

Effect of Glipizide on non-insulin-dependent diabetes mellitus

Jiarui Yuan*

Qingdao No.1 International school, Shandong, China

*Corresponding author: 631402070219@mails.cqjtu.edu.cn

Abstract. Type 2 diabetes mellitus, sometimes referred to as non-insulin-dependent diabetes, (NIDDM). The patient was unable to secrete enough insulin, resulting in elevated blood glucose. Complications during a patient's diseases are common in type 2 diabetes patients. Common type 2 diabetes does not have an age or gender difference. Patients with type 2 diabetes or those under treatment are frequently fat and sedentary. Glipizide, a sulfonylurea medication, is prescribed to people with non-insulin-dependent diabetic mellitus. (type 2 diabetes). There are two common types, oral tablets and sustained-release tablets. The common type of oral tablets is fast-acting tablets. Absorption is rapid and the effect is rapid, because oral tablets have a significant effect and may cause short-term hypoglycemia. The body disintegrates the medication and release it. A contributing factor to type 2 diabetes is having high blood glucose levels, as the pancreas produces less insulin, resulting in a residual overall glucose in the blood. These disorders are often caused by genetics or overweight/physical inactivity. The blood glucose levels of patients with type 2 diabetes are greater than those of ordinary healthy individuals since the condition is a chronic metabolic disorder. Glipizide can be used as an insulin secretagogue to stimulate islet β cells to release insulin, thereby increasing plasma insulin concentration. It also serves as an auxiliary hand in diet and exercise. Different regions have different laws for the use of glipizide. Glipizide can be used in combination with other NIDDM drugs in the United States. It can only be used alone or not in the United Kingdom because of the high risk of aggravating hypoglycemia in patients. Patients who have any cardiovascular or renal disease or have a long history do not mind using these drugs. Such agents are likely to worsen the hypoglycemia associated with the disease. Among many drugs, glipizide is one of the most common sulfonylureas and has a moderate price.

Keywords: Glipizide; NIDDM; Type 2 diabetes; treatment.

1. Introduction

Type 2 diabetes is a condition that affects adults and is typically through genetics or being overweight or obese [1]. Because to inadequate insulin production, glucose cannot be converted into energy, and excess glucose remains in the blood [2], leading in hyperglycemia problems. Symptoms in people with type 2 diabetes are very thirsty – frequent urination, blurred vision, cranky thoughts, fatigue and hunger.

Over 37 million Americans have diabetes, with more than 90 percent having type 2 diabetes, and the general population is 45 and older. At the same time, children who are too obese also have a high probability of developing diabetes from this disease [3].

Type 2 diabetes mellitus, sometimes referred to as non-insulin-dependent diabetes [3]. Glipizide functions as an insulin secretagogue, stimulating the expulsion of insulin from pancreatic β -cells and thereby raising the plasma concentration of insulin [4]. Generally, glipizide is divided into two forms: oral tablets and long-acting tablets, swallowed and eaten [5]. This type of drug is not suitable for insulin-dependent diabetes (type 1 diabetes), because glipizide can only be used for normal patients with insulin secretion [6].

Because this kind of drugs may cause complications such as hypoglycemia and anemia [7]. Also might cause heart disease, kidney disease, oral disease, neurological disease, visual impairment. Compared with other hypoglycemic drugs, glipizide has a higher risk of hypoglycemia. In studies, patients taking glipizide experienced weight gain and uncontrolled blood sugar.

This article primarily discusses the effects and hazards of glipizide in the treatment of non-insulin-dependent diabetes. Glipizide clinical trials. In the diagnosis and treatment of non-insulin-

dependent diabetes, a medication called glipizide and metformin were compared. Glipizide groups that are and are not relevant.

2. Non-insulin-dependent diabetes

Type 2 diabetes mellitus is a chronic metabolic condition that is not insulin-dependent. Patients with type 2 diabetes usually have elevated blood sugar. Causes damage to various parts of the body. Most people with diabetes have type 2 diabetes because of insulin. High blood sugar produced by insufficient secretion in a state of normal glucose maintenance. Generally, non-insulin-dependent diabetes patients are characterized by obesity or height. In recent years, the percentage of NIDDM has risen in sedentary persons, obese people on high-calorie diets, and the elderly.

