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Investigation of Early Diagnosis and Treatment for Diabetes Mellitus Type 1

Jiayong Zhang *

International department, Beijing 101 Middle School, Beijing, 100091, China

* **Corresponding author**: Email: 4john.zhang@beijing101id.com

Abstract: Type I diabetes mellitus (TIDM) is a kind of chronic disease, which caused by autoimmune disorders which result in hyperglycemia and inadequate insulin secretion. Over the past 25 years, knowledge about T1DM has advanced rapidly. These recent progressions in researching T1DM help us better understand the disease in various aspects including genetics, epidemiology, immunology, and pancreatic cancer. Epidemiology, immunology, beta cell phenotype, and disease burden. Why is T1DM thought to be preventable? Several areas of diabetes research have been brought together to suggest therapeutic targets. This article introduces T1DM from its basic definition, world impact, pathology, current existing drug-assistant treatment, and now existing diagnostic tools such as OGTT. This article is based on literature across several fields including Medications, Epidemics, and Statistics. Also, several anti-diabetic drugs that have the potential in participating T1DM treatment as assistance were listed as well. For example, metformin has been recognized as having a huge potential in reducing blood sugar level company with insulin. This article mainly focused on showing information about T1DM and attempting to make several predictions on potential treatments that may be helpful for future patients.

Keywords: Type 1 diabetes; Insulin; Pathology; Diagnostic; Combination treatment.

1. Introduction

TIDM is one of chronic disease, which is characterized by autoimmune destruction and hyperglycemia in pancreas β cells (the ones that produce insulin) basically because of the islets being infiltrated by CD4+, CD8+ T cells, and macrophages. As a common chronic disease, It is approximately 10% of all diabetes cases is T1DM accounts worldwide and is increasing by 2-5% worldwide according to the data from large global epidemiological studies. In the U.S., it affects approximately 1 in 300 people before the age 18. TIDM was not prevailing in Asia, China. In nearly 25 years, even though the cure for T1DM is still difficult, the survival rates and patient health have significantly improved. The development of TIDM is the result of a series of anfractuosity interactions between the islet and immune systems, both innate and adaptive. Also, scientists have investigated antigen-presenting cells (APCs) functions in the presentation process of β-cell peptides. Current research on the efficacy and safety of various hypoglycemic agents suggests that several antidiabetic agents, for example, metformin, pramlintide, and sodium-glucose co-transporter (SGLT) inhibitors may be useful as insulin assistants in treating T1DM. Early diagnosis of diabetes in clinics is usually symptom-based diagnostics targeting characteristics such as recurrent infections, unexplained weight loss, lethargy, thirst, and urination. Patients can even fall into a coma, which is often accompanied by hyperglycemia, in severe cases. In T1DM diagnosis, plasma glucose (PG), or glycosylated hemoglobin [HbA1c] (PG's surrogate), is a key biomarker of diabetes.

2. Pathophysiology of T1DM

2.1. Causes of Type 1 diabetes

Incidence generally increases with age and peaks during adolescence. After puberty, the incidence significantly decreases in young females, while still remains high incidence in male with age 29-35. Large prospective national and international registries have shown that the incidence has increased in most region of the world in recent decades, with a marked increase among young adults.

Studies about analytical epidemiological have shown that the environmental risk factors increase incidence at a young age, including pregnant women, aging, preeclampsia, increased birth weight, cesarean delivery, early introduction of milk proteins, and postpartum growth velocity. The supplementation of optimal vitamin-D is protective after birth immediately. Viruses, which is another environmental risk factor, can induce autoimmunity against β cells, while other stress overloads can affect β cells and accelerate disease progression.

2.2. Immune dysregulation (autoimmunity) of Type I diabetes

Although it was once thought to be an autoimmune disease, while its roots is that T cell-mediated attacks on β cells, which is insulin-producing cell. Nowadays, it is thought to be the result of complex interactions among environmental factors, including the microbiome, and individual genome, metabolism, and immune system, which are vary from case to case. In 1980s, George Eisen Barth developed and published a dexterous conceptual model of TIDM that is still used today. The pathogenesis of TIDM is the result of an anfractuosity interaction between pancreatic beta cells and the innate and adaptive immune systems. Disturbances in β-cells are also thought to play a major role in the development of TID, as is this concept called β-cell suicide. The overexpression of β-cells bearing HLA-I is characteristic of pancreatic sections from cadaveric donors with TIDM. This expression may serve as a kind of homing-signal for cytotoxic T cells. The onset of TIDM is believed to be initiated by the presentation of peptides about β-cell by HLA-I molecule on antigen-presenting cells (APCs). These APC carrying self-antigens

migrates to the pancreas related lymph nodes, where they interact with spontaneous CD4+ T cells and cause spontaneous $CD8^+$ T cells activation. These activated $CD8^+$ T cells migrates to the pancreas islet and lyse the β-cells with autoantigens presented on HLA-I surface molecules. β-cell destruction is exacerbated by the innate immune system including inflammatory cytokines and reactive oxygen released by neutrophils, natural killer cells, and macrophages. This process is exacerbated by deficiencies in regulatory-T cells, which is an important breaker of autoimmunity. Activated $CD4^+$ T cells in the lymph nodes also induce B cells differentiation to plasma cell producing autoantibodies against proteins onβ-cell. These autoantibodies can also be measured in the circulating blood and considered as reliable biomarker of TIDM.

