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A REVIEW ON TYPE-2 DIABETES MELLITUS AND IT'S MANAGEMENT

Burlapalle Subhashini*[1], Bagepalli Srinivas Ashok Kumar[2], Anand Mouna A.[2] and Beedupalli Nawaz[1]

[1]Department of Pharmacology, Noorie College of Pharmacy, Kolar Gold Fields – 563113, Karnataka, India.

[2]Department of Pharmacognosy and Pharmaceutics, Shantha College of Pharmacy, Chickaballapur – 562104, Karnataka, India.

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***Corresponding Author**
Burlapalle Subhashini
Department of Pharmacology, Noorie College of Pharmacy, Kolar Gold Fields – 563113, Karnataka, India.

ABSTRACT

Type 2 diabetes mellitus (DM) is a chronic metabolic disorder which prevalence has been increasing steadily all over the world. As a result it is fast becoming an epidemic in some countries in the world with the number of people affected expected to double in the next decade due to increase in ageing population. No cure has yet been found for the disease, the alternative treatment include lifestyle modifications, treatment of obesity, oral hypoglycemic agents, and insulin sensitizers like metformin, a biguanide that reduces insulin resistance, is still the recommended first line medication especially for obese patients. Other effective medications include non- sulfonylurea secretagogues, thiazolidinediones, alpha glucosidase inhibitors, and insulin. Inhaled insulin was licensed for use in 2006 but has been withdrawn from the market because of low patronage.

KEYWORDS: Diabetes mellitus, hypoglycemic agents, metformin, biguanide, Epidemiology, lifestyle.

INTRODUCTION

Diabetes mellitus (DM) is the one of the oldest diseases known to the man, Diabetes mellitus (DM)was first reported in Egyptian manuscript about 3000 years ago.[1] Diabetes mellitus has been classified into two types that is insulin dependent diabetes mellitus (IDDM, Type I) and non- insulin dependent diabetes mellitus (NIDDM, Type II).[30] In 1936, the difference

between type1 and type 2 DM was clearly made.[2] Type I diabetes mellitus is an autoimmune disease which is characterized by a local inflammatory reaction in and around islets that is followed by selective destruction of insulin secreting cells and whereas Type 2 DM is the most common form of DM characterized by hyperglycemia, insulin resistance, and relative insulin deficiency.[4] Patients with type 2 diabetes mellitus are at an increased risk for the cardiovascular disease.[1,2], peripheral vascular diseases, stroke, neuropathy, renal failure, retinopathy, blindness, amputations.[31] Type 2 DM results from interaction between genetic, environmental and behavioral risk factors.[5,6] People living with the type 2 DM are more vulnerable to various forms of both short-and long-term complications, which often may lead to their premature death.[7]

Epidemiology

In 2011 It was estimated that Globally-366 million people had DM; and by 2030 this number mayrise to 552 million**.** The People with type 2 DM were increasing in every country with 80% of people with DM are living in low and middle-income countries[8] The type 2 DM varies substantially from one geographical region to the other as a result of environmental and lifestyle risk factors.[9] It occurs most frequently in people whose age are inbetween 45 and 64 years and who are obese and who have a family history of diabetes mellitus.[10]

Lifestyle, Genetics, and Medical Conditions

Type 2 DM is due primarily to lifestyle factors and genetics.[11] Genetic plays a crucial role in the etiology and manifestation of type 2 diabetes, Both impairment of beta cell function and an abnormal response to insulin are involved in this.[12] A lifestyle factors are also a important for the development of type 2 DM. life style changes due to urbanization including diet, physical inactivity, stress, smoking and alcohol consumption.[13] Obesity has been found that approximately 55% of cases of type 2 DM[14] The increased rate of childhood obesity between the 1960s and 2000s is believed to have led to the increase in type 2 DM in children and adolescents[15], Environmental toxins may also contribute to increases in the rate of type 2 DM[16] There is a strong inheritable genetic connection in type 2 DM, having relatives with type2 DM increases the risks of developing type 2 DM . among monozygotic twins is close to 100%, and about 25% of those with the disease have a family history of DM.20 Recently, genes discovered to be significantly associated with developing type 2 DM, include TCF7L2, PPARG, FTO, KCNJ11, NOTCH2, WFS1, CDKAL1, IGF2BP2, SLC30A8, JAZF1, and HHEX. KCNJ11.