2.1. Non-insulin-depend diabetes Influence factors

Dietary factors, physical activity factors and metabolic factors affect the presence of type 2 diabetes [8]. Dietary factors because a lot of high fat and high carbohydrate foods will raise blood glucose, VLDL, CM, TG. This increases the quantities of oxygen species that are reactive and causes inflammation. As a result, a mitochondrial malfunction occurs. It does not function properly. Physical activity elements because lack of exercise, as well as extended periods of laying in bed or sitting, contribute to body obesity and raise systemic inflammation. One of these cells acts in the pancreas on insulin-producing beta cells, inhibiting their function[9].

Because of the inability to restore the body's control of blood sugar, the complications of diabetes itself continue to affect the body. Hyperglycemia can lead to the production of mitochondria beyond the normal level, which may persist even after the blood glucose level is controlled and restored. The causes of type 2 diabetes are obesity or little physical activity and unhealthy diet. When the body fat percentage is 30 or more, it induces the interaction between cells and prevents the production and transfer of insulin and glucose between cells. The Women's Health group suggests that participants who walk for more than half an hour a week may delay the onset of type 2 diabetes by causing skeletal muscle cells to contract. Thus enhancing glucose uptake in plasma and reducing fat and body fat percentage[10].

Therefore, the factors that promote the persistence of type 2 diabetes, mainly the stress caused by obesity and blood glucose and the toxic damage to beta cells, lead to the inability to produce enough insulin.

Gender differences in the detection or development of T2DM were observed, with men being more likely to be diagnosed when they were younger and had lower body fat percentage. In women, extreme obesity is more often detected when women are extremely obese. Of course, the main difference is not only in gender, but also in the living environment, living habits, economic status and so on. There are also genetic factors[11].

Among diabetic sequelae, women had a greater death risk for cardiovascular disease and stroke, whereas males had a lower mortality rate for renal disease.

The most important feature of type 2 diabetes in adolescents is obesity. bmi is too high in Asian adolescents. Most have type 2 diabetes. There was no statistically significant gender difference, although the incidence was substantially greater among individuals aged 10 to 19 years. It's different from the prevalence. In comparison, Asians were more likely to change names than Pacific Islanders. However, the prevalence of T2DM varies greatly among regions within Asia[12].

2.2. Pancreatic beta cells

Because beta cells in the pancreas do not generate enough insulin, their integrity must be conserved for the purpose to protect beta cell function. It combines to form preproinsulin, which is created with the aid of proteins in the endoplasmic reticulum (ER), before being transported to the Golgi and split into insulin. When the concentration of glucose rises, it triggers the release of insulin. When glucose

breakdown is activated, intracellular atp or adp increases, leading to the closure of potassium channels. Massive Ca^{2+} entry into the cell leads to insulin exocytosis[13].

The main reason beta cells don't produce enough insulin is because beta cells die. When the body develops other diseases of excess nutrition, such as high blood sugar, obesity and so on. It is likely that beta-cells are stressed and lose islet integrity. Excessively high glucose concentrations lead to local islet inflammation due to islet amyloid peptides synthesized by proinsulinogen in beta cells[14].

2.3. Type2 diabetes symptoms and complications

Thirst is a typical symptom among type 2 diabetes patients. Frequent urination, increased appetite, weariness, hazy eyesight, and poor wound healing are all symptoms of this condition. Infections are common in the disease, and immunity is low[15]. People with type 2 diabetes are more prone to develop illness in all regions of their bodies, including the heart, blood vessels, nerves, and kidneys. Such as cardiovascular diseases, neuropathy of the extremities, nerve damage, chronic kidney disease, cataracts, glaucoma can lead to blindness in severe cases. There is also a higher risk of Alzheimer's disease or other dementia.

3. Mechanism of Glipizide

Glipizide is a second-generation drugs sulfonylurea which is primarily used in the treatment of non-insulin-dependent diabetic mellitus as an addition to diet and exercise. It also has the potential to be used in conjunction with diabetic medications like metformin. These medications are generally used orally[15].

The use of glipizide in patients can stimulate beta cells to release insulin and reduce glucose production, while also producing hypoglycemic effects. Glipizide has low cost, rapid metabolism, and rapid absorption. Although it has a high probability of causing hypoglycemia, hypoglycemia does not occur for a long time because it takes effect quickly and is consumed quickly[15]. More often, short-term hypoglycemia occurs. It usually takes effect half an hour after application, lasts for one to half a day, and is finally excreted in the basal excretion (faeces and urine).

