Results

3.1. Comparison of postprandial blood glucose, fasting insulin, and glycated hemoglobin levels between the study group and the control group

The levels of PBG, FINS, and HbA1c in the early diabetic nephropathy group were higher than those in the control group ($P < 0.01$), as shown in **Table 1**.

Table 1. Comparison of PBG, FINS, and HbA1c levels between the early diabetic nephropathy group and healthy subjects

Group	PBG (mmol/L)	FINS (mU/L)	HbA1c (%)
Early diabetic nephropathy group (n = 43)	11.80 \pm 3.21	11.73 \pm 2.46	8.04 \pm 1.37
Control group (n = 87)	6.72 \pm 0.65	7.73 \pm 1.25	4.86 \pm 0.62
t	3.698	4.021	3.025
P	< 0.01	< 0.01	< 0.01

Abbreviations: FINS, fasting insulin; HbA1c, glycated hemoglobin; PBG, postprandial blood glucose.

3.2. Comparison of postprandial blood glucose, fasting insulin, and glycated hemoglobin levels between the type 2 diabetes group and the early diabetic nephropathy group

The levels of PBG, FINS, and HbA1c in the early diabetic nephropathy group were higher than those in the type 2 diabetes group ($P < 0.01$), as shown in **Table 2**.

Table 2. Comparison of PBG, FINS, and HbA1c levels between the type 2 diabetes group and the early diabetic nephropathy group

Group	PBG (mmol/L)	FINS (mU/L)	HbA1c (%)
Early diabetic nephropathy group (n = 43)	13.42 \pm 3.15	13.55 \pm 2.17	9.13 \pm 1.52
Type 2 diabetes group (n = 53)	10.49 \pm 2.58	10.26 \pm 1.96	7.15 \pm 1.26
t	4.698	3.021	4.025
P	< 0.01	< 0.01	< 0.01

Abbreviations: FINS, fasting insulin; HbA1c, glycated hemoglobin; PBG, postprandial blood glucose.

4. Discussion

4.1. Relationship between glycated hemoglobin and diabetic nephropathy

HbA1c is a multifunctional protein that can regulate glucose metabolism, energy production, and cell growth. When renal function is abnormal, it can increase the glomerular filtration rate and reduce the clearance efficiency of serum proteins. HbA1c can combine with different types of lipids and proteins, such as plasma proteins and tissues, to form complexes. HbA1c can increase the permeability of the glomerular cell membrane, resulting in decreased glomerular filtration rate; at the same time, it can reduce the interactions between glomerular cells, resulting in the inhibition of glomerular cell proliferation or apoptosis. In addition, HbA1c levels are influenced by diet. Studies have shown that HbA1c levels are associated with chronic kidney disease (CKD) and ESRD in diabetic patients. Hence, HbA1c is one of the risk factors leading to CKD and ESRD [6-11].

4.2. Relationship between postprandial blood glucose and fasting insulin levels and diabetic nephropathy

Studies have shown that the levels of PBG and FINS are correlated with glomerular filtration rate and PGA expression was significantly increased in the FINS group compared to the PBG group [10,11]. In human patient samples, the expression of PGA in the type 2 diabetes mellitus group was significantly higher than that in the healthy control group. At the same time, serum and urine PGA levels were also significantly higher in the type 2 diabetes mellitus group compared to the healthy control group. However, no studies have confirmed the specificity and sensitivity of PBG and FINS levels in DN patients. A renal histopathological analysis of type 2 diabetic rats has revealed that PBG and FINS have a significant positive correlation with DN progression. Further studies have found that insulin can reduce urinary albumin excretion by upregulating the expression of PGA in urine cells, thereby reducing the risk of DN progression in type 2 diabetes mellitus. In a histological analysis of the kidneys of type 2 diabetic rats, the level of PGA was found to be significantly elevated in the T2DM group compared with the normal control group, with no significant change in PBG [12,13].

