DOI: https://doi.org/10.53350/pjmhs2115102800

ORIGINAL ARTICLE

Comparison of Efficacy and Safety of Sitagliptin and Glimepiride in Treatment of Type 2 Diabetes Mellitus

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ABSTRACT

Objective: To compare the efficacy and safety of sitagliptin and glimepiride in treatment of type 2 diabetes mellitus.

Design: It was an observational open comparative study.

Study Settings: This study was conducted at Department of Pharmacology over 1 year from March 2017 to March 2018 at DHQ Teaching Hospital, Kohat.

Material and Methods: Sixty (60) patients were enrolled in the study meeting the inclusion criteria. Tablet glimipiride 1 mg and sitagliptin 100 mg was used as the treatment option. Patients were randomly divided into two groups: group Glimepiride (30 patients; administered glimepiride 2 mg daily) and group Sitagliptin (30 patients; administered sitagliptin 100 mg daily). If glycemic control was not reached then patient was excluded from the study and given further treatment for benefit of the patient. The samples of blood were taken at 12 weeks visit to test HbA1c level, fating blood sugar (FBG) and post prandial glucose (PPG) level. At the time of follow up patient were evaluated for efficacy, safety and tolerability. All collected data was entered then analysed in SPSS version 19.0.

Results: A total of 60 patients were enrolled into the study, with 30 in each group. Mean age in sitagliptin group (A) was 45 years, while that of glimeperide group (B) was 47 years. There were 16 males and 14 females in group A, 18 males and 12 females in group B. We found a significant reduction of HbA1C and BMI in group S taking sitagliptin as compared to glimeperide group. ($p<0.05$) Reduction in FBS was comparable in both the groups. ($p>0.05$). Side effects in both the groups mostly included hypoglycemia, and vomiting, nausea and abdominal pain. These side effects were mild and did not need stoppage of medication or resulted in drop outs.

Conclusion: Sitagliptin as an adjunct to present monotherapy with metformin showed significant drop out in HbA1c, PPG and FBG values after treatment of 12 weeks and was non inferior to glimepiride. However, no sitagliptin taking patients observed any episodes of hypoglycemia. Also weight loss was observed in sitagliptin group as compared to glimepiride group..

Keywords: Glimepiride, Sitagliptin, Efficacy, Safety, Type 2 Diabetes Mellitus

INTRODUCTION

Diabetes mellitus is a chronic debilitating disease. It affects people irrespective of age or socioeconomic status.[1] Almost 7.5% of the population of Pakistan suffers from the condition. Upto 300 million are expected to be affected by 2025.2 Mortality due to diabetes in Pakistan is very high.[2] More than 88,000 deaths due to diabetic complications were reported in 2010.[3] This problem poses a significant challenge to the healthcare system as well as the economy especially of an under developed country like ours. Most of those affected are those who belong to in their productive life phase. The complications can lead to disability not just for the individual but also weakens the society by taking away productive members. Poorly controlled diabetes mellitus can cause damage to the eyes, kidneys, nerves, heart and brain.[4]

There are seven groups of antidiabetic drugs discover so far and various drugs are under consideration.[5] For the treatment of type 2 diabetes mellitus that combination of the drugs should be selected which have very less adverse effects and much efficacious.[6] The only FDA approved drugs of sulfonylurea group is Glimepiride. The drug glimepiride have such a valuable characteristics like extrapancreatic effects, optimal secretion of insulin, weight reduction properties, minimal risk of hypoglycemia and its beta-cell friendly property.

Furthermore, glimepiride also have anti-inflammatory, angiogenic properties and being a potent antioxidative and is accepted safe in cardiovascular patients due to its lowest detrimental effects on preconditioning.[7,8,9]

Sitagliptin which is a DPP-4 inhibitors is orally active and routinely prescribed as monotherapy or as an add on therapy. Safety and efficacy of sitagliptin is well established for the treatment of T2DM.[10] These drugs have excellent safety and tolerability profile with no risk of hypoglycemia.[11] These drugs have promising effects on blood glucose, HbA1C, body weight, lipid profile and blood pressure. In addition these drugs have cardio protective properties by improving endothelial function.[12]

To the best of our knowledge there is lack of local published data so the purpose of the current study was to repeat this trial to further confirm the results. The objective of this study was performed to determine the efficacy and safety of sitagliptin as compared to previously established

glimepiride in patients who were uncontrolled on metformin monotherapy. Current study would help in the choice of more suitable treatment option for patients having type 2 DM in future.