Because these agents have a high probability of causing hypoglycemia as a function of action, patients typically start with the lowest dose and increase or decrease glipizide intake depending on the patient's treatment. It is usually regulated in 2.5mg units[16].

4. The structure and function of Glipizide

GLUCOTROL (GLIPIZIDE) patients will have a peak blood drug concentration one to three hours after intravenous or oral administration of the corresponding dose (Fig 1), and the half-life is usually 2 to 4 hours [17]. The route of glipizide administration is very similar in the two groups, but the metabolism is not obvious. In the oral route, normal eating does not affect the action of the drug. The absorption of glipizide in the human body will be delayed by 40 minutes, and in patients taking glipizide tablets, it needs to be advanced by half an hour to ensure that glipizide is effective [18]. There was no specific regimen for medication, and different treatment options were provided according to the patient's blood glucose concentration and the time to peak. Patients usually start with the lowest dose. During the treatment, the glycemic index was detected and the treatment plan was adjusted in time. Glipizide tablets cannot be given a large dose at one time, but should be increased by 2.5 mg or 5mg each time, and each dose change needs a certain interval(the dose can be interrupted or relatively reduced or increased at the time of use, depending on the situation)[14,19]. The maximum single intake dose was 40mg. If the maximum intake dose has been reached, but the condition worsens or does not change, the drug should be replaced immediately to ensure the effectiveness of treatment [20]. Glipizide chemical formula is $\text{C}_{21}\text{H}_{27}\text{N}_5\text{O}_4\text{S}$.

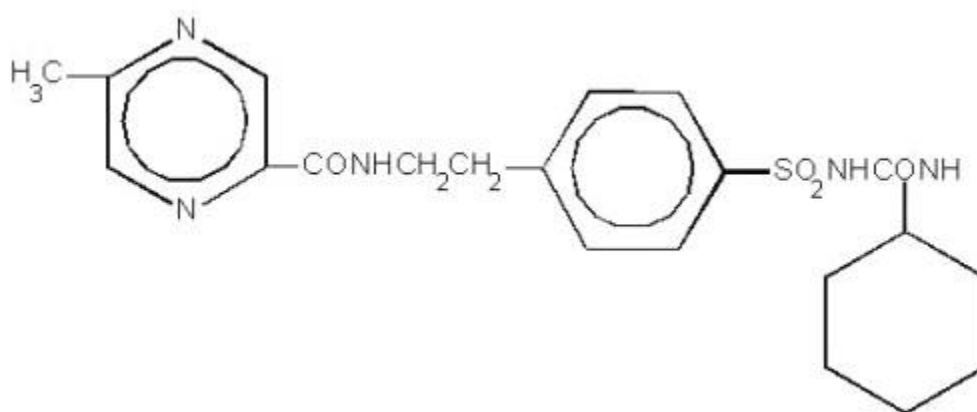


Fig. 1 one references [17].

5. Glipizide side effects

In people with non-insulin-dependent diabetes, glipizide can be used in conjunction with other medicines to minimize the risk of cancer. Glipizide inhibitors can effectively prevent tumor growth and metastasis.

Clinical studies have found that glipizide users have other risk factors for hypoglycemia. Glipizide was used for more than 100 days, and among all users, 22 cases occurred per 1000 person-years. Hospitalization for hypoglycemia due to medication use. Compared with other drugs, glipizide was associated with chronic kidney disease and severe hypoglycemia. Is much higher than other drugs for the treatment of non-insulin-dependent diabetes.

There were seven deaths and more than 10 vascular problems in patients treated with glipizide during the study. Overall glipizide patients gained 1-2kg of body weight.

There was a significant difference in cardiovascular effects between glipizide and metformin, patients receiving therapy for metformin had concerning a half-fold greater incidence of cardiac events than those not treated with metformin. Myocardial infarction, stroke, and mortality from cardiovascular events were among them. The incidence of heart failure, cardiac arrhythmia angina pectoris, coronary artery disease, and other illnesses was similarly greater in the glipizide group than in the metformin group. Although cardiovascular disease is a significant consequence and cause of mortality in type 2 diabetes, the influence of the two diabetes medications on cardiovascular disease varies. In contrast, metformin has a significant benefit in the treatment of cardiovascular disease in type 2 diabetes patients [21].

