ARTÍCULO DE REVISIÓN

TYPE 2 DIABETES MELLITUS: A PREVENTABLE EPIDEMIC

DIABETES MELLITUS TIPO 2: UNA EPIDEMIA PREVENIBLE

Pedro González Morales[1], Francisco Javier Rodríguez Molina[2*], Gladys Josefa Sánchez Cudello[3], Cynthia Olivia Morales Pérez[4]

[1]Estudiante de cuarto año de la carrera de Medicina. Alumno ayudante en la especialidad de Medicina Interna. Universidad de Ciencias Médicas de Cienfuegos.
[2]Estudiante de cuarto año de la carrera de Medicina. Alumno ayudante en la especialidad de Neurocirugía. Universidad de Ciencias Médicas de Cienfuegos.
[3]Estudiante de cuarto año de la carrera de Lenguas Extranjeras. Universidad de Cienfuegos.
[4]Especialista de I grado en Fisiología. Especialista de I grado en Medicina General Integral. Máster en Educación Superior. Universidad de Ciencias Médicas de Cienfuegos.

Correspondencia*: medfjrm970909@ucm.cfg.sld.cu

ABSTRACT

Type 2 diabetes mellitus has been catalogued as one of the many new epidemics of the twenty-first century. It is a multifactorial disease whose prevention constitutes an important objective for the primary level of medical attention. It was the aim of this review to explain the anatomophysiological alterations of type 2 diabetes mellitus. A bibliographical review of 21 sources was carried out. Type 2 diabetes mellitus is classified fundamentally by the presence of resistance to insulin or by a secretory defect thereof. Insulin resistance, metabolic syndrome and atherosclerosis are implicated in its pathogenesis and complications. Its clinical features and the values of glycaemia, be they fasting or postprandial, are indispensable for a diagnosis. A diabetological education that includes an adequate lifestyle will prevent complications and better the quality of life of these patients.

Key words: risk factor, type 2 diabetes mellitus, insulin resistance

RESUMEN

La diabetes mellitus tipo 2 ha sido catalogada como una de las nuevas epidemias del siglo XXI; es un trastorno plurimetabólico y multifactorial cuya prevención es un objetivo importante para el nivel primario de atención médica. El objetivo principal de este material de revisión fue explicar las alteraciones morfofuncionales de la diabetes mellitus tipo 2. Se realizó una revisión de un total de 21 fuentes bibliográficas. Esta enfermedad metabolica se clasifica fundamentalmente por la resistencia a la insulina o por un defecto secretor de la misma. En su patogenia y complicaciones están implicados la insulinorresistencia, el síndrome metabólico y la aterosclerosis. El diagnóstico se realiza a través de los síntomas. El cuadro clínico y los valores de glucemia tanto en ayunas como postprandial son elementos indispensables para el diagnóstico. Una educación diabetológica que incluye un adecuado modo y estilo de vida evitará complicaciones y mejorará la calidad de vida de estos pacientes.

Palabras clave: factor de riesgo, diabetes mellitus tipo 2, insulinorresistencia

INTRODUCTION

Diabetes mellitus (DM), commonly referred to as simply diabetes, encompasses a group of frequent metabolic disorders that share the phenotype of hyperglycaemia. It is an increasingly troubling global health concern given that its prevalence has increased markedly. As a result of a complex interaction between genetics, environmental factors and lifestyle choices, there exist various types of DM. [1]

There are, however, two main categories: DM type 1 and DM type 2. Globally, the majority of DM patients that present are type 2. Unlike type 1 DM, which is denoted as diminished insulin production, type 2 DM is a heterogeneous disorder characterised by impaired cellular responses to insulin, known as insulin resistance, and followed by progressive partial pancreatic β-cell dysfunction. [1,3]

There are also other forms of DM amongst which we find: Diabetes Gravídica, Latent Autoimmune Diabetes of Adulthood (LADA) as well as other specific types. Diabetes Gravídica, also known as gestational diabetes, develops during pregnancy where the gestant's intolerance to glucose first becomes known. Recently, a new type of DM has been discovered, namely LADA, which shares traits and symptoms of both main types of DM. [1,2]

