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SAFETY AND EFFICACY COMPARISION OF THE TENELIGLIPTIN VERSES METFORMIN IN TYPE-II DIABETES MELLITUS

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ABSTRACT

In Our Study Safety and Efficacy Comparison of The Teneligliptin Verses Metformin Type-II Diabetes Mellitus, States that we are taking a total 120 patients were included in our study by the section criteria, both males and females, males are higher majority Population diagnosed by the Type-II DM. A prospective –observational study was conducted at Siddhartha Hospital, Kakinada for a period of six months study was carried out for a period of 6 months January 2018 to July 2018. In the process of case collection we are collecting to the blood samples for the all patients, In addition to effective glycemic control results that suggested teneligliptin is well tolerated in type –II diabetes mellitus along with triglycerides monitoring And of all the above glycemic and non glycemic parameters reports there are no major adverse effects when using of teneligliptin which gives a suitable approach towards the management of type -II DM safely and effectively. The data was analysed by applying the Microsoft Excel 2013 (Microsoft Corporation) And Student Graph Pad Prism. Teneligliptin may show benefits with hypoglycaemia and had chances of increase in triglycerides, monitoring of triglycerides along with teneligliptin therapy is more safe and effective. Using of Teneligliptin verses Metformin, Teneligliptin is reducing the FBS and PPBS at the same time it shows less side effects, better efficacy when compared to the Metformin.

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INTRODUCTION

Diabetes is a common non communicable disease and has reached to epidemic stage in many countries. Globally, 415 million 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, the US, and the Russian Federation reported highest deaths due to diabetes (IDF, 2015). Diabetes affects many organs, and complications due to high blood glucose are an important cause of disability, reduced quality of life, and premature death (IDF, 2015). 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 (IDF, 2015). Diabetes is a chronic disease that requires lifelong medical care and attention for multiple risk reduction and treatment approach beyond glycemic control (American Diabetes Association Strategies for improving care, 2016). Treatment objective must be the prevention of short-term and long-term complications associated with diabetes (American Diabetes Association Foundations of care and comprehensive medical evaluation, 2016). Additionally, patient education and support are important aspects (American Diabetes Association Foundations of care and comprehensive medical evaluation, 2016). This will improve patient outcomes (American Diabetes Association Strategies for improving care, 2016). A multidisciplinary approach is required for the management of diabetes (American Diabetes Association Strategies for improving care, 2016; American Diabetes Association Foundations of care and comprehensive medical evaluation, 2016). 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 (Majumdar *et al*., 2013). 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

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(Tenepure; Teneza) (Kishimoto, 2013; 7. https://aiocdawacs.com [homepage on the Internet] Teneligliptin Data. Feb MAT 2016. Data Source). This review highlights the place of therapy of teneligliptin in the management of T2DM.

Diabetes in India

India is the diabetes capital of the world with 41 million Indians having diabetes; every fifth diabetic in the world is an Indian. It also leads in prevalence of metabolic syndrome as well as obesity[5].Diabetes is fast gaining the status of a potential epidemic in India with more than 62 million diabetic individuals currently diagnosed with the disease.1,2 In 2000, India (31.7 million) topped the world with the highest number of people with diabetes mellitus followed by China (20.8 million) with the United States (17.7 million) in second and third place respectively. According to Wild *et al*.3 the prevalence of diabetes is predicted to double globally from 171 million in 2000 to 366 million in 2030 with a maximum increase in India. It is also predicted that by 2030 diabetes mellitus may afflict up to 79.4 million individuals in India, while China (42.3 million) and the United States (30.3 million) will also see significant increases in those affected by the disease.3,4 India currently faces an uncertain future in relation to the potential burden that diabetes may impose upon the country. The aetiology of diabetes in India is multifactorial and includes genetic factors coupled with environmental influences such as obesity associated with rising living standards, steady urban standards, steady urban migration, and lifestyle changes. Obesity is one of the major risk factors for diabetes, yet there has been little research focusing on this risk factor across India. 6 Furthermore, Indians are genetically predisposed to the development of coronary artery disease due to dyslipidaemia and low levels of high density lipoproteins;14 these determinants make Indians more prone to development of the complications of diabetes at an early age (20-40 years) compared with Caucasians (>50 years) and indicate that diabetes must be carefully screened and monitored regardless of patient age within India (Scott, 2015).

