

Research progress of type 2 diabetes mellitus in adolescents

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Abstract. There is an increase in the prevalence of type 2 diabetes among adolescents. In particular, the prevalence rate of diabetes mellitus patients aged 7-17 years in China ascended from 0.24% in 2002 to 0.52% in 2012. Although the incidence rate is not high, the growth rate is rapid. The main reason why the number of adolescents who suffer from T2DM has been continually rising is that the population of overweight and obese adolescents has been constantly expanding. Research also shows that poor dietary habits and genetic factors also play a crucial role in adolescent patients. As a result, obesity leads to insulin resistance—a condition in which the body's cells find it hard to respond properly to the hormone insulin, and this is the core of type 2 diabetes. This paper points out the current epidemiological characteristics of adolescent T2DM, aiming to provide a reference for the current situation of adolescent T2DM by understanding the pathogenesis, risk factors and the prevention or treatment of adolescent T2DM.

Keywords: Diabetes mellitus, T2DM, Epidemiology, Pathogenesis, Treatment.

1. Introduction

When people eat food, the carbohydrates in the food will be decomposed into glucose after entering the digestive tract. Following that, glucose is transported by blood to the tissue cells of the whole body for aerobic oxidation. In the last phase, oxidative glucose is consumed as energy or stored by the body for future use. In this process, insulin, a hormone produced by islet B cells, is necessary for glucose to enter cells. The binding of insulin and its receptor on target cells appears a signal cascade, which brings glucose transporters to the cell membrane. Therefore, when the human body's cells become resistant to insulin, glucose cannot enter the cells in time to turn into energy, and will stay in the blood to raise blood sugar and make the cells lack nutrition. This is the mechanism of diabetes.

Diabetes can be divided into two types. The first type is type 1 diabetes, which belongs to autoimmune system defect disease. Meanwhile, as the most common disease with the largest number of patients at present, type 2 diabetes is a disease with "insulin resistance type" in which the cells do not respond to insulin and cannot absorb blood sugar because of the failure of insulin and its receptor to bind or problems in signal cascade. What type 2 diabetes mainly be distinguished from type 1 diabetes is the age of onset. Type 1 diabetes mainly occurs under 20 years old, which involves children and adolescents. Conversely, type 2 diabetes almost occurs in adults and the onset age is mostly after 30 years old.

Diabetes mellitus has a multitude of clinical symptoms. To illustrate, when the blood glucose level exceeds the reabsorption capacity of the kidney, it will overflow into the urine, resulting in some typical clinical signs such as unexplained weight loss, increasing hunger (polyphagia), growing urination (polyuria), dehydration, excessive thirst (polydipsia). Apart from this, the long-term high blood sugar levels may pose potential risks to atherosclerosis and diabetic nephropathy. The former increasing the incidence of a series of cardiovascular disease involving coronary heart disease, diabetic cardiomyopathy, and cerebral thrombosis. While the latter, diabetic nephropathy is a progressive kidney disease caused by damage to the capillaries in the kidney's glomeruli due to longstanding diabetes mellitus. It is also an irreversible disease; some patients are likely to end up with kidney failure owing to uremia. Furthermore, Worst of all, there are many other severe complications. For example, the impaired blood vessels in the eyes may culminate in diabetic retinopathy and macular edema, two causes of blindness. Another common threatening complication in people with diabetes mellitus is DKA (Diabetic ketoacidosis) which results from a shortage of

insulin. Meanwhile, one of the dangerous complications is HHS hyperosmolar hyperglycemia state). It can exert neurotoxic effect on diabetic, making them feel numb, tingling and less painful. Plus, lack of nutrition does enormous harm to wound healing which is the main risk factor of further ulceration of the skin. It is frequently observed that the symptom is in the patient's feet. Actually, it is because of those lethal complications that diabetes mellitus can gamble people's lives.

2. Epidemiology of diabetes mellitus

Based on the characteristics of the disease, most studies in the past showed that the adolescent diabetes patients are mainly type 1 diabetes patients, hence it is widely accepted that the incidence of Type 2 diabetes mellitus in adolescents was low. However, more and more scholars have found that the incidence of T2DM in adolescents presents a dramatically rising tendency in recent years.

