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A Comparison of the Efficacy and Safety of Glimepiride and Sitagliptin in Individuals with type 2 Diabetes Mellitus

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ABSTRACT:
Background: One of the main causes of the high cost of treating subjects with Diabetes Mellitus (DM) and society as a whole.
Objective: to compare the safety and efficacy of sitagliptin versus glimepiride in subjects with Type 2 DM who are also receiving Metformin treatment as a background.
Materials and Methods: From March to September 2018, this research will be carried out in an Indian hospital that offers tertiary care. As an add-on therapy for 12 weeks, eligible subjects were randomized to receive sitagliptin 100 mg and glimepiride 2 mg once per day. Demographic information was entered onto a pre-filled proforma. All research participants/subjects received recommendations to maintain a healthy diet and engage in regular exercise. All subjects had their HbA1C, FBS, weight, Alanine aminotransferase (ALT), serum urea, and serum creatinine measurements taken at week 0 and again at the conclusion of the research at week 12. Attainment of the target HbA1C upper normal limit at research's conclusion was the main endpoint.
Results: The trial enrolled a total of 120 subjects, 60 in each category. In category A, there were 32 men and 28 females, and in category B, there were 36 males and 24 females. When compared to the Glimepiride category, category A using sitagliptin showed a significant decrease in HbA1C and BMI. ($p<0.05$). FBS reduction was similar between the two categorys ($p>0.05$). The most common side effects in both categorys were hypoglycaemia, diarrhea, and vomiting. In neither category was there a statistically significant difference in the frequency of occurrence ($p>0.05$).
Conclusion: The results of the current trial provide evidence that sitagliptin is equally effective as glimepiride in improving glycemic control as an add-on medication to metformin and is well tolerated with no significant adverse effects. Sitagliptin outperformed glimepiride and had a lower risk of hypoglycaemia. Additionally, compared to Glimepiride, it was well tolerated and led to weight loss.
Key words: Diabetes Mellitus, Sitagliptin, Glimepiride, HbA1C, BMI

INTRODUCTION

About 180 million individuals worldwide were predicted to have diabetes mellitus (DM), one of the most prevalent chronic disorders in 2008[1]. The incidence and prevalence of type 2 diabetes are increasing exponentially as a result of sedentary lifestyle, obesity, high BMI, decreased physical activity, and longer life expectancy. One of the main causes of the financial burden on subjects and society is this high prevalence rate[2]. Microvascular (retinopathy, nephropathy, and neuropathy)

and macrovascular problems are also greatly increased by type 2 diabetes (coronary heart disorder, cerebrovascular disorder and peripheral vascular disorder). The focus of available therapies is on lowering hyperglycemia and raising insulin sensitivity. These approaches are highly alluring and require focus because they primarily aim to treat the primary problems and prevent complications related to type 2 DM[3-5]. However, glycemic control deteriorates over time despite the abundance of effective treatments. Constant decline in beta-cell function frequently leads to unattainable glycemic management. The major objective of treatment is to manage blood sugar levels by keeping the HbA1C level between 6 and 7% in order to reduce the likelihood of microvascular and macrovascular problems without putting subjects at risk for hypoglycaemia[6-8]. The majority of type 2 DM subjects need more than one anti-diabetic medication, either alone or in conjunction with insulin, as monotherapy increases the risk of complications and inability to maintain glycemic control. The various anti-diabetic medications currently on the market reduce blood glucose levels in various ways. However, the unique pharmacokinetic and pharmacodynamic characteristics of each one place restrictions on their use and dosage titration. Sitagliptin is an oral, once-per day, powerful and highly selective dipeptidyl peptidase-4 (DPP-4) inhibitor that has been given the green light by the US Food and Drug Administration for use in combination with diet and exercise to help adults with type 2 DM improve their glycemic control. Sitagliptin increases fasting and postprandial levels of intact incretins, glucagon-like peptide-1 (GLP-1), and glucose-dependent insulinotropic polypeptide via inhibiting DPP-4 activity (GIP). Incretins have a significant role in increasing the insulin release in response to meals, which helps to regulate glucose levels. GLP-1 also helps to lower glucagon secretion.

These two effects depend on blood glucose levels. When treatment with either medication on its own fails to regulate blood sugar levels, it can be administered alone or in combination with metformin or a thiazolidinedione (pioglitazone or rosiglitazone)[9]. The typical adult dose is 0.1g given once per day. Subjects with moderate-to-severe renal impairment should take 25–50 mg once per day. This research was carried out to compare the safety and efficacy of sitagliptin as compared to glimepiride in subjects whose metformin-alone control was insufficient because there are no significant data regarding the safety and efficacy of this medication in our population.

Objective: to compare the safety and efficacy of sitagliptin versus glimepiride in subjects with Type 2 DM who are also receiving Metformin treatment as a background.

MATERIAL AND METHODS

From March to September 2018, this research will be carried out in an Indian hospital that offers tertiary care. Eligible subjects were randomized to receive sitagliptin 100 mg and glimepiride 2 mg once per day as add-on medication for 12 weeks after receiving approval from the institutional ethics committee. Age, gender, smoking history, and hypertension were among the demographic factors of the research population that were noted on a pre-filled proforma. Throughout the research period, all subjects were encouraged to engage in regular exercise and careful nutrition management. All subjects had their HbA1C, FBS, weight (Kg), Alanine aminotransferase (ALT), serum urea, and serum creatinine measures taken at week 0 and again at the conclusion of the trial at week 12. Attainment of the target HbA1C upper limit normal (ULN) at research's conclusion was the main objective.

