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Medicine

FUTURE IN DIABETES TREATMENT MEDICATION

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ABSTRACT **Background:** Diabetes, a chronic metabolic disorder marked by impaired insulin production or utilization, has reached epidemic proportions around the worlds, AMPK (activated protein kinase) appears to be important. The role of AMPK and potential activators is being studied extensively, and this appears to be the most exciting line of inquiry into a possible cure for T2DM at the moment. **Methodology:** Every three months, patients' glycemic targets are measured to see if they have been met and maintained. **Results:** The treatment plan, depending on the type of diabetes. Eating a healthy diet, maintaining a healthy weight, and engaging in regular physical activity are all important components of diabetes management. **Conclusions:** Diabetic treatment options should be individualized based on patient characteristics such as degree of hyperglycemia, presence of co-morbidities, and patient preference and ability to access treatments; and treatment properties such as effectiveness and durability of lowering blood glucose, risk of hypoglycemia, effectiveness in reducing diabetes complications, effect on body weight, side effects, and contraindications. Also, novel biological safety and effective agents that will improve the quality of life of diabetic patients are being developed in the near future.

KEYWORDS : Diabetes treatment, Future medication of diabetes, AMPK, Diabetes medication, Future treatment of diabetic mellitus.

INTRODUCTION

Diabetes, a chronic metabolic disorder marked by impaired insulin production or utilisation, has reached epidemic proportions around the world. Millions of people are affected by the disease, putting a significant strain on healthcare systems and economies. Diabetes is associated with a variety of complications that have a significant impact on quality of life and increase morbidity and mortality rates among those affected.[1]

The A1C measurement, continuous glucose monitoring (CGM) using time in range (TIR) and/or glucose management indicator (GMI), and blood glucose monitoring (BGM) are used to assess glycemic control. To date, A1C has been the metric used in clinical trials to demonstrate the benefits of improved glycemic control. "Diabetes Technology") is a useful tool for diabetes self-management, which includes meal planning, physical activity, and medication adjustments, especially for people who use insulin.[2]

Type 2 diabetes mellitus (T2DM) is the most common type of diabetes, accounting for roughly 90% of all diabetes cases. It is caused by a combination of insulin resistance and insufficient insulin secretion. T2DM is frequently linked to lifestyle factors such as sedentary behaviour, poor dietary habits, and obesity. Type 1 diabetes (T1DM) is an autoimmune disease that causes the destruction of insulin-producing beta cells in the pancreas, resulting in absolute insulin deficiency. Other types of diabetes, such as gestational diabetes, pose serious health risks, especially to pregnant women and their children.[3]

Diabetes complications are numerous and affect a variety of organ systems. Diabetes' chronic hyperglycemia causes the development of microvascular and macrovascular complications. Microvascular complications primarily affect small blood vessels, such as those in the eyes (diabetic retinopathy), the kidneys (diabetic nephropathy), and the nerves (diabetic neuropathy). Macrovascular complications affect the body's large blood vessels and increase the risk of cardiovascular diseases like coronary artery disease, stroke, and peripheral arterial disease.[4]

Diabetes and its complications necessitate a multifaceted approach that includes lifestyle changes, glucose-lowering medications, and targeted interventions to address specific complications. While conventional diabetes management has advanced, there is a growing interest in investigating alternative therapeutic strategies that offer

improved efficacy, fewer side effects, and disease-modifying potential.[5]

Literature Review

Diabetes mellitus is a chronic metabolic disorder characterised by hyperglycemia, underutilization of blood glucose, and defects in macronutrient metabolism such as carbohydrates, fat, and protein as a result of insulin action disruption. Type 1 diabetes is caused by insulin deficiency caused by pancreatic beta-cell failure. As a result, diabetic patients require exogenous insulin injections, whereas insulin-independent patients do not respond to insulin and can thus be managed through lifestyle changes.

Effective disease-modifying therapies aimed at preserving endogenous insulin production could not only improve these outcomes, but also, if administered early enough in the disease's course, eliminate the need for insulin replacement.[6]

Diabetes Mellitus Pathophysiology, Type 1 And Type 2.

Type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM) are both characterised by abnormally high blood glucose levels, and until the 1930s, when 'insulin-sensitive' and 'insulin-insensitive' diabetes were distinguished, all patients with diabetes were thought to have a shortage of insulin production.