MATERIAL AND METHODS

The study was conducted after getting approval from the hospital's ethical and research committee. Informed consent in written form was taken from enrolled patients after telling them the protocols of the study. It was a randomized controlled trial conducted at Department of Pharmacology over 1 year from March 2017 to March 2018 at DHQ Teaching Hospital, Kohat. Sample size of 60 (30 cases in each group) is calculated with 80% power of test and 95% confidence interval (2-sided).

Patients with age between 18 to 70 years of either sex with type 2 DM, who were taking antidiabetic drug metformin from last 3 months (90 days) and have insufficient glycemic control (levels of HbA1C >7% and HbA1C <10%) were enrolled in the present study. Patients with type-1 diabetes mellitus, who had previously been treated with sitagliptin or had previously been in a study using a DPP-4 inhibitor, alcoholic patients, pregnant and lactating females, females of childbearing age group planning pregnancy in recent future, HIV positive patients, taking weight loss medication, patient who had undergone operation in the last 4 weeks, history of hypersensitivity to any of the investigational agents and other drugs of their class, patients with other systemic illness like congestive cardiac failure, severe respiratory diseases, renal insufficiency, hepatic insufficiency and other terminal illnesses were excluded from the present study.

Tablet glimipiride 1 mg and sitagliptin 100 mg was used as the treatment option. Study cohort was randomly divided into two groups: group Glimepiride (30 patients; administered glimepiride 2 mg daily) and group Sitagliptin (30 patients; administered sitagliptin 100 mg daily). If glycemic control was not reached then patient was excluded from the study and given further treatment for benefit of the patient. Dose of metformin was kept constant throughout study which was 500 mg twice a day and no other hypoglycemic agent was added. If patients was taking medicines for linked illnesses, then in whole period of study doses of these drugs were kept constant.

This treatment was provided for the 12 weeks' time duration and patients was asked to come at follow up after 12 weeks. The samples of blood were taken at 12 weeks visit to test HbA1c level, fating blood sugar (FBG) and post prandial glucose (PPG) level. At the time of follow up patient were evaluated for efficacy, safety and tolerability.

All collected data was entered then analysed in SPSS version 19.0. Quantitative variables such as age and severity score was given as mean ± SD. Qualitative data such as gender and efficacy of the treatment was given as percentages and frequency . The t-test t-test was applied to compare the efficacy between two groups. Data was stratified with age, gender and disease severity. The p-value ≤0.05 was set as a statistically significant.

RESULTS

A total of 60 patients were enrolled into the study, with 30 in each group. Mean age in sitagliptin group (A) was 45 years, while that of glimeperide group (B) was 47 years. There was no statistical difference between the groups in terms of age distribution. There were 16 males and 14 females in group A, 18 males and 12 females in group B. Mean BMI between the groups were also matched without any statistical difference as shown in Table 1.

Baseline reading of HbA1C, fasting blood sugar and BMI were recorded; second reading was taken at 12th week follow up. Both the readings were compared and analyzed using student t test. There was a statistical difference found in the follow up of HbA1C and BMI between the Group A and Group B. We found a significant reduction of HbA1C and BMI in group A taking sitagliptin as compared to glimeperide group. ($p<0.05$) Reduction in FBS was comparable in both the groups. ($p>0.05$) as shown in table 2.

Side effects in both the groups mostly included hypoglycemia, and vomiting, nausea and abdominal pain. The frequency of occurrence in both the groups was similar without a statistical difference ($p>0.05$). These side effects were mild and did not need stoppage of medication or resulted in drop outs.

