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Challenges Facing Family Doctors in Management of Diabetes Mellitus Type 2 in Primary Care

Abdullah Ali Al-Mazrua

Abstract: **This review discusses the current antidiabetes agents and focus on incretin based therapies, which have been shown to improve hyperglycemia, weight and other CV risk factors in patients with T2DM in primary care setting. We carried out a computerized literature search through several medical databases "Medline, Embase, PubMed" up to 2018 January. We hand-searched selected articles for additional citations relevant with our objective. The central factors to take into consideration in taking care of T2DM in primary care are individualizing treatment and entailing the patient in care planning and management. The clinician must utilize an interdisciplinary strategy to care that integrates education and learning and management of hidden conditions. T2DM is a chronic, modern condition that does not need to define the patient. Comprehending and executing evidence-based practice and following clinical technique guidelines improve the quality of first and continuous care, directly influencing the burden of disease, rate of condition development, decrease of comorbidities, and, ultimately, the patient's lifestyle.**

Keywords: **Diabetes Mellitus Type 2, Primary Care.**

1. INTRODUCTION

Type 2 diabetes mellitus (T2DM) is an usual disorder that increases a patient's danger of mortality, typically from CV condition [1].In 2007, 23.6 million people in the United States had DM inning accordance with statistics assembled by the National Institute of Diabetes and Digestive and Kidney Diseases [2].Among adults with DM, 90% to 95% of these instances are T2DM [2].Along with glycemic control, it is important for patients with T2DM to be told regarding the requirement to handle various other cardiovascular (CV) risk elements including overweight or obesity, hypertension and dyslipidemia [3].Unfortunately, control of these variables is less compared to optimum in numerous patients [4].According to information from 1999-2006 in the National Health and Nutrition Examination Survey (NHANES), about half the patients with DM attained a hemoglobin A1C (A1C) of <7.0% [5].Further, only 12.2% of patients with DM attained the suggested combined targets for A1C, blood pressure (BP; <130/80 mm Hg) and low-density lipoprotein cholesterol (LDL-C; <100 mg/dL) throughout this time around period [5]. These searchings for suggest the need for antidiabetes therapies that target not just the fundamental problems of T2DM consisting of insulin resistance and hyperglycemia however likewise address various other CV threat aspects [6].

This review discuss the current antidiabetes agents and focus on incretin based therapies, which have been shown to improve hyperglycemia, weight and other CV risk factors in patients with T2DM in primary care setting.

2. METHODOLOGY

We carried out a computerized literature search through several medical databases "Medline, Embase, PubMed" up to 2018 January. We hand-searched selected articles for additional citations relevant with our objective. We restricted our search only to English language with human subject's studies discussing the Challenges facing family doctors in management of diabetes mellitus type 2 in primary care.

3. DISCUSSION

- **Etiology, risk factors, and pathophysiology**

The mix of extreme caloric intake, reduced caloric result, and obesity results in the development of kind 2 diabetes mellitus (T2DM) in people with a hereditary tendency to the condition [7]-[9].Race and comorbid medical troubles contribute to the point at which the illness establishes. Low birth weight, in addition to birth weight over 9 lb (4.1 kg), is connected with T2DM [8], [10].Environment might also impact T2DM growth and development [10]-[12].

The core problems of T2DM create from chronic hyperglycemia and the interaction of several systemic variables: reduced incretin effect in the digestive tract, raised lipolysis, raised glucose reabsorption in the kidneys, lowered glucose uptake in the muscles, enhanced hepatic glucose manufacturing, enhanced glucagon secretion by pancreatic islet alpha cells, lowered insulin secretion by pancreatic beta cells, and neurotransmitter dysfunction [11]-[14].Age, genetic aspects, and insulin resistance all add to lowering beta cell function [11].

