

Noninsulin Diabetes Medications



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KEYWORDS

- Diabetes medications • Alpha-glucosidase inhibitors • Biguanides • Meglitinides
- Dipeptidyl peptidase 4 inhibitors • Glucagon like peptide-1 agonists
- Selective sodium-glucose transporter-2 inhibitors • Sulfonylureas

KEY POINTS

- Type 2 diabetes can be treated with noninsulin diabetes medications using one drug alone or in combination with different drugs.
- Important properties of the antihyperglycemic agents play a role in the choice of that particular medication for individual patients.
- Selection of antidiabetic medications should be done carefully based on efficacy, impact on weight, hypoglycemia risk, potential side effects, cost, and patient preferences.

INTRODUCTION

The prevalence and incidence of type 2 diabetes (T2DM) are increasing worldwide. In the United States, 29.1 million people or 9.3% of population have diabetes,¹ of which 90% to 95% of people have T2DM. T2DM is the leading cause of cardiovascular disorders, blindness, kidney failure, and amputations. People with diabetes are hospitalized frequently and also have an increased risk of cancer,² mental illness,³ cognitive decline,⁴ liver disease,⁵ and other disabling conditions. Effective management of diabetes is important to prevent and delay complications associated with diabetes.^{1,6} Medical management of diabetes has become increasingly complex and several guidelines and recommendations have been developed to treat diabetes. Hemoglobin A1C target is the major focus of diabetes management.^{6,7} The American Diabetes Association recommends lowering hemoglobin A1c to less than 7.0% in most patients to decrease the incidence of microvascular disease.⁷

Understanding the pathophysiology of diabetes is important to understand its management. Abnormal islet cell function is the key feature of T2DM. In the early stages of disease, insulin production is normal or can be increased, but insulin sensitivity is reduced. Pancreatic beta cells' ability to adequately produce insulin in the presence

Disclosure Statement: There are no commercial or financial conflicts of interest.
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Nurs Clin N Am 52 (2017) 523–537
<http://dx.doi.org/10.1016/j.cnur.2017.07.003>

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of elevated glucose levels is compromised and this incompetence progresses over time. In T2DM, the pancreatic alpha cells secrete more glucagon, which promotes hepatic glucose output. Abnormalities in the incretion system glucagon like peptide-1 and glucose-dependent insulinotropic peptide causes hyperglycemia. Insulin resistance in the target tissues like liver, adipose tissue, and muscle causes hyperglycemia, especially in obese patients. An increased delivery of fatty acids to the liver and their oxidation contributes to increased gluconeogenesis.⁸

It is possible to reverse islet dysfunctions and improve hyperglycemia by enhancing the action of insulin, which decreases beta cell secretory burden. Restriction of dietary intake, bariatric surgery, and use of various antidiabetic medications can improve beta cell dysfunction. The antihyperglycemic agents are directed toward one or more of the above pathophysiologic defects. Many patients may need more than 1 class of medications to adequately treat diabetes.⁷ Each medication's properties should be kept in mind when selecting a particular therapy for an individual patient.⁶

CLASSES OF NONINSULIN DIABETES MEDICATIONS

Pharmacologic therapy of T2DM now has changed greatly owing to new drugs and drug classes available. Noninsulin diabetes medications available in the United States to treat diabetes are as follows.

- Biguanide
- Sulfonylureas
- Meglitinide derivatives
- Alpha-glucosidase inhibitors
- Thiazolidinediones
- Glucagonlike peptide-1 (GLP-1) agonists
- Dipeptidyl peptidase 4 (DPP-4) Inhibitors
- Selective sodium glucose transporter - 2 (SGLT-2) inhibitors
- Amylinomimetic
- Bile acid sequestrant
- Dopamine agonist

Biguanide

This class is the first line treatment for T2DM and prediabetes and is the most widely prescribed diabetes medication. A biguanide decreases insulin resistance and improves insulin sensitivity, and this class is considered to be a cornerstone in the treatment of T2DM. Biguanide reduce hyperglycemia primarily by decreasing hepatic gluconeogenesis and secondarily by increasing the peripheral insulin sensitivity. Metformin does not increase insulin levels or cause weight gain or hypoglycemia, and it is effective, safe, and inexpensive. Metformin may reduce risk of cardiovascular events and death.^{9,10} Metformin is administered orally as immediate release tablets, extended release tablets, or as an oral solution (**Table 1**).

Sulfonylureas

Sulfonylureas are insulin secretagogues that stimulate the release of insulin from pancreatic beta cells, decrease the rate of hepatic glucose production, and increase insulin receptor sensitivity. It can reduce hemoglobin A1c by 1% to 2%; however, as beta cell dysfunction progresses, sulfonylureas become less effective.^{11,12} The main advantage is that it is inexpensive. The main side effect is hypoglycemia. Glyburide, glipizide, and glimepiride are second-generation sulfonylureas

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