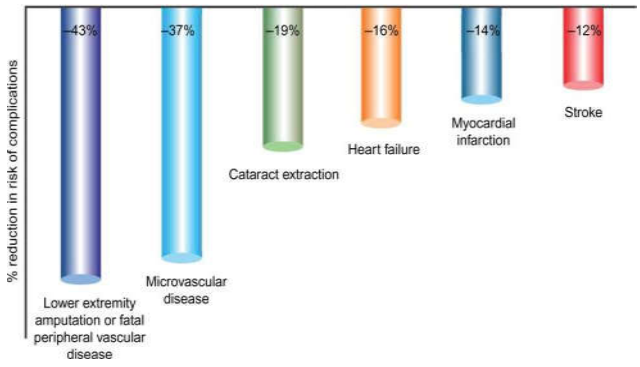

Figure 1. Reduction in risk of long-term complications associated with 1% reduction in HbA1c.

Management of Type-II Diabetes Mellitus

Type-II DM is a chronic progressive disease and involves multiple systems. Diet, exercise, education, pharmacotherapy, and blood glucose monitoring are important pillars for the management of T2DM (Stratton, 2000). Published evidence suggests that even 1% reduction in HbA1c reported significant reduction in the risk of long-term complications associated with T2DM, Various patient and disease factors affect HbA1c targets. Therefore, individualized glycemic goals are always preferred, and tailor-made antidiabetic therapy is recommended in routine clinical practice (Stratton, 2000; Dror Dicker, 2011). Factors determining individual glycemic goal are presented in Table 1.9,11. There are various approaches for initiation and titration of antidiabetic therapy. The American Diabetes Association (ADA) position statement of Standards of Medical Care in Diabetes – 2016 has recommended evidence-based antidiabetic therapy

Teneligliptin

Teneligliptin is a novel oral DPP-4 inhibitor developed by Mitsubishi Tanabe Pharma Co. and approved in Japan in September 2012 for the management of T2DM (Kishimoto, 2013). Currently, teneligliptin is marketed in Japan (Teneria), Argentina (Teneglucon), and India (Tenepure; Teneza) (Table 5) (Kishimoto, 2013; Scott, 2015; https://aiocdawacs.com [homepage on the Internet). Presently, teneligliptin is registered in South Korea and is in the preregistration phase in Indonesia. Additionally, teneligliptin is in phase II clinical trials in Europe, and phase I clinical trials in the US (Xu *et al*., 1999). Teneligliptin, which is classified as peptidomimetic, has a unique structure having five consecutive rings (Edwards *et al*., 1999). Due to this unique structure, teneligliptin acts on S2 extensive sub site of DPP-4; this interaction enhances its potency and selectivity.

Phase of development	Indication	Country
Marketed	T2DM	Japan
Marketed	T2DM	Argentina
Marketed	T2DM	India

Note: Teneligliptin is marketed in Japan,5 Argentina,6 and India.7

Abbreviation: T2DM, type 2 diabetes mellitus.

Figure no 02. Approval status of teneligliptin

Metformin

Metformin hydrochlorides an oral anti hyperglycaemic drug used in the management of type-II diabetes. It improves glucose tolerance in patients with type 2diabetes, lowering both basal and postprandial plasma glucose. Its pharmacologic mechanisms of action are different from other classes of oral anti hyperglycaemic agents. Metformin decreases hepatic glucose production, decreases intestinal absorption of glucose, and improves insulin sensitivity by increasing peripheral glucose uptake and utilization[11].

Aims and Objectives

Compare the safety and efficacy of the Teneligliptin is a DPP inhibitor verses Metformin in Type -II Diabetes Mellitus.

The study was carried out by the following considering objectives

- Collection of Social and Demographic data of the patients such as age, gender, occupation, education, etc...
- Obtain the patients information whether receiving insulin as their ultimate therapy after receiving oral therapy.

