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Review Article

A REVIEW ON DIABETES

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ABSTRACT
When control of insulin levels fails, Diabetes mellitus will result. as a consequence, insulin is used medically to treat some forms of diabetes mellitus. Patients with type 1 diabetes depend on external insulin (most commonly injected subcutaneously) for their survival because the hormone is no longer produced internally. Patients with type 2 diabetes are often insulin resistant, and because of such resistance, may suffer from a "relative" insulin deficiency.
KEYWORD: Diabetes Mellitus, IDDM, NIDDM, Diabetes Insipidus (D.I)

INTRODUCTION

Diabetes is a third leading cause of death (after heart disease and cancer). In many developed countries, it affects world's population. In recent years developed nation have witnessed and explosive increase in prevalence of diabetes. In pre-dominantly related to life style changes and resulting surge in obesity. Improvement in our understanding of the pathogenesis of diabetes, its complication, in therapy and prevention of diabetes are critical to meeting this healthcare change.

Diabetes is a clinical condition characterized by increased in urine level and increased blood sugar level due to insufficient insulin or insulin is not sufficient to its action on its target tissue.

Diabetes is a disease in which the body either fails to produce any insulin (type 1), or the insulin that it does produce is unable to adequately trigger the conversion of food into energy (type 2)[1].

Types of diabetes

Diabetes are mainly classified into two types

1. Diabetes Insipidus.
2. Diabetes Mellitus.

Diabetes insipidus

It is a disease renal convulsion of urine owing either into adequate secretion of vasopressin or ADH from neurophysis or insufficient renal response to a vasopressin. Patient with DI excrete large amount (more than 30ml/kg) urine. It is mainly caused by absence of ADH, very rarely caused by abnormally high rate of the degradation of vasopressinase. Its mainly symptoms are polyuria, polydypsia, polyphagia. It contrast to the sweet urine excreted by patient with diabetes mellitus, hence the urine of diabetes insipidus is a tasteless hence the name is "INSIPIDUS".

They are mainly divided into two parts

- Central diabetes insipidus
- Nephrogenic diabetes insipidus

This both are differentiates in that manner that administration of DESMOPREESINE which will increase urine osmolarity in patient with central diabetes insipidus.

Diabetes Mellitus

Diabetes Mellitus is condition arising from the abnormal metabolism of the carbohydrates, protein and fat caused by either lack of insulin secretion or decrease sensitivity of tissue to insulin.

There are two types of diabetes mellitus

Type: 1 (IDDM) this is called as insulin dependent diabetes mellitus is caused by lack of the insulin secretion.

Type: 2 (NIDDM) It is also called as non insulin dependent diabetes mellitus is caused by decrease sensitivity of target tissue the metabolic effect of insulin. This reduce sensitivity to insulin is often called "insulin resistance".

Both types of diabetes causes metabolism of cell due to which the food stuff alter. The basic effect of insulin lack or insulin resistance to glucose metabolism is to prevent the efficient uptake and utilization of glucose concentration increase and cell utilizing glucose is decreased and utilization of fat and protein increase[2].

Type-1 [IDDM] Diabetes- lack of insulin production by beta cells of pancreas

- Injury to the beta cells of the pancreas or disease that impair insulin production can lead to type-1 diabetes.
- Viral infection or autoimmune disorder may be involved in the destruction of beta cells in many patients with type-2 diabetes.
- Although heredity also play a major role in determine the susceptibility of the beta cells to destruction by the insults.
- In some insults there may be hereditary for beta cell degradation even without viral infection or auto immune disorder.
- The usual onset of type 1 diabetes occur at about 14 years of age in U.S and for this reason it is often called as "juvenile diabetes mellitus".

