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IS METFORMIN AND VILDAGLIPTIN COMBINATION BETTER THAN METFORMIN AND GLIMEPIRIDE COMBINATION FOR THE MANAGEMENT OF TYPE II DIABETES?

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ABSTRACT

Background: In this study, we compared the efficacy and the adverse events of a combination of Metformin-Vildagliptin and Metformin- Glimepiride. **Methods:** During this study, a total of 248 patients who were diagnosed with type II Diabetes Mellitus were taken. The 118 cases were Metformin combined with Vildagliptin and 126 cases were given Metformin combined with Glimepiride. HbA1c was measured at 3 months after the initiation of the treatment. **Results:** The reduction of HbA1c in Metformin + Vildagliptin group was 1.23 ±0.43 and in Metformin + Glimepiride group was 1.12±0.68. This showed that the reduction in HbA1c in both the groups was comparable. Hypoglycemia was more in Metformin + Glimepiride group than the Metformin + Vildagliptin group (p value=0.0001).Other adverse events were not statistically significant. **Conclusion:** The combination of Metformin and Vildagliptin had similar outcomes in reducing HbA1c and similar adverse events when compared to Metformin and Glimepiride, but hypoglycemic events were more common later. Therefore, Metformin and Vildagliptin combination is better than Metformin and Glimepiride combination for the management of type II Diabetes.

KEYWORD: In this study, we compared Metformin + Vildagliptin type II Diabetes.

INTRODUCTION

Diabetes mellitus is a chronic disorder characterized by hyperglycemia and the late development of vascular and neuropathic complications. Regardless of its cause, the disease is associated with a common hormonal defect which is known as insulin deficiency. This may be absolute or relative in the context of coexisting insulin resistance. The effect of insufficient insulin plays a primary role in the metabolic derangements linked to diabetes; hyperglycemia, in turn, plays an important role in disease-related complications.

Classification

The American Diabetes Association classification scheme for diabetes mellitus is summarized in Table 1. Clinical diabetes is divided into four general subclasses: Type 1, primarily caused by autoimmune pancreatic β-cell destruction and characterized by absolute insulin deficiency; Type 2, characterized by insulin resistance and relative insulin deficiency; other specific types of diabetes (associated with identifiable clinical conditions or syndromes); and gestational diabetes mellitus. In addition to these clinical categories, impaired glucose tolerance, impaired fasting glucose, and a high glycol-hemoglobin (HbA1c 5.7 to 6.4%), sometimes referred to as prediabetes. This describes intermediate metabolic states between normal glucose homeostasis and overt diabetes. Both impaired glucose tolerance and impaired fasting glucose significantly increases the risk for the future development of diabetes mellitus and in many

cases are part of the disease's natural history. Patients with any form of diabetes may require insulin therapy; for this reason, the previously used terms "insulin-dependent diabetes (Type 1)" and "non-insulin-dependent diabetes (Type 2)" have been eliminated.

TABLE 1: CLASSIFICATION OF DIABETES MELLITUS

ESTABLISHED DIABETES MELLITUS
Type 1 diabetes, formerly known as insulin-dependent diabetes mellitus or juvenile-onset diabetes (primarily due to β-cell destruction, usually leading to absolute insulin deficiency) Immune mediated Idiopathic Type 2 diabetes, formerly known as non-insulin-dependent diabetes or adult-onset diabetes (may range from predominantly insulin resistance with relative insulin deficiency to predominantly secretory defect with insulin resistance) Other specific types ("secondary diabetes") -Genetic defects of β-cell function (e.g., maturity-onset diabetes of the young, types 1 to 9; point mutations in mitochondrial DNA) -Genetic defects in insulin action (e.g., type A insulin resistance, leprechaunism, Rabson-Mendenhall syndrome, lipoatrophic diabetes) -Disease of the exocrine pancreas (e.g., pancreatitis, trauma, pancreatectomy, neoplasia, cystic fibrosis, hemochromatosis, fibro calculous pancreatopathy) -Endocrinopathies (e.g., acromegaly, Cushing's syndrome, hyperthyroidism, pheochromocytoma, glucagonoma, somato statinoma, aldosteronoma) - Drug or chemical induced (e.g., vapor, pentamidine, nicotinic acid, glucocorticoids, thyroid hormone, diazoxide, β-adrenergic agonists, thiazides, phenytoin, interferon-α) -Infections (e.g., congenital rubella, cytomegalovirus) -Uncommon forms of immune-mediated diabetes (e.g., stiff man syndrome, anti-insulin receptor antibodies) -Other genetic syndromes (e.g., Down syndrome, Klinefelter's syndrome, Turner's syndrome, Wolfram's syndrome, Friedreich's ataxia, Huntington's disease, Laurence-Moon-Biedl syndrome, myotonic dystrophy, porphyria, Prader-Willi syndrome) - Gestational diabetes mellitus
RISK CATEGORIES FOR DIABETES MELLITUS
Impaired fasting glucose Impaired glucose tolerance Increased glycol hemoglobin

