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A Modern Review of Diabetes Mellitus: An Annihilatory Metabolic Disorder

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Abstract

Diabetes mellitus is a disorder occurs due to metabolic problems is most frequent globally. The main indication of diabetes mellitus is a hyperglycemia in blood which is due to inappropriate pancreatic insulin secretion or low insulin-directed fostering of glucose by target cells. Diabetes mellitus can be assorted into several types but the two major types are type 1 and type 2. For type 1 diabetes patients Insulin renewal therapy is the backbone, for patient with type 2 diabetes there must be a control diet and lifestyle modification. In type 2 Insulin is vital when blood glucose are unable to control by nutritional therapy, physical activity and other medication. For the cure of type 2 DM oral hypoglycemic agents are preferred. In type 1 novel approaches like Islet transplantation and artificial pancreas were developed. By using the pathophysiology of type 2 DM there has been developing of novel medications like glucagon-like peptide 1 analogoues: Dipeptidyl peptidase-IV inhibitors, inhibitors of the sodium-glucose cotransporter 2. Due to some complications some drugs were removed from the market.

Keywords: Diabetes mellitus; Pathophysiology; Diagnosis; Management; Novel approaches

Introduction

Diabetes Mellitus (DM) is an endocrinological disorder [1-9] and not a single disorder which is a group of metabolic or heterogeneous affliction resulting from an irregularity in insulin secretions and insulin actions or both. Absence or reduced insulin in turn leads to persistent abnormally high blood sugar and glucose intolerance [10]. It is probably an oldest disease known to man. It is also referred as black-death from the 14th century.

Classification

In this section a description of types are mentioned **(Table 1)**.

Table 1: Classification of diabetis mellitus.

S. No.	Type	Characteristics feature
1	Type 1 (1a and 1b)	Damage of β-cells there by Secretion of insulin was reduced. Self-antibodies damage our own body tissues unknown cause.
2	Type 2	Insulin secretion and insulin resistance causes insulin scantiness. Imperfection of ß-cell functions genetically. Failure in insulin secretion genetically.
3	Other specific types	Pancreatic endocrinopathy. Indigenous infections like rubella and cytomegalovirus induced by drugs or chemicals. Other genetic indisposition.
4	Gestational diabetes	It is a temporary and appears during pregnancy usually develops during third trimester of pregnancy. After delivery, blood sugar levels generally return to normal 3.

Epidemiology

Type 1 diabetes is the most common type of the diabetes in people with lower age groups. The prevalence of type 1 diabetes is increasing in both prosperous and poverty countries. 85-95% of type 2 diabetes is predominant in developing countries.

In the age group between 20-79 there were about 285 million people were consider to have diabetes worldwide in the survey of 2010, by 2030 about 438 million people is expected to have diabetes in 70% of developing countries. 4 Around 7.1% are non-Hispanic whites, 8.4% are Asian Americans, 11.8% are Hispanics, 12.6% are Non-Hispanic blacks, 16.1% are American Indians and Alaska natives.

Etiology

Type 1 diabetes

Auto immune response: It is expressed as a consequence autoimmune disease [11-15], where the beta cells of pancreas are slowly demolished by the body's own immune system which reduces insulin production. In the development of type 1 diabetes both the environmental and genetic predisposing factors are significant, but the exact correlation is still unknown.

Genetical factors: Investigators have commenced at least 18 genetic positions are designated as IDDM1-IDDM18 (Insulin dependent diabetes mellitus), which are related to type 1 diabetes. The IDDM1 (Insulin dependent diabetes millites) region contains the HLA (Human leukocyte antigen) genes that encode proteins called major histocompatibility complex. In this location immune responses are affected by these genes. Other chromosomes and genes continue to be identified. We can predict the onset of clinical diabetes as much as 3 years by the appearance of ICAs frequently.

Environmental factors: Due to abrupt stress like an infection where the β-cells of pancreas falls below 5-10%. Coxsackie viruses are a family of enteric viruses which attack the intestinal tract leads to the destruction of insulin producing pancreatic β cells.

Type 2 diabetes: This kind of diabetes is also has a powerful genetic predisposition. It is suggesting that twins have 100% approaching rate for diabetes. When compared both type 1 and type 2, type 2 has 5-10% of the risk of a child for developing type 2 and 1-2% for type 1. Due to ongoing development of insulin resistance and β-cell dysfunction leads to inability of pancreas for the production of sufficient insulin to conquer insulin resistance. Nearly 85% of population with type 2 diabetes [16-18] are obese that causes insulin resistance. Particularly there is a high risk at intra-abdominal region rather than subcutaneous. To predict the risk of type 2 Body Mass Index (BMI) is used as a measure.