As soon as the cycle of insulin resistance is initiated, other elements add to the transition from insulin resistance to T2DM. Adipocytes resist the antilipolytic impacts of insulin, bring about frequently elevated degrees of free fatty acids (FFA) [13], [14]. Raised FFA degrees also cause gluconeogenesis and promotes hepatic and muscular insulin resistance. Dysfunctional adipocytes produce adipocytokines, setting off an infl ammatory reaction adding to more insulin resistance and atherosclerotic modifications [11], [13], [14].The bigger fat cells have a reduced capability to store fat, leading to the deposition of fat into muscle, liver, beta cells, and the vascular cells of arteries [11].Beta cells in the pancreas are hyperstimulated to overproduce insulin to counter the discovered hyperglycemia [11], [13], [14].The simplistic explanation frequently used is that the beta cells at some point "wear out." This explanation does not define the system by which this takes place; the specific device by which insulin resistance adds to beta cell failure is unknowned. Excess glucose is kept as triglyceride within fat cells and deposited viscerally in musculature in addition to the liver [11].This additionally causes the deposition of lipid metabolites right into beta cells, therefore harming the secretion of insulin. Adiposity brings about lipotoxicity, gauged as elevated levels of FFA, additionally hindering insulin secretion [11], [13], [14].

Paradoxically, glucotoxicity, or long term hyperglycemia, impairs insulin secretion by conflicting with both first- and second-phase insulin secretion.6 Amylin, derived from island amyloid polypeptide (IAPP), is secreted in a one-to-one proportion with insulin. Hence, insulin hypersecretion leads to hypersecretion of IAPP, which is after that deposited as amylin into the beta cells [11], [13], [14].Once again, the system of poisoning is still under research, yet the outcome is progression of beta cell failing. Glucagon-like peptide 1 (GLP-1) and gastric repressive peptide (GIP) add to beta cell failing too [11].As insulin resistance creates and advances, there is a matching shortage in GLP-1 and resistance to GIP [11].As T2DM proceeds, beta cells stand up to the revitalizing result of GIP, resulting in lowered insulin manufacturing [11].

Table 1. Risk factors for T2DM [12].According to the National Institute of Diabetes and Digestive and Kidney Diseases, risk factors for T2DM.

Overweight or obesity
Age 45 or over
Family history of diabetes mellitus
Black, Alaska Native, Native American, Asian American, Hispanic, Native Hawaiian, or Pacific Islander ethnicity
Prehypertension or hypertension
Low levels of high-density lipoprotein, elevated triglyceride levels
Women with a history of gestational diabetes or gave birth to a baby weighing 9 lb (4 kg) or more
Sedentary lifestyle
History of cardiovascular disease
Depression
Polycystic ovarysyndrome
Acanthosis nigricans

- **Diagnosis and monitoring**

Patients should be assessed and monitored for disease symptoms and risk factors, including:

• Polydipsia

• Polyphagia

• Polyuria

• Fatigue

• Blurred vision

• Numbness or tingling

• Nonhealing wounds or sores

• Lower extremity paresthesia

• Candida infections

• Unexplained weight loss[10].

A physical exam should take place every 3 to 6 months based on disease control and should routinely include a general evaluation with additional focus to evaluate:

• Anthropometric measurements at each visit

• BP at each visit

• Intraocular hemorrhages, exudate, and neovascularization every 6 months

• Skin (acanthosis nigricans, Candida infections) at each visit

• Neurologic changes (decrease or absence of light touch, temperature sensation, proprioception, or loss of deep tendon reflexes in ankles) at least annually, but encouraged at each visit

• Feet (muscular tone, changes in toes, wounds, ulcerations, and sensation) at each visit[10]

- **Management**

Regardless of entry A1C, metformin hydrochloride is advised as initial treatment in the treatment of T2DM [7], [15].Metformin is given orally with meals, and the dosage is customized based upon performance and tolerance. Metformin is contraindicated in patients with acute or chronic metabolic acidosis and those with an approximated glomerular filtration rate less compared to 30 mL/min/1.73 m2 [7], [15].A baseline vitamin B12 ought to be acquired prior to starting metformin, and regular monitoring considered after that, due to the fact that metformin has been revealed to prevent the absorption of B12 [7].This is specifically essential in patients with migraine-type headaches because there is a link between B12 deficiency and migraines [16].Proton pump inhibitors have the tendency to inhibit B12 and magnesium absorption, contributing to migraine problems [17].

