The treatment of type 2 diabetes

Xuanwen Yin *

United World College of South East Asia (UWCSEA), Singapore

* Corresponding Author Email: yin153742@gapps.uwcsea.edu.sg

Abstract. Type 2 diabetes, also known as a long-term metabolic condition contributed to by multiple factors, including insulin resistance, hyperglycemia, and impaired beta-cell function, which can be caused by both genetics and environment. The disease is prevalent globally; it is projected that people who have type 2 diabetes will increase to 552 million by 2030, which emphasizes the importance of developing effective management strategies. The aim of this essay will be to evaluate current treatments for this type of diabetes, including lifestyle interventions (dietary management, intermittent fasting, and so on), non-pharmacological approaches (psychological therapies like cognitive behavioral therapy), and pharmacologic therapies (including both first-line and second-line therapies like metformin, sulfonylurea, DPP2 inhibitors, etc.) by considering their effects and potential risks. The analysis aims to investigate individualized and targeted treatments by considering factors like age, comorbidities, and so on, in order to minimize complications and achieve permanent health in people with type 2 diabetes.

Keywords: Type 2 diabetes, individualized treatment, non-pharmacological therapies, cognitive behavioral therapy, pharmacologic therapies.

1. Introduction

Type 2 diabetes is a long-term metabolic disorder primarily marked by insulin resistance, hyperglycaemia, and insufficient insulin production [1]. In contrast to type 2 diabetes, type 1 diabetes is an auto-immune condition defined by a lack of insulin production caused by the destruction of pancreatic beta cell. Genetic and environmental influences can also contribute to the onset of type 1 diabetes. Although the causes of the two diabetes are different, they might develop the same features in the long term, such as the presence of insulin resistance and dysfunction in the beta cells. As of 2021, patients with type 2 diabetes were already around 366 million worldwide; the data predicts that it will increase to 552 million by 2030. The disease developed through multiple nonmodifiable risk factors such as age, genetics, etc., and also through modifiable factors (Poor diet habits, physical inactivity, and tobacco use are all included). Evidence from diabetes prevention programs shows that weight management would be more effective compared with using insulin-sensitizing drugs in terms of reducing long-term risk. In response to the global burden, many countries are expected to improve weight management, such as taxes on sugar-sweetened beverages, although the long-term impact of these policies remains uncertain [2]. The level of blood glucose is regulated by insulin, which plays an essential role in this process. In type 2 diabetes patients, impaired feedback between insulin action and secretion leads to high blood glucose. Insulin is produced insufficiently during beta-cell dysfunction, which might be caused by genetic and environmental factors. Obesity, which often leads to hyperglycaemia and hyperlipidaemia, demonstrates that beta cells are subjected to toxic pressures like inflammation and ER stress, influenced by the patient's genetic susceptibility. This can result in the loss of islet integrity, ultimately leading to beta-cell failure and worsening hyperglycaemia. Moreover, insulin resistance (a reduced response of insulin-sensitive tissues to insulin) would cause an increase in glucose level; less glucose would be absorbed by the liver for storage and muscle for cell respiration [3].

Due to the variety of type 2 diabetes, it is essential to explore tailored, specific, and targeted therapies. For instance, the classification of patients' age is a key factor. Compared with the elderly, younger patients have a relatively higher risk of complications and death. However, the risk of comorbidities and hypoglycaemia in the elderly becomes more complicated during treatment. Therefore, treatment for different types of patients should be individualized and have broader

glycemic targets. By 2024, treatments for type 2 diabetes are evolving toward individualized care—shifting from solely controlling blood glucose to setting personalized glucose and weight goals, prioritizing cardiovascular protection, minimizing hypoglycaemia risk and kidney complications, and addressing each patient's unique needs. At the same time, the availability and cost of drugs are also of vital importance; the goal is to develop accessible drugs that serve patients and aim to improve their quality of life [4]. This essay aims to analyse and evaluate current treatments for type 2 diabetes, emphasizing the importance of individualization, to improve long-term health outcomes and quality of life.

