Analysis of Metabolic Factors Associated with Hyperuricemia in Diabetes Mellitus

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Abstract: After the occurrence of diabetes in patients, with the increase of the course of disease and the increase of the age of patients, the incidence of other combined diseases in patients is also increasing. Diabetes combined with hyperuricemia is a common clinical disease, and 40% of patients with diabetes will develop hyperuricemia and other complications, which not only makes the treatment of the disease more difficult, but also increases the burden of the hospital. Therefore, to analyze the metabolic factors related to hyperfatemia, and to provide a reference for the clinical exploration of active and effective treatment.

Keywords: Diabetes Mellitus; Hyperuricemia; Metabolic Factors

Introduction

Diabetes mellitus is a common chronic disease in clinical practice, and patients are often complicated with hyperglycemia, hyperuricemia and other complications. Related studies have shown that there is a certain relationship between hyperuricemia and diabetes[1]. This paper studies the internal pathogenesis and rules of diabetes combined with hyperuricemia, providing a new basis for the clinical prevention and treatment of diabetes combined with hyperuricemia.

1. Overview of the correlation between hyperuricemia and diabetes mellitus

Hyperuricemia refers to the hypersaturated state of urate in the extracellular fluid. It is characterized by the disorder of purine metabolism and the increase of uric acid in the body. It is generally believed that hyperuricemia should be considered when blood uric acid ≥420umol/L(7mg/L) in males and ≥360umol/L(6mg/L) in females.

Uric acid (UA) is the end product of purine metabolism in the human body. One third of purines in the body come from food breakdown, two thirds are synthesized by the body itself, and most purines are oxidized and metabolized by the liver into uric acid. The daily production is approximately equal to the excretion, 1/3 is excreted by the intestine, and 2/3 is excreted by the kidney. The kidney is the main way of uric acid excretion. After blood uric acid is filtered from the glomeruli, 98% of uric acid is reabsorbed by the proximal tubules, and finally, less than 10% of uric acid is excreted into the urine by the distal convoluted tubules. Blood uric acid (SUA) concentration depends on the balance between the amount of purine synthesis, the amount of ingested and the amount of uric acid excreted. If uric acid is generated too much or excreted too little, uric acid metabolism will lose balance, and uric acid will accumulate in the body, leading to elevated blood uric acid, hyperuricemia (HUA), and a series of pathophysiological changes.

With the rapid development of economy in recent years, the occurrence of hyperuricemia not only gradually increases, but also tends to occur at an earlier age. At present, it is clinically found that the age of 30 to 39 years old is prone to hyperuricemia, which may be related to genetic factors, mental factors, lifestyle (diet, alcohol consumption, physical

exercise). After puberty, serum uric acid levels increase more rapidly in men than in women and peak at age 50. The serum uric acid level of females does not rise significantly after puberty, but rapidly rises to a level similar to that of males after menopause, possibly because estrogen can promote the excretion of uric acid by the kidney. In the 40 to 59 age group, hyperuricemia is associated with a cluster of diseases, such as hyperuricemia with hyperuricemia, hypertension, obesity, and diabetes. This is mainly related to metabolic risk factors such as renal excretory dysfunction and insulin resistance. It is worth exploring the relationship between diabetes mellitus combined with hyperuricemia and these metabolic diseases.

2. Analysis of metabolic factors related to hyperuricemia in diabetes mellitus

Uric acid is the end product of purine metabolism in the body. In the body, uric acid is mainly degraded by urate oxidase (uricase) in the liver to produce allantoin, and then excreted by the kidney. Uric acid levels in the body is mainly affected by two aspects, on the one hand is to make increased uric acid to produce factors (10%), such as high purine or protein diet is taken, alcohol consumption, the high level of cell metabolism, and the shortcomings of the purine metabolic enzymes, etc., on the other hand is reduce uric acid excretion factor (90%), two-thirds of renal excretion by the blood uric acid, a third by the bowels, After glomerular filtration, 98% of uric acid is reabsorbed by proximal tubules, and less than 10% is finally excreted into urine by distal convoluted tubules[3]. For example, the renal excretion capacity decreases, the glomerular filtration rate decreases, the renal tubular reabsorption increases (such as the use of thiazide diuretics), and the blood uric acid increases.