The enhancement of other therapy techniques is displayed in the American Association of Clinical Endocrinologists (AACE)/ American College of Endocrinology (ACE) 2017 Glycemic Control Algorithm and the Executive Summary [15].There are many effective means to get to the AACE/ACE endpoint of glycemic control with an A1C of 6.5% or less for reduced hypoglycemic risk patients [15].A goal range A1C of 6.5% to 8% is appropriate if the patient is at higher threat for difficulties if a target of 6.5% would certainly cause a damaging end result [15].Metformin continuouslies be the fi rst-line treatment as a result of its low cost and general tolerability [7], [15].Although, arguments could be produced various other representatives as ideal for the patient. Based upon the entry A1C, it may be suitable to start the patient on two representatives. With the impact of GLP-1 on the core flaws of T2DM, weight, and BP, a GLP-1 receptor agonist is an excellent option for a second-line agent, although patients might be unwilling to start shots [15].Dipeptidyl peptidase 4 (DPP-4) preventions might be an appropriate choice to a GLP-1 receptor agonist since this class raises incretin degrees of GLP- 1 and GIP with a minimal effect on A1C and the core problems [15].Sodium glucose cotransporter-2 (SGLT-2) preventions enhance renal excretion of as much as regarding 100 g of sugar daily using micturition [18].Alpha glucosidase preventions block digestion of carbohydrates in the digestive tract by hindering the essential enzymes

[19].Insulin resistance is straight dealt with using thiazolidinediones (TZD) [20].Sulfonylureas (SU) and glinides (GLN) work directly on the beta cells to boost insulin secretion [21]. While both colesevelam and bromocriptine have a small glucose-lowering effect, neither are consistently recommended for glycemic management due to the negative response profile of each [22].

Additional medicines to be thought about for initiation at beginning of T2DM, particularly in the visibility of hypertension, include an angiotensin-converting enzyme inhibitor (ACEI), angiotensin II receptor blocker (ARB), thiazide-like diuretic, or a calcium network blocker (CCB) [7].The Eighth Joint National Committee (JNC-8) combined suggestions for BP management in adults by establishing similar treatment objectives for all people detected with hypertension except in cases where details proof supports different goals for particular subpopulations [23].JNC-8 recommends a treatment objective of systolic BP much less than 140 mm Hg based upon expert point of view [23] The ADA medication considerations remain in positioning with the JNC-8 grade B (modest) suggestion [7], [23].In the presence of cardiac arrest, preliminary treatment with a thiazide-like diuretic was extra effective in improving end results than ACEIs, which had higher effectiveness than CCBs; nonetheless, the evidence was not strong enough to recommend one medication class over an additional [23].Thiazidelike diuretics and CCBs are shown for first treatment for Black patients [23].No matter race or the visibility of diabetic issues, hypertension therapy in the existence of chronic kidney illness should consist of an ACEI or an ARB [23] Reproductive therapy should take place with women of reproductive age prior to initiating ACEI or ARB treatment [7].

Aspirin, utilized to lower the proinflammatory impact of lipotoxicity, might be started based upon the computed atherosclerotic cardiovascular disease (ASCVD) threat [7].The use of an HMG-CoA reductase prevention (statin) may be shown to minimize ASCVD risk. The option of statin is based on the degree of risk [7], [24].The statins most generally selected are (from many powerful to the very least powerful): rosuvastatin, atorvastatin, pitavastatin, simvastatin, lovastatin, pravastatin, and fluvastatin.

Table 2. Common medications for T2DM treatment [25]-[30].

Drug class and mechanism of action	**Advantages**	**Disadvantages/considerations**
Biguanides ↓ hepatic glucogenesis	•↓risk for weight gain, hypoglycemia •↓ cardiovascular (CV) risk	• Gastrointestinal (GI) adverse reactions •↑ risk for lactic acidosis • May exacerbate heart failure (HF) • Use with caution with kidney insuffi ciency • May exacerbate hypoxemia • May cause dehydration
GLP-1 receptor agonists ↑ glucose-dependent insulin secretion, ↓ gastric emptying, ↓ inappropriate glucagon secretion, weight loss, ↑ beta cell proliferation and regeneration	• All act independently of insulin with ↓ risk for hypoglycemia	• Contraindicated in medullary thyroid cancer •Risk for pancreatitis •Varied delivery vehicles and needle sizes •Some require mixing and delay after mixing
SGLT-2 inhibitors ↑ renal excretion of glucose	• All act independently of insulin • weight loss • ↓ BP	•May ↑genital Candida infections •May ↑ risk for urinary tract infections •Kidney function must be adequate and monitored. • May ↑ growth rate of certain tumors
DPP-4 inhibitors ↑ secretion of insulin, ↓ secretion of glucagon	• Low hypoglycemia risk • Weight neutral	• ↑ risk for pancreatitis • Most require adequate kidney and liver function and monitoring • Hypersensitivity, may ↑ joint pain
TZDs ↑ insulin sensitivity	•Limited risk for hypoglycemia • ↓high-density lipoprotein cholesterol •↓ triglycerides •↓CV risk, ongoing efficacy	• ↑ weight gain • ↑ risk for HF • ↑ edema •↑ low-density lipoprotein cholesterol •↑ fracture risk in predisposed patients • ↑ risk for bladder cancer • No concomitant use with SGLT-2 inhibitor