The medical name, *diabetes mellitus*, derives from words whose etymologies are rooted in Greek and Latin. Diabetes has its origin in a Greek word that means to come out with force. The most obvious sign of diabetes is to urinate excessively. Mellitus derives from a Latin word which means sweet as honey, given that the urine of a diabetic contains an excess of glucose. [4]

DM was already known before the age of Jesus Christ. In Ebers' papyrus, discovered in Egypt and dating back to the 15th century B.C., symptoms that appear to correspond with DM were already being described. It was Aretheo of Cappadocia who, in the second century of the Christian age, gave this illness the name diabetes. Galleon too referred to diabetes during the second century A.C. Avicenna spoke with clear precision on the topic in the eleventh century A.C. in her famous Canon of Medicine. After a long interval, it was Thomas Willis who gave a masterful description of diabetes and it has henceforth become recognised by its symptomatology as a clinical entity. It was he who, making reference to the sweet taste of the urine, gave it the name diabetes mellitus. [2]

The prevalence of DM has increased markedly in the last two decades in countries with low and middle income, not to mention countries with high income where it is even more widespread. This trend, which is almost completely due to type 2 DM, is expected to continue rising. According to the International Diabetes Federation (IDF), at least 371 million people have diabetes in 2012, which is predicted to be 552 million by 2030. [3,5]

The Pan-American Health Organisation (PAHO), through the "Initiative for Diabetes in the Americas" and the IDF, estimated that there were 18 million Latin-Americans diagnosed with DM in 2010, 25 million in 2014 and, according to forecasts from the same organisations, these figures should increase to approximately 40 million by the year 2025. [6]

In Cuba, during 2011, the total population was 11 244 543. In that very year, the prevalence of DM in the country was 45.7/1 000 people, with predominance in the 60-64 age group where the rate was 181/1 000. DM was also the eighth most common cause of death with 2 236 people passing away. This constituted a gross rate of 19.9/100 000 citizens. These figures are very discouraging, especially when one considers the marked increase in prevalence. At the moment, on a global level, 90 to 95% of cases that present DM present type 2 DM and this also constitutes the principal health problem in the thirty families assigned to the authors. Therein lies the importance of this bibliographical review. [7]

What are the anatomophysiological alterations of type 2 DM that have made it one of the new epidemics of the 21st century?

Our objective was directed to explain the anatomophysiological alterations of type 2 diabetes mellitus.

DEVELOPMENT

Classification

Type 2 DM is characterised by predominant insulin resistance with a relative deficit of insulin secretion or by a predominant secretory defect with relative resistance to insulin. As a result of insulin resistance, the β-cells of the Islets of Langerhans of the endocrine pancreas secrete insulin for the control of blood glucose in abnormally high levels. Nowadays, the diet and lifestyle choices of people tend towards increased caloric intake and sedentary behaviour, both of which promote the development of obesity. [1,3]

Pathogenesis

Type 2 DM possesses four relevant features in its pathogenesis. These are: 1) insulin resistance, 2) hepatic overproduction of glucose, 3) intolerance to glucose and 4) the altered functioning of pancreatic β-cells. [4]

Metabolic Syndrome and Resistance to Insulin

Central obesity, associated with other risk factors, constitutes the metabolic syndrome (MS), whose basic feature is insulin resistance. Insulin resistance is also present in arterial hypertension and atherosclerosis. Changes in organ and cellular function, such as pre-receptor abnormalities, a deficit in the number of or affinity for insulin receptors, deficient glucose transport and the deficient translation of the signal by the receptor, contribute to the appearance of insulin resistance. Insulin resistance is expressed at a hepatic level with an overproduction of glucose and at a cellular and tisular level with an underutilisation thereof, which metabolically includes the defect of proinsulin activation by the enzyme glycogen synthase in skeletal muscle and the deficient suppression of lipolysis. [6,7]

As a result of a hyperinsulinaemic inability to supress gluconeogenesis, we see the onset of a hepatic overproduction of glucose. This overproduction in turn, leads to Impaired Fasting Glucose (IFG) readings as well as the reduction of hepatic glucose storage in the postprandial period. This incessant hepatic gluconeogenesis occurs during a relatively early stage in the development of DM, though it probably occurs after the initial insulinic secretory alterations and the appearance of insulin resistance in skeletal muscle. [1,6]