- Assess the dose of the hypoglycaemic agent.
- Assess the state of their life style diet modifications after starting the therapy.
- Assess and compare the efficacy of teneligliptin verses Metformin
- Assess the glycemic lab reports of the patient before and after the treatment whether two open labelled groups.

MATERIALS AND METHODS

Study Site: The study was conducted at Siddhartha Hospital, Kakinada.

Study Duration: The study was carried out for a period of 6 months from January 2018 to July 2018.

Study Design: The study was a prospective –observational study.

Study Criteria: The patients visited to the hospital were enrolled into the study by considering the following inclusion and exclusion criteria after taking consent from the patients/attenders of the patients in a suitably designed informed consent form.

Inclusion Criteria

- Patients of either gender and above 12 years
- Patients diagnosed with type-II diabetes
- Patients prescribed with oral hypo glycemic agents as monotherapy.
- Patients who are willing to participate in the study

Exclusion Criteria

- Patients who are not willing to participate in the study
- Immunosupp
- ressed patients.
- Patients who are suffering with other than the Type-II Diabetes

Analysis of Data

The data was analysed by applying the Microsoft Excel 2013 (Microsoft Corporation) And Student Graph Pad Prism.

Source of the Study

The data for the study was collected from

- Patients Case Sheets,
- Laboratory Investigations of the patients and other relevant resources.

Study Procedure

A prospective study was carried out at Siddhartha Hospital, Kakinada. The patients were enrolled into the study by considering the study criteria after taking their consent to participate into the study. From the enrolled patients the data was collected from the case sheets and other relevant resources in a suitably designed data collection form.

The following data will be collected

Socio Demographic Data

- Name
- Age
- Gender
- Occupation
- Education
- Height
- Weight
- Family history
- Co-morbid conditions

Disease State

- Severity of diabetes

Treatment Data

- Dose of the Oral hypoglycaemic agents prescribed
- Class of oral hypoglycaemic agent prescribed
- Therapeutic out comes

The collected data was analysed by using standard text books, journals, and internet sources and by other resources.
Finally the collected data was compared with Microsoft Excel 2013(Microsoft Corporation)

RESULTS

Gender Distribution of the Study Population: We are taking total 120 patients with type 2 diabetes were enrolled in the study out of which 63(45%) were male patients and 57 (55%) were female patients.

Table 2. Gender details of the patients enrolled in the study

S No	Gender	Numberof Patients (n=114)	Percentage
1	MALE	63	45%
2	FEMALE	57	55%

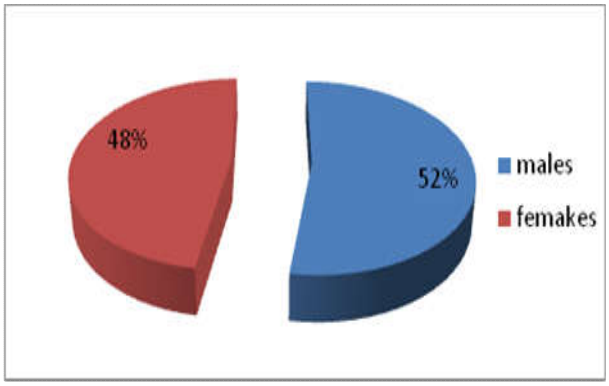

Figure 01. Based On the Study Distribution of Study Population

Based On the Age Distribution of Study Population: We are taking Out of 120 patients 8(7%) patients were in the age range between 18-25 years, 10(8%) patients were in the age range between 26-40, 69(57%) patients were in the age range between 41-55, 13(11%) patients were in the age range between 61-80, 20(17%) patients were in the age range

between 81-85. Among these 41-60 age range patients were high in number, 18-25 age range patients were low.

