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Diabetes and the importance of insulin

E. Bhavya

Associate Professor, Department of Pharmacy Practice, School of Pharmaceutical Sciences, Vels Institute of Science, Technology And Advanced Studies (VISTAS), Pallavaram, Chennai-117

Corresponding author email: bhavya.sps@velsuniv.ac.in

G. Sanjay

Department of Pharmacy Practice, School of Pharmaceutical Sciences, Vels Institute of Science Technology and Advanced Studies (VISTAS), Pallavaram, Chennai-117

Abstract--Diabetes mellitus is a collection of metabolic illnesses marked by chronic hyperglycemia caused by insulin production, insulin action, or both. Insulin is secreted in pancreatic beta cells. Insulin deficiency produces a rise in blood glucose levels, causing problems with carbohydrate, lipid, and protein metabolism. With the progression of the condition, tissue or vascular damage occurs, resulting in severe diabetes consequences such as retinopathy, neuropathy, nephropathy, cardiovascular problems, and ulceration. Without any comprehensive preventive and control measures, the worldwide prevalence of diabetes would continue to rise. Diabetes can be controlled non-pharmacologically by diet and exercise or pharmacologically by oral hypoglycemic agents and insulin. Insulin therapy is more effective in managing DM and is preferred in case of emergency hyperglycemic conditions. Moreover, Insulin's physiological function and clinical significance are often associated with its involvement in glucose homeostasis. Several types of insulin have shown effective results in the management of DM. Insulin pen devices provide several benefits over the classic insulin bottle and syringe technique. Insulin pumps have been offered as an alternative to traditional insulin injections for the management of type 1 diabetes mellitus patients. Thus it is safe and efficient in the treatment of diabetes mellitus (DM).

Keywords--Diabetes mellitus, Insulin, pathophysiology, diagnosis, clinical manifestation.

Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by abnormal blood glucose levels and caused by a deficiency in insulin production, insulin action, or both in pancreatic beta cells (1). Polyuria, polydipsia, polyphagia are the most common clinical manifestation of DM. Genetic factors and a sedentary lifestyle are thought to be the primary reason for developing DM (2). Moreover, without any comprehensive preventive and control measures, the worldwide prevalence of diabetes would continue to rise (3). Obesity, lack of physical activities may increase the risk of DM. The lack of insulin causes metabolic irregularities in carbohydrates, lipids, and proteins. Retinopathy, neuropathy, nephropathy, cardiovascular problems, and ulceration are all severe diabetes complications. Due to these complications and uncontrolled diabetes can cause stupor, coma and death (4-6). The importance of insulin and diabetes mellitus is highlighted in this review.

History

The name diabetes mellitus is derived from the Greek and Latin terms for "siphon" and "sweet," respectively. Between 250 and 300 BC, Apollonius of Memphis coined the term "diabetes". The name diabetes mellitus was coined because of the urine's sweetness. University of Toronto researchers, Mering and Minkowski, found in 1889 that diabetes is mostly caused by the pancreas. Banting, Best, and James Collip found in 1922 that effective therapy for diabetes was available. The pancreas of cows was used to extract the insulin hormone (7). Egyptian papyri, ancient Indian and Chinese medical literature, as well as the work of ancient Greek and Arab physicians, all contain descriptions. Aretaeus of Cappadocia gave the first accurate description of diabetes in the 2nd century AD, coining the term diabetes, while Thomas Willis added the term Mellitus to the disease in the 17th century, in an attempt to describe the unusually sweet taste of the urine. Frederick Banting and Charles Best built on Minkowski and Mering's experiment in 1921. They separated insulin from pancreatic islets and administered it to type 1 diabetic patients, saving millions of lives and ushering in a new era in diabetes therapy (8).

Etiology

There are two types of endocrine cells in the pancreas' islets of Langerhans: insulin-producing beta cells and glucagon-secreting alpha cells. The glucose environment causes beta and alpha cells to change their hormone production levels on a regular basis. The glucose levels become skewed when the equilibrium between insulin and glucagon is disrupted. Insulin is either missing or has reduced activity (insulin resistance) in diabetics, resulting in hyperglycemia. Type 1 diabetes, type 2 diabetes, maturity-onset diabetes of the young (MODY), neonatal diabetes, gestational diabetes, and secondary causes such as endocrinopathies, steroid usage, and so on are all types of diabetes. T1DM is expected to afflict children and adolescents, but T2DM is thought to affect middle-aged and older individuals who have long-term hyperglycemia as a result of poor lifestyle and nutritional choices.