More often than not, most of the adolescents with type 2 diabetes are asymptomatic. Therefore, most of the current studies and reports are local and lack the overall prevalence of type 2 diabetes among adolescents in the world. For instance, some Japanese researchers found that the incidence rate of T2DM in Japan aged 6-12 years increased from 7.3/100000 to 13.9/100000[1], which is closely related to the changes in eating habits and the increase in teenagers with obesity in Japan in the last ten years. Similar research was a survey from multiple centers in China, showing that among 4,337,836 discharged patients aged 0-18, the prevalence of new type 2 diabetes (per 100000 people) was 8.0. It pays to point out that type 2 diabetes increased from 4.1 to 7.1 and 10.0 in every five years, which revealed an expansion over double the figure for adolescents. The study also found that developed areas in China had a higher prevalence compared to less developed areas type 2 diabetes: 15.16 vs. 1.64], related to a sharply growing number of obese children in developed areas. Also, a study from a fagot Campagna and other researchers exhibited that among 15 -to -19-year-old North American Indians, prevalence of type 2 diabetes was higher than the figure for people of the same age in other parts of the United States. More importantly, prevalence for Pima Indian adolescents between 1987 and 1996 was six times as much as that of Pima Indian adolescents between 1967 and 1976. Besides, the number of adolescents with type 2 diabetes among African Americans and whites in Ohio accounted for a very large share of all cases of diabetes. The study also showed that in the United States, the majority of adolescent type 2 diabetes patients are residents in backward and poor areas or belong to the low-income group, which was contrary to China. This reflects the regional differences in the epidemic characteristics of juvenile diabetes.

3. The pathogenic factors of diabetes mellitus

3.1. Genetic factors affect the onset of diabetes mellitus

MODY (maturity-onset diabetes of the young) was named by Fajans and Tattersall in 1975 after analyzing a series of reports since 1950. It is a single gene mutation diabetes with features of autosomal dominant inheritance and early onset age. Besides, its primary clinical manifestation is a significant increase in the level of non-ketotic glycemic in adolescents, which is identical to adult with type 2 diabetes mellitus. Actually, if a teenager's family has a first-degree or second-degree relative with T2DM, he or she is more likely to suffer from T2DM than teenagers of the same age or the same obesity level. Many studies proved that adolescent patients with T2DM were closely related to their genes and family disease history. The family of patients with MODY caused by glucokinase (GCK) gene mutation have been investigated and reported to the gene mutation sites [2]. It was found that there was a heterozygous missense mutation of c.485g > A in the exon of GCK gene in 5 members of the family for three consecutive generations. Among the 5 members, the proband was consistent with MODY2 patients, and all the rest four members are patients with diabetes or impaired glucose regulation. It is of great significance for the correct molecular genetic diagnosis method given in the report to the diagnosis of type 2 diabetes in adolescents and the clinical consultation of the disease.

Similarly, Ravi P Sahu and others have studied the etiology of type 2 diabetes in non-obese Indian adolescents and found that it is related to islet autoimmunity and hepatocyte nuclear factor 1 α and mitochondrial gene mutations. Glutamic acid decarboxylase antibody was detected in 3% of patients, mitochondrial A3243G mutation was detected in 1% of patients, and MODY3 mutation (r200w) was detected in 3% of patients [3]. It was found that the proband developed diabetes at the age of 17, and they had a family history of diabetes for three generations and serious microvascular complications, demonstrating that β Cellular autoimmunity and HNF-1 α Gene mutation were the main causes of T2DM in northern Indian adolescents.

In conclusion, Gene and family history are independent risk factors for type 2 diabetes in adolescents, but such patients are often asymptomatic in the early stage. Consequently, the American Diabetes Association recommends that overweight children whose BMI exceeds the 85th percentile of children of the same age and sex and who have two or more of the following risk factors should be screened [6]: those with a family history of diabetes in their first or second degree relatives, those with high-risk races, and those with insulin resistance phenotypes (hypertension, lipid metabolism disorder, hyperinsulinemia, acanthosis nigricans, polycystic ovary syndrome). Screening should be started at the age of 10 (or adolescence) and checked every 2 years. The screening method includes the determination of FPG or PPG.

3.2. Obesity

The rising obesity rate is the most important risk factor for the increasing number of adolescent type 2 diabetes patients. According to the latest data in the report on nutrition and chronic diseases of Chinese residents (2020), 19% of children aged 6-17 years old and 10.4% of children under 6 years old are overweight or obese currently. In total, there are already 600 million overweight and obese people in China, ranking the first place in the worldwide. More importantly, there was a radical mass in the obesity levels whether in the city or the countryside. Compared to Western countries, the rate of overweight or obesity was higher in upper-income group. It is largely due to the fact that the radically shifting dietary patterns and lifestyles of teenagers with the rapid transformation of China's economy and society. Many people are keen to junk food and carbonated drinks, which are high in sugar content. In addition, the pressure of fast-paced life and study make teenagers accustomed to sitting for a long time and failing to have breakfast frequently. Moreover, many of them gobble food too fast, which leads to an increase in appetite.