The pathophysiology of the two diseases has been extensively researched since then, and T1DM is now relatively well understood. To summarise, the patient's immune system attacks and destroys beta cells in the pancreatic islets, resulting in insulin deficiency. The causes of the immune response are unknown, but they are thought to be both genetic and environmental.[7]

T2DM pathophysiology is still poorly understood today. Most patients have insulin resistance when they are diagnosed: the pancreas produces insulin, but the body cannot use it effectively. The pancreas initially compensates by producing more insulin, and patients have increased beta-cell mass. Insulin production will eventually decline, typically several years after diagnosis, with a corresponding drop in beta-cell mass, and many people with T2DM will eventually require insulin. Although the underlying cause is unknown, it is believed that liver, fat, and muscle cells, in addition to pancreatic beta cells, all play a role.[8]

Excess glucose binds to free amino groups in tissue or blood proteins and body fluid in the chronic state, interfering with their functions. This nonenzymatic reaction produces advanced glycosylation end products (AGEs). The glycation reaction alters the structure and function of biomolecules, particularly proteins. Diabetes complications are known to be exacerbated by AGE formation.

Diabetes can be treated and controlled in a variety of ways, including the administration of insulin or hypoglycemic drugs, dietary control, and exercise. Furthermore, chemical drugs have low long-term efficacy, are prohibitively expensive, and have severe side effects, such that some patients cannot tolerate prolonged treatment or high dosages of these drugs. Herbal medicines, on the other hand, are regarded as potential sources of medication due to their beneficial effects, negligible side effects in clinical trials, and low cost. [9]

Although insulin pump technology has advanced, today's pumps deliver insulin subcutaneously, and the delay while insulin is absorbed into the bloodstream limits software's ability to accurately regulate blood glucose. Intravenous insulin delivery has been hampered by catheter complications, and surgically implanted pumps are costly. None of these technological challenges are insignificant, but given the rate of technological advancement, we can expect more practical options for patients within the next ten years.[10]

Pharmacological Solutions

Due to its relatively modest glucose-lowering effects, bromocriptine is likely to be used in only a minority of patients, but it may spark new avenues of research for diabetes treatments, as is always the case when new drug classes are identified.

Metformin is also associated with weight loss, though the amount lost is insufficient to meet FDA weight loss drug criteria (at least 5% of body weight). Metformin is now recommended by guidelines for preventing or delaying diabetes in people with elevated glucose levels and a BMI greater than 35 kg/m2 [11]

AMPK (activated protein kinase) appears to be important. The role of AMPK and potential activators is being studied extensively, and this appears to be the most exciting line of inquiry into a possible cure for T2DM at the moment.

Previous study has revealed the role of AMPK signalling in improving insulin sensitivity for diabetic patients. Furthermore, AMPK upregulation protects cells from stress and cell death.[12]

We often think of glucose as the fuel for cells, but it is only one of the fuels used to produce adenosine triphosphate (ATP), the actual energy source in every cell. Individual cells' energy balance is maintained by the enzyme AMP-activated protein kinase (AMPK), which is activated when the ATP-to-adenosine monophosphate (AMP) ratio falls. Because AMPK is the'master switch' that regulates energy intake and expenditure, it is a potential therapeutic target in T2DM patients. If AMPK can be activated, the resulting signaling pathways could be manipulated to restore energy balance, making people more fit and less likely to develop insulin resistance, without requiring a reduction in energy intake or weight loss.[13]

Some of these theoretical effects are already being confirmed by studies of AMPK activators. Sedentary mice, for example, were shown to improve treadmill performance when given an oral AMPK agonist called AICAR. The polyphenol resveratrol, an AMPK modulator found in red wine, appears to protect mice from diet-induced obesity and insulin resistance. It has also been shown to mimic the effects of calorie restriction in obese people.[14]

Different complexes of AMPK localise to the liver, adipocytes, or skeletal muscles, and a drug targeting these complexes with high specificity could selectively restore energy balance without harming other tissues.

AMPK activation (green lines) stimulates energy-generating pathways while inhibiting energy-consuming pathways (red lines) in several tissues. AMPK activation increases glucose uptake and fatty acid oxidation in skeletal muscle and the heart. AMPK activity in the liver inhibits fatty acid and cholesterol synthesis. AMPK activation also reduces lipolysis and lipogenesis in adipose tissue. AMPK activation in pancreatic -cells is linked to decreased insulin secretion. AMPK activation increases food intake in the hypothalamus.[15]

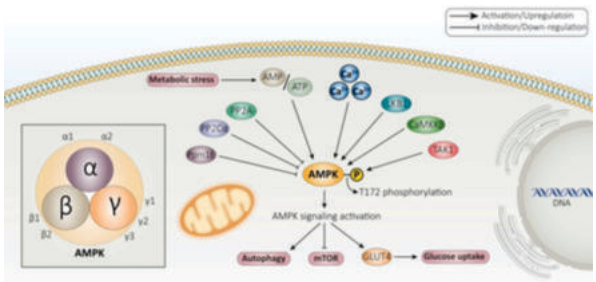

Fig (2): AMPK Signaling Activation

Phlorizin was later discovered to be a non-specific inhibitor of sodium-glucose cotransporter (SGLT) proteins, and several different types of SGLT proteins have been identified since then. These proteins perform their functions independently of insulin. Inhibiting these proteins was found to result in changes that favourably improve carbohydrate metabolism, making it an appealing concept for diabetes treatment.