Way of living modification, consisting of weight loss as proper and decrease of lower nutritional value fats (including transfat and hydrogenated fat), need to be reviewed [7], [24].For patients with raised triglyceride levels, intensive way of life modification could be necessary, particularly if the triglycerides rise in the presence of reduced degrees of high-density lipoprotein (HDL) [7], [24].Additional causes of hypertriglyceridemia ought to be checked out in patients with degrees more than 500 mg/dL [7], [24].Pancreatitis is a risk in these patients, and therapy aimed at danger decrease ought to be thought about [7].The medical professional ought to realize that statin therapy could need to be modified based upon tolerability and healing action [7]. Statins utilized in mix with fibrates have not improved ASCVD outcomes and supply no additional decrease in low-density lipoprotein cholesterol (LDL-C), minimal HDL improvement, and only moderate triglyceride improvement [7], [24].In a similar way, the addition of niacin to a statin has not revealed substantial improvement in cardio end results and has been connected to hyperglycemia, rise in hepatic function researches, stomach damaging reactions, and altitudes in uric acid [24].

Moderate-intensity treatment could be increased with using ezetimibe [7], [24].In patients with current acute coronary disorder and an LDL-C of 50 mg/dL or greater, combination therapy with ezetimibe contributed to moderate-intensity statin treatment supplies higher benefit compared to a statin alone [7].In patients with both T2DM and confirmed atherosclerotic heart disease, the proof suggests way of living adjustment must be combined with high-intensity statin therapy utilizing atorvastatin or rosuvastatin [7], [24].Moderate-intensity or high-intensity therapy ought to be considered in enhancement to way of living alteration for grown-up patients under age 40 that have been identified with T2DM and possess various other ASCVD threat variables [7], [24].There is a tiny benefit to carrying out moderate strength statin treatment along with way of living changes for patients in between ages 40 and 75 that have nothing else ASCVD danger variables other than the diagnosis of T2DM [7], [24].

4. CONCLUSION

Type 2 diabetes poses lots of difficulties for primary care team in preventing and handling complications. Efficient management is important because the problem is connected with major problems which may result in a decrease in both longevity and lifestyle. The central factors to take into consideration in taking care of T2DM in primary care are individualizing treatment and entailing the patient in care planning and management. The clinician must utilize an interdisciplinary strategy to care that integrates education and learning and management of hidden conditions. T2DM is a chronic, modern condition that does not need to define the patient. Comprehending and executing evidence-based practice and following clinical technique guidelines improve the quality of first and continuous care, directly influencing the burden of disease, rate of condition development, decrease of comorbidities, and, ultimately, the patient's lifestyle.

REFERENCES

[1] Suadicani P, Hein HO, Eyben FE, et al. Metabolic and lifestyle predictors of ischemic heart disease and all-cause mortality among normal weight, overweight, and obese men: a 16-year follow-up in the Copenhagen Male Study. Metab Syndr Relat Disord 2009;7:97–104.

[2] National Diabetes Information Clearinghouse. National diabetes statistics, 2007. Available at: http://diabetes.niddk.nih.gov/dm/pubs/ statistics/. Last update: June 2008. Accessed July 24, 2009.

[3] American Diabetes Association. Standards of medical care in diabetes—2009. Diabetes Care 2009;32(suppl 1):S1–61.

[4] Nathan DM, Buse JB, Davidson MB, et al; American Diabetes Association; European Association for Study of Diabetes. Medical management of hyperglycemia in type 2 diabetes: a consensus algorithm for the initiation and adjustment of therapy: a consensus statement of the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care 2009;32:193–203.