Table 2. Age Distribution of the Study Population

S No	Age Range	Numberofpatients (n=120)	percentage (%)
1	18-25	8	7%
2	26-40	10	8%
3	41-60	69	57%
4	61-80	13	11%
5	81-85	20	17%

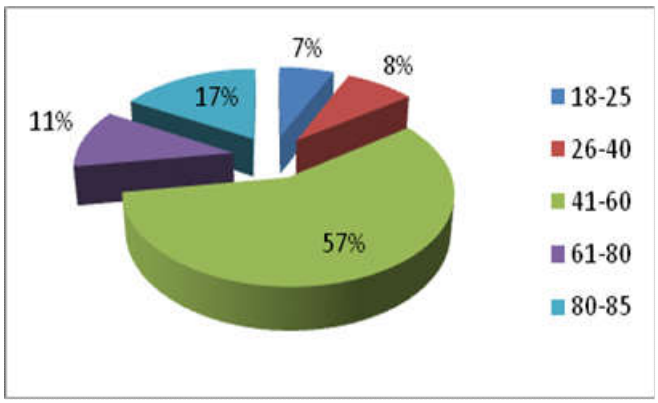

Figure No 02. Based On the Age Distribution of Study Population

Based On the Body Mass Index of Study Population: We are taking Out of 120 patients 8(7%) patients were under weight, 52(43%) patients were normal weight, 42(35%) patients were overweight, and 18 (15%) patients were obese.

Table 3. Body Mass Index of the Study Population

SNO	BMI	Weight Status	Number of Patients	Percentage (%)
1	Below 18.5	Under Weight	8	7%
2	18.5-24.9	Normal and Healthy Weight	52	43%
3	25.0-29.9	Overweight	42	35%
4	Above 30	Obese	18	15%

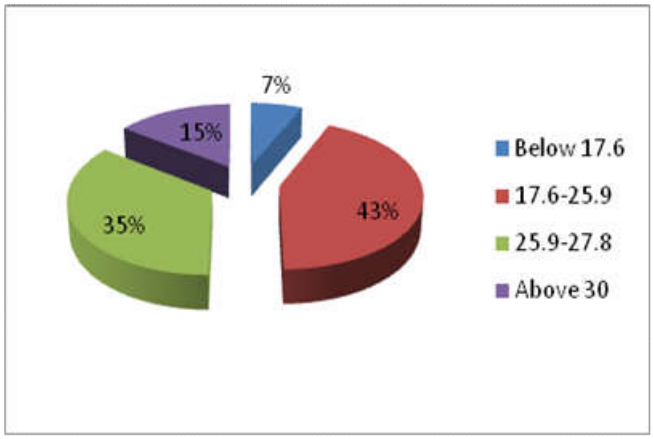

Figure 3. Based On the Distribution of Body Mass Index Study Population

Based On the Duration of the Disease: We are taking out of 120 patients 12 (10%) patients were of below 1 year of duration, 93(82%) patients were of 1-10years of duration, 8(7%) patients were of 11-20 years of duration and 1 (1%) patients were of 21-30 years of duration.

Table 5. Duration of disease of the patients

S No	Disease Duration	Number of Patients(N=120)	Percentage (%)
1	BELOW 1	16	13%
2	1-10	95	79%
3	11-20	7	6%
4	21-30	2	2%

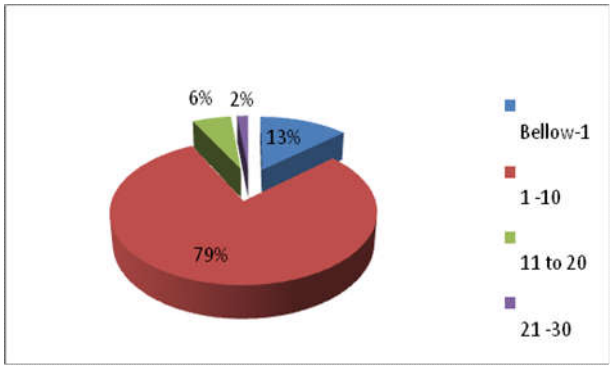

Figure 4. Bases on the Duration of Disease of Study Population

Teneligliptin Verses Metformin: We are taking Out of 200 patients 75 (62%) patients were using on teneligliptin and 45(38%) Patients were using Metformin in our Research.