An amount of studies has confirmed that obesity plays an important role in abnormal blood glucose and T2DM.

In the study of Yu Changyang [4], 77 obese adolescents and 18 non-obese youths with a family history of diabetes were subjected to oral glucose tolerance test. After comparative analysis of 7 glucose metabolism indexes, it was found that HPG, fins, pins, pins / 2 HPG and HOMA IR in the obese group were remarkably higher than those in the non-obese group. At the same time, among the 77 obese patients, there are 3 cases with type 2 diabetes, one of them had no family history of diabetes. Additionally, 12 cases had IGT, and 31 cases had hyperinsulinemia. The result presented that the abnormal degree of glucose metabolism of obese people is higher than that of non-obese people, and the risk of diabetes is higher.

In a survey of 60 adolescent patients with type 2 diabetes admitted to the second hospital of Fuzhou City [5], the researchers divided the observation group into non-abdominal obesity group (group A), mild abdominal obesity group (group B), moderate abdominal obesity group (Group C) and severe abdominal obesity group (Group D) according to the degree of abdominal obesity. The fasting blood glucose, postprandial blood glucose, glycosylated hemoglobin, plasma TC and TG levels of the four groups were tested respectively. The indexes measured in group D were higher than those in group A, and the fasting blood glucose, postprandial blood glucose, glycated hemoglobin, plasma TC and TG levels in group B, group C and group D increased in turn. The results show that the degree of abdominal obesity can adversely affect the glucose and lipid metabolism of adolescents with type 2 diabetes. The higher the degree of abdominal obesity, the higher the related indicators of diabetes. In

addition, the study mainly found the relationship between the degree of abdominal obesity and the content of liver fat. With the aggravation of abdominal obesity, the content of fatty liver in patients increases, and the risk of developing into fatty liver also increases. It can be seen that the degree of abdominal obesity affects the probability of diabetes complications like fatty-liver in adolescent diabetes patients.

It is frequently observed that cardiovascular disease is the main cause of death in adult diabetes patients. Meanwhile, obesity is a common risk factor for T2DM complicated with cardiovascular disease. Italian scholars conducted oral glucose tolerance tests on 7 obese children with T2DM, 17 obese children and 8 non-obese children with control analysis. The study found that compared with the non-obese belonging to control group, β Cell function, area under insulin curve and glucose degradation index decreased significantly among obese non-t2dm children and obese T2DM children. In the two obese children groups, the vagal index descended progressively and the sympathetic index ascended. More importantly, this change was especially obvious in T2DM children. It is self-evident that severe insulin resistance and β Cell failure can cause damage to the early cardiac autonomic pattern in the obese T2DM children group.

3.3. Other influence factors

In fact, there is also a certain correlation between mental stress and adolescent type 2 diabetes. First of all, under the condition of mental tension, emotional excitement and various kinds of stress, it will cause the secretion of a large number of blood glucose hormones to increase, such as growth hormone, norepinephrine, trypsin and adrenocortical hormone. Secondly, under stress, teenagers are more likely to develop bad habits such as smoking, overeating to relieve stress. A researcher reviewed the data of more than 1.5 million 18-year-old Swedish men recruited into the army from 1969 to 1997, and found that compared with those with the highest stress tolerance at the age of 18, those with the lowest stress tolerance were 51% more likely to be diagnosed with type 2 diabetes later. Although there is no research that can prove the direct causal relationship between stress and adolescent type 2 diabetes, there is no doubt that stress can indirectly affect the lifestyle and physical condition of adolescents, leading to an increased risk of developing type 2 diabetes.

4. Proposed therapies for T2DM

4.1. kinesitherapy

Exercise therapy is a basic treatment method for a host of chronic diseases. Numerous studies have shown that physical training has significant clinical effects on the treatment and prevention of type 2 diabetes mellitus.

