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Original Research Article

A study of effectiveness of addition of drug teneligliptin to metformin, glimepiride, pioglitazone combination in type II diabetic patients

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ABSTRACT

Background: Diabetes is a most prevalent chronic disease and has reached to alarming stage in almost all developed and developing countries. Worldwide approximately four hundred millions of people are living with diabetes and it is a leading cause of death. Aims and objectives is to study effectiveness of addition of drug Teneligliptin to Metformin, Glimepiride, Pioglitazone combination in type II Diabetic patients.
Methods: This was a cross sectional study carried out in the department of Medicine of a tertiary health care centre during the one year period i.e. January 2017 to January 2018 in the type II diabetic patients. Out of all type II diabetic patients 40 patients who were on the treatment for hypoglycemia with drugs Metformin, Glimepiride, Pioglitazone were selected out of these randomly 20 patients were continued on the previous treatment (Group B) and remaining 20 were given additional drug Teneligliptin (Group A). The statistical analysis was done by unpaired t-test and chi-square test analyzed by SPSS 19 version of software.
Results: In this study Authors have seen that the average age in both the groups was comparable i.e. 36.78±6.74 and 38.92±5.87 ($p>0.05$, $t=1.24$, $df=38$), the sex ration was also similar in both the group ($p>0.43$, $\chi2=0.43$, $df=1$) and the HbA1C was comparable at 1st Wk. 10±4.56 - 9.87±3.42 ($p>0.05$, $t=1.023$, $df=38$) and 4th Wk. 8±5.23 - 9.67±4.52 ($p>0.05$, $t=1.0804$, $df=38$) but significantly differed at 8th Wk. 7.12±2.34 - 9.92±3.56 ($p<0.01$, $t=3.82$, $df=38$), 12th Wk. 5.98±1.98 - 9.24±2.79 ($p<0.001$, $t=4.26$, $df=38$) respectively in Group A and B.
Conclusions: It can be concluded from this study that the addition of Teneligliptin significantly reduced the HbA1c level at the end of 4th wk. and hence superior to conventional Metformin, Glimepiride, Pioglitazone only combination treatment.

Keywords: Glimepiride, Metformin, Pioglitazone, Teneligliptin, Type II diabetes

INTRODUCTION

Diabetes is a most prevalent chronic disease and has reached to alarming stage in almost all developed and developing countries. Worldwide approximately four hundred millions of people are living with diabetes and it is a leading cause of death. This number is expected to rise to 642 million by 2040. A mortality burden of 5 million was noted with diabetes. The People's Republic of China, India, US, and Russian Federation reported highest deaths due to diabetes.[1] Diabetes affects many organs and complications due to high blood glucose are an important cause of disability, reduced quality of life, and premature death.[1] In 2015, globally, ~5 million people aged between 20 years and 79 years died due to diabetes; this accounts for one death every 6 seconds.[1] Diabetes is a chronic disease that requires lifelong medical care and attention for multiple risk reduction and treatment approach beyond glycaemic control.[2] Treatment objective must be the prevention of short-term and long-term complications associated with diabetes.[3] Additionally, patient education and support are important

aspects.[3] This will improve patient outcomes. A multidisciplinary approach is required for the management of diabetes.[2,3] Considering the huge epidemic of type 2 diabetes mellitus (T2DM), newer therapies that improve efficacy, tolerability, and long-term compliance and prevent complications associated with T2DM are always required and preferred.[4] Recently, a new and relatively economic dipeptidyl peptidase 4 (DPP-4) inhibitor, teneligliptin, has been made available in some countries such as Japan (Teneria), Argentina (Teneglucon®), and India (Tenepure; Teneza).[5-7] Authors have studied the effectiveness of teneligliptin with respect to glycemia in the management of T2DM.

METHODS

This was a cross sectional study carried out in the department of Medicine of a tertiary health care centre during the one year period i.e. January 2017 to January 2018 in the type II diabetic patients. Out of all type II diabetic patients 40 patients who were on the treatment for hypoglycaemia with drugs Metformin, Glimepiride, Pioglitazone were selected out of these randomly 20 patients were continued on the previous treatment (Group B) and remaining 20 were given additional drug Teneligliptin (Group A). The glycaemic control was monitored with respect to glycosylated Hb. (HbA1C) at 1st Wk, 4th Wk., 8th Wk, 12th Wk. after starting the treatment. The statistical analysis was done by unpaired t-test and chi-square test analysed by SPSS 19 version of software.

Inclusion criteria

- Patients with type 2DM not adequately controlled with tripe drug (Metformin, Glimepiride, Pioglitazone).

Exclusion criteria

- Patients with type 2DM with comorbidities like renal failure, ischemic heart disease with congestive cardiac failure, diabetic nephropathy.

RESULTS

Total 40 patients divided in two groups A and B as shown in table 1, the mean age in group A was 36.78 with standard deviation of 6.74 and in group B mean age was 38.92 with standard deviation 5.87.

Table 1: Distribution of the patients as per the socio demographic characters.

		Group A (20)	Group B (20)	p-value
Average age (Mean±SD)		36.78±6.74	38.92±5.87	p>0.05, t=1.24, df=38
Sex	Male	12	14	p>0.43, χ^2=0.43, df=1
	Female	8	6	

Table 2: Distribution of the patients as per the HbA1c level in two different treatment groups.