Type 1 diabetes mellitus is defined by the loss of beta cells in the pancreas as a consequence of the complete death of beta cells, insulin is either nonexistent or severely low. Type 2 diabetes has a more gradual development, with an imbalance between insulin levels and insulin sensitivity leading to an insulin functional deficit. Insulin resistance may be due to a variety of factors, although it is most typically caused by obesity and age. The genetic composition of both types is important as a risk factor. Numerous loci related to diabetes mellitus have been found as a result of intensive investigation of the human genome. Polymorphisms in the major histocompatibility complex (MHC) and the human leukocyte antigen have been proven to influence the likelihood of developing type 1 diabetes (T1DM) (HLA). Due to the combination of genetics and lifestyle, T2DM is a more difficult condition. T2DM seems to have a more hereditary profile than T1DM. The vast majority of persons who have T2DM also have at least one parent who has the disease. Gestational diabetes mellitus is a term that refers to glucose intolerance that occurs during pregnancy. Other specific types include relatively various uncommon conditions primarily such as genetically defined forms of diabetes and diabetes relating to other diseases or the use of drugs (9).

Pathophysiology

When it comes to the disease's pathogenesis, unusually high blood glucose levels are caused by a breakdown in the feedback loops between insulin action and insulin production. The body's ability to maintain normal glucose levels is impaired in the event of cell malfunction, which reduces insulin production. IR, on the other hand, increases hepatic glucose synthesis while decreasing muscle, liver, and adipose tissue glucose absorption (10). The pancreatic beta cells are damaged by hyperglycemia alone, and this leads to a reduced ability to produce insulin. An impaired metabolic state occurs as a result of the hyperglycemic cycle. In this setting, blood glucose levels exceeding 180 mg/dL are often called hyperglycemic, although there is no clear cutoff point because of the multiplicity of processes. Serum glucose levels exceeding 250 mg/dL are known to produce polyuria and polydipsia, however, the impact varies from person to person. Excess fatty acids and proinflammatory cytokines cause insulin resistance, which causes glucose transit to be impeded and fat breakdown to be increased. Due to an insufficient reaction to the production of insulin, the body reacts improperly by raising glucagon, adding to hyperglycemia further. Chronic hyperglycemia also results in the glycation of proteins and lipids without the need for enzymes. Glycation causes damage to the retina, kidney, and peripheral nerves' tiny blood vessels. Increased glucose levels accelerate the process. This damage results in the traditional diabetes consequences of diabetic retinopathy, nephropathy, and neuropathy, as well as the avoidable complications of blindness, dialysis, and amputation (11).

Insulin

Insulin, the body's sole hormone-containing 51 amino acids, with a molecular weight of 5802 which is capable of reducing plasma glucose levels, is secreted by pancreatic cells. Diabetes mellitus is caused by impaired or inadequate insulin production (12). Insulin's physiological function and clinical significance are often associated with its involvement in glucose homeostasis (13). There have been

numerous developments in rapid or long-acting insulin, which have improved both their sensitivity and their injection-to-onset profile. The smallest of changes in basic protein structures allowed for either inhibition or promotion of micro precipitation in insulin variants when administered subcutaneously, allowing for greater control over insulin doses and injection-to-onset times (long-acting analogs) (14). Insulin that is physiologically comparable to human insulin is made using swine pancreatic insulin, recombinant DNA technology, or chemical modification of pig insulin. Insulin analogues have been developed by modifying the sequence of amino acids of an insulin molecule (15)

Insulin resistance

Insulin resistance is clinically defined as the inability of a given amount of exogenous or endogenous insulin to enhance glucose absorption and utilization in a person to the same extent as it does in the normal population. Insulin action occurs when insulin binds to its plasma membrane receptor and communicates with the rest of the cell through a sequence of protein-protein interactions. Intracellular insulin action is regulated by two major protein-protein interaction cascades: one controls intermediate metabolism and the other controls growth and mitotic activity. Many theories have been proposed to explain how insulin resistance and insulin resistance syndrome arise. These include the following: (1) genetic anomalies in one or more insulin action cascade proteins (2) starvation of the fetus (3) a rise in visceral obesity. The "Insulin Resistance Syndrome" or "The Metabolic Syndrome" is a collection of cardiovascular-metabolic illnesses that may result in diabetes. It is possible that this combination of defects may develop into type 2 diabetes and may cause accelerated atherosclerosis, hypertension, or polycystic ovary syndrome (PCOS) depending on the individual's family history (16).