Sodium-glucose cotransporter 1 (SGLT1) proteins are glucose transporters with high affinity but low capacity. They are found in the small intestine as well as the kidney's proximal tubule. Inhibiting SGLT1 can cause gastrointestinal problems, including severe diarrhea. The SGLT1 proteins in the kidney's proximal convoluted tubule account for less than 10% of filtered glucose reabsorption. The role of SGLT1 proteins in the intestine is still unknown, but evidence from dual inhibitors suggests that they may play a role.[16]

Because of their weight loss and antihypertensive properties, SGLT2 inhibitors may be a useful option in obese and hypertensive patients.

Insulin

Insulin is used to treat patients with all types of diabetes. Human insulin preparations (both NPH and regular insulin) do not mimic

endogenous insulin secretion (both basal and postprandial). Then insulin analogues were created (aspart, lispro, glulisine, detemir, glargine, degludec, and U-300). They have improved the flexibility and effectiveness of diabetes management. Both are present in very rapid-acting insulin analogues: For pre-meal coverage, it is faster and has a shorter duration of action than regular insulin, whereas long-acting analogues have a longer duration of action, allowing once-daily dosing; it also has less day-to-day variability.Insulin degludec reduced HbA1c as well as insulin glargine, with a lower risk of confirmed and nocturnal hypoglycemia.[17]

Biological Solutions

In recent years, natural products and their derivatives have received a lot of attention as potential therapeutic agents for diabetes and its complications. These compounds, derived from various natural sources such as plants, animals, fungi, and microorganisms, provide a wide range of bioactive constituents with diverse pharmacological activities. Using natural products in diabetes research not only provides a rich source of novel compounds, but it also capitalises on traditional medicinal knowledge passed down through generations. [18]

Natural products frequently have pleiotropic effects, which means they can target multiple pathways at the same time. This trait is especially important in the complicated pathophysiology of diabetes, where dysregulation occurs at multiple levels. Natural products and their derivatives have the potential to provide comprehensive and synergistic benefits in diabetes management by addressing multiple underlying mechanisms at the same time.[19]

Polyphenols derived from Ochrophyta/Phaeophyceae (brown algae), including flavonoids and phenolic acids, have sparked interest due to their potential anti-diabetic properties. These compounds have antioxidant and anti-inflammatory properties, which can aid in the reduction of oxidative stress and chronic inflammation associated with diabetes. Some brown algae-derived polyphenols, such as phlorotannins, have been shown to inhibit -glucosidase and -amylase enzymes, resulting in lower glucose absorption and better glycemic control.[20]

Fucoxanthin, a carotenoid found in brown algae, has shown promise in diabetes management by improving insulin sensitivity by stimulating glucose uptake in skeletal muscle cells and adipocytes. Furthermore, certain algae-derived pigments have antioxidant and anti-inflammatory properties, suggesting that they may play a role in reducing diabetes-related complications.

Algae-derived compounds have been found to influence pancreatic -cell insulin secretion. Some compounds have been shown to increase insulin secretion in response to elevated glucose levels, assisting in the maintenance of proper glucose homeostasis. This effect is especially beneficial in people who have impaired insulin secretion, such as people with type 2 diabetes.[21]

The scientific name "Anethum" is derived from the Greek word "anethon" and the colloquial name "dill."

Fig. (3): Plant And Seed Of Dill

In diabetic models, administration of various AG seed and leaf extracts, as well as its essential oil, significantly reduced triglycerides, total cholesterol, low-density lipoprotein cholesterol (LDL-C), very-low-density lipoprotein cholesterol (VLDL-C), and glucose levels, while increasing HDL-C levels. Many studies, on the other hand, have found that AG has hypoglycemic and antioxidant activity. AG's antioxidant activity is due to the presence of phenolic proanthocyanidins and flavonoids in its constituents. [22]

Methodology

Every three months, patients' glycemic targets are measured to see if they have been met and maintained. A 14-day CGM assessment of TIR and GMI can be used in clinical management as a surrogate for A1C.

