Review Article

TYPE 2 DIABETES: A REVIEW OF CURRENT TRENDS

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ABSTRACT

Diabetes mellitus type 2 (DM) is a chronic metabolic disorder in which the frequency has become worldwide. Because of this, there is always an epidemic in some countries of the world, with the number of people affected is expected that within the next decade to double due to the increasing aging of the population, thus increasing the existing burden of health care providers, particularly in the less developed countries. This review is based on a search Medline, Cochrane Database of Systemic journals and references to the literature list at the bottom.Subject heading and key wordsused include type 2 diabetes, the prevalence, the current diagnosis and therapy in progress. Onlyarticles in English were included. Early detection and diagnosis is still for the World Health Organization (WHO) and the American Diabetes Association (ADA) criteria include clinical and laboratory parameters. No cure has been found yet for the disease;Treatment details, however, include lifestyle changes, treatment of obesity, oral hypoglycemic agents and insulin sensitizers such as metformin, a biguanidethat reduces insulin resistance, is still the first-line drug specifically for overweight patients.Other effective drugs includesnonsulfonylureasecretagogues, thiazolidinediones, inhibitors of alpha-glucosidase and insulin.Recent research in the pathophysiology of type 2 diabetes has led to the introduction of new drugs such as glucagon-like peptide 1 analogoues: Dipeptidyl peptidase-IV inhibitors of the sodium-glucose cotransporter 2 and 11s-1-hydroxysteroid dehydrogenase, glucokinase activators of insulin release and pancreatic-G-protein-coupled fatty-acid-receptor agonists, glucagon receptor antagonists, inhibitors of the hepatic metabolism of glucose production and fast release bromocriptine. Inhaled insulin has been approved in 2006, but was withdrawn from the market due to low patronage.

Key Words: Type 2 diabetes, Diagnosis, Administration, New medicines

INTRODUCTION

Diabetes mellitus (DM) is perhaps one of the oldest diseases known to mankind. It was first mention in Egyptian manuscript about 3000 years ago[1]. In 1936 the difference between type 1 and type 2 DM madesignificantly[2].Type 2 diabetes is described (as non-insulin dependent DM earlier) as a component of the metabolic syndrome in 1988[3]. Type 2 diabetes,the most common form of DM characterized by hyperglycemia, insulin resistance and insulin deficiency[4].Type 2 DM results from the interaction of genetic, environmental and behavioral risk factors[5, 6]. People with type 2diabetes are more susceptible to various forms of short- and long-term complications that often lead to premature death. This trend of increasing morbidity and mortality is seen in patients with diabetes type 2 because of truism that type DM, insidious onset and late recognition, particularly in poor developing countries such resources Africa[7].

Epidemiology

It is estimated that 366 million people had DM in 2011; 2030 will be 552 million increased [8].The number of people with type 2 diabetes is increasing in all countries with 80% of people with DM living in low and middle income countries.DM caused 4.6 million deaths in 2011[8]. It is estimated that 439 million people suffer from type 2 diabetes since year 2030[9]. The incidence of type 2 diabetes ranges from one geographic area to another, due to lifestyleand environmental risk factors[10]. The literature has shown that there is little available data on type 2 diabetes prevalence in Africa as a whole.Study data trends based tip of Africa to show a dramatic increase in the prevalence of rural and urban areas, and both gender equally[11]. The majority of the weight in Africa appears to be type 2 DM, to be less than 10% of cases ofDMis type 1 DM[11].A 2011 Centre for Disease Control and Prevention (CDC) report estimates that DM affects about 25.8 million people in the United States (7.8% of the population) in 2010, with 90% to 95% of which is type 2 -DM[12].It is expected that

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the prevalence of diabetes in patients with type 2 diabetes, it is important that adults will increase in the next two decades, and much of the increase will be in developing countries, where the majority of patients are aged between 45 and 64 years[13].It is estimated that the state equal to or even greater than the previous one in the developing countries, which will be completed double taxation arising from the current trend of moving from non-communicable diseases contacts