Type 2 diabetes mellitus (T2DM) is one of the most common chronic disorders in adults, and constitutes a major global and growing public health problem particularly in developing countries. It is expected that the number of diabetes mellitus (DM) patients will rise from 366 million in the year 2011 to 552 million by 2030. Insulin resistance, in addition to a deficit in insulin secretion, is one of the core defect in Type 2 diabetes and is manifested in skeletal muscle, adipose tissue and the liver. The abnormality result n increased lipolysis in adipose tissue with resulting elevation of free fatty acids, and ultimately leading to raised triglyceride levels. It also leads to decreased total glucose clearance in the periphery and increased fasting plasma glucose (FPG), thus adding to the chronic progression of the disease. In a high percentage of patients, insulin resistance is associated with dyslipidemia, hypertension, and other components of the metabolic syndrome.

Oral glucose-lowering agents usually target one or more sites of the pathophysiology and Metformin is recommended by most guidelines as first line therapy for T2DM. Once initial monotherapy starts to lose its effect, long term management with combination therapy with two oral agents (e.g., metformin plus a sulfonylurea or metformin plus a DPP-4 inhibitors) is often necessary. For a long time, sulfonylureas have been recommended as a second-line treatment for Type 2 diabetes when metformin alone was not enough to achieve adequate glycemic control despite being effective in improving glycemic control. Sulfonylurea use is limited by the high rate of hypoglycemia. Recent breakthrough in the understanding of incretin-based therapies have provided additional options for the treatment of Type 2 diabetes, including glucagon-like peptide-1 receptor agonists and dipeptidyl peptidase-4 inhibitors. Among dipeptidyl peptidase-4 inhibitors, vildagliptin has been licensed at the recommended dose of 50 mg twice daily, in combination with metformin.

In the present study, we compared the efficacy and the adverse events of combination of Metformin-Vildagliptin and Metformin- Glimepiride in 248 patients.

METHODS

In our study, we took 248 patients in a tertiary care center who were diagnosed with Diabetes Mellitus type II. 120 patients were given Metformin and Vildagliptin combination out of which 2 patients were lost / did not comply with the regimen properly so only 118 patients

were left in the group. In the Metformin and Glimepiride group, there were 128 patients and 1 patient was lost in follow up and only 127 patients were left. The patients were followed up for a period of 3 months after the initiation of the treatment. HbA1c was measured at the end of 3 months and adverse events during this 3 month period was also noted. The data was analyzed with the help of chi-square test and level of significance was kept at p value<0.05.

RESULTS

The baseline characteristics of the patient population are described in Table 1. The duration of diabetes was 4.98± 2.13 years in Metformin + Vildagliptin group and 5.68± 1.59 years in Metformin + Glimepiride group. Mean HbA1c at the initiation of the treatment was 8.56± 0.75 in Metformin + Vildagliptin group and 8.13± 0.95 in Metformin + Glimepiride group. The reduction of HbA1c in Metformin + Vildagliptin group was 1.23±0.43 and in Metformin + Glimepiride group was 1.12±0.68. This showed that the reduction in HbA1c in both the groups was comparable.

Table 1: Baseline characteristics of the patients

Variable	Metformin + Vildagliptin (n=118)	Metformin + Glimepiride (n=126)
Age (yrs)	55.68 ± 9.86	57.35 ± 10.42
Male (%)	78(66.10%)	88(69.84%)
Female (%)	40(33.90%)	38(30.16%)
BMI (kg/m2)	23.04± 7.58	22.64± 4.38
Duration of Diabetes(yrs)	4.98± 2.13	5.68± 1.59
HbA1c	8.56± 0.75	8.13± 0.95

The adverse events in both the groups are showed in table 2. There were some differences in the incidence of the adverse events in the two groups but it was not significant and hence cannot be compared. The major adverse event was hypoglycemia which was more in the Metformin + Glimepiride group and this was significant (p value= 0.0001).

