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Review Article

A REVIEW ON TREATMENT AND PREVENTION OF DIABETES MELLITUS

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ABSTRACT

Diabetes mellitus is an endocrinological and metabolic disorder with an increasing global prevalence and incidence. High blood glucose levels are symptomatic of diabetes mellitus as a consequence of inadequate pancreatic insulin secretion or poor insulin-directed mobilization of glucose by target cells. Diabetes mellitus is aggravated by and associated with metabolic complications that can subsequently lead to premature death. The diagnosis of diabetes in an asymptomatic subject should never be made on the basis of a single abnormal blood glucose value. For the asymptomatic person, at least one additional plasma/blood glucose test result with a value in the diabetic range is essential, either fasting, from a random (casual) sample, or from the oral glucose tolerance test (OGTT). If such samples fail to confirm the diagnosis of diabetes mellitus, it will usually be advisable to maintain surveillance with periodic re–testing until the diagnostic situation becomes clear. In these circumstances, the clinician should take into consideration such additional factors as ethnicity, family history, age, adiposity, and concomitant disorders, before deciding on a diagnostic or therapeutic course of action. An alternative to blood glucose estimation or the OGTT has long been sought to simplify the diagnosis of diabetes. Diabetes is a metabolic disorder that can be prevented through lifestyle modification, diet control, and control of overweight and obesity. Education of the populace is still key to the control of this emerging epidemic. Novel drugs are being developed, yet no cure is available in sight for the disease, despite new insight into the pathophysiology of the disease.

Keywords: Diabetes mellitus, Insulin, Blood glucose levels, Hyperglycemia, Type1 diabetes, Type 2 diabetes.

INTRODUCTION

Diabetes

Diabetes mellitus is a metabolic disorder characterized by elevated blood glucose levels and disturbances in carbohydrates, fats and protein metabolism.

Diabetes occurs either because of a lack of insulin or because of the presence of factors that oppose the action of insulin. The result of the insufficient action of insulin is an increase in blood glucose concentration (hyperglycemias). Many other metabolic abnormalities occur, notably an increase in ketone bodies in the blood when there is a severe lack of insulin [1, 2].

Diabetes mellitus, often simply referred to as diabetes, is a group of metabolic diseases in which a person has high blood glucose, either because the body does not produce enough insulin, or because cells do not respond to the insulin that is produced. This high blood glucose produces the classical symptoms of polyuria (frequent urination), polydipsia (increased thirst) and polyphagia (increased hunger) [3, 4].

Types of diabetes

There are three main types of diabetes.

Type 1 diabetes mellitus

Type 1 diabetes mellitus (also referred as Insulin-Dependent Diabetes Mellitus, IDDM or juvenile diabetes) is characterized by loss of the insulin-producing beta cells of the islets of Langerhans in the pancreas leading to insulin deficiency. It can be immune-mediated or idiopathic. Type 1 diabetes mellitus usually manifests in childhood or adolescence, and the patients require exogenous insulin because of the destruction of insulin producing β-cells in the pancreas by an autoimmune reaction. Most affected people are otherwise healthy and of a healthy weight when onset occurs. Sensitivity and responsiveness to insulin are usually normal, especially in the early stages [5, 6].

Type 2 diabetes mellitus

Type 2 diabetes mellitus (also referred as Non-Insulin-Dependent Diabetes Mellitus, NIDDM or adult-onset diabetes) is characterized by insulin resistance (a condition in which cells fail to use insulin properly, sometimes combined with an absolute insulin deficiency). The defective responsiveness of body tissues to insulin is believed to involve the insulin receptor. Type 2 diabetes mellitus is the most common type. Type 2 diabetes mellitus ranges from those with predominant insulin resistance associated with relative insulin deficiency to those with a predominantly insulin secretory defect with insulin resistance. The prevalence of type 2 diabetes mellitus begins to rise in early middle age and increases along with age. Exogenous insulin is not always a necessity for these patients because insulin production is frequently high compared to that of type 1 diabetes mellitus. In the early stage of type 2 diabetes mellitus, the predominant abnormality is reduced insulin sensitivity. At this stage, hyperglycemia can be reversed by a variety of measures and medications that improve insulin sensitivity or reduce glucose production by the liver [7].

