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Overview of Diabetes mechanism and therapy

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Abstract. The diabetes patients continuous increasing these days and many therapies come out. Till now, there is about 0.537 billion patients and mainly above forty years old and had a high proportion in Africa and Asia. Now drug treatment, operation and life management to reduce the negative effect cause by diabetes or even cure. The mechanism of diabetes type 1 is a kind of autoimmune disease and mostly mediated by T lymphocytes, islet beta cells are attacked and destroyed, causing inflammation, resulting in absolute insufficient insulin secretion and onset. Type 2 diabetes is caused by insufficient amount of inuslin.

Keywords: epidemiology, mechanism, therapy.

1. Introduction

The history related to diabetes can date back to 1550 BC, there was record of ancient Egypt patient who has the same kinds of symptoms with diabetes nowadays and the word of "diabetes" was first used till 200 BC which has a vivid description. After that until 18 century, England doctor Matthew Dobson figured out that blood was also sweet, and people found the relationship of diabetes with pancreas. In the early 20 century, England doctor Edward Albert Sharpey-Schafer fond that the diabetes had resulted by lack of secretion of certain substance by the pancreas and figured out which part of resulted that. But doctors treated this kind of disease with normal saline and tried diet therapy to see if can sustain patients' life. Until Frederick Banting successfully extracted insulin from dogs' and cows' pancreases in 1921. Throughout the world, there are two kinds of diabetes, one is type1 diabetes and another one is type2 diabetes and has a total amount of patients about 0.537 billion patients according to data from IDF and the number will increase to 0.783 billion by prediction. In developed country, with the advanced medical instruments and experienced medical workers, they have a relative steady number of cases, but mostly cases increase occur in developing country and have about 9 million patients which illustrate diabetes have a greater morbidity rate especially in developing countries since their life style change due to country's economy development. Gender doesn't really affect the probability to gain this kind of disease. Talking to age of onset, most cases are common under forty years old and has a trend of getting younger. Type1 is basically congenital result by gene or immune system. Type2 is a kind of acquired disease, mainly caused by unhealth habit and age. The clinical manifestation could be polydipsia, polyuria and polyphagia and weight loss. There are four ways for diagnosis: Fasting Plasma Glucose, Oral Glucose Tolerance Test, Glycated Hemoglobin and Random Blood Glucose Test. Firstly, talk about the FPG which requires patients to be with an empty stomach for at least eight hour and take the blood from vein to detect blood glucose concentration. If random blood glucose ≥ 11.1 mmol/L (200 mg/dL) with classic symptoms of diabetes, then can be diagnosis as diabetes. Another is OGTT, which is measure blood

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glucose concentration any time and if larger than 11.1mmol/L can be diagnosis as diabetes. Thirdly, is to measure the glycated glucose concentration in red blood cell which can provide average glucose level in blood in the past 3months.The fourth way is to use OGTT which test patients who fasting for eight hours and ingest 75g glucose solution and measure the concentration of glucose in blood after two hours. The symptoms mainly be extremely thirsty, pee more frequently, poor eyesight and unawareness weight loss. Type 1 diabetes mainly due to self-immune system attack β cell in pancreas which result in secreting insufficient insulin or even stop. Type 2 diabetes mainly due to insulin resistance which cause pancreas need to secrete more insulin to balance the blood glucose level and as time passed doesn't have the ability to secrete enough insulin, result in dysglycemia. The main medical treatment method has four types: drug therapy, insulin injection, insulin pump and operation. Drugs can be Metformin or other inhibitor, main target is to increase the sensitivity of insulin, produce more insulin or excrete more glucose out of the body. Insulin injection means we inject insulin into body to make sure the level of insulin in the body is enough for maintain glucose concentration in the blood vessel and most excess glucose turn into glycogen. The insulin pump is same with the insulin injection, but it can automatically inject the insulin when detecting to a high blood glucose concentration which is helpful for those patients have a large fluctuation in blood glucose concentration. There are two types of operation one is for obesity to reduce the weight while other one is to insert a new pancreas islet [1,2,3].

