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SAFETY AND EFFICACY OF TENELIGLIPTIN OVER OTHER HYPOGLYCEMIC AGENTS IN TYPE-2 DIABETES

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Abstract

*To compare the safety and efficacy of the Teneligliptin a DPP inhibitor over other hypoglycaemic agents in Type II Diabetes Mellitus. .It is a prospective –observational study in this study was conducted at, Pradeep Diabetic Centre, Rajamahendravaram and the study was carried out for a period of 6 months from Feb 2016 to July 2016, and we are taking total of 114 patients with type 2 diabetes, in our study concludes the combination of Teneligliptin with other oral hypoglycaemic agents have been shown to improve glycaemic control efficiently when compare with the monotherapy shown inadequate glycaemic control. Patients of either gender and above 12 years, Patients diagnosed with type-II diabetes, Patients prescribed with oral hypo glycaemic agents as monotherapy, combination of oral hypoglycaemic agents along with insulin. The data and laboratory reports were collected from the case sheets of the patients and relevant sources. In this study was carried out by considering the collecting of socio demographic data of the patients such as age, gender, occupation, education and to obtain the information of patients receiving insulin as their ultimate therapy after receiving oral therapy and to assess the number, type and dose of oral hypoglycaemic drugs as prescribed and Dose of the insulin and other oral hypoglycaemic drugs that are shown in desirable therapeutic outcome or not. As well as we assess the state of their life style diet modifications after starting the therapy and compare the efficacy of Teneligliptin with combination of oral hypoglycaemic and monotherapy finally we assess the glycaemic laboratory reports of the patient before and after the treatment. In the data was analysed by applying statistics by **SPSS** (Statistical Package for the Social Sciences).*

Key Words: *Teneligliptin, Hypoglycaemia, Case Study, 114 Patients, 6 Months.*

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1.0 INTRODUCTION:

Diabetes mellitus is probably one of the oldest diseases known to man. It was first reported in Egypt about 3000 years ago. In 1936, the distinction between type- and type2 Diabetes mellitus was clearly made. Type-II Diabetes mellitus was first described as a component of a metabolic syndrome in 1988.[1] Sushruta (6th century BCE) was the one who identified diabetes and classified it as Madhumeha .He further identified it with obesity and sedentary lifestyle, and also advising exercises which can help to "cure" it. The Indians tested for diabetes by observing whether ants were attracted to a person's urine, , and called the disorder "sweet urine disease" (Madhumeha).[2]Diabetes mellitus (DM) is a chronic metabolic disorder in which prevalence has been increasing steadily all over the world. As a result of this trend, it is fast becoming an epidemic in many countries of the world with the number of people affected expected to double in the next decade due to increase in ageing and population, thereby adding to the already existing burden for healthcare providers, especially in poorly developed countries.[1]As at 2013, 382 million people have diabetes world wide . Type-II makes up about 90% of the cases. This is equal to 8.3% of the adult population with equal rates in both women and men.[3]In 2014, the International Diabetes Federation (IDF) estimated that diabetes resulted in 4.9 million deaths. The World Health Organization (WHO) estimated that diabetes resulted in 1.5 million deaths in 2012, making it the 8th leading cause of death . The discrepancy between the two estimates is due to the fact that cardiovascular diseases are often the cause of death for individuals with diabetes; the IDF uses modelling to estimate the amount of deaths that could be attributed to diabetes. More than 80% of diabetic deaths occur in low and middle- income countries.[3]The first nationwide study on the prevalence of Type-II diabetes mellitus (T2DM) reported 2.1% and 1.5% prevalence in the urban and rural populations of India, respectively. [4] The present research work aims at the combination of Teneligliptin with other oral hypoglycaemic agents have been shown to improve glycaemic control efficient when compare with the monotherapy shown inadequate glycaemic control of adult men and woman over a region in Rajahmundry for a period of 6 months.

1.1 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.[6]

1.2 Pathophysiology

Normal regulation of glucose metabolism is determined by a feedback loop involving the islet β-cell and insulin-sensitive tissues in which tissue sensitivity to insulin determines the magnitude of the β-cell response. When insulin resistance is present, the β-cell maintains normal glucose tolerance by increasing insulin output. It is done only when the β-cell is incapable of releasing sufficient insulin in the presence of insulin resistance that glucose levels rise. While β-cell dysfunction has a clear genetic component, environmental changes play a vital role.[7]

This feedback loop relies on crosstalk between the β-cell and the insulin sensitive tissues . Insulin released in response to β-cell stimulation mediates the uptake of glucose, amino acids and fatty acids by insulin-sensitive tissues. In turn, these tissues feedback information to the islet regarding their need for insulin, the mediator of which has not yet been identified but is likely to involve integration between the brain and humoral systems. When insulin

resistance is present, as seen most commonly with obesity, the β-cell increases its insulin output to maintain normal glucose tolerance. However, when the β-cell is incapable of this task, the result is an elevation in plasma glucose.[7]