Continuous glucose monitoring is an electronic system that records glucose levels from a sensor placed under the skin every few minutes. The system can send alerts when levels are too high or too low, and information can be transmitted to a mobile device such as a phone.

In addition measuring of blood pressure and cholesterol-lowering medications, as well as low-dose aspirin, to help prevent heart and blood vessel disease.[23]

A random blood sugar test was performed. A blood sample will be drawn at random. A blood sugar level of 200 milligrammes per deciliter (mg/dL) — 11.1 millimoles per litre (mmol/L) — or higher, regardless of when you last ate, indicates diabetes.

A fasting blood sugar test is performed. After you haven't eaten anything the night before (fast), a blood sample will be taken. Fasting blood sugar levels of less than 100 mg/dL (5.6 mmol/L) are considered normal. Prediabetes is defined as fasting blood sugar levels ranging from 100 to 125 mg/dL (5.6 to 6.9 mmol/L). Diabetes is diagnosed when your blood sugar level is 126 mg/dL (7 mmol/L) or higher on two separate tests.[24]

Test for glucose tolerance. You must fast overnight for this test. The fasting blood sugar level is then determined. Then you drink a sugary liquid, and your blood sugar levels are checked every two hours for the next two hours.

Normal blood sugar levels are less than 140 mg/dL (7.8 mmol/L). After two hours, a reading of more than 200 mg/dL (11.1 mmol/L) indicates diabetes. Prediabetes is defined as a blood sugar level between 140 and 199 mg/dL (7.8 mmol/L and 11.0 mmol/L).

RESULTS

Blood sugar monitoring, insulin, and oral medications may all be part of treatment plan, depending on the type of diabetes. Eating a healthy diet, maintaining a healthy weight, and engaging in regular physical activity are all important components of diabetes management.

Type 2 diabetes management entails the following steps:

- Eating well is important.
- Exercise on a regular basis.
- Weight reduction.
- Diabetes medication or insulin therapy could be used.
- Monitoring of blood sugar levels.

Physical Exercise

Exercise is essential for losing or maintaining a healthy weight. It also aids in blood sugar control. Before beginning or changing your exercise programme, consult with your doctor to ensure that the activities are safe for you.

Aerobic activity. Choose a fun aerobic exercise like walking, swimming, biking, or running. Adults should aim for at least 150 minutes of moderate aerobic exercise per week, or 30 minutes of moderate aerobic exercise on most days of the week.

Resistance training. Resistance exercise improves your strength, balance, and ability to perform daily activities more easily. Weightlifting, yoga, and callisthenics are examples of resistance exercises. Adults with type 2 diabetes should aim for two to three resistance exercise sessions per week.

Limit your inactivity. Long periods of inactivity, such as sitting at a computer, can be broken up to help control blood sugar levels. Every 30 minutes, take a few minutes to stand, walk around, or do some light activity.

Weight Reduction

Weight loss improves control of blood sugar, cholesterol, triglycerides, and blood pressure.

Hyperglycemic hyperosmolar nonketotic syndrome (HHNS). This life-threatening condition includes a blood sugar reading higher than 600 mg/dL (33.3 mmol/L).

DISCUSSION

Diabetes treatments for both type 1 and type 2:
nsulin injections or the use of an insulin pump, frequent blood sugar checks, and carbohydrate counting are all part of type 1 diabetes

treatment. Pancreas or islet cell transplantation may be an option for some people with type 1 diabetes.

Treatment for type 2 diabetes consists primarily of lifestyle changes, blood sugar monitoring, and the use of oral diabetes medications, insulin, or both.[25]

Physical activity and exercise are important components of diabetes treatment. Promoting exercise within a specific plan provides numerous benefits in general: Increased insulin sensitivity in tissues, benefits in lipid profile and blood pressure, weight maintenance or loss, cardiovascular benefits, better quality of life, psychological well-being, and depression improvement. Both aerobic and resistance exercises have demonstrated benefits in people with diabetes through increased glucose uptake and decreased insulin resistance.[26]

CONCLUSIONS

Diabetic treatment options should be individualised based on patient characteristics such as degree of hyperglycemia, presence of co-morbidities, and patient preference and ability to access treatments; and treatment properties such as effectiveness and durability of lowering blood glucose, risk of hypoglycemia, effectiveness in reducing diabetes complications, effect on body weight, side effects, and contraindications. Also, novel biological safety and effective agents that will improve the quality of life of diabetic patients are being developed in the near future.

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