4.3. Relationship between postprandial blood glucose and fasting insulin levels and renal injury

The kidney is a complex system comprising many important cells, blood vessels, and nerves. The kidney plays an important role in maintaining fluid balance through glomerular filtration, renal tubular secretion, and glomerular reabsorption. This complex organ that is composed of abundant ECM plays an important role in maintaining the stability of the internal environment. PBG is mainly secreted by epithelial cells and is the main component of the renal barrier. As people's understanding of PBG continues to grow, its influence on human bodily functions has garnered widespread attention.

FINS is mainly synthesized by fibroblasts. Fibroblasts can secrete various growth factors and collagen, and they are one of the main components of the ECM in the kidney. In renal injury, with the changes in ECM composition, renal tubular reabsorption capacity weakens or is impaired, which in turn results in decreased urine concentrating function. The kidney is highly sensitive to glucose toxicity and hypoxia-induced inflammatory response, which is also one of the main pathological mechanisms of DN. Injury to renal tubular epithelial cells can cause a series of clinical changes, such as tubular structural changes and epithelial-mesenchymal transition. DN and diabetic kidney injury are very similar in pathology, but there are certain differences in their pathological mechanisms. The early stage of DN manifests as decreased glomerular filtration rate, glomerulosclerosis, and progression of interstitial fibrosis, but the manifestations of kidney injury vary in different stages, and its occurrence is associated with many different factors, such as diabetes, inflammation, oxidative stress, and metabolic disorders. Patients with CKD are more likely to develop clinical manifestations in the early stage (1–3 years), while patients with type 2 diabetes have a higher probability of developing early kidney disease (3–4 years); in addition, the rate of progression is faster. However, studies have shown no significant difference in patients with advanced renal insufficiency. The pathogenesis of DN is very complex and has not been fully elucidated. The pathological changes of diabetic kidney include glomerular injury, renal tubular cell injury, and microvascular disease, and these changes eventually lead to renal tubular epithelial cell apoptosis and glomerulosclerosis, which are the main causes of early DN. FINS, a pro-inflammatory cytokine, participates in various pathological processes, such as glomerular injury, tubular epithelial cell injury, tubular apoptosis, and tubular fibrosis; it plays an important role in early DN. PBG, on the other hand, is not only involved in renal interstitial injury, but also related to renal interstitial fibrosis. Studies have found that PBG may also contribute to the development of early DN [12-16].

4.4. Significance of postprandial blood glucose, fasting insulin, and glycated hemoglobin in the prevention of early diabetic nephropathy

HbA1c can bind to a variety of enzymes that regulate ECM metabolism and promote its degradation, thus participating in kidney injury. The serum levels of PBG, FINS, and HbA1c in patients with type 2 diabetes were significantly elevated. In a mouse model of type 2 diabetes, PBG was positively correlated with HbA1c concentration, whereas FINS was not significantly correlated with HbA1c^[15,16]. Serum PBG, FINS, and HbA1c levels were elevated in patients with type 2 diabetes, and serum PBG levels were positively correlated with acute kidney injury ($P < 0.05$); FINS was found to be associated with the progression of DN. Serum creatinine, blood urea nitrogen, creatinine clearance rate, and glomerular filtration rate in patients with type 2 diabetes were significantly higher than those in the normal healthy group ($P < 0.05$); meanwhile, a positive correlation was observed between urinary protein excretion rate and PBG ($P < 0.05$). Hyperglycemia can activate the nuclear factor kappa light chain enhancer of activated B cells (NF- κ B) pathway, cause renal oxidative stress, generate a large amount of reactive oxygen species, and lead to apoptosis as well as the destruction of renal tubular epithelial cells, while PBG may contribute to renal injury by inhibiting apoptosis. The exposure to inflammatory factors may cause infiltration of a large number of inflammatory cells and tissue damage and may result in increased permeability of the glomerular membrane and thickened glomerular basement membrane.

In conclusion, PBG, FINS, and HbA1c are factors that affect the occurrence of DN in patients with type 2 diabetes, and the occurrence of DN in type 2 diabetes can be effectively prevented by controlling the levels of PBG, FINS, and HbA1c.

Disclosure statement

The authors declare no conflict of interest.

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