Type 1 diabetes may develop very abruptly over for period of a few days or weeks with two major principal

1) Increase blood glucose.
2) Increase utilization of fat for energy

Type-2 [NIDDM]/ adult onset diabetes

Type 2 is more common then type 1 accounting of about 90% of all classes of diabetes mellitus. In most cases the onset of type 2 diabetes occurs after age 30, often between 50 to 60. Disease develops gradually therefore this syndrome is refered to as 'Adult Onset Diabetes'. However in recent study shows patient are mainly below 20 years type-2 diabetes. The main risk factor for type 2 diabetes in children is obesity and as well as adult. Type 2 diabetes in contrast with type 1 is that associate with increase plasma insulin concentration. This occurs as a compensatory response by the pancreatic beta cells for diminished sensitivity of target tissue to the metabolic effect of insulin a condition referred to as 'insulin resistance'. The decrease in insulin sensitivity impairs carbohydrate utilization and storage, rising the blood glucose and stimulating a compensatory increase in insulin secretion. Development of insulin resistance and impair glucose metabolism is usually a gradual process beginning with excess weight gain and obesity. The mechanism that links receptor activation with multiple cellular effects. Insulin resistance in part of cascade of disorder that is often called as the "metabolic syndrome". Some features include

- Obesity especially accumulation of abdominal fat.
- Insulin resistance.
- Fasting hyperglycemia.
- Hypertension.

Lipid abnormalities such as increase blood triglyceride and decrease blood high density lipoprotein- cholesterol[3].

Symptoms of Diabetes

Excessive thirst, Frequent urination, Weight loss, Blurred vision, Increased hunger, Frequent skin, bladder or gum infections, Irritability, Tingling or numbness in hands or feet, Slow to heal wounds, Extreme unexplained fatigue, Sometimes there are no symptoms (type 2).

Complications

Ketoacidosis: - The body prefers to use sugar for energy, but when it is not available fat is utilized. When fat is utilized certain acid substance are produced known as ketone bodies. This disturbs the normal acid- base balance which results in severe acidosis.

Obesity: - Insulin therapy without dietary restriction may leads to obesity.

Arteriosclerosis: - Hardening of arteries occurs much more frequently in diabetic patient. This happens particularly in lower extremities where deep ulcer may form in the feet or legs and gangrene may result from the secondary infection.

Cataract: - Occurs more frequently in older diabetes. Diabetes retinitis more frequently in children.

Infection: - Diabetes is more susceptible to infection of skin such as boils, carbuncles and generalized itching.

Nephropathy: - One of the most serious complications is damage to kidney and albuminuria, hypertension, edema of various parts of body occurs.

Hypoglycemia: - The hypoglycemia may result from over dosage of insulin, failure to it or ingestion of alcohol. Insulin allergy and resistance may get develop[4].

Pathophysiology

The following process illustrates how the blood glucose level is maintained within the normal limit by beta cells of islets of langerhans of pancreas. Glucose is converted to glycogen in presence of insulin. This process is called "GLYCOGENESIS". Glycogen is converted to glucose in presence of glucagon. This process is called "GLYCOGENOLYSIS". Glucagon's also stimulate the process of gluconeogenesis.

The various action of insulin is as follows

- It increases the glucose uptake by muscle and fat.
- It inhibits gluconeogenesis.
- Conversion of glucose to glycogen and fatty acid promotes.
- Conversion of fatty acid to triglycerides and reverse reaction is inhibited.
- Conversion of amino acid to protein promoted and reverse reaction inhibited. The normal fasting blood sugar level lies between 80-120 mg % whereas meals it rise 150 mg %.
- Due to low level of insulin there is metabolism of fatty acid leading to formation of ketone bodies and acidosis.
- There is a hyperglycemia and glycosuria resulting in dehydration[5].

Treatment

Controlling your blood sugar is essential to feel healthy and avoiding long term complications of diabetes. Some

people are able to control their blood sugar with diet and exercise alone. Others may need to use insulin or other medications in addition to lifestyle changes. In either case, monitoring your blood sugar is a key part of your treatment program. A healthy diet and exercise should be placed as a priority for diabetes treatment. Second you might also try some of the diabetic treatment using alternative medicine. Third, follow yours doctors prescriptions. And last, pancreas or islet cell transplantation may be an option for people whose kidneys are failing or who aren't responding to other treatments. Keep in mind that the amount of sugar in your blood is constantly changing. Self- monitoring helps you learn what makes your blood sugar level s rise and fall, so you can make adjustment in your treatment. Factors that affect your blood sugar include:

Food: - Food raises your blood sugar level? Its highest 1 to 2 hour after meal. What and how much you eat, and the time of day, also affect your blood sugar level.