6. Limitations of glipizide

Alcoholism leads to hypoglycemia, which may be exacerbated by concomitant glipizide consumption [15]. In a easy way to explain, instead of metabolize glucose, liver will choose to metabolize the alcohol. Also ethanol inhibits gluconeogenesis [22]. Chronic alcoholism is not suitable for Glipizide as a therapeutic agent. But the occasional small dose of alcohol can help. Rapid intake of large amounts of alcohol without food can cause hypoglycemia through the inhibition of gluconeogenesis and glycogenolysis. By activating insulin, a modest amount of alcohol can minimize the incidence of type 2 diabetes.

It is not indicated in patients with type 1 diabetes, as it should only be used in patients who produce normal insulin. It should not be used in pregnant women because glipizide and its Cousins cross the placenta. Certain conditions can lead to complications or genetic disorders in the newborn or unborn fetus.

It is not recommended for the elderly, malnourished patients, patients with other serious medical conditions, or patients with liver and kidney problems. Because it may lead to hypoglycemic episodes.

This leads to the aggravation of the original disease. Glipizide treatment in people with a deficiency in glucose-6-phosphate dehydrogenase may result in hemolytic anemia.

The conditions listed below are not recommended/indicated for glipizide: adrenal insufficiency, hypopituitarism, malnutrition, hypoglycemia, anemia, type 1 diabetes, fever, infection, surgery, cardiovascular diseases, kidney disease, the elderly. All the patients who participated in the trial were middle-aged and over 40 years old.

Under time-specific conditions, the mean rate of weight loss was less and the mean rate of weight gain was greater with glipizine than with dapagliflozin after the trial. Glycemic instability leading to discontinuation of dapagliflozin was observed in less than 0.5% of patients. But it was more than 3.5% in the glipizide group. Over the course of the trial, complications such as rhinitis, hypertension, diarrhea, and dizziness were much greater in the patients who used bichin every other day than in the patients who used dapagliflozin.

Glipizide had similar reduction efficacy compared with sitagliptin, but sitagliptin was generally better tolerated in comparison. The risk of hypoglycemia and weight fluctuation was reduced. Sitagliptin and glipizide had similar reductions in a1c at week 54. Glipizide and sitagliptin were three times more likely to affect hypoglycemia [23]. Compared with glipizide, glipizide caused more weight, height and complications. But glipizide is also a relatively quick and effective drug.

The lowest cost diabetes treatment strategy is to use glipizide, whereas the total cost per patient is between US \$4500 and US \$5000. Those using metformin range from \$5,000 to \$5,300. glipizide is the least expensive to administer in the same class or in a first-line regimen. (In 2000) prices would continue to rise based on impacts such as COVID-19 and economic inflation.

7. Conclusion

The main consequence of type 2 diabetes is pancreatic beta cell dysfunction, which do not produce enough insulin. This causes too much glucose to remain in the blood, producing hyperglycemia. The most common type 2 diabetes patients are those with unhealthy diet, obesity (high body fat rate), and lack of exercise. Factors can be influenced by living environment and geographical location. There are numerous therapies available for non-insulin-dependent diabetic mellitus. This page mostly discusses glipizide therapy. Among pancreatic drugs, glibitz is a common and affordable treatment. Glipizide is commonly used in conjunction with other medicines such as metformin. Patients need to swallow glipizide oral tablets half an hour in advance to ensure maximum effect. Glipizide is not recommended as the primary treatment for patients with alcoholism, the elderly, or heart/kidney disease. The efficacy of these drugs is very significant. If the patient takes too large dose at one time, it is likely to cause hypoglycemia or aggravation of hypoglycemia. In clinical trials, compared with glipizide and other drugs, glipizide resulted in higher hypoglycemia index, more complications, and weight gain in patients. For the prospect of glipizide in the future, the corresponding complications are reduced and the suitable population is increased. The main problem leading to hypoglycemia can be improved.