2. Lifestyle and Non-Pharmacological interventions

2.1. Dietary Modifications

Obesity is one of the significant factors that often lead to hyperglycaemia and hyperlipidaemia, which would eventually lead to the failure of beta cells and worsening hyperglycaemia. Hence, weight management and dietary modifications are essential for minimizing the long-term risk of type 2 diabetes. Obesity and metabolic syndrome, also known as MetS, combine a series of metabolic disorders such as central obesity, insulin resistance, hypertriglyceridemia, and so on. It is also considered a main risk factor in the 21st-century epidemic of type 2 diabetes and heart disease. The factors contributing to MetS can be both modifiable and non-modifiable. Fortunately, individuals can lower their risk of death by controlling their weight, adhering to a nutritious diet, and engaging in physical exercise. Intermittent fasting is an alternative to continuous caloric restriction (which involves lowering overall caloric intake while maintaining adequate nutrition), which requires the eating pattern to be with little or no consumption of calories. To investigate whether fasting has an effect on insulin resistance and prediabetes, Halberg et al. conducted an intermittent fasting experiment on eight healthy men, that is, fasting for up to 20 hours every other day. The results indicated that, although there was no obvious change in body weight, insulin sensitivity was improved, and the rate of insulin-mediated glucose extraction increased significantly. Therefore, this experiment demonstrated the potential of intermittent fasting to enhance the rate of insulin-mediated glucose absorption.

2.2. Physical Activity

In addition, enhancing physical exercise helps regulate blood sugar levels and prevent their deterioration. Studies show that individuals at risk for type 2 diabetes can be able to lower their risk by 45% over a period of 2 years or longer by exercising at moderate or vigorous intensity for a total of 150 minutes per week. Examples of aerobic exercises, such as running, walking, and cycling, can enhance insulin sensitivity and vascular function while also reducing body fat. Studies show that if one can consistently engaging in 150 minutes of moderate to vigorous aerobic exercise per week, distributed at least three days per week, the positive impact on insulin sensitivity will last for 48 hours [5].

2.3. Behavioral and Psychological Support

Diabetes also interacts with other diseases such as depression and anxiety (in terms of biological and psychosocial aspects, etc.), complicating its treatment. Therefore, cognitive behavioral therapy (CBT) is also a method for treating diabetes, but it focuses more on the psychological aspect, helping to improve self-care ideas and beliefs and assisting in improving patients' behavioral disorders and blood sugar control. Motivational interviewing (MI), on the other hand, is used to enhance patients' engagement and enthusiasm. According to research on CBT, researchers recruited 20 young participants who underwent six CBT and MI sessions within three months, completing a series of assessments (including self-efficacy, generalized anxiety, depression, etc.). The results showed that among the 14 participants who completed the study, the number of diabetes distress and generalized anxiety disorders, and so on, was significantly reduced. Therefore, this experiment demonstrated the

effectiveness of CBT and MI and is conducive to improving the mental health and self-management of diabetic patients [6].

3. Pharmacologic Therapies for Glycemic Control

3.1. First-Line Therapy

In addition to lifestyle and diet control, pharmacologic therapy is also a way for glycemic control. One type of treatment is metformin, a first-line therapy due to the effects on glucose control. Metformin could lower blood sugar levels in the human body while also affecting muscle and gut bacteria [7]. Specifically, metformin lowers glucose output in the liver by reducing gluconeogenesis and glycogenolysis, which is the breakdown of glycogen. The mechanism of metformin works in several ways: by controlling enzyme activity, reducing the liver's uptake of materials that are needed for glucose, interfering with glucagon signaling, and so on [8]. Metformin could help increase patients' insulin sensitivity and lower fasting insulin levels for people who have abnormal glucose metabolism. In addition, metformin would have stronger glucose control if combined with other drugs, such as glibenclamide, troglitazone, and so on. Metformin is also appropriate for women who get pregnant with type 2 diabetes to use; for PCOS, metformin can reduce more body weight than using rosiglitazone. However, it is worth noting that metformin may still cause some side effects. For instance, it may cause lactic acidosis, which could lead to symptoms such as dizziness, drowsiness, breathing difficulties, and heart problems in patients. Although metformin itself does not cause hypoglycaemia, if taken together with other medications, it may lead to symptoms such as hypoglycaemia [9].