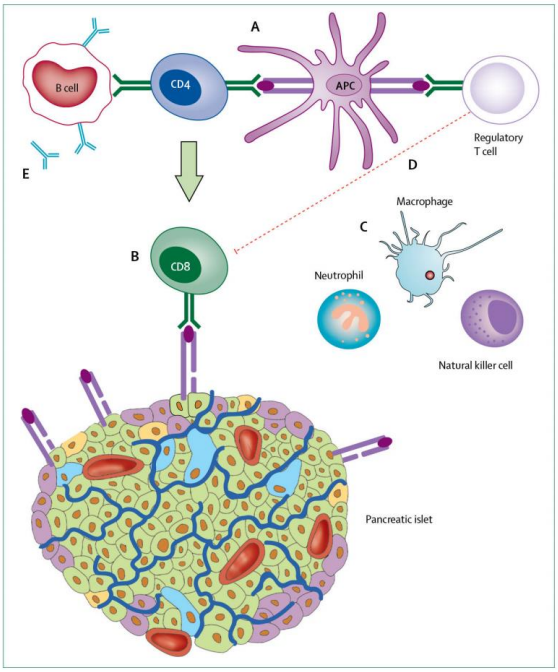

Figure 1. The immunopathogenesis of type I diabetes.

3. Diagnosis of TIDM

3.1. Diagnostic criteria of TIDM

Traditional methods of diagnosing diabetes are usually based on symptoms including frequent thirst and urination, unexplained body weight loss, lethargy, or severe coma with hyperglycemia. The oGTT should only be considered for diagnostic status if the most recent blood glucose level is within an undefined range (i.e., between values that confirm and exclude diabetes). Fasting blood glucose measurements 2-75 hours after oral g-glucose are sufficient for oGTT. In children, oral glucose tolerance is weight dependent and is 1.75 g/kg when using an adult diagnostic croissant.

3.2. Diagnostic requirement of TIDM

The requirements for diagnosing TIDM in individuals bearing many different symptoms and hyperglycemia differ from those of asymptomatic individuals with blood glucose levels slightly above the diagnostic threshold. Severe hyperglycemia occurring with acute infection, traumatic illness, or cardiovascular disease may be transient and should not be considered a diagnosis of diabetes. In asymptomatic subjects, it is essential to add at least one plasma or glucose test results with values in the diabetic range, including fast sample, oral glucose tolerance test (OGTT), or random sample. If these samples do not show confirmed results, it is usually best to continue monitoring until the diagnostic picture is clearer and to repeat the tests regularly. In this case, physicians should consider other factors such as family history, age, obesity, and comorbidities before making a diagnosis and treatment plan. It is important to remember that in asymptomatic individuals, the diagnosis of diabetes should not just base on a single index, such as blood glucose abnormality. Alternatives to the blood glucose test or OGTT have been sought to simplify the diagnosis of diabetes. Glycosylated hemoglobin, which reflects average blood glucose levels over several weeks, is considered one such test. Although its sensitivity and specificity are comparable or nearly comparable to glucose measurements, it is not yet available in many different regions of the world and is not be well standardized, so its application cannot be recommended at this time.

3.3. Diagnostic tools for TIDM

Plasma glucose (PG) including glycosylated hemoglobin is the most specific biomarker of diabetes. It is debatable whether diabetes is an upper limit of the continuous glucose distribution or discrete entity. the diagnostic criteria for diabetes including two indexes: blood glucose associated with the risk of developing microvascular complications that is diabetes-specific, retinopathy, and the population distribution of blood glucose. The balance of the blood glucose levels and the retinopathy have allowed the identification of blood glucose quartiles with increased risk of retinopathy, which is used as thresholds for diabetes diagnosis. A bimodal distribution model of PG, which was first described in 1971 in the Pima Indian Study and subsequently, was verified in other populations with a high prevalence of TIDM, but it has not been observed in all populations. In the DETECT-2 study, the bimodal distribution of FPG was found in 5/27 populations, and a bimodal distribution of 2-h blood glucose (2-h PG) in 8/26 populations.