During the early stages of the disorder, glucose tolerance appears normal in spite of the presence of insulin resistance. This is because the β-cells in the Islets of Langerhans compensate by increasing the production of insulin thus leading to a state of hyperinsulinaemia. However, as the disorder progresses, the pancreas becomes incapable of sustaining this hyperinsulinaemic state. This leads to the appearance of Impaired Glucose Tolerance (IGT), which is characterised by large elevations of postprandial glycaemia. When insulin secretion declines yet further and hepatic gluconeogenesis increases, we see the onset of diabetes manifested as IFG. As a final consequence, we see the destruction of the pancreatic β-cells. [1,8,9]

Atherosclerosis and type 2 DM

Central obesity (also known as abdominal obesity) associated with MS, whose basic feature is insulin resistance, is also characterised by a proinflammatory and prothrombotic state. Visceral adipocytes are more resistant to insulin than subcutaneous ones and this leads to an increase in the number of fatty acids that enter the liver. This also increases the hepatic synthesis of triglycerides. All of this has two immediate consequences: hepatic steatosis occurs and hepatic formation of Very Low Density Lipoproteins (VLDL) increases. As a result of the insufficient activity of lipoprotein lipase (an insulin-dependent endothelial enzyme), this surge in the liberation of VLDL and the reduction in plasmatic clearance thereof leads to hypertriglyceridaemia. [10,15]

Diagnosis

Internationally, criteria for the diagnosis of DM have been proposed based on the following premises: 1) the spectrum of fasting plasmatic glucose (FPG), and 2) DM is defined as the level of glycaemia at which the specific complications of DM occur. The habitual methods for the diagnosis of diabetes are based on various laboratory tests

carried out with the urine and blood of the patient, such as: tests for glycosuria, values of fasting glycaemia and the glucose tolerance curve. [1,16]

In order to determine the quantity of glucose that is lost through urination, professionals of the health sciences will use either simple methods that can be done in a consultation or more complex quantitative analytical procedures. In general, a normal person loses undetectable quantities of glucose; whereas a person with DM will lose quantities of glucose that are either slightly or highly elevated in correspondence with the severity of their affliction and the amount of carbohydrates that they ingest. At the beginning of the morning, the level of fasting glycaemia is normally from 80 to 90 mg/dL or less than 7 mmol/L and it is considered that 110mg/dL represent the superior limit of normality. A fasting glycaemia in excess of this value or over 11 mmol/L tends to indicate DM. Much less frequently, we find a hypophysial or adrenal diabetes. [8]

Clinical Features and Complications

Type 2 DM frequently presents in our medium in people above the age of 45 with a family history of diabetes, and it is associated with central obesity and arterial hypertension. The chronic complications of diabetes are present in an elevated percentage of patients at the initial moment of diagnosis. [1, 11]

Type 2 DM manifests itself by signs and symptoms in accordance with its characteristic hyperglycaemia or its specific complications. Associated with acute hyperglycaemia we find: Polyuria, polydipsia, polyphagia, asthenia, weight loss, blurred vision and superficial infections such as mycosis and vaginitis. In relation with chronic complications: paraesthesia, cramps/spasms, absence of peripheral pulses, varying grades of diabetic retinopathy etc. [17, 18]

It is proposed that in the progression toward type 2 DM, the plurimetabolic disorders, and the atherogenic and thrombogenic endothelial processes that give rise to the complications of the disease, develop and evolve in parallel with the deterioration of glucose tolerance. These disorders are associated fundamentally with insulin resistance and hyperinsulinaemia. [11]

Studies carried out in Cuba show that patients with type 2 DM of recent diagnosis present: microangiopathic complications in a significant frequency; asymptomatic peripheral neuropathies of the lower extremities (75%); diabetic retinopathy (8%) and diabetic nephropathy (11%). In a study comprising 302 patients from six different regions of Argentina with a recent diagnosis of type 2 DM, chronic complications were found in 156 of them of which there were 70 with microvascular complications (diabetic neuropathies, nephropathies and retinopathies) and the rest were macrovascular complications such as coronary sickness and silent myocardial infarctions. [11]