References

- [1] Correa R, Quintanilla Rodriguez BS, Nappe TM. Glipizide. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing, 2023.
- [2] Bethesda (MD): National Library of Medicine (US), National Center for Biotechnology Information. PubChem Compound Summary for CID 3478, Glipizide, 2023.
- [3] Glipizide: Medlineplus Drug Information. MedlinePlus, U.S. National Library of Medicine,
- [4] Glipizide. Uses, Interactions, Mechanism of Action | DrugBank Online,
- [5] Type 2 Diabetes: Symptoms, Causes, Diagnosis, and Treatment. WebMD, WebMD,
- [6] Type 2 Diabetes. Centers for Disease Control and Prevention, Centers for Disease Control and Prevention, 2022.

- [7] van de Wiel. Diabetes Mellitus and Alcohol. Diabetes/Metabolism Research and Reviews, U.S. National Library of Medicine
- [8] Sun H, Saeedi P, et al. IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. *Diabetes Res Clin Pract*, 2022,183:109119.
- [9] Cheng JWM, Badreldin HA, Patel DK, Bhatt SH. Antidiabetic agents and cardiovascular outcomes in patients with heart diseases. *Curr Med Res Opin*, 2017, 33(6):985-992.
- [10] Lo C, et.al. Insulin and glucose-lowering agents for treating people with diabetes and chronic kidney disease. *Cochrane Database Syst Rev*, 2018, 9(9):CD011798.
- [11] Nauck MA, et.al. Dapagliflozin versus glipizide as add-on therapy in patients with type 2 diabetes who have inadequate glycemic control with metformin: a randomized, 52-week, double-blind, active-controlled noninferiority trial. *Diabetes Care*, 2011, 34(9):2015-22.
- [12] Qi, C., Zhou, et.al. Glipizide, an antidiabetic drug, suppresses tumor growth and metastasis by inhibiting angiogenesis. *Oncotarget*, 2014, 5(20): 9966-9979.
- [13] Zhou, et.al. Sentinel Modular Program for Propensity-Score Matched Cohort Analyses: Application to Glyburide, Glipizide, and Serious Hypoglycemia. *Epidemiology (Cambridge, Mass.)*,2017, 28(6): 838.
- [14] Arjona Ferreira, et.al. Efficacy and Safety of Sitagliptin Versus Glipizide in Patients with Type 2 Diabetes and Moderate-to-Severe Chronic Renal Insufficiency. *Diabetes Care*, 2013, 36(5): 1067-1073.
- [15] Nauck, M. A.,et.al. Dapagliflozin Versus Glipizide as Add-on Therapy in Patients with Type 2 Diabetes Who Have Inadequate Glycemic Control with Metformin: A randomized, 52-week, double-blind, active-controlled noninferiority trial. *Diabetes Care*, 34(9), 2015-2022.
- [16] Kautzky-Willer A, et.al. Sex and Gender Differences in Risk, Pathophysiology and Complications of Type 2 Diabetes Mellitus. *Endocr Rev*. 2016,37(3):278-316.
- [17] Diabetes mellitus. Merck Manual Professional Version. Accessed Dec. 7, 2020.
- [18] Liu LL, Yi JP, et.al; SEARCH for Diabetes in Youth Study Group. Type 1 and Type 2 diabetes in Asian and Pacific Islander U.S. youth: the SEARCH for Diabetes in Youth Study. *Diabetes Care*, 2009, Suppl 2: S133-40.
- [19] Foster RH, Plosker GL. Glipizide. A review of the pharmacoeconomic implications of the extended-release formulation in type 2 diabetes mellitus. *Pharmacoeconomics*, 2000, 18(3):289-306.
- [20] Jie H, Yifei Z, et. al. on behalf of the SPREAD-DIMCAD Investigators; Effects of Metformin Versus Glipizide on Cardiovascular Outcomes in Patients with Type 2 Diabetes and Coronary Artery Disease. *Diabetes Care* 1, 2013, 36 (5): 1304–1311.
- [21] “GLUCOTROL®Clinical Pharmacology (Glipizide).” GLUCOTROL® Clinical Pharmacology (Glipizide) | Pfizer Medical Information - US,
- [22] Correa R, Quintanilla Rodriguez BS, Nappe TM. Glipizide.In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing.
- [23] GLUCOTROL®Description (Glipizide). GLUCOTROL® Description (Glipizide)Pfizer Medical Information - US