

Incidence of Hypoglycemia and Other Side Effects in Patients of Type 2 Diabetes Mellitus Treated with Glimepiride versus Glibenclamide

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ABSTRACT

Background: Sulfonylureas were among the first oral antihyperglycemic agents developed, but patients on a sulfonylureas experience hypoglycemia. Severe hypoglycemia was a potentially life-threatening condition. **Objective:** The aim of the study was to compare the frequency of hypoglycemia in patients with type 2 diabetes treated with glimepiride versus glibenclamide. **Material & Methods:** Total 50 patients were included in the study. These patients were divided in group I & II. Group I (n=25): Patients were given Tab. Glibenclamide. Group II (n=25): Patients were given Tab. Glimepiride for 24 weeks. **Results:** Patients with glibenclamide experienced hypoglycemia (12%) and weight gain (4%) as the main adverse effects while patients with glimepiride had no such adverse effects. **Conclusion:** In people with type 2 diabetes, glimepiride was associated with fewer episodes of hypoglycemia than glibenclamide.

Keywords: Type 2 diabetes mellitus, glimepiride, glibenclamide, hypoglycemia, sulfonylureas.

INTRODUCTION

Diabetes mellitus is a chronic disease that occurs when the pancreas does not produce enough insulin leading to hyperglycemia and requires life-long pharmacological and non pharmacological management to prevent complications such as cardiovascular disease, retinopathy, nephropathy, and neuropathy.^[1] Type 2 diabetes mellitus is the most common form

of diabetes comprising of 90% to 95% of all diabetes cases.^[2] An estimated 346 million people worldwide live with diabetes, resulting in 3.4 million deaths in 2004, with more than 80% of these deaths occurring in low- and middle income countries.^[3] The fastest growing age group of people with diabetes is between 40 to 59 years and the worldwide 2011 estimated prevalence of diabetes is the elderly population (60 years

and above) is between 15% to 20%.^[4] Diabetes is the leading cause of renal failure, visual impairment and blindness and increases the risk of lower limb amputation. Additionally, patients living with diabetes may need 2 to 3 fold more health-care resources compared to people without diabetes and diabetes care may require allocation of up to 15% of national health care budgets.^[5] Sulfonylureas were among the first oral antihyperglycemic agents developed, and they are still commonly used today because they are inexpensive and well tolerated.^[6] Glibenclamide and Glimepiride both are second generation sulfonylureas. Since glibenclamide came onto the market in 1983, glibenclamide has been one of the most popular sulfonylureas. The American Diabetes Association (ADA) recommends the use of these agents as part of a stepwise approach to treating type 2 diabetes mellitus.^[7] Sulfonylureas aim to reduce diabetes associated hyperglycemia by acting on the pancreatic beta cell channels (ATP-K channel) to facilitate insulin secretion.^[8] The primary difference between glibenclamide and glimepiride is the prolonged half-life of glibenclamide at 10 hours compared average half-life of 5 hours for glimepiride.^[9] The pharmacokinetic parameters of half-life, elimination and volume of distribution are also increased to a greater extent for glibenclamide compared to glimepiride.^[10] However, all sulfonylureas are hepatically metabolized and renally cleared, therefore, are subject to slower elimination in the elderly due to the age-associated decrease in renal function.^[11] Furthermore, compared to glimepiride, glibenclamide has a higher affinity for pancreatic beta-cell receptors, greater propensity for accumulation of active metabolites and greater penetration of pancreatic tissue.^[12] Sulfonylureas are generally well tolerated as a class; however,

the pharmacokinetic differences within the agents can have significant clinical implications for patients. The pharmacokinetic differences are amplified and particularly noticeable in the elderly patient.^[13] One of the most common side effects of sulfonylureas is hypoglycemia, that if left untreated can lead to altered mental status, seizures, coma or death.^[14] An estimated 20% of the patients on sulfonylureas experience hypoglycemia within a 6-month period.^[15]

MATERIALS & METHODS

In the study we compared the safety of two second generation sulfonylureas, glimepiride and glibenclamide for the treatment of type 2 diabetes mellitus. This is a randomized, parallel group study which was conducted in the patients suffering from type 2 diabetes mellitus by the Department of Pharmacology in association with Department of Medicine at Maharishi Markandeshwar Institute of Medical Sciences & Research (MMIMSR), Mullana Ambala. Total 50 patients were included in the study. These patients were divided in group I & II. Group I (25 patients): This group included the eligible patients diagnosed with type 2 diabetes mellitus and these patients were given Glibenclamide in dose range of 5-15 mg/day, for 24 weeks. Group II (25 patients): These patients were administered Glimepiride in dose range of 1-6 mg/day, for 24 weeks. At each visit, the patients were asked about compliance and any adverse drug reaction experienced. A detailed medical history was obtained. Careful general physical examination along with systemic examination was done. Any adverse effects reported by the patient or investigator were recorded and analyzed. Safety and tolerability evaluation was based upon both self reported adverse effects and the recorded adverse effects.