Table 2: Adverse events in the population

	Metformin+ Vildagliptin (n=118)	Metformin + Glimepiride (n=126)	P value
Presence of adverse event/events	12	23	0.071
Medication discontinuation due to adverse events	0	2	0.169
Vomiting	3	1	0.282
Abdominal pain	0	0	1
Overall gastrointestinal adverse events	7	2	0.078
Hypoglycemia	3	26	0.0001

DISCUSSION

Targeting hyperglycemia is key importance in the management of Type 2 diabetes mellitus, because lowering glycaemia reduces both acute symptoms and the risk of, retinopathy and cardiovascular disease. Also, Insulin resistance and pancreatic cell dysfunction are the two main pathophysiological features of T2DM, hence proper treatment for such disease should target both these defects. These days there are many medicines available and even these medicines have different combinations. Metformin is the most commonly used medicine. In many patients, proper glycemic control is not achieved with the use of single agent Metformin. Therefore, the combination of both medicines is used. Metformin is combined with sulfonylureas like Glimepiride or DPP-4 inhibitor like Vildagliptin. Metformin + Glimepiride is cheaper than Metformin + Vildagliptin combination. But some studies show that Metformin + Vildagliptin combination is better than Metformin + Glimepiride in terms of efficacy. Thus in this study, we tried to compare the efficacy and the adverse events in both combinations in Indian population.

Vildagliptin is an oral and highly selective dipeptidyl peptidase-4 (DPP-4) inhibitor which prevents the rapid degradation of endogenous glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic peptide (GIP). This increases the levels of the intact and active form of endogenous GLP-1. Vildagliptin improves glycemic control in Type 2 diabetic patients. Either monotherapy or administered in combination with metformin, sulfonylurea, thiazolidinedione or insulin. Improvements in glycemic control are mediated

primarily by increased insulin secretion and the suppression of glucagon secretion. Both of these effects depend on plasma glucose concentration, indicating that insulin secretion is suppressed and glucagon secretion is stimulated under low-blood glucose conditions. Vildagliptin has not demonstrated any effects on body weight and does not evoke severe hypoglycemia.

Glimepiride is a potent oral hypoglycemic agent and second generation sulfonylureas. It is commonly prescribed as a monotherapy or as a component of combination therapy for the treatment of type 2 diabetic patients over 60 years of age. Although sulfonylurea is well-known as being effective in lowering blood glucose, it also induces body weight gain and severe hypoglycemia.

In our study, we found that the combination of vildagliptin and metformin did not promote weight gain and offered clear advantages in terms of a reduction in the incidence of hypoglycemia. Therefore, Vildagliptin represents an appealing therapeutic option in patients with T2DM who fail to meet target HbA_{1c} with metformin monotherapy, particularly those with mild hyperglycemia and older or more fragile individuals who are more susceptible to hypoglycemia. The present study demonstrated that Vildagliptin has a favorable AE profile compared with Glimepiride with respect to hypoglycemia. Patients in the Vildagliptin group experienced a lower incidence of confirmed hypoglycemia and fewer episodes of hypoglycemia than did those in the Glimepiride group.

CONCLUSION

The reduction in HbA1c was same in both the groups. Hypoglycemia was more in Metformin + Glimepiride group as compared to the other. Other adverse events were same in both the groups. This shows that Metformin + Vildagliptin combination is a better combination than Metformin + Glimepiride.

REFERENCES

1. Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications of insulin-dependent diabetes mellitus. *N Engl J Med*., 1993; 329: 927.
2. Vildagliptin efficacy in combination with Metformin among Jordanian patients with Type 2 diabetes mellitus inadequately controlled with Metformin. Al Omari M1, Khader Y1, Dauod AS1, Beni Yonis OA1, Khassawneh AH1.
3. Comparative efficacy of Glimepiride and/or Metformin with insulin in Type 2 diabetes. Kabadi UM1, Kabadi M.
4. Comparison of Vildagliptin and Glimepiride: effects on glycemic control, fat tolerance and inflammatory markers in people with type 2 diabetes Derosa G1, Bonaventura A, Bianchi L, Romano D, Fogari E, D'Angelo A, Maffioli P.
5. Comparison of Vildagliptin-Metformin and Glimepiride-Metformin Treatments in Type 2 Diabetic Patients. Hyun Jeong Jeon and Tae Keun Oh.
6. Vildagliptin – Benefit assessment according to §35a Social Code Book V.
7. Fifty-two-week efficacy and safety of Vildagliptin vs. Glimepiride in patients with Type 2 diabetes mellitus inadequately controlled on Metformin monotherapy E. Ferrannini, V. Fonseca, B. Zinman, D. Matthews, B. Ahrén, S. Byiers, Q. Shao, S. Dejager.
8.