Table 5. Teneligliptin Verses Metformin Using On the Patients

S No	Drugs	Number of patients (n=114)	Percentage (%)
1	Teneligliptin	75	62%
2	Metormin	45	38%

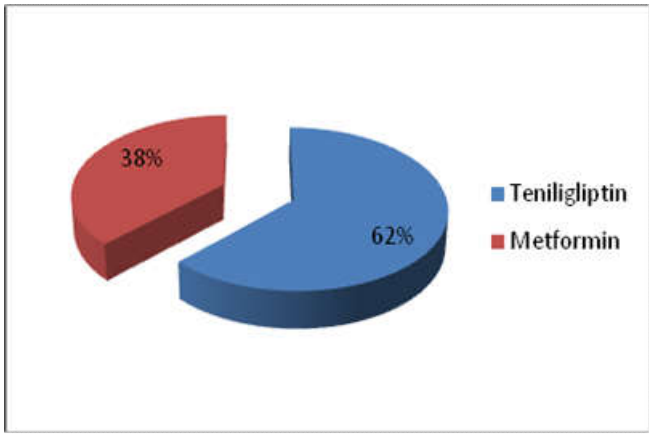

Figure 5. Teneligliptin verses Metformin therapy in the study Population

Adverse Drug Reactions: We are taking out of 120 patients 79(93%) patients were reported with mild range of side effects, 6(7%) patients were reported with moderate range of side effects and none of the patients shown severe range of side effects. We are taking out of 120 patients 45(38%) were administered it resulted in a decrease in FBS, PPBS and HBA1C which was maintained for a 24 week study the changes in FBS (mean±SD) from base line to be (42.29167±30.05427), PPBS (61.50000±40.603), HBA1C (.43333±.19035) and an increase in triglyceride levels (mean± SD) from base line was(-7.37500±2.222). HBA1C, FBS, PPBS were statistically significantly lower at 24 week than at base line (p value<0.0001).

Table 6. Adverse drug reactions of the patients

S No	Category	No of Patients	Percentage %
1	MILD	79	93%
2	MODERATE	6	7%
3	SEVERE	0	0%

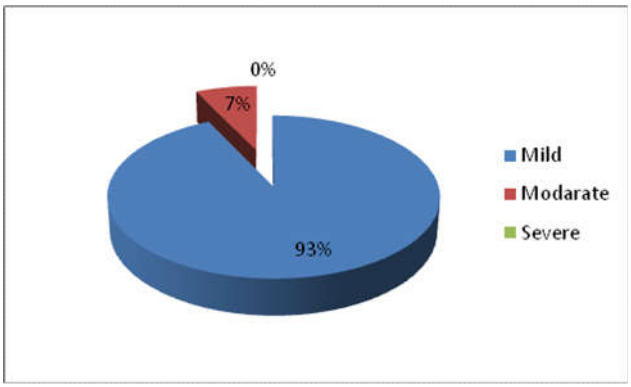

Figure 6. Adverse Drug Reactions in the Study Population

Glycemic and non glycemic parameters before and after the treatment with teneligliptin: We are taking out of 120 patients 75(62%) were administered with teneligliptin as a resulted in a increase in FBS, PPBS, HBA1C, LDL, HDL and triglycerides which was maintained for a 24 week study the changes in FBS (mean±SD) from base line were(-12. 41±5. 53), PPBS (70-33. 66±10. 95), HBA1C (-.200±.112), LDL(-1. 41±2.46), HDL(2.33±1.87) and triglyceride levels (mean± SD) from base line to be 24 were(-11. 91±4. 96). HBA1C, FBS, PPBS were statistically significantly lower at 24 week than at base line (p value<0.0001).

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DISCUSSION

During the study period, a total of 130 patients were enrolled by considering study criteria, out of them 114 (88%) patients were completely followed and 16 (12%) patients were withdrawn from the study as the patients were not willing to continue the therapy. We are taking out of 120 patients, 63 (52%) were male patients and 57 (48%) were female patients. This indicates that there were, more number of male patients having type-II diabetes mellitus when compared to female patients. Out of 120 patients 8 (7%) patients were in the age range between 18-25 years, 10(8%) patients were in the age range between 26-40, 69(57%) patients were in the age range between 41-60, 13(11%) patients were in the age range between 56-70, 20(17%) patients were in the age range between 71-85. The age distribution of the patients reveals that, majority of type 2 diabetes were in the age of 41-60 age range patients were high in number, 18-25 age range patients were low.