Pathophysiology

Type 1 diabetes

This type of diabetes is a long lasting autoimmune disease, where there is selective demolition of insulin producing pancreatic β-cells. When there is transplantation of pancreas from twin donars to chronic diabetic twin recipients in the absence of immune suppression is complicated due to elevated heterogenecity of pancreatic lesions of β-cells which are rapidly annihilated, and then there is development of massive insulitis by using infiltrating T lympocytes which measures an amnestic autoimmune reaction.

Type 2 diabetes

As a consequence of insulin resistance, abnormality of insulin production and ongoing pancreatic β-cell failure leads to insulin insensitivity which is a characteristic feature of Type 2 Diabetis Mellitus **(Table 2)**.

Table 2: Data of venous plasma glucose**.**

Type	Diagnosis	Venous Plasma Glucose
Normal	Fasting and 2 h post-prandial	<6.0 mmol/m
		<7.8 mmol/m
Diabetis	Fasting or 2 h post-prandial	≥7.0 mmol/m
		≥11.1 mmol/m
Impaired Glucose Tolerance	Fasting and 2 h post-prandial	<7.0 mmol/m
		7.8-11.0 mmol/m
Impaired Fasting Glycemia	Fasting	6.0-6.9 mmol/m

Management

Approach considerations

Goals which includes in taking care of patients with diabetes are to eradicate the symptoms or to slow down the developing risk factors includes blood pressure and glycaemia, control of lipids which reduces macro vascular risk and stoppage of smoking and maintaining aspirin therapy.

General management of diabetic patient's education: Education must need:

- Disease process treatment option.
- Food plan.
- Physical activity plan.
- Awareness of given medication for diabetes.
- Monitoring of blood sugar levels.
- Awareness of acute and chronic issues.
- Psychosocial issues.
- Promoting health strategies.

Medical nutrition therapy: Dietary calculation is based on the body weight in pounds which is multiplied by 10 to maintain a kilo joule/kilocalorie which is essential, plus 30-100% added for physical task. The diet must include 50-55% carbohydrates, 30% fat Fiber (of which not more than 10% should be saturated fatty acids, and 15-20% proteins).

Physical activity: Inactive lifestyle is a strong risk factor for Type 2 diabetes, so exercise is useful in patients.

Type 1 diabetes

Insulins are the first choice to treat type 1 diabetes & they can be administered by injections and insulin pump. Insulins are of three type's rapid acting, long acting and intermediate acting. Some insulins like regular insulin (HUMULIN 70/30, NOVOLIN 70/30), Insulin isophane (HUMULIN N, NOVOLIN N),

and insulin glulisine (APIDRA), insulin lispro (HUMALOG), insulin aspart (NOVOLOG). Some long acting insulins are glargine (LANTUS), detemir (LEVEMIR). Pramlintide (SYMLIN) inj. is a synthetic version of a chemical free hormone which is amylin provided by β cells and some angiotensin receptor blockers; ACE inhibitors, aspirin and cholesterol lowering drugs are used.

Islet grafting was been explored as a therapy for type 1 diabetes in selected patients with inadequate glucose control despite insulin therapy. Artificial pancreas is a closed loop insulin delivery. It is linked with a continous monitor of glucose to insulin pump. The device which delivers correct amount of insulin automatically when the monitor specify the need for the pump.

Type 2 diabetes

Pharmacological therapy: Oral hypoglycaemic agents are useful in the treatment of type 2 DM and insulin also includes in it and those agents include Sulphonylureas, Alpha glucosidase inhibitors, Biguanides and Thiazolidenediones. The main aim is to correct metabolic disorder like resistance to insulin and insufficient insulin secretion. They are given in combination with a suitable diet and changes in lifestyle. They show loss of weight, increase glycaemic control [19] decrease the risk of cardiac problems **(Table 3)**.

Table 3: Pharmacological therapy.

S. No.	Type of drug	Drug generic	Brand name
1	Sulphonylureas	Glimepiride	AMARYL
		Glipizide	DIABETA
		Glyburide	GLYNASE GLUCOTROL
2	Biguanides	Metformin	GLUCOPHAGE
3	Thiazolidinediones	Pioglitazone	ACTOS, AVANDIA
4	Alphaglucosidase inhibitors	Acarbose	PRECOSE, GLYSET
5	Meglitinides	Nateglinide	PRANDIN, STARLIX

Best choice of drug for type 2 diabetes mellitus: Metformin does not promote weight gain and has advantageous effects on several cardiac risk factors. Accordingly, it is majorly indicated as the optional drug for most patients with type 2 diabetes. In Current guidelines from the American Diabetes Association (ADA), European Association for Study of Diabetes (EASD) and American Association of Clinical Endocrinologist (AACE) or American College of Endocrinology (ACE) recommended early initiation of metformin as first line agent for type 2 diabetes mellitus.

