ISSN: 0975-5160

Available online on www.ijtpr.com

International Journal of Toxicological and Pharmacological Research 2021; 11(2); 42-46

Original Research Article

A Comparative Study of Effectiveness and Tolerability of Metformin and Combination of Metformin and Teneligliptin in the Treatment of Type II Diabetes Mellitus Patients

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Received: 01-03-2021 / Revised: 05-04-2021 / Accepted: 22-04-2021
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Conflict of interest: Nil

Abstract

Introduction: Diabetes Mellitus is a chronic Metabolic disorder affecting large population all over the world.Metformin is a first line drug therapy for the Management of Type II Diabetes Mellitus especially in obese patients. Now a days a new drug Dipeptidyl Peptidase 4 Inhibitors (DPP-4), Teneligliptin is more effective in combination with Metformin than Metformin monotherapy in patients with inadequately controlled Plasma Glucose levels.

Objective: To compare the effectiveness and tolerability of Metformin and combination of Metformin and Teneligliptin in the treatment of Type II Diabetes Mellitus Patients.

Materials and Methods: It was an observational study on 35 patients each in metformin group and Metformin with Teneligliptin group. After enrollment in study follow up was done at 8 weeks of therapy.

Results: The change in fasting blood glucose (FBG) in Group A was from 150.18 + 3.75 to 140.3 + 3.41 mg/dl and Group B was from 154.68 + 3.6 to 122.36 + 2.57 mg/dl. Changes in both the groups were statistically significant with P-value < 0.00001. The change in post prandial blood sugar in Group A was from 188.68 + 8.4 to 169.66 + 3.62 mg/dl and Group B was from 187.5 + 10.29 to 152.08 + 5.19 mg/dl. Changes in both the groups were statistically significant with P-value < 0.00001

Conclusion: The addition of Teneligliptin (20 mg) to Metformin treatment was effective in controlling blood glucose (Fasting and Post Prandial) and was well tolerated in patients with Type II DM. It provided clinically significant glycemic control.

Keywords: Metformin, Teneligliptin, Type II Diabetes Mellitus.

Introduction

Diabetes Mellitus is a group of metabolic disorder, characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The term "Diabetes was first used by Greek Appolonius of Memphis. It was Briton John in late 1700s who added the term mellitus meaning "from honey". The Treatment for Diabetes Mellitus was discovered in 1921 by two Canadians Frederick Banting & Charles. 382 million people had diabetes in 2013. By 2035, this number will rise to 592 million. In 'India 65.1 million people had diabetes in 2013 [1]. By 2035 this number will increase by 70.6%. Type II DM accounts for more than 90% of all Diabetes Mellitus [2].

In treatment of Type II Diabetes Mellitus, Metformin is the first choice for oral medication. Metformin has inhibitory action on gluconeogenesis in liver. It decreases hepatic glucose production, decrease intestinal absorption of glucose and improves insulin sensitivity by increasing peripheral glucose uptake and utilization. Incretins are a group of metabolic hormones that stimulate a decrease in Plasma Glucose levels[3]. There are two main Incretin hormones in humans :Gastric Inhibitory Polypeptide (GIP) and Glucagon-like Peptide-1(GLP-1) are secreted from the Intestine on ingestion of glucose or nutrients to stimulate Insulin secretion from Pancreatic beta cells .Incretins released after eating, stimulates synthesis of insulin and glucagon from pancreatic beta and alpha cells respectively.They are involved in the physiologic regulation of glucose homeostasis. DPP-4 inhibitor enhance levels of the active incretin hormones that are released in the circulation after digestion of meal.[4] GLP and GIP increase insulin release and thereby decrease the post meal rise in glucose concentration and reduce fasting glucose concentration. Teneligliptin is a DPP-4 inhibitor. [5] It competitively inhibits the enzyme DPP-4 thereby increasing and prolonging the action of these hormones. DPP-4 inhibitor improves glycaemic control by reducing both fasting and postprandial levels without weight gain in the patients of Type II Diabetes Mellitus [6] By blocking inactivation of incretin, Teneligliptin increase active incretins levels which helps in the treatment of Type II Diabetes Mellitus. The addition of Teneligliptin with Metformin may improve glycacmic control.[7] The present study was planned with the aim to analyze efficacy and safety of Metformin alone and combination of Metformin and Teneligliptin in Type II diabetic patients[8].

Aim and Objective

Diabetes Mellitus is a chronic Metabolic disorder characterized by Insulin insensitivity as a result of Insulin resistance, declining Insulin production and eventually Pancreatic beta-cell failure.Earlier many studies have been done with different drugs for their comparative safety and efficacy in the management of Diabetes Mellitus. Through our study,We aim to compare the Effectiveness and Tolerability of Metformin and combination of Metformin and Teneligliptin in the treatment of Type II Diabetes Mellitus Patients.

Materials and Methods

This prospective, randomized, open, comparative observational study was conducted in Department of Pharmacology, PMCH, Patna. This was 8 weeks study between 22 December 2020 to 16 February 2021 in 70 Type II Diabetes Mellitus patients (male 48 and female 22).With age ranging between 30 to 70 years visiting outdoor of Medicine Department, Patna Medical College and Hospital (PMCH), Patna.

The following categories of patients were enrolled in the study

Inclusion Criteria.

a) Type II Diabetes Mellitus patients without any comorbidity.
b) Patients not on drugs which cause either hypoglycemia or hyperglycemia.
c) Written and informed consent form was taken from each patients before the start of study.

The following categories of patients were excluded from the study.

Exclusion Criteria

(1) Patients with type I Diabetes Mellitus.
(2) Patients not willing to give consent.
(3) Patients with any co-morbid condition.