Hypertension is capable of accelerating diabetic complications, especially nephropathy and cardiovascular pathologies. The treatment of the same should first and foremost be centred on lifestyle modifications such as weight loss, exercise, stress reduction and sodium restrictions. Hypotensive drugs should be selected by taking into consideration the advantages and disadvantages of each medication within the profile of the individual's risk factors. [1]

Another recurrent complication in patients with type 2 DM is the diabetic foot ulcer. Wound healing is an innate mechanism of action that works reliably most of the time. A key feature of wound healing is stepwise repair of lost extracellular matrix (ECM) that forms the largest component of the dermal skin layer. However, in some patients, certain disorders or physiological insult disturbs the wound healing process. DM is one such metabolic disorder that impedes the normal steps of the wound healing process. Many studies show a prolonged inflammatory phase in diabetic wounds, which cause a delay in the formation of mature granulation tissue and a parallel reduction in wound tensile strength. These wounds are difficult to heal due to the poor sanguine irrigation of the feet in diabetic patients and oftentimes will lead to amputations. [18]

In a healthy patient's blood, there are small traces of acetoacetic acid. However, in a severe case of DM, its concentration increases markedly and it turns into acetone. Acetone is a volatile substance and is vaporised in exhaled air. As a consequence, it becomes possible to obtain a diagnosis of DM due to the acetonic odour of the patient's breath – which is in and of itself a chronic complication of DM. [1, 8, 18]

CONCLUSIONS

1. Type 2 diabetes mellitus is a plurimetabolic and multifactorial disorder and is classified fundamentally by the presence of resistance to insulin or by a secretory defect thereof.
2. Insulin resistance, metabolic syndrome and atherosclerosis are implicated in its pathogenesis and complications.
3. Its clinical features and the values of glycaemia, be they fasting or postprandial, are indispensable for a diagnosis.

BIBLIOGRAPHICAL REFERENCES

1. Kasper DL, Braunwald E, Fauci AS, Hauser SL, Longo DL, Jameson JL, et al. HARRISON: Principios de Medicina Interna. 19thEd. New York: McGraw-Hill Companies; 2017. p. 8849 – 8936.
2. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2014 Jan;37 Suppl 1:S81-90. doi: 10.2337/dc14-S081. PubMed PMID: 24357215..
3. Wilson RD, Islam MS. Effects of white mulberry (Morus alba) leaf tea investigated in a type 2 diabetes model of rats. Acta Pol Pharm. 2015 Jan-Feb;72(1):153-60. PubMed PMID: 25850211..
4. Lindsay RS, Funahashi T, Hanson RL, Matsuzawa Y, Tanaka S, Tataranni PA, Knowler WC, Krakoff J. Adiponectin and development of type 2 diabetes in the Pima Indian population. Lancet. 2002 Jul 6;360(9326):57-8. PubMed PMID: 12114044.
5. Safari M, Yazdanpanah B, Yazdanpanah B, Mobasheri A. A population-based screening of type 2 diabetes in high-risk population of Yasuj, Iran. J Health Popul Nutr. 2014 Dec;32(4):677-86. PubMed PMID: 25895201; PubMed Central PMCID: PMC4438698.
6. Cambizaca Mora GP, Castañeda Abascal I, Sanabria G. Sobrepeso, obesidad y diabetes mellitus 2 en adolescents de América Latina en 2000 – 2010. Rev Cubana Med Gen Integral [Internet]. 2015 [citado 21 Oct 2018];31(2): [aprox. 17 p.]. Disponible en: http://www.revmgi.sld.cu/index.php/mgi/article/view/15/11
7. Casanova Morenol MC, Trasancos Delgado M. Ancianos con diabetes mellitus de tipo 2: retos actuales para la salud pública cubana. MEDISAN [Internet]. 2013 Ago [citado 21 Oct 2018];17(8): [aprox. 16 p.]. Disponible en: http://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S1029-30192013000800001&lng=es
8. Guyton A C, Hall J E. Tratado de Fisiología Médica. 9th ed. Habana: Ecimed; 2006 p. 1063 – 1077.
9. Cardellá Rosales L, Hernández Fernández R, Upmann Ponce de León C, Vicedo Tomey A, Pérez Díaz A, Sierra Figueredo S, et al. Bioquímica Médica T. IV. 26th ed. La Habana: ECIMED; 2005. p. 1305 – 1311.
10. Miguel Soca PE. Riesgo vascular en pacientes diabéticos con obesidad. Rev Cubana Med Gen Integral [Internet]. 2016 [citado 21 Oct 2018];32(1): [aprox. 23 p.]. Disponible en: http://revmgi.sld.cu/index.php/mgi/article/view/143.
11. Valdés Ramos E, Camps Arjona MC. Características clínicas y frecuencia de complicaciones crónicas en personas con diabetes mellitus tipo 2 de diagnóstico reciente. Rev Cubana Med General Integral [Internet]. 2013 [cited 2015 Dec 22]; 29(2): 121-31. Available at: http://scielo.sld.cu/scielo.php?script=sci_artt