[5] Cheung BM, Ong KL, Cherny SS, et al. Diabetes prevalence and therapeutic target achievement in the United States, 1999 to 2006. Am J Med 2009;122:443–53.

[6] Stonehouse AH, Holcombe JH, Kendall DM. Management of type 2 diabetes: the role of incretin mimetics. Expert Opin Pharmacother 2006;7:2095–105.

[7] American Diabetes Association. Standards of Medical Care in Diabetes—2017. Diabetes Care. 2017;40(suppl 1):S1-S135.

[8] Qiao Q. Epidemiology of type 2 diabetes. 2012. www.eurekaselect.com/ 101704/volume/1.

[9] Unger J. Diabetes Management in Primary Care. Philadelphia, PA: Wolters Kluwer Health; 2015.

[10] Khardori R. Type 2 diabetes mellitus: practice essentials, background, pathophysiology. Emedicine. 2017. http://emedicine.medscape.com/article/117853- overview.

[11] DeFronzo RA. From the triumvirate to the ominous octet: a new paradigm for the treatment of type 2 diabetes mellitus. Diabetes. 2009;58(4): 773-795.

[12] National Institute of Diabetes and Digestive and Kidney Diseases. Risk factors for type 2 diabetes. www.niddk.nih.gov/health-information/diabetes/overview/risk-factors-type-2-diabetes.

[13] DeFronzo RA, Eldor R, Abdul-Ghani M. Pathophysiologic approach to therapy in patients with newly diagnosed type 2 diabetes. Diabetes Care. 2013;36(suppl 2):S127-S138.

[14] DeFronzo RA, Triplitt CL, Abdul-Ghani M, Cersosimo E. Novel agents for the treatment of type 2 diabetes. Diabetes Spectr. 2014;27(2):100-112.

[15] Garber AJ, Abrahamson MJ, Barzilay JI, et al. Consensus statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the comprehensive type 2 diabetes management algorithm—2017 executive summary. Endocr Pract. 2017;23(2): 207-238.

[16] I˙pçiog˘lu O, Özcan Ö, Gültepe M, Tekeli H, S¸enol M. Functional vitamin B12 defi ciency represented by elevated urine methylmalonic acid levels in patients with migraine. Turk J Med Sci. 2008;38(5):409-414.

[17] Liang JF, Chen YT, Fuh JL, et al. Proton pump inhibitor-related headaches: a nationwide population-based case-crossover study in Taiwan. Cephalalgia. 2015;35(3):203-210.

[18] Mosley JF 2nd, Smith L, Everton E, Fellner C. Sodium-glucose linked transporter 2 (SGLT2) inhibitors in the management of type-2 diabetes: a drug class overview. P T. 2015;40(7):451-462.

[19] McCulloch D. Alpha-glucosidase inhibitors and lipase inhibitors for treatment of diabetes mellitus. 2017. UpToDate. www.uptodate.com.

[20] McCulloch D. Thiazolidinediones in the treatment of diabetes mellitus. UpToDate. 2017. www.uptodate.com.

[21] McCulloch D. Sulfonylureas and meglitinides in the treatment of diabetes mellitus. UpToDate. 2017. www.uptodate.com.

[22] McCulloch D. Management of persistent hyperglycemia in type 2 diabetes mellitus. UpToDate. 2017. www.uptodate.com.

[23] James PA, Oparil S, Carter BL, et al. 2014 Evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). JAMA. 2014;311(5):507-520.

[24] Stone NJ, Robinson JG, Lichtenstein AH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2014;129(25 suppl 2):S1-S45.

[25] Lexicomp. Metformin: drug information. UpToDate. 2017. www.uptodate. com.

[26] Lexicomp. Canaglifl ozin: drug information. UpToDate. 2017. www.uptodate. com.

[27] Lexicomp. Alogliptin: drug information. UpToDate. 2017. www.uptodate.com.

[28] Lexicomp. Miglitol: drug information. UpToDate. 2017. www.uptodate.com.

[29] Lexicomp. Repaglinide: drug information. UpToDate. 2017. www.uptodate.com

[30] Lexicomp. Detemir: drug information. UpToDate. 2017. www.uptodate.com