First and foremost, sports therapy is very effective in controlling blood sugar level and promoting the metabolism of glucose and lipid in the body. Regular exercise can promote the muscle tissue's uptake of glucose in the blood, reduce blood sugar, increase the consumption of liver glycogen and muscle glycogen during exercise, relieve the hyperglycemia state, and convert blood sugar into glycogen for storage after exercise, further reducing blood sugar. A study of 80 diabetic patients selected from the Second People's Hospital of Taizhou City proved this point [6]. The patients were divided into the routine group and the control group. In the routine group, diet control and drug therapy were the main methods, combined with some aerobic exercise. The control group developed a moderate intensity exercise program for the patients according to the specific conditions of the patients. The patients were required to exercise for more than 5 days a week, for more than 1 hour a day, and for three consecutive months. When jogging, the total distance should be maintained at 6-8 km. At the same time period, the medical staff guided the patients to do some conventional resistance exercises as an auxiliary treatment. It can be seen from the results of the experiment that the levels of serum insulin (Fins), the levels of serum insulin levels (Fins), HbA1C, Triglycerides (TG) and fasting blood-glucose (FBG) in the control group were obviously lower than those in the routine

group, which shows that scientific exercise program for patients is conducive to reducing blood lipid and glucose levels in patients with type 2 diabetes mellitus. Besides, the decrease of serum insulin level also shows that exercise therapy can improve insulin function in patients with type 2 diabetes mellitus. Exercise can effectively improve body mass. The insulin secretion of type 2 diabetic patients is reduced during exercise. Exercise increases the blood circulation, thus increasing the binding rate of insulin and receptors. The metabolic reaction is constantly enhanced after binding with receptors, thus increasing insulin sensitivity, weakening insulin resistance and improving glucose metabolism. Moreover, sports therapy is rewarding for the prevention of complications of type 2 diabetes mellitus. Numerous acute and chronic consequences of diabetes, including coronary heart disease, hypertension, diabetic nephropathy, neuropathy, etc., can be brought on by poor glycemic control. Mild to severe hypertension can be efficiently treated by exercise, which also thickens and elongates blood vessel walls. In diabetic people, high-intensity aerobic exercise considerably lowers mortality and cardiovascular disease. The researchers investigated 301 subjects and divided them into exercise group and control group. There was no significant difference between the two groups in gender, age, course of disease, BMI, proportion of patients with hypertension and hyperlipidemia. Meanwhile, the prevalence of DN, DR and DMA in the two groups was similar before exercise intervention. After 12 months, the prevalence of DN in the exercise group was lower than that in the control group, and the number of DN patients in the exercise group decreased after the exercise intervention, and some patients' DN was reversed. It can be seen that exercise therapy is effective in preventing chronic vascular complications.

4.2. Diet therapy

In reality, compared with traditional diet, a significant number of children and adolescents are enthusiastically fond of fast food, carbonated drinks and high-calorie snacks nowadays. Such a high salt, sugar and cholesterol diet leads the number of obese patients to soar, which increase the probability of TD2M. Consequently, as an important precaution or treatment, dietary control is essential for adolescents with type 2 diabetes. 94 patients with type 2 diabetes who were diagnosed and treated in a community were selected as the study subjects [7], and they were divided into experimental group and reference group. Among them, the reference group was treated with conventional drugs, and the experimental group was given diet control on this basis. The experiment took many measures including diversification of dietary structure, strict control of intake and dietary supervision. At the beginning, the subjects ate coarse grains and fine grains together, and gradually used corn, oats, pumpkins and other coarse grains as the staple food rather than rice and noodles. In addition, the medical staff also strictly regulated the daily intake of the patients according to their conditions, including how much fruit and vegetables they should eat each day, whether the protein is enough, whether potassium should be supplemented, etc. All requirements are very specific and rigorous. Most of all, the medical staff should instruct the family members to strictly supervise whether the patients eat according to the regulations, and also need to adjust the diet plan regularly according to the actual condition of the patients. After taking different measures and after a period of time, the treatment effectiveness and quality of life scoring indicators of patients in the experimental group after taking diet control treatment were higher than those in the reference group, and the clinical indicators and depression scoring indicators were lower than those in the reference group, which fully demonstrated that diet control treatment had significant effect on improving the prognosis of patients with type II diabetes.

4.3. Medical treatment

At present, type 2 diabetes in adolescents cannot be eradicated. Once diagnosed with type 2 diabetes, patients need to start drug treatment in addition to diet and exercise therapy. The specific drug treatment plan needs to be formulated according to the patient's own clinical symptoms. There are two main drugs for treatment of type 2 diabetes in adolescents.