Exercise and physical activity:- In general, the more active you are, the lower your blood sugar. Physical activity causes sugar to be transported to your cells, where its used for energy.

Medication

Insulin and oral diabetes medications deliberately work to lower your blood sugar. But medications you take for other condition may affect glucose level. Corticosteroids, in particulars may raise blood sugar level.

Illness: - The physical stress of a cold and other illness causes to produce hormones that raise your blood sugar level. The additional sugar helps promote healing. But if you have diabetes, this can be a problem. In addition, a fever increases your metabolism and how quickly sugar is utilized, which can alter amount of insulin you need.

Alcohol: - Even a small amount of alcohol about 2 ounces can cause your sugar levels to fall too low. But sometimes alcohol can cause sugar level to rise. The alcohol counts as carbohydrate calories in your diet.

Fluctuation in hormone level: - The female hormone estrogen typically makes cells more responsive to insulin, and progesterone makes cell more resistant. Although these two hormones fluctuate throughout the menstrual cycle, the majority of women don't notice a corresponding change in blood sugar level.

A healthy diet: - Contrary to popular myth, there's no "diabetes diet" Furthermore, having diabetes doesn't mean you to eat only bland, boring foods. Instead, it means you'll eat more fruits, vegetables and whole grains, foods that are high in nutrition and low in fat and calories[6].

Anti- Diabetic Drugs

Insulin

Oral Hypoglycemicagents

Sulphonyl urea: e.g; Carbutamide, Tolbutamide, Chlorpropramide, Acetahexamide, Glebenclaimide (betanase), Glipizide (glibense).

Biguanides e.g; Phenformin, Metformin.

Thiazolidine diones: Triglitazone, Ciglitazone, Piglitazone, Euglitazone.

Alpha- glycosidase inhibitor: eg; Acarbose

Insulin: - Insulin is a polypeptide hormone produced by the cells "BETA cells of islets of langerhans of pancreas". It has profound influence on the metabolism of carbohydrate, fat and protein. Insulin is considered as anabolic hormone as it promotes the synthesis of glycogen, triglycerols and proteins. The hormone has been implicated in the development of diabetes mellitus. Insulin occupied as a special place in the history of biochemistry as well as medicine. Insulin was the first hormone to be isolated purified and synthesized[7].

Mechanism

Insulin binds to a specific receptor on the surface of its target cells. The receptor is a large trans- membrane glycoprotein complex consisting two alpha and beta subunit. The alpha subunit is are entirely extra cellular and each carries an insulin binding site where as beta subunit are trans- membrane protein with tyrosine kinase activity. The activity is suppressed by the alpha subunit. But insulin binding caused a conformational change that caused phosphorylation of multiple other intra cellular enzymes. The net effect in to activate some of enzyme while the inactivating enzyme other

In this way insulin direct produced desired effect on carbohydrate, fat and protein metabolism.

- Glucose transport,
- Protein synthesis,
- Fat synthesis,
- Glucose synthesis,
- Growth and gene expression[8].

Pharmacokinetic

Insulin is not taken orally because of gastric acid degrades insulin. Insulin injected into the subcutaneous tissue of the abdomen, buttok, anterior thigh or dorsal arm. Absorption occurs most rapid from abdominal wall followed by arm, buttok and thigh. The abdomen currently is preferred site for injection in the morning because it absorbed 20-30 % faster from the site of arm. Now insulin also given in intra muscular route. Pulmonary absorption of insulin occurs and inhalation of an aerosol is promising route of administration. Insulin is inactivated by the enzyme "gluthathione insulin Trans hydrogenase" in the liver which break up bi-sulphide

bond of cystein between two chain. Normal man secretes 50 units of insulin daily. Pancreas content is about 200 units. The rate of insulin is influenced by various factors. Its half life is approximately 10 min. Its peak effect is achieved quickly within few hours[9].