Out of 120 patients 8(7%) patients were under weight, 52 (43%) patients were normal weight, 42 (35%) patients were overweight, and 18 (15%) patients were obese. The above study shows that 43% patients were with highest BMI and 4% of patients were with low BMI. Out of 120 patients 16 (13%) patients were of below 1 year of duration, 95 (79%) patients were of 1-10years of duration, 7(6%) patients were of 11-20 years of duration and 2 (2%) patients were of 21-30 years of duration.

Table 7. Statistical analysis of patients with Metformin

S no	Characteristics	Before	After	Mean±stan-dard
1	Systolic	133.7500±14.9818	130.0000±11.4208	3.75000±7.109
2	Diastolic	85.4167±7.79028	87.0833±10.41703	-1.66±10.072
3	FBS	181.2083+/54.017	138.9167±37.8163	42.29±30.05
4	PPBS	269.0417±66.84	207.5417±52.1911	61.50±40.6
5	HBA1C	6.8833±.634	6.45±.551	.433±.190
6	LDL	148.8333±23.89	149.5833±23.51	-.750±1.939
7	HDL	32.25±6.76	32.83±6.98	-.583±2.50
8	TRIGLYCERICES	162.8750±21.092	170.25±19.79	-7.375±2.22

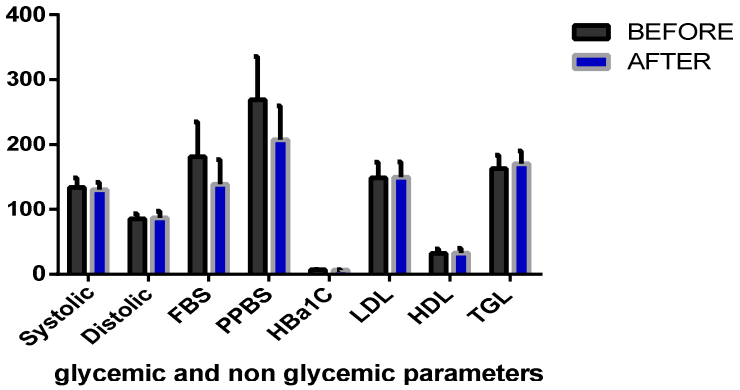

Figure . Statistical Analysis of Patients with Metformin in Study Population

Table 9. Statistical analysis of patients with Teneligliptin monotherapy

S no	Characteristics	Before	After	Mean±stand-ard
1	Systolic	132.5±19.128	122.5000±10.5529	10.0±12.06
2	Diastolic	89.1667±9.0033	78.3333±7.1774	10.83±9.96
3	FBS	142.83±12.171	155.2500±11.2664	-12.41±5.53
4	PPBS	222.9167±16.703	256.5833±13.607	-33.66±10.95
5	HBA1C	6. 6583±.46213	6.8583±.47570	-.200±.112
6	LDL	138.8333±18.4776	140. 25±17.90442	-1.41±2. 46
7	HDL	34.4167±6.90794	32.0833±7.64506	2.33±1. 87
8	TRIGLYCERICES	155.25±15.196	167.16±14.134	-11. 91±4.96

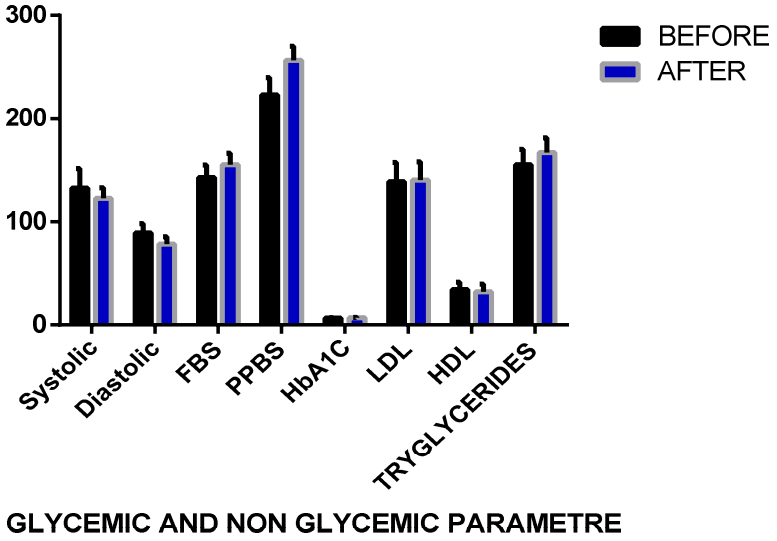

Figure 8. Statistical Analysis of Patients with Teneligliptin Monotherapy in Study Population