2. Mechanism

2.1. type one diabetes

It caused by autoimmune deficiency and mainly due to inheritance and has a low probability by pathogen or chemicals from the environment. The T cell has two types, Th1 and Th2 which these two stimulate to cell-mediated immunity and humoral immunity. The pathogens, chemicals and dead β cell result increase portion of Th1 which secrete cytokines like IL12, IL2 and IFN-y which cause inflammation occurred in part of the pancreas and let some β cell been killed. After that, the antigen of β cell were present to Th and produce specific antibody to pancreas islet β cell called ICA which increase the concentration of inflammatory cell and let blood insulin concentration drop. It's the gene disease of multifactorial inheritance and is caused mainly by HLA which based on the short chain of human's six chromosome. Haploid types A1, C1, B56, DR4, DQ8 have very high absolute risk. Nearly 50% of the genetic risk can be attributed to HLA genes near D region II genes (DR, DQ, DP). The study found that the susceptibility genes of type 1 diabetes include 57 non-aspartic acid in HLA-DQ b1 chain (which is a protective gene when it is aspartic acid) and 52 arginine in HLA-DQ A1 chain [4,5,6].

2.2. type two diabetes

Type 2 diabetes mainly result by the signal transmission problem and insulin receptor dysfunction included receptor gene mutations, abnormal of transport protein GluT4 and the transmission of signal. Also, low sensitivity of pancreas islet β cell cause insufficient secretion of insulin which may cause by missing of glucose transport protein (GluT2). The gene mutation like SUR, Glut-G, mt-G also plays a role in influence insulin secretion. For example, mt-DNA has a circular double-stranded structure, and its mutation will lead to the oxidative phosphorylase system of islet beta cells which make less ATP and result in insufficient energy supply, influence the function of islet beta cells and reduce the synthesis and secretion of INS. The mt-G mutation also affects the oxidative phosphorylase system of skeletal muscle, the anaerobic glycolysis of sugar is enhanced, the production of lactic acid is increased, the liver gluconogenesis is enhanced, and the blood sugar is raised which lead to diabetes [4,7,8]. However, the gene mutations not always lead to diabetes unless gene directly exposed to the environmental factors, such as obesity, series infection.

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3. Therapeutic method

3.1. Therapy for Type1,2 diabetes

Insulin injection. The insulin can divide into many types from rapid to long term effective insulin from short time to more than 24 hours. Insulin can be injected by pump or injection by patients [9,10].

Pancreas islet insertion (Surgery). Some of the patients can treat by pancreatic islets transplantation which allow the function of insulin secretion like a normal people if there is no immunological rejection.

Stem cell therapy. The main aim of use stem cell is to regenerate and replace the damaged B-cell and may be in the future will become a treatment method.

3.2. Therapy for Type2 diabetes

Biguanides-a kind of drug inhibit liver producing glucose which reduce the blood glucose concentration, lower the sensitivity of liver to the glucagon and increase the sensitivity to the surrounding of the insulin. The kind of drug most suitable for the people who is obesity with diabetes Type 2. The administration way of this kind of drug is mostly with food in batches to control the blood glucose concentration smoothly and the regular detect of blood glucose is also required in order to see if this drug is effective [11].

Sulfonylurea Drug-two generations of drugs and the latest type has a less negative effect. This kind of drug can stimulate the B-cell to excrete insulin like a competitive inhibitor to block the Potassium channel and cell membrane depolarization which activate the Calcium channels open to let Calcium ion into the cell and insulin storage to excrete by exocytosis from cell to increase insulin secretion. The insulin increase reduces amount of glucose secretion and production from pancreas and promote glucose transport to the whole body. This kind of medicine most suitable for the patients with diabetes Type 2 who still has the ability to secrete insulin and has a relatively normal weight. Patients usually take this drug with small amount usually before meals and change the dose dependent on the situation for every 1-2 weeks and can corporate with other kinds of drugs [12,13].

DDP-4 inhibitor-It's a kind of drug through inhibiting DPP-4 which is an enzyme which mainly degrade GLP-1 and GIP which increase the production of insulin and reduce production in glucagon and DPP-4 inhibitor prevent this enzyme from degrading GLP-1 and GIP to increase their half-life period from only a few minutes which make sure the insulin is enough. When patients have a low or normal glucose concentration, there is no effect due to this kind of reaction relies on glucose. It's a kind of drugs has a smaller negative effect compare to the second drug mentioned before and suitable for the patients relative old with a risk of glucopenia or who don't want to use high risk drugs [14,15].

4. Conclusion

The DDP-4 inhibitor binds with the DDP-4 reduce production glucagon and increase production of insulin and more glucose convert into glycogen. However, this kind of drug may respiratory tract infection and rare allergic patients may exist. While Sulfonylurea Drug, there is risk of glucopenia, weight increase, blood platelets decrease and allergic reaction. Biguanides may cause Gastrointestinal adverse reaction and lactic acidosis, but it's quite suitable for obesity patients and doesn't lead to glucopenia. The DDP-4 has a relatively low negative effect and the future development of stem cell therapy may give less negative due to it just replace the damaged B-cell which secrete insulin.

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