Combinations of antidiabetic drugs with Metformin to treat diabetes: Metformin+Sulphonyl ureas-decrease in HbA1C (0.8–1.5%) than drug alone.

- Metformin+Insulin-improve glycaemic control limit changes in body weight & reduce insulin requirements.
- Metformin+Thiazolinedinediones-decreased concentration of HbA1C & improve insulin sensitivity.
- Metformin+α-glycosidase inhibitors-decrease in HbA1C.
- Metformin+Glifozins are used in combinations now a day to treat type 2 diabetes.

New inventions developed in curingdiabetes: The current class of drugs include GLP-1 mimetics, DPP-4 Inhibitors, SGLT-2 Inhibitors, Amylin mimetics, Dual PPAR agonist.

GLP-1 mimetics (or) agonist: Glucagon like peptide (GLP-1) are mainly used in the treatment of type 2 diabetes which are given by injection to regulate glucose level there by stimulating glucose dependent secretion of insulin. GLP-1 mimetics are powerful in increasing glycaemia control and promote weight reduction by mimicing the mechanism of action of an endogenous stomach and intestinal hormones **(Table 4)**.

Table 4: Drugs used.

S. No.	Name of the Drug	Brand Name
1	Exenatide	BYETTA
2	Liroglutide	VICOZA
3	Lixisenatide	LYXUMIA
4	Albiglutide	TANZEUM

DPP-4 inhibitors (Gliptins): It is a new class of oral diabetic drugs which help in weight loss as well as decrease in blood sugar level and they work by an enzyme which destroys a group of gastrointestinal hormones called incretins. DPP-4 inhibitors are prescribed for type 2 diabetes mellitus patients who do not well respond to metformin and sulphonyl ureas.

Amylin analogues or agonist: These are injectables which are used in treating both type 1 & type 2 Diabetes and are administered before meals.They inhibit the release of glucagon while eating, slows food emptying from the stomach. Pramlintide acetate (SYMLIN) is the class of drug available in US which is administered by subcutaneous injections. In the UK it is unapproved by National institute for health and care excellence (NICE) because it can significantly raise the risk of severe hypoglycaemia **(Table 5)**.

Table 5: Different brands used.

S. No.	Name of the drug	Brand name
1	Sitagliptin	JANUVIA
2	Vildagliptin	GALVUS
3	Saxagliptin	ONGLYZA
4	Kinagliptin	TRADJENTA was approved for use in the USA

SGLT- 2 inhibitors: Selective sodium glucose transporter-2 is used to treat type 2 diabetes mellitus. These agents lower the

kidney glucose margin levels resulting in an increased amount of glucose which will be excreted in the urine **(Table 6)**.

Table 6: SGLT-2 inhibitors.

S. No.	Name of the drug	Brand name
1	Canagliflozin (It was the drug first approved in united states to treat diabetes).	INVOKANA
2	Empagliflozin	JARDINCE
3	Dapazliflozin	FARXIGA

Dual PPAR agonist (Peroxisome Proliferator Activated Receptor): Nuclear receptor PPAR γ agonists are used to reduce hyperglycemia combained with metabolic syndrome & type 2 Diabetes. It was the main target of fibrate drugs which is a class of amphipathic carboxylic acids. Being potent in normalisation of sugar levels in blood, now a days PPAR γ agonist in thiazolidinedione type will have many worst adverse effects like fluid retention, oedema and congestive heart failure **(Table 7)**.

Table 7: Dual ppar agonist.

S.no.	Name of the drug	Brand name
1	Clofibrate	ATROMID-S
2	Gemifibrozil	LOPID
3	Bezafibrate	BEZALIP
4	Fenofibrate	TRICOR

Removal drugs of type 2 diabetes from the market: In 2006 inhaled insulin was given license for use but it was withdrawn from the market because it has less encouragement. Troglitazone (REZULIN) was not recommended & removed from market due to its potential high hepatotoxicity [20-23]. Phenformin & buformin causes severe lactic acidosis, rosiglitazone (AVANDIA) causes high risk of heart attack & death, but continues to be available in the US, pioglitazone (ACTOS) worsen the heart failure in some patients, due to these reasons these drugs are eliminated from the market.

Conclusion

This review acts as a brief introduction for diabetes which is a growing health care problem affecting individual's health, health care system and the economy of the whole world. In the hospital the health professionals will meet patients with diabetes. It is the role of them to be properly educated about diabetes and the most current recommended treatments. New drugs are developing to treat diabetes and these important roles have a great impact on the prevention and management of this disease which improves patient's quality of life.

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