Table 1: Baseline characteristics of the randomised population

Parameters	Sitagliptin	Glimeperide	p Value
Age	45±4.3	47±903.2	0.56
Sex M/F	16 14	18 12	0.76
BMI	23±2.5	22±2.9	0.64
Disease duration year	9 ± 3	10 ± 21	0.65

Table 2: Showing comparison of primary end points between both the groups at follow ups

	Sitagliptin Group		Glimeperide Group		
	Baseline	Week 12	Baseline	Week 12	P-value
HbA1C(%)	8.02±0.56	6.48±0.23	7.98±0.60	7.02±0.30	0.04
FBS	170±7.8	120±5.8	165±6.6	123±4.3	0.1
BMI	27±2.1	24.1±1.5	28.0±2.3	27.03±1.6	0.02
Weight	62.06±7.02	60.57±6.66	64.59±7.9	66.06±8.02	0.05

Table 3: Comparison of adverse drug reactions reported in both the groups

	Sitagliptin G	Glimeperide G	
Hypoglycemia	3.5	4.11	0.56
Nausea	12.8	11.4	0.98
Vomiting	6.0	3.11	0.76
Abdominal pain	4.5	5.25	0.44

DISCUSSION

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. Maintaining HbA1C at a range of 6-7% is taken as adequate and reflects a good control of

DM.[13] 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.[14]

In our study, Sitagliptin group achieved higher reduction in HbA1C in contrast with glimepiride group patients however the difference was statistically insignificant; p>0.05. Similar results were reported by other studies. In study by Arechavaleta et al.[15], there were 65% of patients achieving target HbA1C of <7%.

In a similar study by Charbonnel et al.(2006)[16] reported that 47 percent patients who were taking sitagliptin attained the targeted HbA1c. Fasting blood sugar was decreased in both groups but statistically significant difference was not observed in these two groups. Goldstein et al. (2017)[17] reported that 63.9 mg/dl reduction in fasting blood sugar was observed due to sitagliptin. Charbonnel et al.(2006)[16] reported that 50 mg/dl reduction in fasting blood sugar was noted due to sitagliptin from values of baseline, while it decreased to 42mg/dl in patients of glimeperide group.

In results of our study it was observed that BMI decrease in both glimeperide and sitagliptin group patients. Similar results were reported by Nauck et al. (2007)[18] that a significant reduction in weight in patients of sitagliptin group was observed as compare to patients glimepiride group. There was no major side effects of the drugs were observed in both groups. In group sitagliptin at baseline mean weight was 48.23±2.15 kgs and in group glimeperide was 49.61±3.21 kg. Similarly mean duration of diabetes was 4.56±1.24 years and 4.34±1.12 years in group S and group G respectively.[19]

Srivastava et al, in their study of 50 patients who were uncontrolled on metformin monotherapy reported a significant reduction in HbA1c, FBG and 2HPPG values with sitagliptin addition, when compared to baseline values ($p < 0.05$).[20] They also reported a decrease in bodyweight (-0.102kg) in sitagliptin group compared to glimepiride group (0.493 kg) where weight gain was observed.[20]

Anjoom et al in a similar study involving 60 T2DM patientsreported a significant difference in HbA1c, between glimepiride (8.79±0.11 and 7.32±0.11% ($p < 0.001$)) and sitagliptin (8.98±0.13 and 7.09±0.13% ($p < 0.001$)) group at 24 weeks follow up compared tobaseline values which is almost similar to the present study observations.[21]

Another study done by Hayati et al with 95 T2DM patients, who were previously taking metformin and glimepiride and adding sitagliptin as a third agent significantly reduced HbA1c by 0.41% ($P<0.007$) as compared to dual therapy alone, about 18.27% achieved their HbA1c targets.[14]

CONCLUSION

Sitagliptin as an adjunct to present monotherapy with metformin showed significant drop out in HbA1c, PPG and FBG values after treatment of 12 weeks and was non inferior to glimepiride. However, no sitagliptin taking patients observed any episodes of hypoglycemia. Also weight loss was observed in sitagliptin group as compared to glimepiride group.

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