ext&pid=S0864-21252013000200003&lng=es
12. Flores Paredes A. Actividad física y prevalencia de sobrepeso y obesidad en adolescentes escolares de 12 a 18 años de la ciudad de juliaca 2015. Rev Investig Altoandin [Internet]. 2017 Mar [citado 12 Oct 2018];19(1): [aprox. 18 p.]. Disponible en: http://www.scielo.org.pe/scielo.php?script=sci_arttext&pid=S2313-29572017000100011&lng=es
13. Miguel Soca PE. Riesgo vascular en pacientes diabéticos con obesidad. Rev Cubana Med Gen Integral [Internet]. 2016 [citado 12 Oct 2018];32(1): [aprox. 16 p.]. Disponible en. http://scielo.sld.cu/pdf/mgi/v32n1/mgi02116.pdf
14. Benítez Rojas A, Martínez Ponce LM, González Martín L, Rojas Pérez S. Actualización en criterios para el diagnóstico de la diabetes mellitus. Revista Universidad Médica Pinareña, [S.l.], v. 13, n. 1, p. 1-45, sep. 2017. ISSN 1990-7990. Disponible en: http://galeno.pri.sld.cu/index.php/galeno/article/view/439/html
15. Tarragó Amaya E, Miguel Soca PE, Cruz Lage LA, Santiesteban Lozano Y. Factores de riesgo y prevención de la cardiopatía isquémica. CCN [Internet]. 2012 [citado 12 Oct 2018];16 (2): [aprox. 18 p.]. Disponible en: http://www.revcocmed.sld.cu/index.php/cocmed/article/view/505
16. Masood T, Kushwaha RS, Singh R, Sailwal S, Pandey H, Varma A, Singh RK, Cornelissen G. Circadian rhythm of serum 25 (OH) vitamin D, calcium and phosphorus levels in the treatment and management of type-2 diabetic patients. Drug Discov Ther. 2015 Feb;9(1):70-4. doi: 10.5582/ddt.2015.01002. PubMed PMID: 25788054.
17. Chan WK, Tan AT, Vethakkan SR, Tah PC, Vijayananthan A, Goh KL. Low physical activity and energy dense Malaysian foods are associated with non-alcoholic fatty liver disease in centrally obese but not in non-centrally obese patients with diabetes mellitus. Asia Pac J Clin Nutr. 2015;24(2):289-98. doi: 10.6133/apjcn.2015.24.2.15. PubMed PMID: 26078246.
18. Vicente Peña R, Rodríguez Porto AL, Sánchez Zulueta E, Quintana López L, Riverón González JM, Ledo Grogués D. Diagnóstico y Tratamiento en Medicina Interna. 2ed. Habana: ECIMED; 2016. p. 391 – 441.

Cita del artículo

González Morales P, Rodríguez Molina FJ, Sánchez Cudello GJ, Morales Pérez CO. Diabetes mellitus tipo 2: una epidemia prevenible. INMEDSUR [Internet]. Nov 2018-Feb 2019; 1 (1): 78-83.