Regulation of insulin secretion in human pancreatic islets

Insulin is secreted by pancreatic cells, the only hormone in the body capable of reducing plasma glucose levels. Diabetes mellitus is caused by impaired or inadequate insulin production. The cell is electrically excitable; as glucose levels rise, it depolarizes and begins to generate action potentials. The electrophysiology of mouse cells has been widely studied, as the cell's function in insulin production. Similar investigations on human cells have been conducted more recently. Numerous and significant variations between human and rat cells have been discovered. Cellular features of human pancreatic cells, including glucose sensing and insulin exocytosis, are discussed in this section. Ion channel complements underlie the glucose-induced electrical activity that results in exocytosis release, as well as cell regulation of exocytosis (17).

Clinical manifestation

Many people underestimate the clinical characteristics of diabetes due to the disease's continuous course. The public is unaware that harm may begin many years before symptoms manifest. This is problematic since early detection of symptoms may aid in quickly bringing the condition under control and preventing vascular problems. (18) Polyuria, polydipsia, weight loss, and, in certain cases,

polyphagia and hazy eyesight are all symptoms of severe hyperglycemia. Chronic hyperglycemia may also impair development and increase susceptibility to some illnesses. Untreated diabetes may result in acute, life-threatening complications such as hyperglycemia with ketoacidosis or nonketotic hyperosmolar syndrome. Diabetes-related long-term complications include retinopathy, which can result in vision loss; nephropathy, which can result in renal failure; peripheral neuropathy, which can result in foot ulcers, amputations, and Charcot's joints; and autonomic neuropathy, which can result in gastrointestinal, genitourinary, cardiovascular, and sexual dysfunction. The risk of developing atherosclerotic cardiovascular, peripheral arterial, and cerebral vascular disease is significantly increased in diabetics. Individuals with diabetes often have hypertension and impaired lipoprotein metabolism (19).

Diagnosis

Diabetic patients may be diagnosed with hyperglycemia based on their history and a single blood glucose level of at least 200 mg per dL (11.1 mmol per L). Diagnostic criteria may also include an A1C level of 6.5% or above, a fasting blood glucose level more than 126 mg/dl (7.0mmol/L), or two-hour blood sugar levels greater than 200 mg/dl after an oral glucose tolerance test including a 75-gram glucose load. To confirm the diagnosis, 126 mg/dL of fasting plasma glucose or an oral glucose tolerance test with 75-g glucose load with a 2-hour plasma glucose level of 200 mg/dL or above may be employed. Testing should be performed the next day (20).A1C is a frequently used indicator for chronic glycemia. It is calculated by averaging blood glucose levels over a two- to three-month period. Following an exhaustive evaluation of both current and developing epidemiological information, the expert Committee suggested using the A1C test to diagnose diabetes, with a 6.5 percent threshold, and the ADA supports this conclusion (21).Screening for gestational diabetes (GDM) around 24-28 weeks of pregnancy is advised in women who have never had diabetes before since GDM is asymptomatic. The possibilities of getting Diabetes is more likely to develop if there is a history of Gestational diabetes mellitus (22).Even in the absence of clinical hyperglycemia, a second confirmatory laboratory test (FPG, A1C, 2hPG in a 75 g OGTT) is required when just one test indicates that a patient is diabetic. The diagnosis of diabetes is verified if the results of two distinct tests are obtained and both are over the diagnostic limits. 2hPG is for 2-hour plasma glucose; A1C stands for glycated hemoglobin; FPG stands for fasting plasma glucose; OGTT stands for oral glucose tolerance test and PG stands for plasma glucose (23)

Insulin Delivery Devices

Insulin pen

Insulin pen devices are intended to give patients a simple and straightforward method of administering insulin. They are classified into two types: reusable, durable pens and disposable, prefilled pens. These insulin pen devices provide several benefits over the classic insulin bottle and syringe technique. Additionally, insulin pens have been shown to be less uncomfortable than the vial-and-syringe approach and are often linked with increased patient preference and social acceptance. As a consequence, this form of insulin administration may eventually

aid in glucose control improvement and should be considered when prescription insulin products (24).

