Impact of Early Addition of Teneligliptin to Metformin in Type 2 Diabetic Patients

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ABSTRACT

Introduction: Diabetes is a noncommunicable disease. Present study assessed the effectiveness of early addition of Cost effective teneligliptin to Metformin in Type 2 Diabetes Mellitus patients.

Material and Methods: 100 subjects were enrolled, of which only 28 subjects were eligible for the study. The study group comprised of 28 subjects who were on metformin monotherapy i.e. between 1000gms to 2000gms per day. 500 mg of metformin in the study group was replaced with DPPIV inhibitor- teneligliptin 20mg per day. In order to study the efficacy of combination therapy versus metformin monotherapy Paired t test was performed after completion of 12weeks of therapy.

Result: The efficacy of combination therapy was assessed by Paired t test. It was observed that the mean FBS after addition of teneligliptin was (109.36 mg/dl ± 10.92) when compared to (118.07mg/dl ±12.76) in the Metformin monotherapy (t value: 4.98; p value <0.001) there was significant decrease in Fasting blood glucose level after addition of teneligliptin. The mean PPBS after addition of teneligliptin was (182.61 mg/dl ±33.05) when compared to (203.18mg/dl ±38.04) in the Metformin monotherapy (t value: 7.76; p value <0.001) there was significant decrease in post prandial blood glucose level after addition of teneligliptin. The mean baseline HbA1c after addition of teneligliptin was (7.44% ±0.35) when compared to (7.65% ±0.38) in the Metformin monotherapy (t value: 7.12; p value <0.001) there was significant decrease in HbA1C level after addition of teneligliptin. The incidence of Gastro-intestinal adverse events was more in metformin monotherapy than addition of teneligliptin however it was not statically significant. In addition there was no statically significant change observed with respect to lipid profile, body weight, Insulin Levels and HOMA score.

Conclusion: Teneligliptin was selected for the study because it has longer half-life, dual mode of elimination, superadded it is cost effective and cheaper in India than compared to other DPPIV inhibitors, due to its cheaper cost the compliance was better with respect to usage of teneligliptin. Ultimately Teneligliptin add-on to Metformin during the early course of treatment would be a multimodal approach in treatment of Diabetic patients further it could help in delaying the exhaustion of pancreatic islet function.

Keywords: Diabetes Mellitus, Teneligliptin, Metformin, DPP-4, Glycemic Control, Glycosylated Hemoglobulin, Fasting Blood Glucose, Post prandial Glucose

INTRODUCTION

Worldwide nearly 415 million people are suffering from diabetes and poor glycemic control leading to macro and microvascular complication. Experts have shown the figure of expected Diabetes patient could be 642 million by 2040. It has been noted that there is increased incidence of death due to diabetes and its complication in the following countries like India, Republic of China, USA, and Russian Federation.

Teneligliptin have a structure which is unique and binds to S1, S2, and S2 extensive subsite of DPP-4 enzyme. It is recommended Once-a-day administration.[1] Excretion of Teneligliptin metabolites is by dual mode. Present study assessed the effectiveness of early addition of Cost effective teneligliptin to Metformin in Type 2 Diabetes Mellitus patients.

MATERIAL AND METHODS

100 subjects were enrolled in the Deccan College of Medical Sciences, of which only 28 subjects were eligible for the study. The study group comprised of 28 subjects who were on metformin monotherapy i.e. between 1000 gms to 2000 gms per day. 500 mg of metformin in the study group was replaced with DPPIV inhibitor- teneligliptin 20mg per day. In order to study the efficacy of combination therapy versus metformin monotherapy

Inclusion criteria: Patients on metformin monotherapy with Glycated haemoglobin (HbA1c) of 7.0–9.0%, men and women age group 20 years to 60 years.

Exclusion criteria: Type 1 diabetes mellitus, Pre-existing renal, hepatic or cardiac disease, and Patients on various OHA like Alpha Glucosidase Inhibitors, Sulphonylurea, SGLT 2 Inhibitors, and Insulin.

STATISTICAL ANALYSIS

Statistical analysis was done by using SPSS version 17.0. Descriptive statistics were used for categorical variables. The efficacy of combination therapy was assessed by Paired t test. In order to study the efficacy of combination therapy versus metformin monotherapy Paired t test was performed after completion of 12weeks of therapy.

RESULT

The primary endpoint of the study was to monitor the changes in HbA1c levels, FBS, PPBS, BMI, HOMA score and Insulin levels from baseline to week 12. It was observed that the mean FBS after addition of teneligliptin was (109.36 mg/dl ± 10.92) when compared to (118.07mg/dl ±12.76) in the Metformin monotherapy (t value: 4.98; p value <0.001) there was significant decrease in Fasting blood glucose level after addition of teneligliptin. The mean PPBS after addition of teneligliptin

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DISCUSSION

European Association of the Study of Diabetes and American Diabetes Association guidelines have recommend Metformin as a first line drug to be used in Type 2 Diabetes Mellitus patient. If there is Glycemic variability with metformin, add on drugs drug like DPP-4, or Other OHA's or Insulin to be considered depending on the clinical scenario.

Teneligliptin have a structure which is unique and binds to S1, S2, and S2 extensive subsite of DPP-4 enzyme. It is recommended Once-a-day administration.[1] DPP-4 enzyme inhibition occurs maximum within 2 hours and >50% inhibition has been noted at 24 hours; no drug–drug interaction. Excretion of Teneligliptin metabolites is by dual mode i.e. hepatic (~35%) and renal (~65%) routes. Drug dosage adjustment is not necessary even in patients with renal impairment due to its long half-life and it helps in stabilizing the glycemic fluctuations throughout the day.[1-4] Moreover multiple trails on DPP-4 inhibitors have shown better glycemic control in type 2 diabetes mellitus patients and these patients had minimal risk of hypoglycemia and weight gain.

Scott R et.al (2008), Bosi E (2007), has done the study for 16 weeks. Study subjected received combination therapy of teneligliptin and metformin therapy. The result of this study was similar to or slightly higher than the results of previous studies performed with other DPP-4 inhibitors.[5-6]

A meta-analysis by Kim.et al.2013 showed a significant lowering of Glycemic level lowering in Asian than in non-Asian people who were on Dpp-4.[7]

Kadowaki T et.al 2013 studied the effect of combination of teneligliptin with pioglitazone in Japanese patient. Results of this study showed significant reductions in HbA_{1c} when compared with the placebo group.[8]

Fukuda-Tsuru et al (2012), Pederson RA et.al (1998), reported that oral fat-loading test was given to Zucker fatty rats followed with administration of teneligliptin. It was shown that there was reduction in the levels of postprandial triglycerides levels, free fatty acids and there was also significant increase in the levels of GLP-1 and insulin levels.[9-11]

Eto et al (2012) study has shown that there was no significant different between the teneligliptin and placebo groups during the study conducted.[12]

CONCLUSION

Teneligliptin was selected for the study because it has longer half-life, dual mode of elimination, superadded it is cost effective and cheaper in India than compared to other DPPIV inhibitors, due to its cheaper cost the compliance was better with respect to usage of teneligliptin. Ultimately Teneligliptin add-on to Metformin during the early course of treatment would be a multimodal approach in treatment of Diabetic patients further it could help in delaying the exhaustion of pancreatic islet function. The present study was only for 28 patients, a larger cohort of patients and a further follow up is required to assess the side effects, HOMA score and BMI in the patients as there was a decrease which is not significant.

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