RESULTS

Patients were randomly divided in two groups:

Group I (n=25): Patients were given Tab. Glibenclamide (5-15 mg/day) orally for 24 weeks. Group II (n=25): Patients were given Tab. Glimepiride (1-6 mg/day) orally for 24 weeks.

Table 1: Adverse effects observed during the study.

ADRs	GROUP I		GROUP II	
	n(no. of patients)	%	n (no. of patients)	%
Nausea/vomiting	2	8	1	4
Constipation	1	4	0	0
Hypoglycemia	3	12	1	4
Weight gain	1	4	0	0
Headache	1	4	1	4

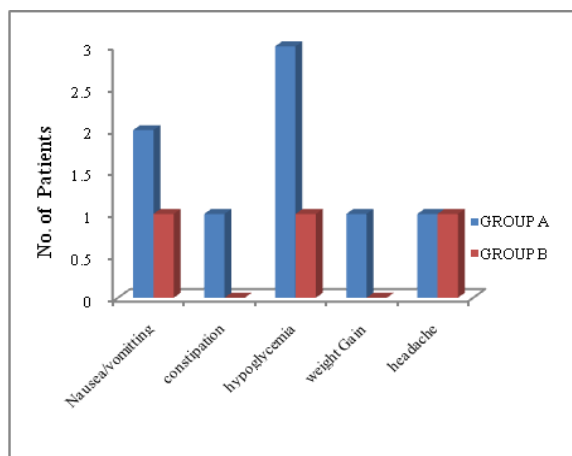


Figure 1: Adverse Effects observed during the study.

DISCUSSION

Diabetes mellitus is a worldwide disease which affecting most of the population. There are a number of new agents for the treatment of type 2 diabetes mellitus but oral sulfonylureas remain a cornerstone of therapy. Glibenclamide thus appears to be a useful addition to the range of oral hypoglycemic sulfonylurea, because of its potency (and its expense) it is probably best used as second or third line of attack in patients whose blood glucose control is inadequate with other therapy.^[16] Glibenclamide can also increase insulin

sensitivity greater than other sulfonylureas, and due to its long half-life, can lead to increased insulin release for longer periods after cessation of the medication, especially in decreased renal function.^[17] One of the most common side effects of glibenclamide is low blood sugar or hypoglycemia. Glibenclamide has the potential to cause a number of other unwanted, but not dangerous side effects. One of the most commonly experienced effects is weight gain, which can be mitigated through diet and exercise. Gastrointestinal side effects of glibenclamide include constipation, diarrhea, nausea, vomiting, abdominal pain and loss of appetite. Glimepiride is comparatively a newer second generation oral hypoglycemic agent belonging to sulfonylurea group. Adverse effect profile of glimepiride is similar to glibenclamide; although chances of hypoglycemia are little bit less with glimepiride. It has pharmacokinetic properties that make it less prone to cause hypoglycemia in renal dysfunction than glibenclamide.^[18] During this study when we compare both drugs it was found that patients in Group I experienced hypoglycemia (12%) and weight gain (4%) as the main adverse effects while patients in Group II had no such adverse effects. Nausea, vomiting and headache occurred with almost similar frequency in both the groups. (Table 1 and Figure 1)

The result of the study was similar with the following studies:

Draeger KE et al. conducted a study in which it was found that fewer hypoglycemic reactions occurred with glimepiride than with glibenclamide.^[19] Another study conducted by Vray M et al. also pointed out that there was a significant increase in weight in the patients treated with glibenclamide. Holstein A et al. conducted a prospective, population-based

and found that glimepiride was associated with fewer episodes of severe hypoglycemia than glibenclamide.^[20] Holstein A et al. During the study registered total 93 episodes of severe hypoglycemia, 37 on glimepiride and 56 on glibenclamide.^[21] Similarly Hamaguchi T et al. observed a significant reduction in weight with glimepiride.^[22]

CONCLUSION

Glimepiride and glibenclamide both the drugs were well tolerated but in people with type 2 diabetes, glimepiride was associated with fewer episodes of hypoglycemia and no weight gain than glibenclamide

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