Pathophysiology

Type 2 DM is characterized by insulin insensitivity as result it leads to insulin resistance, declining production of insulin, and even it leads to pancreatic beta-cell failure.[17,18] This leads to a decrease in glucose transport into the liver, muscle cells, and fat cells. There is an increase in the breakdown of fat with hyperglycemia. The involvement of impaired alpha-cell function has recently been recognized in the pathophysiology of type 2 DM.30 As a result of this dysfunction, glucagon and hepatic glucose levels that rise during fasting are not suppressed A majority of individuals are suffering from type 2 DM are due to obese, with central visceral adiposity. The adipose tissue plays a crucial role in the pathogenesis of type 2 Diabetes mellitus. Although the predominant theory used to explain this link is the portal/visceral hypothesis giving a key role in elevated non-esterified fatty acid concentrations, two new emerging theories are the ectopic fat storage syndrome (deposition of triglycerides in muscle, liver and pancreatic cells). These two hypotheses constitute the framework for the study of the interplay between insulin resistance and betacell dysfunction in type 2 DM as well as between our obesogenic environment and DM risk in the next decade.[18]

Screening and Diagnosis

The test recommended for screening of type 2 DM are same as that for making diagnosis, with the result that a positive screen is equivalent to a diagnosis of pre-diabetes or DM.[19] About 30%of patients with type 2 DM already have microvascular complications at the time of diagnosis suggesting that they have had the disease for more than 5 years at the time of diagnosis.[20] It is still based on the American Diabetic Association (ADA) guidelines of 1997 or World Health Organization (WHO) National diabetic group criteria of 2006, which is for a single raised glucose reading with symptoms (polyuria, polydipsia, polyphagia and weight loss), otherwise raised values on two occasions, of either fasting plasma glucose (FPG) ≥7.0 mmol/L (126 mg/dL) or with an oral glucose tolerance test (OGTT), two hours after the oral dose a plasma glucose ≥11.1 mmol/L (200 mg/dL). The 1997 ADA recommendations for diagnosis of DM focus on the FPG, while WHO focuses on the OGTT.[19] The glycated hemoglobin (HbA1c) and fructosamine is also stilluseful for determining blood sugar control over time. However, practicing physicians frequently employ other measures in addition to those recommended. In July 2009, the International Expert Committee (IEC) recommended the additional diagnostic criteria of an HbA1c result ≥6.5% for DM. This committee suggested that the use of the term pre-diabetes may be phased out but identified the range of

HbA1c levels ≥6.0% and <6.5%.[21]

Management

Studies have shown that, there is an chance of significant reduction in type 2 DM with a combination of maintenance of body mass index of 25 kg/m2, eating high fibre and unsaturated fat and diet low in saturated and trans-fats and glycemic index, regular exercise, abstinence from smoking and moderate consumption of alcohol.[5,22, 23, 24]

The majority of type 2 DM can be prevented by lifestyle modification. Patients with type 2 DM should receive a medical nutrition evaluation; lifestyle recommendations should be tailoredaccording to physical and functional ability.[25]

Pharmacological Agents

1) Sulfonylureas
2) Meglitinides
3) Metformin (a biguanide),
4) Thiazolidinediones (TZDs),
5) Alpha glucosidase inhibitors,
6) Incretin-Based Therapies
7) Dipeptidyl peptidase IV (DPP-4) inhibitors,
8) Insulin
9) Bromocriptine

Sulfonylureas

Sulfonylureas are well tolerated but they stimulate endogenous insulin secretion, they carry a riskof hypoglycemia[25] Elderly patients, with DM who are treated with sulfonylureas have a 38% increased risk of hypoglycemia compared to younger patients[26] Glyburide is associated with higher rates of hypoglycemia compared to glipizide[27] Some of the risk factors for hypoglycemiaare age-related impaired renal function. Use of long acting sulfonylurea such as glyburide should be avoided in elderly patients with DM and use of short-acting glipizide should be preferred.[25]

Meglitinides

Meglitinides, Repaglinide and nateglinide are non-sulfonylurea secretagogues which act on the ATP-dependent K-channel in the pancreatic beta cells thereby stimulating the release of

insulin from the beta cells, similar to sulfonylurea, though the binding site is different.44 Meglitinides have a rapid onset and a short duration of action (4-6 hrs) and thus lower risk of hypoglycemia. Meglitinides are given before meals for postprandial blood glucose control. Preprandial administration allows flexibility in case a meal is missed without increased risk of hypoglycemia.

Biguanides

Biguanides, metformin is the most commonly used in overweight and obese patients, suppresses hepatic glucose production, increases insulin sensitivity, enhances glucose uptake by phosphorylating GLUT-enhancer factor, increases fatty acid oxidation, and decreases the absorption of glucose from the gastrointestinal tract. It has a low incidence of hypoglycemia compared to sulfonylureas.[28]

Bromocriptine

Bromocriptine has recently been developed for the treatment of type 2 DM. the mechanism of action is not clear. Studies have shown that they reduce the mean HbA1c levels by 0.0% to 0.2% after 24 weeks of therapy.[29]

CONCLUSION

Conclusion Type 2 DM is a metabolic disease that can be prevented through lifestyle modification,diet control, and control of overweight and obesity. Education of the populace is still key to the control of this emerging epidemic. Novel drugs are being developed, yet no cure is available in sight for the disease, despite new insight into the pathophysiology of the disease. Management should be tailored to improve the quality of life of individuals with type 2 DM.

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