Type-II diabetes results when pancreatic beta cells are unable to secrete sufficient insulin to maintain normoglycemia,2nd typically in the context of increasing peripheral insulin resistance.[8]Genes and the environment together are important determinants of insulin resistance and β- cell dysfunction. As our gene pool has not changed in recent times, environmental changes have been critical in determining the Type-II diabetes epidemic.[9] Advances in technology and analytical approaches have led to the discovery of genes linked to Type-II diabetes. Using the candidate gene approach, PPARγ was the first gene identified18. Since then, using largely genome-wide association studies (GWAS), over 50 gene loci have been linked to Type-II diabetes19. Further, 53 loci have been linked to glucose and insulin concentrations, of which 33 also link to Type-II diabetes, but do not always associate with both fasting and 2-hour glucose19,20. While a few loci are associated with obesity and insulin resistance, the vast majority are linked to the β-cell21.[9]

1.3 Management of Type-Ii Diabetes

Management recommendations will include nutrition therapy, physical activity, self- management approaches and pharmacologic therapy.[10] Blood sugar control - The goal of treatment in Type-II diabetes is to keep blood sugar levels at normal or near-normal levels. Careful control of blood sugars can help prevent the long-term effects of poorly controlled blood sugar (diabetic complications of the eye, kidney, and cardiovascular system. Patients who are identified with prediabetes should be referred for education and life-style interventions to a qualified health professional (which may include clinician, dietician, nursing staff and pharmacist).Intensive lifestyle change or programs have been proven effective in delaying or preventing the onset of diabetes by about 50-58%. Effective lifestyle changes include setting achievable goals, obtaining weight loss when needed (between 5-10% of total body weight is recommended), and increasing physical activity to a minimum of 150 minutes per week (Tuomilehto, 2001).Patients with IGT, IFG or an A1c should be referred to an effective ongoing support program targeting weight loss of 7% of body weight and increasing physical activity to at least 150 minutes per week of moderate activity such as walking.

- Metformin therapy for prevention of T2DM may be considered in those patients meeting criteria for prediabetes.
- At least annual monitoring for the development of diabetes in those with prediabetes may be utilized.
- Screening for and treatment of modifiable risk factors for CVD are suggested.[10]

Pharmacological therapy of Type-II diabetes has changed dramatically in the last 10 years, with new drugs and drug classes becoming available. These drugs allow for the use of combination oral therapy, often with improvement of glycaemic control that was previously beyond the reach of medical therapy.

1.4 Metformin

Metformin hydrochlorides an oral anti hyperglycaemic drug used in the management of type2 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]

1.5 Sulfonylurea's

The sulfonylurea agents are the oldest class of oral anti-diabetes therapies and are currently used as second-line or add-on treatment options for Type-II diabetes. The agents stimulate pancreatic beta-cells to produce insulin, increase cellular uptake and utilization of glucose, and decrease glucose production in the liver.[12] sulfonylureas are useful only in patients with some ß-cell function. Sulfonylurea's may also have extrapancreatic effects, one of which is to increase tissue sensitivity to insulin, but the clinical importance of these effects is minima.[13]

1.6 Meglitinides

The meglitinides are short-acting glucose-lowering drugs for therapy of patients with Type-II diabetes alone or in combination with metformin. They are structurally different than sulfonylureas, but act similarly by regulating ATP-dependent potassium channels in pancreatic ß-cells, thereby increasing insulin secretion .[18] Repaglinide appears to act via different receptors than sulfonylureas. It is less effective than glyburide at higher blood glucose concentrations, and does not increase insulin exocytosis .[13]

1.7 Thiazolidinediones

Thiazolidinediones (glitazones), a new class of antidiabetic drugs, have been developed. These drugs are potent and highly selective agonists for peroxisome proliferators-activated receptors (PPAR Á), directly improving insulin sensitivity at the sites of insulin action in Type-II diabetes patients. Thiazolidinediones seem to have pleiotropic vascular protective effects, as they appear to improve diabetic dyslipidaemia, hypertension and abnormalities of the co- agulation-fibrinolysis system, thus reducing the overall cardiovascular risk in patients with the metabolic syndrome.[14]