3.2. Second-Line and Add-On Therapies

Many second-line therapies, such as sulfonylurea, can be used to treat type 2 diabetes when first-line therapies like metformin no longer work. Sulfonylurea is an oral drug for diabetes that stimulates insulin secretion by shutting down potassium channels in pancreatic beta cells. However, sulfonylurea might cause hypoglycaemia since it is a glucose-independent stimulation of insulin secretion; in severe cases, it can develop into loss of consciousness and coma, with a risk three times that of other drugs [10]. Another treatment is thiazolidinediones drugs (TZDs), which are the only drugs that mainly work by improving insulin sensitivity. Nevertheless, due to concerns regarding side effects and adverse events, these medications are presently not utilized. Troglitazone, rosiglitazone, and pioglitazone are examples of TZDs, while troglitazone left the market in 2000 due to concerns of liver problems, which can be due to hepatotoxic reactive metabolites. TZDs may also cause water retention (peripheral edema of the lower extremities), and the prevalence rate can be as high as 18% when used in combination with insulin. If it is too severe, it can also lead to heart failure. Therefore, TZDs are contraindicated in patients with heart failure [11]. Compared with TZDs, dipeptidyl peptidase-4 (DPP4) inhibitors are and more effective and can be used in combination with another basic insulin. They work by boosting insulin release in response to glucose and controlling glucagon production. Additionally, they can lower HbA1c by 0.6-0.8% and do not cause weight gain or extra risk of hypoglycemia. Sodium glucose cotransporter 2 (SGLT2) inhibitors are used to block SGLT2, it is primarily located in the proximal tubule of the human kidney and is responsible for around 90% of glucose reabsorption. Inhibitors can cause more glucose and sodium to be excreted in urine to balance blood sugar level; they can also help promote water loss (osmotic diuresis) and reduce body weight and blood pressure. Moreover, SGLT2 inhibitors can also benefit the cardiovascular system and kidney in patients who have type 2 diabetes [12]. Since type 2 diabetes raises the risk of heart related disease—a major factor contributes to death in these patients—it is crucial to consider cardiovascular health when developing treatments. Atherosclerotic cardiovascular disease (ASCVD) is one of the diseases that many type 2 diabetes patients have in common. Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are a treatment that has been found to minimize the risk of CV diseases by having several mechanisms that are thought to protect the heart and blood vessels through

targeted modulation of mediators of large and small vessel function as well as blood flow regulation GLP-1 RAs can also improve blood pressure, cholesterol, and triglycerides [13]. Last but not least, insulin therapy remains the most commonly used treatment for patients who have type 2 diabetes. However, primary care providers often find it challenging to manage insulin initiation and titration. The American Diabetes Association recommends that if a patient's hemoglobin A1C does not improve following three months of triple combination therapy, that is, for patients whose blood sugar levels are still above the normal range, the initiation of basal insulin could increase by 10 –15% once or twice weekly from the original 10 units/day. If the patient still fails to reach the target after adjusting insulin initiation and titration, treatment can be carried out by injecting a rapid-acting insulin injection twice or more before meals or by adding GLP-1 receptor agonists and other methods.

4. Conclusion

In conclusion, type 2 diabetes is a chronic disease caused by factors such as insulin resistance, beta cell dysfunction, and lifestyle. Current evidence highlights the importance of lifestyle improvement and weight management in the treatment of this disease. Countries can reduce the long-term risk of diabetes by formulating strategies, such as imposing taxes on sugary beverages and so on. In addition, discussions on non-pharmacological interventions also include intermittent fasting, enhanced physical exercise, cognitive behavioral therapy, and other methods, aiming to enhance insulin sensitivity and regulate blood sugar levels. Moreover, due to the heterogeneity of type 2 diabetes, it is crucial to study personalized and targeted treatments. The essay discussed pharmacologic therapies for glycemic control, including metformin as a first-line therapy, sulfonylureas as second-line treatments, thiazolidinediones, DPP-4 inhibitors, SGLT2 inhibitors, and the most common insulin therapies. Furthermore, the essay not only summarizes the characteristics and advantages of various drug types but also considers their potential risks and impacts.

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