Inclusion criteria:

1. Type 2 DM subjects on metformin monotherapy with poor glycemic control
2. Values of FBS and PPBS exceeding 100 mg/dl and 140 mg/dl, respectively

3. Individuals with HbA1C levels greater than 7%
4. Both male and female subjects are included.

Exclusion criteria:

1. Research participants with a history of medication allergies or sensitivity
2. Pregnant women with type I diabetes
3. those with compromised liver and kidney functions,
4. Uncontrolled diabetes, defined as a fasting blood sugar (FBS) level of 300 mg/dl or higher (HbA1C > 9%),
5. The research excluded participants with unstable angina and uncontrolled hypertension.

Statistical Analysis

SPSS for Windows was used to analyze every piece of data. With PS software, the sample size was determined using an 80% power. Chi-square (x2) for categorical variables and student 't' test for continuous variables, as necessary, were used to compare the two categorys. A p value of 0.05 or lower was considered significant.

RESULTS

The trial enrolled a total of 120 subjects, 60 in each category. After employing a randomization software, the category was assigned. The mean age in the sitagliptin category (A) was 45 years, compared to 47 years in the glimiperide category (B). Regarding age distribution, there was no significant difference between the categorys. In category A, there were 32 men and 28 females, and in category B, there were 36 males and 24 females. The categorys' average BMIs were also matched, with no statistically significant differences.

Table 1: Demographic Data

	Demographic Data		
	Sitagliptin	Glimiperide	p Value
Age in years(Mean±SD)	45±4.15	47±903.1	0.56
Sex(M/F)	32/28	36/24	0.76
BMI(Mean±SD)	23±2.25	22±2.45	0.64

Table 2: comparison

	Sitagliptin Category		Glimiperide Category		
	Baseline	Week 12	Baseline	Week 12	p Value
HbA1C(%)	8.02±0.28	6.48±0.12	7.98±0.3	7.02±0.15	0.04
FBS	170±7.4	120±5.4	165±6.3	123±4.15	0.1
BMI	27±2.05	24.1±1.25	28.0±2.15	27.03±1.3	0.02

HbA1C, fasting blood sugar, and BMI baseline readings were kept; a second reading was done at the 12-week follow-up. The student t test was used to compare and assess both readings. In the HbA1C and BMI follow-up, there was a statistically significant difference between Categorys A and B. When category A using sitagliptin was compared to the category taking glimepiride, we discovered a substantial decrease in HbA1C and BMI. ($p<0.05$). FBS reduction was equivalent between the two categorys. ($p>0.05$)

Table 3: Side Effect Profile

Side Effect Profile			
	Sitagliptin Category	Glimiperide Category	p Vlaue
Hypoglycaemia	6	4	0.56
Diarrhoea	4	2	0.98
Vomiting	4	6	0.76
Others	2	4	0.44

The most common side effects in both categorys were hypoglycaemia, diarrhea, and vomiting. There was no statistical difference in the frequency of occurrence between the two categorys ($p>0.05$). These side effects were minor, necessitated no prescription interruptions, and did not cause any dropouts.

DISCUSSION

Diabetes mellitus is a major risk factor for developing numerous complications ranging from microvascular injury to organ failure. The primary objective of the treatment of DM is to maintain the blood glucose levels in the normal range. HbA1C is a marker of that parameter that reflects the glucose control over past 2 to 3 months[10]. Maintaining HbA1C at a range of 6-7% is taken as adequate and reflects a good control of DM. The American Diabetes Association guidelines state that metformin, along with lifestyle changes, should be considered first-line therapy in subjects with type 2 DM. If glycemic control not successfully achieved and DM still remains uncontrolled during step-1/first line therapy, then employment of step-2 may be needed which includes sulfonylureas, thiazolinediones or insulin etc.

Metformin and TZDs are the two major drugs in treatment of DM, act by treating the insulin resistance, however they have got no action on declining the progression of beta cell function which observed in subjects with type 2 DM. So, there is need of newer treatment approaches[11]. Targeting the incretin mimetic hormone is one among them. GLP-1, an incretin hormone, is released when blood glucose levels are elevated, GLP- 1 stimulates insulin secretion, decreases glucagon secretion, improves beta-cell function, and slows gastric emptying. There will be reduction in the production of GLP-1 in subjects with type 2 DM. DPP-4 is the enzyme the causes rapid degradation of GLP-1 when it is produced.

So, the action of GLP-1 hormone can be prolonged inhibiting the enzyme with DPP-4 by drugs like Sitagliptin. Once the blood glucose level approaches normal, the amounts of insulin released and glucagon suppressed diminishes, thus preventing an “overshoot” and subsequent hypoglycaemia which is seen with some other oral hypoglycemic agents. In our research, Sitagliptin category achieved higher reduction in HbA1C as compared to subjects in Glimepiride category but the difference was not statistically significant. Similar results were reported by other studies. In research by Arechavaleta et al., there were 65% of subjects achieving target HbA1C of <7%. Similarly in a research by Charbonnelet al, in subjects using sitagliptin, 47% of them achieved target HbA1C[12]. FBS was decreased in both categorys, although there was no statistically significant difference between them. The outcome matched what other research had shown. In a trial by Goldstein et al., sitagliptin reduced FBS by 63.9 mg/dl. FBS was decreased in a research by Charbonnelet et al. by 50 mg/dl in the

sitagliptin category from baseline, compared to 42 mg/dl in the glimiperide category[13]. Both the Sitagliptin and Glimiperide categorys in our research's subjects experienced a decline in BMI, although the sitagliptin category's decline was statistically significantly greater than the glimiperide category's. Similar to this, in the Naucket al. trial, the sitagliptin category lost much less weight than the glimepiride category.

CONCLUSION

As an add-on therapy to metformin, sitagliptin appears to be as effective as glimepiride in improving glycemic control and is well tolerated with no significant side effects, according to the results of the current research. There were no significant negative effects detected in our trial.

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