The occurrence of hyperuricemia in diabetic patients is the result of increased production or decreased excretion. The reasons may be as follows :① Microangiopaplasia is common in diabetic patients, and renal microangiopaplasia leads to renal ischemia and decreased renal blood flow, while uric acid excretion is directly proportional to renal blood flow, so blood uric acid increases. ② Uric acid, as one of the most widely distributed water-soluble antioxidants in the human body, has the property of iron as a mixture, which can reduce the incidence of lipid peroxidation and stabilize the serum ascorbic acid from oxidation. In some patients, oxidative stress is aggravated and large blood vessels are damaged. Uric acid compensatively increases to counter this oxidative reaction, resulting in hyperuricemia. ③ Elevated serum uric acid can further damage islet B cells. Hyperuricemia is also one of the clinical manifestations of metabolic syndrome. The pathogenesis of diabetic hyperuricemia is also related to hyperinsulinemia caused by insulin resistance. Because it increases urinary sodium excretion in proximal convoluted tubules, it competitively inhibits uric acid excretion. It is known that glucose and uric acid are competitively reabsorbed in the proximal convoluted tubules of the kidney. Increased excretion of urine sugar will competitively inhibit uric acid reabsorption, resulting in a decrease in blood uric acid level. When blood glucose is well controlled, urine sugar decreases, uric acid reabsorption increases, and blood uric acid increases. It is suggested that the decrease of renal function can increase the serum uric acid level, 8 but the blood glucose level is not the cause of the abnormal uric acid metabolism. Studies have shown that body weight is an independent risk factor for diabetes mellitus complicated with hyperuricemia. The mechanism of association between obesity and hyperuricemia may be the decreased expression or clearance of leptin gene in serum of patients with hyperuricemia. Atherosclerosis induced by high level of serum uric acid in patients with diabetes may be deposited directly in the arteriolar wall through uric acid stones, and then damage the intima through purine metabolism and lipid metabolism. Hyperuric acid, hyperglycemia and hyperlipidemia have superposed pathogenic effects to accelerate the process of atherosclerosis, while hypertension can also cause renal microvascular sclerosis, increase the concentration of angiotensin and catecholamines, reduce renal blood flow, and accumulate hypoxic lactic acid in local tissues, which compete with blood uric acid for excretion, and increase blood uric acid[4].

On the other hand, uric acid crystals in diabetes can promote blood pressure by stimulating renin angiotensin system

and inhibiting nitric oxide synthesis[5]. At the same time, uric acid crystals are deposited in the vessel wall, which promote lipid peroxidation, increase the generation of oxygen free radicals, and participate in the inflammatory reaction. Recent studies have also found that hypertension is related to genes related to vascular proliferation and sclerosis, such as upregulation of uric acid transporter I and cyclooxygenase-2 genes on vascular wall. It can be seen that hyperuricemia is closely related to hypertension and its atherosclerotic complications. Stepwise regression analysis showed that Ccr, body weight and LDL-C were independent risk factors for diabetes mellitus complicated with hyperuricemia. These results indicated that the increase of serum uric acid level in diabetes mellitus was closely related to obesity, lipid metabolism disorder, elevated blood pressure, IR and metabolic syndrome. Elevated serum uric acid level is an important characteristic of insulin resistance syndrome.

3. The prevention of hyperuricemia

For asymptomatic hyperuricemia patients with family history of gout or blood uric acid >535umol/L and 24h urine uric acid >5.9mmol/L, drugs should be used to reduce uric acid. At present, drugs to reduce uric acid are mainly divided into two kinds: uric acid excreting drugs (benbromarone) and uric acid inhibiting drugs (allopurinol), the former can inhibit uric acid. Reabsorption of uric acid by renal tubules increases uric acid excretion. Generally applicable to the type of uric acid excretion reduction, taking method :50mg, once a day. Allopurinol can inhibit the activity of xanthine oxidase, thereby reducing the biosynthesis of uric acid and decreasing the concentration of blood uric acid. Allopurinol is commonly used in patients with increased uric acid production. How to take: Starting dose 50mg, 3 times a day, gradually increased to 300-600mg/d. It is worth pointing out that the above two types of drugs must be used after the control of acute inflammation in gouty arthritis (2 weeks after the acute attack). Colchicine or non-steroidal anti-inflammatory drugs should be used in acute gout attacks.

4. Summary

To sum up, high uric acid hematic disease is common complications of diabetes, are caused by lipid metabolism disorders in body, is in patients with atherosclerosis, stroke and other chronic cardiovascular disease risk factors, treatment and prevention of diabetic high blood uric acid is an important content of current medical research, is of great significance to reduce chronic cardiovascular disease clinically. Since hyperuric acid, hyperglycemia, dyslipidemia and hypertension complement each other and promote the formation of atherosclerosis and the aggravation of insulin resistance, it is necessary to not only control fasting blood glucose, blood pressure, blood lipids and obesity, but also pay attention to the risk factor of hyperuric acid in patients with T2DM and give timely treatment relevant interventions.

References

[1] Marco Meloni, Valentina Izzo, Erika Vainieri, Laura Giurato,Valeria Ruotolo,Luigi Uccioli.Management of negative pressure wound therapy in the treatment of diabetic foot ulcers[J]. World Journal of Orthopedics: 2015,6(4):387-393.

[2] Liu JC, Tang CY, Lu SY et al., a famous Chinese medicine practitioner in China, discusses the pathogenesis characteristics of adolescent central obesity based on "qi change theory"[J].Journal of Hainan Medical College,2020(8):56-60.

[3] Pan LB, Han P, Ma SR, et al. Abnormal metabolism of gut microbiota reveals the possible molecular mechanism of nephropathy induced by hyperuricemia [J]. Journal of pharmaceutical sciences, 2020,0(2):249-261.

[4] Cappuuio FP, Strazzullo P, Farinaro E, et al. Reduction of serum uric acid by hormonal replacement therapy in postmenopausal with hyperuricemia. Lancet, 1999, 354: 650.