The above study reveals that the highest disease duration was of 1-10 years and the lowest disease duration was 21-30 years. Out of 120 patients 75 (62%) patients were on teneligliptin and 45(38%) patients were on Metformin. The study indicates that majority of patients (62%) were under the prescription of teneligliptin and the lowest (38%) were on Metformin therapy. Out of 120 patients 79 (93%) patients were reported with mild range of side effects,6 (7%) patients were reported with moderate range of side effects and none of the patients shown severe range of side effects.

Out of 114 patients 26 (23%) were administered with teneligliptin as a combination therapy to sulfonyl urease resulted in a decrease in FBS, PPBS and HbA1C which was maintained for a 24 week study the changes in FBS (mean±SD) from base line were (54.30±45.60), PPBS (71.692±45.35), HbA1C (0.488±0.233) and an increase in triglyceride levels (mean± SD) from base line was (-7.5±1.555). HbA1C, FBS, PPBS were statistically significantly lower at 24 week than at base line (p-value <0.0001). We are taking out of 120 patients 45(38%) were administered it resulted in a decrease in FBS, PPBS and HBA1C which was maintained for a 24 week study the changes in FBS (mean±SD) from base line to be (42.29167±30.05427), PPBS (61.50000±40.603), HBA1C (.43333±.19035) and an increase in triglyceride levels (mean± SD) from base line was(-7.37500±2.222). HBA1C, FBS, PPBS were statistically significantly lower at 24 week than at base line (p value<0.0001). We are taking out of 120 patients 75(62%) were administered with teneligliptin as a resulted in a increase in FBS, PPBS, HBA1C, LDL, HDL and triglycerides which was maintained for a 24 week study the changes in FBS (mean±SD) from base line were (-12. 41±5. 53), PPBS (70-33. 66±10. 95), HBA1C (-.200±.112), LDL (-1. 41±2.46), HDL (2.33±1.87) and triglyceride levels (mean± SD) from base line to be 24 were (-11. 91±4. 96). HBA1C, FBS, PPBS were statistically significantly lower at 24 week than at base line (p value<0.0001)

Safety and Tolerability of the Current Research

In our study is to tell that the teneligliptin reported with mild adverse events which can be treated easily by taking healthy drinks as most of the patients were reported with general weakness, constipation which can be treated easily by suggesting to have high fiber food in their diet which can also lowers the cardio vascular events by maintaining the lipid profile And Very low number of patients were reported with moderate to severe adverse effects which gives a clear information on teneligliptin usage as appropriate.

Conclusion

In our study conclude that the In addition to effective glycemic control results that suggested teneligliptin is well tolerated in type –II diabetes mellitus along with triglycerides monitoring. And teneligliptin of all the above glycemic and non glycemic parameters reports no major adverse effects which gives a suitable approach towards the management of type -II DM safely and effectively. Teneligliptin may show benefits with hypoglycaemia and had chances of increase in triglycerides, monitoring of triglycerides along with teneligliptin therapy is more safe and effective. Finally the authors conclude that the using of verses Metformin,

Teneligliptin is reducing the FBS and PPBS at the same time it shows less side effects, better efficacy when compared to the Metformin.

Acknowledgement

The authors specially thank Dr. M. Aditya Krishna, Managing Director, Siddhartha Hospital, for providing an opportunity to carry out the research work.

Conflict Of Interest

The authors do not have any conflicts of interest.

List of Abbreviations

DM-II -Diabetes Mellitus-II

DPP-4 Inhibitors - Inhibitors of Dipeptidyl Peptidase 4.

HbA1c- Haemoglobin A1c

ADA- American Diabetes Association

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