Lifestyle, Genetics, and Medical Conditions

Type 2 diabetes is caused primarily by lifestyle factors and genetics[15]. A number of lifestyle factors are known to develop type 2 diabetes. These are physical inactivity, lack of exercise, cigarettesmoking and generous consumption of alcohol[16]. Obesity has been found to contribute about 55% of cases of type 2 DM[17].The increased rate of childhood obesity between the 1960s and 2000s is believed to have led to an increase of type 2 diabetes in children and adolescents[18]. Environmental toxins may contribute to the recent increase in the rate of type 2 diabetes.Found a weak positive correlation between the concentration in the urine of bisphenol A, a component of some plastics, and the incidence of type 2 DM[19].There is a strong hereditary genetic connection in type 2 DM with relatives (especially first degree) with type 2 diabetes increases the risk of type 2 diabetes significantly. Agreement between monozygotic twins is close to 100%, and about 25% of People with the disease have a family history of DM[20].Recently discovered genes associated significantly with type 2 diabetes include TCF7L2, PPARG, FTO, KCNJ11, NOTCH2, WFS1, CDKAL1, IGF2BP2, SLC30A8 and JAZF1 HHEX. KCNJ11 (potassium internal channel correction, subfamily J, member 11), encodes the islet ATP-sensitive potassium channel Kir6.2 and TCF7L2 (transcription factor 7-like 2) regulates proglucagon gene expression and thus production glucagonlike peptide-1[21]. Furthermore, obesity (which is an independent risk factor for type 2 diabetes) is strongly inherited[22].Monogenic forms as Maturity-onset diabetes of the young (MODY), constitutes up to 5% of cases[23]. There are many diseases that can potentially cause or exacerbate type 2 diabetes, including obesity, hypertension, high cholesterol (combined hyperlipidemia), often referred to as conditions of metabolic syndrome (also known as syndrome X, Reaven's syndrome known) [24]. Other causes include acromegaly Cushing's syndrome, thyrotoxicosis, pheochromocytoma, chronic pancreatitis, cancer and drugs[25]. Additional factors found that the risk for type 2 diabetes with increasing age, diet rich in fat [26] and a less active lifestyle[27].

Pathophysiology

Type 2 diabetes is an insulin sensitivity due to insulin resistance, reduced insulin production, and pancreatic beta cells can failure[28, 29]. This results in a reduction in glucose transport in the liver, muscle and fat cells. There is an increase in the distribution of fat in hyperglycemia. The inclusion of the modified alpha-cell function has been detected recently in the pathophysiology of type 2 DM[30]. As a result of dysfunction, glucagon and hepatic glucose levels which are increased during fasting, is not removed with a meal. Since insufficient insulin levels and increased insulin resistance that results in hyperglycemia. The incretins are important mediators of the intestine of the release of insulin, and in the case of GLP-1, suppress glucagon. Although the activity of GIP is impaired in individuals with type 2 diabetes remain intact GLP-1 insulinotropic action and hence the GLP-1 is a potentially useful therapeutic option[30].However, since the GIP; GLP-1 is rapidly inactivated by DPP-IV in vivo. Two therapeutic approaches have been developed to solve this problem: GLP-1 analogues with increased half-life and DPPIV inhibitors that prevent the breakdown of endogenous GLP-1 and GIP[30].The two classes of agents have shown promise improved, with the ability to not only normalize postprandial glucose and fasting, but also for the function and beta cell mass. Investigations are under way, the role of mitochondrial dysfunction in the development of insulin resistance and etiology of type 2 DM[31]. Also very important is adipose tissue, as endocrine organ hypothesis(various Adipokytokines secretion, ieleptin, TNF-alpha,resistin and adiponectin resistance Insulin involved and possibly a dysfunction of beta cells) [30]. The majority of people with type 2 diabetes are overweight, with central visceral obesity. Therefore, fat plays an important role in the pathogenesis of type 2 diabetes, although the prevailing theory used to explain this connection, the gate / visceral case gives a key role in non-esterified high fatty acid concentrations, two new theories resulting trumpets fat storage syndrome (triglyceride accumulation in muscle, liver and pancreatic cells). These two assumptions are the framework for the study of the interaction of insulin resistance and beta cell dysfunction in type 2 diabetes and between us obesogenicenvironment and the risk of DM in the next decade[30].

Screening and Diagnosis

Tests for screening and diagnosis of DM are readily available. The recommended test is the same as for the diagnosis of prediabetes or DM[32]. Although approximately 25% of patients already type 2 diabetes have microvascular complications at diagnosis, suggesting a diagnosis, so it is a positive effect equivalent to that had the disease for more than five years old, when diagnosis[33]. It is still in the American Diabetes Association (ADA) guidelines of 1997 or the World Health Organization (WHO) national criteria diabetic group in 2006, which is for a single elevated glucose reading levels with the primary symptoms (polyuria, polydipsia, and polyphagia weight loss) Otherwise set values twice or fasting plasma glucose (FPG) ≥7.0 mmol / L (126 mg / dL) or Oral glucose tolerance test (OGTT), two hours after the oral dose of plasma glucose ≥11.1 mmol/L (200 mg/dL) [32] recommen-