Post treatment duration (Wks.)	Group A (20)	Group B (20)	p-value
1st Wk.	10 ± 4.56	9.87±3.42	p>0.05, t=1.023, df=38
4th Wk.	8± 5.23	9.67±4.52	p>0.05 ,t=1.0804, df=38
8th Wk.	7.12 ± 2.34	9.92±3.56	p<0.01, t=3.82, df=38,
12th Wk.	5.98± 1.98	9.24±2.79	p<0.001, t=4.26, df=38,

It shows that the average age in both the groups was comparable i.e. 36.78±6.74 and 38.92±5.87 (p>0.05, t=1.24, df=38), There were 12 male and 8 female in group A, 14 male and 6 female in group B. Nearly equal no of male and female patients are there, the sex ration was also similar in both the group (p>0.43, χ^2=0.43, df=1).

As shown in table 2 the baseline (1st week) HbA1c in both group was nearly equal, 10 and 9.87 in group A and B respectively. There was marginal reduction at the end of 4th week in group A as compared to group B. The further fall in HbA1c was observed at the end of 8th week 7.12 (group A) but was not seen in group B. At the end of 12th week group A showed fairly well controlled HbA1c.

In brief the HbA1C was comparable at 1st Wk. 10±4.56 - 9.87±3.42 (p>0.05, t=1.023, df=38) and 4th Wk. 8±5.23 - 9.67±4.52 (p>0.05, t=1.0804, df=38) but significantly differed at 8th Wk. 7.12±2.34 - 9.92±3.56 (p<0.01, t=3.82, df=38), 12th Wk. 5.98±1.98- 9.24±2.79 (p<0.001, t=4.26, df=38) respectively in Group A and B.

This study shows that addition of 4th drug as teneligliptin in patients with type 2DM not having adequate glycaemic control with triple drug combination(Metformin,

Glimepiride, Pioglitazone) reduces HbA1c significantly and bring patient in acceptable glycaemic control.

DISCUSSION

Incretin hormones are released by the small intestine in response to a meal. One of these incretins, glucagon-like peptide-1 (GLP-1), plays a critical role in the regulation of postprandial glucose (PPG) by stimulating insulin secretion and inhibiting glucagon secretion in a glucose dependent manner.[8,9] However, as GLP-1 is rapidly degraded by dipeptidyl peptidase-4 (DPP-4).[10,11] DPP-4 inhibitors were developed to increase the endogenous GLP-1 levels, and hence lower blood glucose levels in a glucose-dependent manner. Eto T. et al. previously reported that once-daily administration of teneligliptin significantly increased postprandial plasma levels of active GLP-1 in type 2 diabetes mellitus (T2DM) patients and that the PPG-lowering effects of once-daily teneligliptin were sustained throughout the day.[12] T. Kadowaki have also found that teneligliptin monotherapy achieved significant reductions in haemoglobin A1c (HbA1c) [placebo-subtracted least-squares (LS) mean change: -0.9, -0.9 and -1.0% for 10, 20 and 40 mg teneligliptin, respectively; all, p <0.001] and fasting plasma glucose (FPG) levels (-17.8, -16.9 and -20.0 mg/dl, respectively), and was generally well tolerated in Japanese patients with T2DM.[13] Sulphonylureas are widely used because of their low price and their well-established efficacy and safety. Furthermore, they are often used as the initial antidiabetic drug in Japan.[14] However, sulphonylureas do require some attention because of the risk of hypoglycaemia and weight gain, together with their limited durability in clinical use. Both incretin-related drugs and sulphonylureas stimulate insulin secretion from pancreatic β-cells through independent pathways.[15,16] although there is some evidence to suggest that both pathways may incorporate Epac2, a cAMP sensor.[17] which may mediate some of the effects of both classes of drugs on insulin secretion. Therefore, administration of a sulphonylurea in combination with an incretin-related drug is potentially very useful, and many studies have tested combinations of these drugs.[18,19]

In this study Authors have seen that The average age in both the groups was comparable i.e. 36.78±6.74 and 38.92±5.87 ($p>0.05$, $t=1.24$, $df=38$), the sex ration was also similar in both the group ($p>0.43$, $\chi^2=0.43$, $df=1$) and The HbA1c was comparable at 1st Wk. 10±4.56 - 9.87±3.42 ($p>0.05$, $t=1.023$, $df=38$) and 4th Wk. 8±5.23 - 9.67±4.52 ($p>0.05$, $t=1.0804$, $df=38$) but significantly differed at 8th Wk. 7.12±2.34 - 9.92±3.56 ($p<0.01$, $t=3.82$, $df=38$), 12th Wk. 5.98±1.98 - 9.24±2.79 ($p<0.001$, $t=4.26$,$df=38$) respectively in Group A and B.

This was similar to Meta-analysis done by T. Kadowaki they found Teneligliptin reduced HbA1c significantly compared with placebo at week 12.[20] The placebo-subtracted change in HbA1c was -1.0±0.1% [least-squares (LS) Mean±SE., p <0.001].

CONCLUSION

It can be concluded from this study that the addition of Teneligliptin significantly reduced the HbA1C level at the end of 4th wk. and hence superior to conventional Metformin, Glimepiride, Pioglitazone only combination treatment. Patients of type 2DM who are not adequately controlled with conventional triple drug combination and not willing for insulin therapy can be given Teneligliptin as add on therapy.

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