4. Anti-diabetic drugs

Intensive insulin therapy as a standard of care for patients with TID, which has been shown to reduce perennial microvascular and macrovascular-complications of diabetes. However, the blood glucose remains poorly controlled in most patients with TID. Many people with TID have poor blood sugar control, even with standard treatment, and increasing insulin doses is often with a risk of hypoglycemia and weight gain, which is associated with an increased risk of cardiovascular disease. Those overweight or obese patients with TID is increasing in Western countries, according to the prospective follow-up report of the TIDM and Diabetes Mellitus (DPV) study. The increasing prevalence of obesity is accompanied by insulin resistance in patients with TID, and a combination of insulin and antidiabetic drugs may be the best solution. The safety and efficacy of various hypoglycemic agents including drugs and adipates, have been studied and results suggest that certain antidiabetic agents may be used as adjunctive therapy to insulin in TID. These include pramlintide, metformin, sodium-glucose cotransporter inhibitors (SGLT), agonists against GLP-1 receptor, dipeptidyl peptidase 4inhibitors, thiazolidinediones, and another antidepressants medicine.

4.1. Metformin

The metformin in T1D has been repeatedly recommended, and many studies have shown improved glycemic control, as measured by reduced HbA1c levels. Although metformin did not increase the incidence of severe hypoglycemia, the role of metformin in mild hypoglycemia remains unclear and requires lots of further study by continuous monitoring of blood glucose levels.

Metformin is a kind of oral antidiabetic drug commonly used as a first-line drug for type II diabetes treatment. This effect has multiple mechanisms, including decreased hepatic glucose production, increased muscle glucose uptake, and increased hepatic and muscle glucose sensitivity to insulin. Furthermore, the REMOVAL trial showed that metformin lowered low-density lipoprotein cholesterol and slowed the progression of atherosclerosis, suggesting a role for metformin in the treatment of cardiovascular disease in patients with TID.

4.2. Pramlintide

These physiological roles of amylase were confirmed by the results of a clinical trial in patients with TID, in which subcutaneous administration of pramlintide (a synthetic analog) combined with prandial insulin instead of l-amylase corrected postprandial hyperglycemia. Gastric emptying is thought to slow and improve postprandial blood sugar. tour. In addition, 24-h blood glucose profile and serum fructosamine concentration [10], so pramlintide can improve glycemic control and reduce morbidity in T1D patients without weight gain. At least you can.

4.3. SGLT-2 Inhibition

SGLT-2 inhibitor is a novel antidiabetic drug that were first launched for the treatment of type II diabetes in 2013. Small number of studies suggest that SGLT-2 inhibitors may be effective in addressing some unmet needs in patients with TID [11]. These include increasing mean blood sugar by reducing glucose excursions and postprandial hyperglycemia without increasing hypoglycemia and promoting weight loss by reducing the dose of insulin used in combination with the drug.

5. Conclusions

As a chronic disease, T1DM is an autoimmune disease as well. T1DM can be simply concluded because of the destruction and hyperglycemia in the islets. According to statistics, T1DM is rapidly increasing worldwide, affecting approximately 1 in 300 people under the age of 18 in the U.S. About 10% of all diabetes cases are patients of T1DM, which millions of them spread around the West hemisphere. Despite advances in technology, many patients with T1DM still lack access to the latest treatments because of poor glycemic control and the high cost of even basic therapies, since the treatment could be life-long. Causes of T1DM could be multiple, such as age, bacterial infection, and Beta cell overload. The pathogenesis of T1DM involves a series of complex interactions between pancreas islet β-cells and our immune systems. For example, a recent study revealed the direct cause of T1DM is the infiltration of $CD4^+$, $CD8^+$ T cells, and macrophages to the pancreas can result in hyperglycemia in islets which eventually destroys the normal functioning β-cells. Early diagnosis, such as OGTT manifestation, can help the patient find potential inflation in their pancreas, thus relieving and controlling the extent of T1DM. Also, since the high blood sugar level has been considered a symptom of T1DM, an OTGG test is recommended since the temporary increase in blood sugar can be the result of other infections or normal body regulations. Receiving an OTGG diagnosis is emphasized here since the treatment for curing T1DM could be lifelong and extremely costly to some families, thus the preciseness of the doctor's judgment is important. Besides early diagnosis, several anti-diabetic drugs can be effective assistance company with insulin in curing T1DM, including Metformin, Pramlintide, and treatment of Sodium–Glucose Cotransporter 2 Inhibition, which enable the human body to behave more improved glycemic controls and reduce human blood glucose level in a higher scale. Since anti-diabetic drugs improve the efficiency of insulin, the patient's cost of buying insulin can be lowered. As all being said, the future tendency in treating T1DM is likely to focus on the combination treatment of Insulin and anti-diabetic drugs since insulin is the core in lowering human blood glucose levels and those anti-diabetic drugs are key to improving the efficiency of taking insulin.

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