dations from the 1997 ADA for the diagnosis of DM emphasis fasting glucose, whereas WHO concentrates on OGTT[32]. The glycosylated hemoglobin (HbA1c), and fructosamine, is always useful to determine the control of blood glucose with time. But doctors often practiced using other measures than those recommended. In July 2009, the International Expert Committee (IEC)recommended additional diagnostic criteria for HbA1c result ≥6.5% for DM. The Commission proposed that the term prediabetes can be eliminated, but defines the range of HbA1c ≥6.0% and detection <6.5% in subjects with high risk of developing DM[34]. As with glucose-based tests, there is no definite threshold of HbA1c at which normality ends and DM begins[32]. The IEC has decided to comment on a cut-off point for the diagnosis of diabetes, that emphasizes the particularity that this balanced position and the cost of impersonation diabetic subjects by minimal clinical consequences of delayed diagnosis apatientwith anHbA1c level <6.5% [34].

Management

The lifestyle and dietary changes. Studies have shown that there is a significant reduction in the incidence of type 2 diabetes with a combination of the feed body mass index of 25 kg / m^2, eat fiber and unsaturated fatty acids and low nutritional dietary saturated fats and trans-fats and glycemic index, regular exercise, abstention from smoking and moderate drinking alcohol[5, 16, 35-37]. Suggesting that the majority of Type 2 diabetes can be prevented by lifestyle changes. Patients with type 2 diabetes should receive medical evaluation of the diet; Lifestyle recommendations should be adapted to the physical and functional ability[38].

Pharmacological agents

Biguanide

Biguanides, metformin is the most commonly used in patients in overweight and obese, suppresses hepatic glucose production, increases sensitivity to insulin increases glucose uptake by phosphorylation GLUT-activating agent, increases fatty acid oxidation and reduced absorption of glucose from the digestive tract[39]. Research published in 2008, also shows the mechanism of action of metformin that activation of AMP-activated protein kinase, an enzyme that plays a role in the expression of hepatic gluconeogenesis genes40. Because of concerns about the development of lactic acidosis, metformin should be used with caution in elderly diabetic patients with renal insufficiency. It has a low incidence of hypoglycaemia than sulfonylureas[39].

Sulfonylureas

This is generally well tolerated, but because stimulate secretion of endogenous insulin, the risk of wear hypoglycemia[38]. Elderly patients with diabetes who are treated with sulfonylurea have an increased risk of hypoglycaemia by 36% compared to younger patients[41]. Glyburide is associated with higher rates of hypoglycemia compared with glipizide[42]. Some of these risk factors for hypoglycaemia depends on the age-related renal insufficiency, concomitant administration of insulin sensitizers or older than 60 years, calculated from the hospital recently, alcohol abuse, the reduction of calories, different drugs or actions sulfonylurea drugs[43]. Using long-acting sulfonylurea glibenclamide should be avoided in elderly patients with diabetes mellitus and the use of short-acting glipizide to preferred[38].

Meglitinides

Repaglinide and nateglinide are non-sulfonylurea secretagogues act on the ATP-dependent K channels in pancreatic beta cells and stimulating the release of insulin from beta-cells, similar to sulfonylurea, although the binding site is different[44]. Meglitinides have rapid onset and short duration of action (4-6 hours), and therefore a lower risk of hypoglycemia. The meglitinides are given before meals for postprandial glucose control. Preprandial administration allows for flexibility in case a meal lost, no increased risk hypoglycemia[45]. Mainlyrepaglinide is metabolised by the liver in very small amounts and excreted by the kidneys and therefore, dose adjustment in patients with renal impairment is required, except with end stage renal disease[44] failure.

Thiazolidinediones

It is a thiazolidinedione insulin sensitizer, selective ligands peroxisome proliferator-activated transcription factor gamma. These are the first drugs to treat patients[46]with the basic problem of insulin resistance in type 2 diabetes, whose course now consists mainly pioglitazone on the contained use of rosiglitazone by the Food and Drug Administration recommended (FDA) recently because of increased cardiovascular events reported in rosiglitazone[36]. Use of pioglitazone is not associated with hypoglycemia and can be used in patients with renal impairment and therefore tolerated in older adults. On the other hand, due to concerns about peripheral edema, fluid retention and fracture risk in women, whose use is limited in older adults with diabetes. Pioglitazone should be avoided in elderly patients with congestive heart failure, and is contraindicated in patients with class III-IV heart failure[47].