Gestational diabetes mellitus

Gestational diabetes mellitus (GDM) is seen in pregnancy when women, who have never had diabetes before, have a high blood glucose level during pregnancy. It may precede the development of type 2 diabetes mellitus. It resembles type 2 diabetes mellitus in several respects, involving a combination of relatively inadequate insulin secretion and responsiveness. It occurs in about 2-5% of all pregnancies and may improve or disappear after delivery [8, 9].

Table 1: Difference between type1 and type2 diabetes

Type 1 diabetes mellitus	Type 2 diabetes mellitus
Inflammatory reaction in islets	No insulitis
Islets of β-cells destroyed	β-cells function
Islet cell antibodies	No islet cell antibodies
HLA-related	Not HLA-related
Not directly inherited	Strong genetic basis (some cases)

Symptoms of diabetes

- Polyuria (frequent urination)

- Blurred vision
- Erectile dysfunction
- Pain or numbness in the feet or hands
- Bladder, kidney, skin, or other infections, fatigue and weight loss
- Polyphagia (increased hunger)
- Polydipsia (increased thirst) [10, 11]

Diagnosis

Diabetes mellitus is characterized by recurrent or persistent hyperglycemia, and is diagnosed by demonstrating any one of the following:

- Fasting plasma glucose level ≥ 7.0 mmol/l (126 mg/dL).
- Plasma glucose ≥ 11.1 mmol/l (200 mg/dL) two hours after a 75 g oral glucose load as in a glucose tolerance test.
- Hyperglycemia and casual plasma glucose 11.1 mmol/l (200 mg/dL).
- Glycated hemoglobin (Hb A1C) ≥ 8.5%.

A positive result, in the absence of unequivocal hyperglycemia, should be confirmed by a repeat of any of the above-listed methods on a different day. It is preferable to measure a fasting glucose level because of the ease of measurement and the considerable time commitment of formal glucose tolerance testing, which takes two hr to complete and offers no prognostic advantage over the fasting test. According to the current definition, two fasting glucose measurements above 126 mg/dL (7 mmol/l) are considered diagnostic for diabetes mellitus. People with fasting glucose levels from 100 to 125 mg/dL (5.6-8.9 mmol/l) are considered to have impaired fasting glucose. Patients with plasma glucose at or above 140 mg/dL (7.8 mmol/l), but not over 200 mg/dL (11.1 mmol/l), two hr after a 75 g oral glucose load are considered to have impaired glucose tolerance (table 2). Of these two pre-diabetic states, the latter, in particular, is a major risk factor for progression to full-blown diabetes mellitus as well as cardiovascular disease [12-14].

Table 2: Diabetes criteria

Condition	Glucose after 2 h mmol/l (mg/dL)	Fasting glucose mmol/l (mg/dL)
Normal	<7.8 (<140)	<8.1 (<110)
Impaired fasting glycaemia	<7.8 (<140)	≥ 8.1(≥110) & <7.0(<126)
Impaired glucose tolerance	≥7.8 (≥140)	<7.0 (<126)
Diabetes mellitus	≥11.1 (≥200)	≥7.0 (≥126)

Table 3: Medications for type 2 diabetes

Drug	Comments
Secretagogues: **Sulfonylureas-** **1st generation** e. g Tolbutamide Tolazamide Chloropropamide	• These medications have been largely replaced by 2nd generation sulfonylureas. Because they are cleared hepatically, these medications should be avoided in patients with abnormal liver function.
Secretagogues: **Sulfonylureas-** **2nd generation** e. g Glyburide Glipizide Glimepiride	• Consider using in patients starting oral therapy who have normal hepatic/renal function and in patients already on an insulin sensitizer who need additional glucose lowering. • Avoid using in patients with impaired renal function (creatinine clearance<60 ml/min) or who are elderly. There is a risk of hypoglycemia for those who skip meals.
Secretagogues: **Nonsulfonylurea** e. g. Repaglinide Nateglinide	• Consider using in patients with modest postprandial hyperglycemia and in patients who have the irregular timing of meals. These agents can be used in patients with renal impairment.
Biguanides: e. g. Metformin	• Good first-line agent for overweight or obese patients. Consider using in patients already on a secretagogue who need additional glucose lowering. • Avoid in patients with renal or hepatic impairment or class III or IV heart failure.
Alpha-glucosidase inhibitors: e. g. Acarbose Miglitol	• Consider using in patients who have primarily postprandial hyperglycemia. • Avoid in patients with gastrointestinal disease or hepatic or renal insufficiency. • May be used in combination with sensitizers or sulfonylurea secretagogues but not with non sulfonylurea secretagogues.
Thiazolidinediones: e. g. Rosiglitazone Pioglitazone	• These agents are used as monotherapy in patients on a secretagogues or metformin. • Avoid in patients with abnormal hepatic function or class III or IV heart failure. • They may cause weight gain and/or peripheral edema.
Dipeptidyl peptidase IV inhibitors e. g. Sitagliptin	This drug is used as monotherapy or in conjunction with Metformin or thiazolidinediones in patients with type 2 diabetes for whom diet and exercise or their current drug regimen is insufficient as treatment.

