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Review article

Diabetes Mellitus and Insulin Resistance Physiology

[1]Dr M C Tayade , [2]Dr R G Latti

[1]Associate Professor, Department of Physiology, Rural Medical College, Pravara Institute of Medical Sciences, Loni, Tal. Rahata, Dist. Ahmednager, India

[2]Professor and HOD , Department of Physiology, Rural Medical College, Pravara Institute of Medical Sciences, Loni, Tal. Rahata, Dist. Ahmednager, India

Corresponding author: Dr Motilal C Tayade ; Email: drmctayade@gmail.com

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Abstract:

Diabetes mellitus is a heterogeneous group of metabolic disorders characterized by chronic hyperglycemia. Diabetes mellitus is caused by complex interaction of genetics, environmental factors, and life style choices. Depending on the etiology of diabetes mellitus, factors contributing to hyperglycemia may resulting from defects in insulin secretion, insulin action, or both. [1] The effects of diabetes mellitus include long term damage, dysfunction, and failure of various organs, especially the eyes, kidneys, heart, and blood vessels. Diabetes may present with characteristic symptoms such as thirst, polyuria, blurring of vision, weight loss, and polyphagia, and in its most severe forms with ketoacidosis or nonketotic hyperosmolarity, which in the absence of effective treatment, leads to stupor, coma, and death. Type 2 diabetes is the most common form of diabetes. Patients with type 2 diabetes usually have insulin resistance and relative, rather than absolute, insulin deficiency. Insulin resistance has also been arbitrarily defined as the requirement of 200 or more units of insulin per day to attain glycemic control and to prevent ketosis. Evidence is presented that shows that free fatty acids (FFA) are one important link between obesity, insulin resistance, and type 2 diabetes. Plasma FFA levels are elevated in most obese subjects, and physiological elevations of plasma FFA inhibit insulin-stimulated glucose uptake into muscle.

Keywords: Diabetes mellitus, metabolic disorders

Background:

Diabetes mellitus is a heterogeneous group of metabolic disorders characterized by chronic hyperglycemia. Diabetes mellitus is caused by complex interaction of genetics, environmental factors, and life style choices. Depending on the etiology of diabetes mellitus, factors contributing to hyperglycemia may resulting from defects in insulin secretion, insulin action, or both. [1] The effects of diabetes mellitus include long term damage, dysfunction, and failure of various organs, especially the eyes, kidneys, heart, and blood vessels. Diabetes may present with characteristic symptoms such as thirst, polyuria, blurring of vision, weight loss, and polyphagia, and in its most severe forms with ketoacidosis or nonketotic hyperosmolarity, which in the absence of effective treatment, leads to stupor, coma, and death. Type 2 diabetes is the most common form of diabetes. Patients with type 2 diabetes usually have insulin resistance and relative, rather than absolute, insulin deficiency. At the time of diagnosis of diabetes, and often throughout their lifetimes, these patients do not need insulin treatment to survive, although ultimately

many require it for glycemic control. This form of diabetes is associated with progressive P-cell failure with increasing duration of diabetes.[2]

Review

Most patients with type 2 diabetes are obese when they develop diabetes, and obesity aggravates the insulin resistance. Type 2 diabetes frequently goes undiagnosed for many years because the hyperglycemia develops gradually and in the earlier stages is not severe enough to produce the classic symptoms of diabetes; however, such patients are at increased risk of developing macrovascular and microvascular complications. Their circulating insulin levels may be normal or elevated yet insufficient to control blood glucose levels within the normal range because of their insulin resistance. Thus, they have relative, rather than absolute, insulinopenia. Insulin resistance may improve with weight reduction or pharmacologic treatment and results in normalization of their glycemia. Type 2 diabetes is seen frequently in women who have a previous history of gestational diabetes and in individuals with other characteristics of the insulin resistance syndrome, such as hypertension or dyslipidemia[3]

However, Al C assays are now highly standardized so that their results can be uniformly applied both temporally and across populations. In their recent report an International Expert Committee, after an extensive review of both established and emerging epidemiological evidence, recommended the use of the Al C test to diagnose diabetes, with a threshold of 6.5%, and ADA affirms this decision.

The diagnostic Al C cut point of 6.5% is associated with an inflection point for retinopathy prevalence, as are the diagnostic thresholds for FPG and 2-h PG . The diagnostic test should be performed using a method that is certified by the National Glycohemoglobin Standardization Program (NGSP)and standardized or traceable to the Diabetes Control and Complications Trial reference assay(DCCT). Point of care AlC assays are not sufficiently accurate at this time to use for diagnostic purposes.

The AlC has several advantages to the FPG, including greater convenience, since fasting is not required, evidence to suggest greater preanalytical stability, and less day to day perturbations during periods of stress and illness. These advantages, however, must be balanced by greater cost, the limited availability of A1C testing in certain regions of the developing world, and the incomplete correlation between Al C and average glucose in certain individuals. In addition, the A1C can be misleading in patients with certain forms of anemia and hemoglobinopathies, For patients with a hemoglobinopathy but normal red cell turnover,such as sickle cell trait, an AlC assay without interference from abnormal hemoglobins should be used .For conditions with abnormal red cell turnover, such as anemias from hemolysis and iron deficiency, the diagnosis of diabetes must employ glucose criteria exclusively[4]

Insulin resistance

It is generally accepted that insulin resistance plays a major role in the development of type 2 diabetes[4] . Obesity, particularly visceral or central as evidenced by the hip waist ratio is very common in type 2 diabetes mellitus.

Adipocytes secrete a number of biologic products (leptin, TNF -alpha, free fatty acids, resistin and adiponectin) that modulate insulin secretion, insulin action and body weight and may contribute to insulin resistance. In the early stages of the disorder, glucose tolerance remains normal, despite insulin resistance because pancreatic beta cells

compensate by increasing insulin output. As insulin resistance and compensatory hyperinsulinemia progress, the pancreatic islets in certain individuals are unable to sustain the hyperinsulinemic state.

Impaired glucose tolerance (IGT) characterized by elevations in postprandial glucose, then develops. Further decline in insulin secretion and an increase in hepatic glucose production lead to overt diabetes with fasting hyperglycemia, ultimately beta cell failure may ensue. Markers of inflammation such as interleukin 6 and C reactive protein are often elevated in type 2 diabetes.[5]

Another emerging theory proposes that elevated levels of free fatty acids, a common feature of obesity may contribute to the pathogenesis of type 2 diabetes.

Insulin resistance is a state in which a given concentration of insulin produces a less-than-expected biological effect. (See Pathophysiology.) Insulin resistance has also been arbitrarily defined as the requirement of 200 or more units of insulin per day to attain glycemic control and to prevent ketosis. Evidence is presented that shows that free fatty acids (FFA) are one important link between obesity, insulin resistance, and type 2 diabetes. Plasma FFA levels are elevated in most obese subjects, and physiological elevations of plasma FFA inhibit insulin-stimulated glucose uptake into muscle.

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