Alpha-Glucosidase Inhibitors

Acarbose, miglitol and voglibose not be used widely for the treatment of type 2 diabetes subjects, but rather safe and effective. These agents are more effective in postprandial hyperglycemia and should be avoided in patients with significant renal impairment. Their use is generally limited due to the high rate of side effects such as diarrhea and flatulence[38]. Voglibose which is newer drug, in one study it was shown

that glucose tolerance compared to the delay of progression of the disease and the number of patients that improve significantly normoglycemia[48].

Incretin-based therapies

1 (GLP-1) analogues with glucagon peptide is the basis of the treatments based on targeting incretin control[49] this little-known function of DM pathogenesis will lead to sustained improvement in glycemic control and improve body weight. Designed for use as monotherapy in addition to diet and exercise, or in combination with oral antidiabetic agents in adults examples of type 2 diabetes are available exenatide-imitative and secretory Liraglutide[38]. There is no risk of hypoglycemia using the GLP-1 treatment (except when combined with insulin secretagogues). Moreover, the emerging incretin therapies are based on data that may have a positive impact on inflammation, cardiovascular and liver health, sleep and central nervous system[49].

Dipeptidyl peptidase-IV inhibitors

Inhibitors of dipeptidylpeptidase (DPP) IV inhibitsdipeptidyl peptidase-4 (DPP-4), a ubiquitous enzyme is rapidly inactivated both GLP-1 and GIP increase active levels of these hormones, thereby improving islet function and glycemic control in type 2 DM[50]. DPP-4 inhibitors are a new class of anti-diabetogenic drugs that provide comparable efficacy to current therapies. It is suitable as monotherapy in patients inadequately controlled by diet and exercise and as adjunct therapy in combination with metformin, thiazolidinediones and insulin controlled. DPP-4 inhibitors are well tolerated, leading to lower risk of causing hypoglycemia and weight neutral. However, they are relatively expensive[50]. The long-term sustainability of effect on glycemic control and the morphology of the beta cells and the function established yet[50, 51].

Insulin

Insulin is used alone or in combination with oral hypoglycemic agents. The increase in the basal insulin therapy helpful if some beta cell function. Instead of an insulin basal-bolus is necessary if the depletion of beta cells. Emergency treatment using replacement is necessary if the toxicity of glucose, which should mimic the normal release of insulin by the beta cells of pancreas[52]. Insulin is available in injectable forms - rapid-acting, short-acting, intermediate-acting and long-acting. Long acting form is less likely to induce hypoglycemia than forms Quick.

Insulin analogues

Insulin therapy is limited its ability to mimic the normal physiological insulin secretion. Average traditional activity for long-term insulins (insulin NPH, Lente insulin and Ultralente) from the non-absorption and action tips, hypoglycemia[53,54]may cause the pharmacokinetic profiles of new insulin analogues limited differ from those of insulin and whose onset and duration ranging from fast action expands. Currently, two fast-acting insulin analogues lispro and insulin aspart and long-acting insulin analog, insulin glargine, is available[53, 54].

The future of treatment with inhaled insulin drug

Inhaling form of fast-acting insulin, in 2006[55], were available then. The European Medicines Evaluation Agency and the FDA approved for the treatment of type 1 and type 2 DM in adults[55-57]. It is a form of fast-acting insulin is indicated for use in patients with type 1 and adults with type 2 diabetes and has the convenience of administration directly into the lungs. However, studies have shown that inhaled insulin is as effective as, but not better than short acting insulin [55], recalled by the manufacturer, in October 2007 because of poor sales.

Bromocriptine

Quick release bromocriptine has recently been developed for the treatment of type 2 diabetes, however, the mechanism of action is unclear. Studies have shown that reducing the average HbA1c of 0.0% to 0.2% at 24 weeks therapy[58].

Other

Inhibitors of the sodium-glucose co-transporter 2, to increase the urinary excretion of glucose and inhibitor of 11β-hydroxysteroid dehydrogenase. The effect of glucocorticoids on liver and fat insulin releasing glucokinase acid receptors and agonists acids linked to G-proteins pancreas, glucagon receptor antagonists and of glucose production in the liver metabolism inhibitors are patients[59] for evaluating the development of a new drug therapy for type 2 diabetes.

DISCUSSION

Type 2 diabetes is a metabolic disease that can be prevented through changes in lifestyle, diet control and management of overweight and obesity. The education of the population is still the key to controlling these thresholds epidemic.

CONCLUSION

Thus new drugs are developed, but there is no cure for the disease is available, although a new light on the pathophysiology of the disease. Management should be able to improve the quality of life of type 2 diabetes.

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