Prevention

The onset of type 2 diabetes can be delayed or prevented through proper nutrition and regular exercise. Intensive lifestyle measures may reduce the risk by over half.

Management

Management of type 2 diabetes focuses on lifestyle interventions, lowering other cardiovascular risk factors, and maintaining blood glucose levels in the normal range. Self-monitoring of blood glucose for people with newly diagnosed type 2 diabetes is recommended by the National Health Services.

Lifestyle

Aerobic exercise is beneficial in diabetes with a greater amount of exercise yielding better results. It leads to a decrease in HbA1C, improved insulin resistance, and a better $V0_2$ max. Resistance training is also useful, and the combination of both types of exercise

may be most effective. A diabetic diet that promotes weight loss is important. The best diet type is a low glycemic index diet has been found to improve blood sugar control. Culturally appropriate education may help people with type 2 diabetes control their blood sugar levels, for up to six months at least.

Medications

The two major categories of Oral Hypoglycemic Drugs are Insulin Secretagogues and Insulin Sensitizers that enhance insulin action.

Insulin secretagogues

Insulin secretagogues stimulate pancreatic secretion of insulin, which in turn decreases hepatic glucose production and enhances the uptake of glucose by muscle. There are two classes of secretagogues: sulfonylurea and non-sulfonylurea secretagogues.

Insulin sensitizers

Agents that enhance insulin action work through several mechanisms. They may inhibit glucose absorption, inhibit hepatic gluconeogenesis and glycogenolysis, or increase glucose uptake in fat and muscle. These medications fall into three categories: biguanides (metformin), thiazolidinediones, and alpha-glucosidase inhibitors [14, 15].

Recent advances

New insight into how diabetes leads to blindness

Diabetic retinopathy is the leading cause of vision impairment and blindness among working age Americans. Retinopathy is caused by high blood glucose levels that lead to the abnormal development of tiny blood vessels in the eye. A number of landmark studies have demonstrated that intensive glycemic control reduces the development and progression of diabetic retinopathy. However, exactly how high blood glucose levels disrupt blood vessel development in the eye is not completely understood.

Pathway scientist identifies possible trigger for type 1 diabetes

Type 1 diabetes occurs when the body's immune system attacks and destroys the insulin-producing cells in the pancreas. There is no cure for type 1 diabetes, which affects about 1.25 million Americans. In order to prevent or reverse the development of type 1 diabetes, it is essential to understand why and how the immune system attacks the body's own cells.

The diabetes-depression connection

Diabetes and depression are closely linked. A lifelong condition like diabetes takes a toll on mental health. Depression, in turn, makes it harder to find the motivation to care for diabetes: getting exercise, eating right, and completing other basic tasks are difficult when you're struggling just to get out of bed in the morning.

Very low effort muscular activity and diabetes risk

American Diabetes Association-funded researcher Dr. Marc T. Hamilton is studying how light physical activity, such as interrupting sedentary time with standing and walking, impacts glucose and fat metabolism in people who do not exercise.

Improving pregnancy outcomes in obese mothers starts with healthy eggs obese women have increased rates of infertility, and once they are pregnant, they experience higher rates of miscarriage, gestational diabetes, preeclampsia, and other pregnancy complications. Association-funded researcher Dr. Kelle Moley is working to understand how obesity impacts reproduction, not only for women seeking to become pregnant now but also for the health and wellness of future generations [16].

CONCLUSION

Diabetes is a metabolic disorder that can be prevented through lifestyle modification, diet control, and control of overweight and obesity. Education of the populace is still key to the control of this emerging epidemic. Novel drugs are being developed, yet no cure is available in sight for the disease, despite new insight into the pathophysiology of the disease.

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CONFLICT OF INTERESTS

Declare none

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