Table No-1: Classification of oral hypoglycaemic agents

Class	Generic name (brand name)	Mechanism of action	When to take it	Adverse effects
Sulfonylureas	Gliclazide Glimepiride Glyburide Natéglinide	Stimulate the pancreas to produce more insulin Stimulate	Before meals (≤ 30 minutes); Do not take at bedtime	Hypoglycemia (low blood sugar)
Méglitinides	Natéglinide Répaglinide	Stimulate the pancreas to produce more insulin	Before meals (≤ 15 minutes); Do not take at bedtime	Hypoglycemia (low blood sugar)
Biguanides	Metformine Metformine with extended release	Reduce the production of glucose by the liver	During meals At dinner	Diarrhea,metallic aftertaste, nausea
Thiazolidinediones (TZD)	Pioglitazone Rosiglitazone	Increase insulin sensitivity of the body cells and reduce the production of glucose by the liver With	With or without food, at the same time each day	Swelling due to water retention, weight gain Pioglitazone : increased risk of bladder cancer Rosiglitazone: increased risk of non-fatal heart attack.
Alpha-glycosidase inhibitors	Acarbose Linagliptine	Slow the absorption of carbohydrates (sugar) With	With the first mouthful of a meal	Bloating and flatulence
Dipeptidyl-peptidase-4 (DPP-4) inhibitors Glucagon-like	Linagliptine Saxagliptine Sitagliptine Alogliptine	Intensify the effect of intestinal hormones (incretines) involved in the control of blood sugar Mimic	With or without food, at the same time each day	Pharyngitis, headache
Glucagon-like peptide-1 (GLP-1) agonist	Exenatide Liraglutide Canaglifozine	Mimic the effect of certain intestinal hormones (incretines) involved in the control of blood sugar	Injection to take 0 to 60 minutes before breakfast or dinner Injection to take with or without food, at the same time each day	Nausea, diarrhoea, vomiting
Sodium glucose co- transporter 2 inhibitors (SGLT2)	Canaglifozine Dapagliflozine	Help eliminate glucose in the urine	Before the first meal of the day Any time of day, with or without food	Genital and urinary infections, more frequent urination

The following pills combine 2 classes of anti diabetic drugs:

- Thiazolidinedione + biguanide
- DPP-4 inhibitors + biguanide[15]

1.8 Dpp-4 Inhibitors

Dipeptidyl peptidase-4 (DPP-4) inhibitors have recently emerged as a new class of anti diabetic that show favorable results in improving glycemic control with a minimal risk of hypoglycaemia and weight gain**.** Incretin hormones,1–3namely glucagon-like peptide-1 (GLP-1) and glucose –dependent insulinotropic polypeptide (GIP), are released from entero endocrine cells and enhance insulin secretion.1,2,4–6Incretins are rapidly inactivated by the enzyme dipeptidylpeptidase-4 (DPP-4), and have a very short half-life (t1/2) as a result. DPP-4 inhibitors increase the levels of active GLP-1 and GIP by inhibiting DPP-4 enzymatic activity; thus, in patients with diabetes, these inhibitors improve hyperglycemia in a glucose-dependent manner by increasing serum insulin levels and decreasing serum glucagon levels.7–13 Therefore, incretin-related agents such as DPP-4 inhibitors are promising drugs that can decrease glucose fluctuations in diabetic patients and have emerged as a new class of anti diabetic**.** [16]

Although the described DPP-4 inhibitors are all competitive reversible inhibitors, it can be difficult to compare them using data reported in individual studies, because these are influenced by differences in the assay conditions used to estimate the extent of DPP-4 inhibition.The DPP-4 inhibitors are all orally available and is rapidly absorbed, withsignificant inhibitionofplasmaDPP-4 activity being seen within 5 min of administration. Oral bioavailability in humans is generally high (~87% for sitagliptin [33], 85% for vildagliptin [34] and ~67% for saxagliptin [35]), although somewhat lower for linagliptin (~30%).[17]

1.9 Teneligliptin

[Brand name]: Tenelia, afoglip, teniva, tenglyn, teneza, tenebite, tiban, Tablets 20 mg

[Non-proprietary name]: Teneligliptin Hydro bromide Hydrate (JAN*)

[Applicant]: Mitsubishi Tanabe Pharma Corporation

[Date of applicatication]: August 26, 2011

[Dosage form/Strength]: Each tablet contains TeneligliptinHydro bromide Hydrate, equivalent to 20 mg of teneligliptin

[Application classification]: Prescription drug (1) Drug with a new active ingredient

[Results of deliberation]: In the meeting held on April 27, 2012, the First Committee on New Drugs concluded that the product may be approved and that this result should be presented to the Pharmaceutical Affairs Department of the Pharmaceutical Affairs and Food Sanitation Council.The product is not classified as a biological product or a specified biological product, the re-examination period is 8 years, and neither the drug substance nor the drug product is classified as a poisonous drug or a powerful drug.[18]