Insulin pen devices provide a number of benefits over the conventional vial-and-syringe method of insulin administration, including increased patient satisfaction and adherence, the convenience of use, enhanced accuracy for administering tiny doses of insulin, social acceptability, and reduced reported injection pain. Pens have gotten more user-friendly in recent years, and some kinds are quite straightforward to use, needing little or no training. Understanding the design enhancements made to pens, both to meet patient demands and as a consequence of better technology underlying the device mechanics, is critical for encouraging the adoption of insulin pen devices(25).

Insulin Syringes:

Generally, insulin is administered subcutaneously using syringes indicated in insulin units. The manner in which units are stated may vary based on the syringe's size and manufacturer. Insulin syringes are available in sizes of 0.3, 0.5, 1, and 2 mL. Needles come in a variety of lengths. The laws regulating the procurement of syringes vary significantly by state. Numerous medical devices have been created to mitigate the risk of needle sticking and other sharps injuries in accordance with current OSHA guidelines. The use of some insulin syringes now available with engineered sharps injury prevention (ESIP) may obstruct efficient insulin self-administration training. During insulin self-administration education, an individual patient evaluation should guide the use of an ESIP insulin syringe. Syringes should never be shared due to the possibility of contracting a blood-borne viral illness (e.g., acquired immune deficiency syndrome or hepatitis). Travelers should be informed that insulin in the strength U-40 is accessible outside the United States. To avoid dosing errors, syringes calibrated to the concentration of U-40 insulin must be used (26).

Jet injector:

In recent years, people with diabetes mellitus have increasingly employed jet insulin injections. Jet injectors may get contaminated with germs over time if they are not cleaned properly; cleaning every two weeks is advised. By cultivating jet injectors in daily use by 19 diabetic patients, we evaluated the incidence of bacterial contamination. On blood agar plates, swabs from the inner chambers were cultivated. Only one of twenty cultures grew bacteria, and the recovered organism was a putative contaminant that could not be recognized as a common pathogen. Jet injectors are very unlikely to get colonized by germs or to transmit the infection to patients who use them to administer insulin. Colonization is unlikely to occur as a result of the antibacterial preservatives included to commercial insulin formulations. Additional data based on a larger sample size would be beneficial in further elucidating the infection risk related to jet injectors (27).

Insulin Pump:

Insulin pumps have been offered as an alternative to traditional insulin injections for the management of type 1 diabetes mellitus patients. Insulin pump research and development, as well as the manufacture of smart pumps, provide patients with increased dose accuracy, flexibility, and simplicity of use (29). All of these goals may be achieved to a large extent with the use of an insulin pump or CSII treatment. For individuals with type 2 diabetes (DKA), CSII is a better option than multiple daily injections (MDI) because of its rapid-acting insulin, more flexibility in meal and snack schedule, and the use of programmed basal rates to optimize nocturnal glycemic control (30). There are now seven manufacturers of insulin pumps on the market: Medtronic MiniMed, Roche's Disetronic Medical Systems, Animas (Johnson & Johnson), Deltec (Smiths Group), Sooil, Nipro, and Insulet Cooperation Ltd. The amount of rapid-acting insulin to be administered by the pump is calculated based on the total daily dose of injectable insulin when starting insulin pump therapy. The optimum total daily dose for pump therapy is usually considered to be a 20% reduction in the total daily dose of insulin. The pump delivers half of this amount to address basal insulin demands. The 'rule of 500,' which divides the number 500 by the total daily injected dose of insulin in units to provide an insulin-to-carbohydrate ratio, is used to predict the initial bolus doses of insulin during meals(31).

Conclusion

In the beyond decade, there was a high-pace evolution in diabetes technology to enhance the nice of existence and to increase the durability of topics with diabetes. Though there had been commendable traits withinside the presently to be had gadgets, lots of the ones had been prohibitively high priced. Though there are numerous high-priced remedies the above sorts of insulin transport gadgets had been gambling a first-rate position in the subject of diabetes and pharma. Furthermore, our superior information on the types of diabetes and their devices based on case studies and reviews have given a clear understanding to the patient and there is a wide exposure to devices in the field of pharma. Hence we can conclude Insulin is both safe and effective in the management of DM.

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