Patients were randomly distributed into two groups Group A and Group B each of 35 patients.

Group A: Comprised of patients receiving Metformin (500 mg orally twice daily)

Group B: Comprised of patients receiving combination of Metformin (500 mg orally twice daily) and Teneligliptin (20 mg orally once in a day). Baseline fasting (FPG) and Post-Prandial Plasma Glucose (PPPG) levels were measured. Follow up was done at 8 weeks of therapy. At 8 weeks FPG level and PPPG level were measured and safety of drugs were noted.

Results

Table 1: Age and Gender distribution of patients in the 2 groups.

Characteristics	Group A	Group B
Age (Years, mean)	53.9	59.3
Gender (numbers		
Male	23	25
Female	12	10

Table 2: Comparison of changes in Fasting Plasma Glucose level in mg/dl at 0 and 8 weeks in Group A and Group B.

Group	Baseline (Mean±SD) 0 week	8 weeks (Mean±SD)	Reduction in glucose level (Mean±SD)	P. Value
Group A Metformin 1000 mg (n=35)	150.18±3.75	140.3±3.41	9.88 ±3.41	<.00001
Group B Metformin 1000 mg+Teneligliptin 20mg (n=35)	154.68±3.6	122.36±2.57	32.32 ± 1.03	<.00001

Table 3: Comparison of change in Post Prandial Plasma glucose level in mg/dl at 0 and 8 weeks in Group A and Group B.

Group	Baseline (Mean±SD) 0 week	8 weeks (Mean±SD)	Reduction in glucose level (Mean±SD)	P. Value
Group A Metformin 1000 mg (n=35)	188.68±8.4	169.66±3.62	19.02 ±4.78	<.00001
Group B Metformin 1000 mg+Teneligliptin 20mg (n=35)	187.5±10.29	152.08±5.19	35.42 ± 5.10	<.00001

Table 4: Comparison of Adverse Drug effects between two group.

Adverse effect	Group A (n=35)	Group B (n=35)
Vomiting	9 (26%)	3 (8%)
Abdominal Pain	3 (8%)	1 (2%)
Diarrhea	4 (12%)	1(2%)

The change in fasting Plasma Glucose in Group A was from 150.18 + 3.75 to 140.3 + 3.41 mg/dl and Group B was from 154.68 + 3.6 to 122.36 + 2.57 mg/dl. Changes in both the groups were highly statistically significant with p-value < 0.00001.

The change in Post-Prandial Plasma Glucose in Group A was from 188.68 + 8.4 to 169.66 + 3.62 mg/dl and Group B was from 187.5 + 10.29 to 152.08 + 5.19 mg/dl. Changes in both the groups were statistically highly significant with p-value < 0.00001.

The difference between Group A and Group B for reduction in Plasma Glucose (both fasting and post-prandial) was also statistically significant.

The safety analysis was performed on all patients who completed the study. A total 50% of the patients reported adverse effects like vomiting (26%) abdominal pain (8%), diarrhea (12%) metallic taste (6%) in the group A whereas a Total 14% patients reported adverse effects like vomiting (8)% abdominal pain (2%) diarrhea (2%), metallic taste (2%) in the group B(Table No. 4)

Disscussion

American Diabetic Association guidelines have recommended Metformin as first line drug to be used in Type II Diabetes Mellitus patients [9]. If there is glycemic variability with Metformin, add on other antidiabetic drug depending on the clinical scenario should be done.

An approach to delay the glycaemic deterioration in patients, starting the combinational therapy at initial early stage was proposed, with outcome of preservation of functioning of beta cells.

The present study showed that the combination of Metformin and Teneligliptin is more effective than Metformin alone in Type II Diabetes Mellitus patients.

Teneligliptin was having good overall safety profile including low risk of hypoglycemia and was well tolerated in patients of Type II Diabetes Mellitus [10].

The reduction in Fasting Plasma Glucose at 8 weeks was Significantly higher in Group B than Group A. The reduction in also Post-Prandial Plasma glucose level at 8 weeks was higher in Group B than Group A.

Pubmed, Medline Embase and Cochrane library concluded that Teneligliptin produced absolute reduction in glycated haemoglobin level [11]. There was greater decrease of Fasting Plasma Glucose (FPG) level. WMD-18.32%, 95% cl (-21.05 to -15.60) P < 0.00001 [12]. Teneligliptin also significantly decreased the Post-Prandial Plasma glucose (WMD-46.94%, 95% cl (-51.58 to -42.30), p < 0.00001. The efficacy of addition of daily one dose of Teneligliptin 20 mg with ongoing Metformin therapy in Type II Diabetes Mellitus patients who had insignificant glycacmic control with monotherapy using Metformin was significant. [13] When patients were treated with single antidiabetic drug, they were able to achieve and maintain glycacmic control to a lesser extent.. Therefore many patients required combination of antidiabetic drugs. In the present study the improvement in glycemic control was the key finding after addition of Teneligliptin to patients with Metformin monotherapy and inadequate glycaemic control [14].

The incidence of Adverse effects was less in Metformin and Teneligliptin combination group. The adverse effects in Group A were noted to be higher than Group B patients. Cochrane library also showed that addition of single dose daily of Teneligliptin 20 mg was well tolerated along with Metformin therapy in patients treated with metformin alone and having inadequate glycaemic control [15].

Conclusion

The addition of Teneligliptin (20 mg) to Metformin treatment was more effective in controlling Plasma Glucose (Fasting and Postprandial) and was well tolerated in patients with Type II Diabetes Mellitus compared to Metformin monotherapy in Type II Diabetes Mellitus. It provided clinically significant glyceamic control.

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