Side Effect

Allergy: - This infrequent is due to contaminating protein very rare with human purified insulin.

Edema: - Some patients develop short lived dependent edema. When instrument therapy is stated.

Clinical

Metformin in patient with type 2 diabetes. It does not stimulate type 2 patient and in consequences useful in majority patients who are obese and fail in treatment of diet alone. It does not hypoglycemic and can be combined with sulphonyl ureas, glitazone and insulin[10].

CONCLUSION

A number of innovations in insulin therapy are currently under trial attempts. Attempts are continuing to make alternative routes of insulin delivery (nasal and oral) practicable. Liposome's in-capsulated insulin is being tried. Analogues of insulin with differing pharmacokinetic profile have been synthesized.

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Table 1: History of Diabetes

1552 B.C.	Earliest known record of diabetes mentioned on 3rd Dynasty Egyptian papyrus by physician Hesy –Ra; mentions polyuria (frequent urination) as a symptom.
1st Century A.D.	Diabetes described by Arateus as 'the melting down of flesh and limbs into urine.'
164 A.D.	Greek physician Galen of Pergamum mistakenly diagnosis diabetes as an ailment of the kidneys.
Up to 11th Century	Diabetes commonly diagnosed by 'water tasters', who drank the urine of those suspected of having diabetes; the urine of people with diabetes was thought to be sweet tasting. The Latin word for honey (referring to its sweetness) , 'mellitus', is added to the term diabetes as a result.
16th Century	Paracelsus identifies diabetes as a serious General disorder.
Early 19th Century	First chemical tests developed to indicate and measure the presence of sugar in the urine.
Late 19th	Italian diabetes specialist, Catoni , isolates his patients under lock and key in order to get them to follow their diets.
1900-1915	'Fad' diabetes diets include: the 'oat cure' , the milk diet, the rice cure, potato therapy and even the use of opium!
1919	Frederick Allen publishes Total Dietary Regulation in the treatment of diabetes;, and a case record of 76 out of 100 diabetes patient.
1919-20	Allen establishes the first treatment clinic in the USA.
Summer 1921	Insulin is "discovered". A de-pancreatized dog is successfully treated with insulin.
1944	Standard insulin syringe is developed, helping to make diabetes management more uniform.
1955	Oral drugs are introduced to help lower blood glucose level.
1959	Two major types of diabetes are recognized: Type 1 (insulin dependent) and Type 2 (non insulin dependent) diabetes.
1970	Blood glucose meter, Insulin pump and Laser techniques are developed
1983	First biosynthetic human insulin is introduced
1998	The United Kingdom Prospective Diabetes is published.

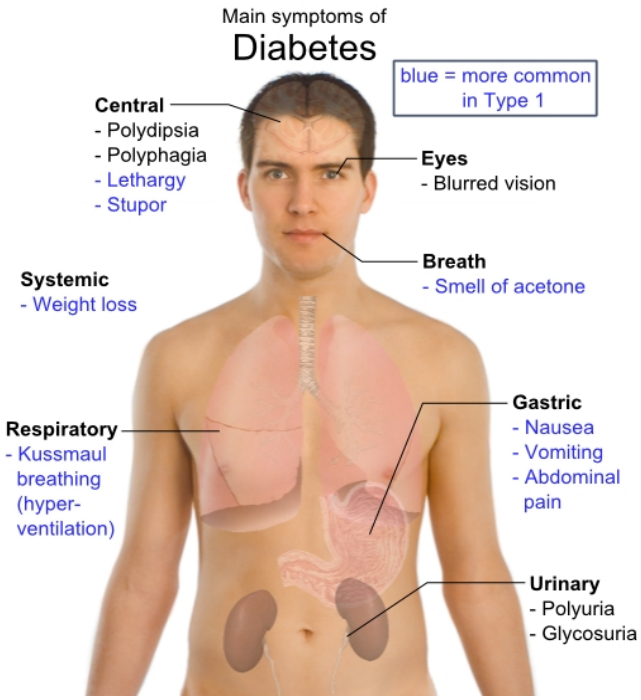

Figure 1: Symptoms of Diabetes