

Use of Glimepiride in Special Populations

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Abstract

Glimepiride, a sulfonylurea (SU), has emerged as a drug of choice due to its insulin secretagogue activity with other added benefits. As compared to other sulfonylureas, glimepiride has low hypoglycemic effects, and its use is relatively safe even in special populations of type 2 diabetes mellitus patients, such as the elderly; patients with hepatic and renal diseases; and young people with diabetes. However, SUs including glimepiride might have hypoglycemic effects to various extents, and hence, their use in these special populations should be monitored. The use of newer SUs especially glimepiride is pertinent in Indian settings because of their low cost and proven benefits. Here we discuss the use of glimepiride in special population of people with diabetes mellitus.

Introduction

A part from the appropriate selection of the type of sulfonylurea (SU) for treatment of type 2 diabetes mellitus, it is also essential to select the patient populations appropriately for SU therapy. In order to gain optimum therapeutic benefits, emphasis should be on proper selection of patients and drugs, accurate dosage, timing, and frequency of the drug administration. All patients do not necessarily benefit from the same drug, e.g. those patients who are at risk of hypoglycemia, like patients with hepatic or renal impairment, hypoadrenalism or hypothyroidism, should not be treated with potent SUs. Likewise, the preferred SU for use in pregnancy might not be suitable for patients with renal impairment. Sulfonylureas that do not inhibit ischemic pre-conditioning and therefore may be prescribed for diabetic patients with stable coronary artery disease.¹ Glimepiride, a SU, has been found to be safe for use in the treatment of a wide array of people with type 2 diabetes mellitus. Here we will discuss the safety and efficacy of the use of glimepiride in special populations of people with type 2 diabetes mellitus.

Glimepiride in the Elderly

Although SUs are usually well tolerated in people with diabetes, they have usually been associated with hypoglycemic effects. Different SUs have variable hypoglycemic effects; therefore, some of them are safe to be used in elderly patients while others are

not. A study on the comparative effect of SUs in elderly patients revealed that while some of the SUs, such as glimepiride and modified release gliclazide can be used in elderly patients due to relatively lower hypoglycemic effects; the use of glibenclamide should be restricted in such populations.² Furthermore, the use of SUs, such as glimepiride as a drug of choice for elderly type 2 diabetes mellitus patients has been recommended by several guidelines, including International Diabetes Federation and Canadian guidelines.³

Glimepiride in Patients with Renal Impairment

In patients with chronic kidney disease and being treated with SUs, prolonged hypoglycemia is a significant problem. Some of the SUs, such as glibenclamide (glyburide), have metabolites that have a hypoglycemic effect and are, therefore, associated with prolonged hypoglycemia in patients with renal failure. Other SUs, such as glimepiride, have been found to be relatively safer to use in people with diabetes who have chronic kidney disease.⁴

The altered insulin requirements in people with diabetes and acute renal failure must be monitored carefully.

Lower dose of insulin and SU or temporarily withholding the SU is required for patients with acute renal failure. As their renal function improves, insulin requirements also increase, and the dose of oral and injectable agents can be increased accordingly. Poor daily caloric intake and emesis are two important considerations that must be kept in mind while monitoring patients with diabetes and renal impairment.⁴

Glimepiride in Patients with Liver Disease

Since most SUs are metabolized in the liver, hepatic impairment in people with diabetes may cause accumulation of the drug, causing hypoglycemia. Hypoalbuminemia can result in hypoglycemia due to the increase in the concentration of free drug. Patients may have reduced ability to counteract hypoglycemia in some conditions such as decompensated cirrhosis. Therefore, the response of such patients to antidiabetic therapy should be monitored closely and drugs safe for use in hepatic impairment may be preferred.² Therefore, SUs with mild hypoglycemic effects, such as glimepiride should be used with caution in patients with liver disease.

Glimepiride in Patients with Cardiovascular Disease

The risk of developing cardiovascular disease (CVD) is higher in those with diabetes, thereby, necessitating the cardiovascular-safe profile of antidiabetic drugs. In the Veterans Affairs Diabetes Trial that included 1791 military veterans, it was revealed that the use of glimepiride therapy was associated with a 17% reduced risk in the rate of CV events in comparison to standard therapy. A meta-analysis showed that SUs are not associated with enhanced risk for cardiovascular

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Table 1: Effects of glimepiride on special populations of type 2 diabetes mellitus patients

Types of special population	Effects of glimepiride
Elderly patients	Lower hypoglycemic effects than the first generation SUs. Recommended as the 'drug of choice' for elderly patients with diabetes by several guidelines including the International Diabetes Federation and Canadian guidelines. ³
Patients with renal compromise	Relatively safer in patients with diabetes with chronic kidney disease. ⁴
Patients with liver disease	The use of SUs, including glimepiride, in hepatic dysfunction should be monitored closely since these patients are susceptible to hypoglycemia. ³
Cardiovascular patients	Glimepiride has a cardio-safe profile compared to other SUs. ³

mortality, stroke, or all-cause mortality.³ Glimepiride has also been postulated to cause less glycemic variability than the older SUs such as glibenclamide.⁵ The Cardiovascular Outcome Study of Linagliptin Versus Glimepiride in Patients with Type 2 Diabetes (CAROLINA) trial evaluated the comparative effects of linagliptin and glimepiride on cardiovascular morbidity and mortality. This recent study demonstrated that in terms of time to first major adverse cardiovascular event in type 2 diabetes mellitus patients with cardiovascular risk, glimepiride was non-inferior to linagliptin.⁶

Glimepiride in Young People with Type 2 Diabetes Mellitus

Although evidence on the use of SUs in children is quite limited, a single-blind active-controlled study was

conducted over a period of 26 weeks in 285 pediatric patients with type 2 diabetes mellitus.^{3,7} The study revealed that glimepiride was equally effective in HbA_{1c} reduction as metformin, with similar rates of hypoglycemia. Guidelines also indicate that a SU must be the drug of choice, for the treatment of Maturity-Onset Diabetes of the Young.^{3,8}

The effects of glimepiride on different special populations of type 2 diabetes mellitus patients have been summarized in Table 1.

Conclusion

Glimepiride has emerged as a drug of choice for the treatment of type 2 diabetes mellitus. Apart from the glucose-lowering effects of glimepiride by increasing insulin release from the pancreatic beta-cells, it also has a lower risk of hypoglycaemia among SUs. The use of glimepiride has been recommended even in special populations of type 2 diabetes mellitus patients who require caution during hyperglycemia therapy. Glimepiride is safe to use in patients with cardiovascular risk, cardiovascular disease and in younger patients with diabetes. However, since it can cause hypoglycemia, which is a common limitation of SU therapy, its use in the elderly, and people with renal or hepatic impairment should be monitored.

Conflict of Interest

SK is an employee of Sanofi India. All other authors report no conflicts of interest.

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