Oral hypoglycemic drugs are the first choice for the treatment of juvenile patients with type 2 diabetes. First and foremost, Glimepiride, a sulfonylurea drug, belonging first line drugs for type 2 diabetes. The main mechanism of it is to stimulate insulin release through binding β Sulfonylurea receptors on the cell surface [8]. In addition, it also reduces the metabolism of insulin, enhances the sensitivity of target cells to insulin and improves the binding ability of insulin and its receptor. But it can also cause liver damage and blood system damage, and even lead to persistent hypoglycemia symptoms, just like insulin. Therefore, medical staff need to tell patients to check blood routine and liver function regularly, and understand the symptoms of hypoglycemia and first aid measures. Apart from that, there is a safer drug named Rieglinide which has a much lower risk of hypoglycemia than sulfonylurea drugs. Its pharmacological action is similar to that of sulfonylurea drugs, characterized by rapid oral absorption and multiple times of pre-meal medication. Therefore, it is also referred as a blood glucose regulator during meals. In addition to these two drugs that promote insulin secretion, there is also an important drug for the treatment of juvenile type 2 diabetes called metformin, which belongs to biguanide drugs. Its advantage is that it can reduce the blood sugar, blood lipid and weight of patients. Metformin has a wide range of pharmacological effects. Metformin can decompose glucose into lactic acid through glycolysis by ingesting glucose in the blood, with the purpose of increasing the uptake and utilization of glucose by human muscle tissue, adipose tissue, liver cells and other surrounding tissues. It can increase the absorption of glucose in the intestine and block the glucose from entering the blood during this process. In addition, it can improve the binding between insulin and its receptor and the post receptor mechanism, thereby improving insulin resistance. It also inhibits the release of glucagon. Metformin is completely insulin independent β Cell function, so it will not cause hypoglycemia, which is superior to other drugs [9].

Furthermore, once patients have clinical symptoms of type 2 diabetes, insulin injection will become a necessary treatment [10]. Insulin mainly simulates physiological insulin secretion to maintain blood glucose stability of patients. To illustrate, there are three main sources of blood sugar, namely, sugar in food, liver glycogen and some non-sugar substances. Insulin prevents the sugar in food from being digested and absorbed into the blood by the human body, prevents the liver glycogen from being decomposed, and resists the conversion of non-sugar substances into glucose. In addition, insulin also helps the oxidation and decomposition of glucose into carbon dioxide, water and energy. If glucose cannot be consumed, insulin can promote its synthesis and store it as liver glycogen and muscle glycogen. Insulin also enables glucose to be converted into fatty acids, amino acids and other non-sugar substances. Although insulin is very effective in controlling blood sugar, it also has many adverse reactions. The most common is hypoglycemic reaction caused by excessive insulin dosage. In addition, patients may have tolerance to insulin, allergic reaction, local swelling, etc. For adolescent patients treated with insulin injection, medical staff should strictly monitor their daily drug dosage, and let patients or their families know the symptoms of adverse reactions, so as to find these adverse reactions as soon as possible and treat them.

At present, most treatment plans are formulated according to the specific symptoms of patients. Patients are mainly divided into patients with stable metabolism and patients with unstable metabolism. Asymptomatic patients, due to their stable metabolism, should take metformin at a dose of 500mg/dx7d, and gradually increase the dose of 500mg every week to 1000mg twice a day in the next three to four weeks. If the patient has clinical symptoms of diabetes but has no ketosis or ketoketoacidosis, metformin should be used together with insulin injection. One time/day medium effect insulin (NPH) or basic amount of insulin (from 0.25-0.5U/kg) can often effectively control the abnormal metabolism of patients. After the patient's condition is stable, insulin will not be stopped, but the dosage can be reduced by 30%~50% each time, until metformin is used alone, which usually takes 4 to 6 weeks. In fact, because the metabolic capacity of adolescents is still at a high level, most adolescents can be well controlled with metformin alone after being diagnosed.

5. Conclusion

Type 2 diabetes is a chronic metabolic disease, which occurs most frequently in people over 40 years old. However, due to the soaring number of obese people in recent years, the incidence rate of type 2 diabetes among adolescents in various regions has also increased year by year. This phenomenon will also become a trend in the future. Gene is the main factor affecting adolescent's disease, and gene diagnosis is also an important means to make adolescent's type 2 diabetes can be detected and prevented early. At present, with the change of people's lifestyle, obesity has become the main pathogenic factor of most adolescent type 2 diabetes patients. Therefore, in addition to drug treatment, controlling diet and exercise and fundamentally changing bad living habits can better control type 2 diabetes.

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