- Teneligliptin consists of a considerably rigid J shaped structure formed by five rings, four which are directly connected,the loss in entropy is small upon binding to DPP-4.
- The carbonyl group of teneligliptin, derived from the peptide mimetic, forms a hydrogen bond with the side chain of Asn710.
- For teneligliptin, introduction of the ‘’anchor lock domain’’, which binds to the S2 extensive subsite, increased the activity by 1500-fold over the corresponding fragment that binds to S1 and S2 only.
- Because of above mentioned unique features teneligliptin is one of the most potent DPP4 inhibitors

1.10 Therapeuticindications

Teneligliptin Tablets are indicated as a monotherapy adjunct to diet and exercise to improve glycemic control in adults with Type-II diabetes mellitus (T2DM).

1.11 Contraindications

Teneligliptin Tablets are contraindicated in patients with:

- Hypersensitivity to the drug or any of its components
- Severe ketosis, diabetic coma or pre-coma and also for immediate remedy in type –I diabetes
- Severe trauma, before and after surgery and when the blood glucose has to be controlled with insulin injection**.**[19]

1.12 Pregnancy and Lactation

Teneligliptin should be used in pregnant women or in women who may possibly be pregnant only if the expected therapeutic benefits’ outweigh the possible risks associated with treatment of this product in pregnant women has not been established. Furthermore, the transfer to embryo in animal studies (rats) has been reported.)Breast-feeding must be discontinued during administration of this product in

lactating women (transfer to milk in animal studies (rats) has been reported.).

1.13 Undesirable Effects

The following adverse reactions have been identified in the clinical trials of Teneligliptin:

In clinical trials conducted in Japan, 232 adverse reactions to this drug (including abnormal laboratory tests) were reported in 156 patients (9.5%) of total 1645 patients. The most adverse reactions were hypoglycaemia in 43 patients (2.6%) and constipation in 14 patients (0.9%**).**[20]

2.0 Aims and Objectives

To compare the safety and efficacy of the Teneligliptin a DPP inhibitor over other hypoglycaemic agents in Type -II Diabetes Mellitus.

The study was carried out by considering the following objectives.

2.1 Objectives

- To collect socio demographic data of the patients such as age, gender, occupation, education, etc...
- To obtain the information of patients receiving insulin as their ultimate therapy after receiving oral therapy.
- To assess the number of oral hypoglycaemic drugs prescribed.
- To assess the type of oral hypoglycaemic agents.
- To assess the dose of the hypoglycaemic agents.
- To assess the state of their life style diet modifications after starting the therapy.
- To assess and compare the efficacy of Teneligliptin with combination of oral hypoglycemics and monotherapy. To assess the glycaemic lab reports of the patient before an

3.0 Materials and Methods of Collecting Data

3.1 Study Site

The study was conducted at, Pradeep Diabetic Centre**,** Rajamahendravaram.

3.2 Study Duration

The study was carried out for a period of 6 months from Feb 2016 to July 2016.

3.3 Study Design

The study was a prospective –observational study.

3.4 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.

3.5 Inclusion Criteria

- Patients of either gender and above 12 years
- Patients diagnosed with type-II diabetes
- Patients prescribed with oral hypo glycaemic agents as monotherapy, combination of oral hypoglycaemic agents along with insulin.
- Patients willing to participate in the study

3.6 Exclusion Criteria

- Patients not willing to participate in the study
- Immunosuppressed patients
- Diabetic Patients other than type-II diabetes.

3.7 Analysis of Data

The data was analysed by applying statistics by SPSS (Statistical Package for the Social Sciences) software where ever required.

3.8 Source of the Study

The data for the study was collected from,

- Case sheets of the patients,
- Lab reports of the patients and other relevant resources.

3.9 Study Procedure

A prospective study was carried out at Pradeep Diabetic Centre, Rajamahendravaram, after getting ethical clearance from institutional ethics committee and with the prior permission from the hospital administration. 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

3.10 Socio Demographic Data

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

3.11 Disease State

- Severity of diabetes

3.12 Treatment Data

- Dose of the Oral hypoglycaemic agents prescribed
- Class of oral hypoglycaemic agent prescribed
- Dose of the insulin 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 standard guidelines like mean, standard, significant 2 tailed tests in SPSS and ANOVA in PRISM PAD Software.

4.0 RESULTS:

4.1 Gender Distribution

A total of 114 patients with type 2 diabetes were enrolled in the study out of which 51(45%) were male patients and 63 (55%) were female patients.

S NO	GENDER	NUMBEROF PATIENTS(n=114)	PERCENTAGE
1	MALE	51	45%
2	FEMALE	63	55%

Table No-2: Gender Details of the Patients Enrolled In the Study

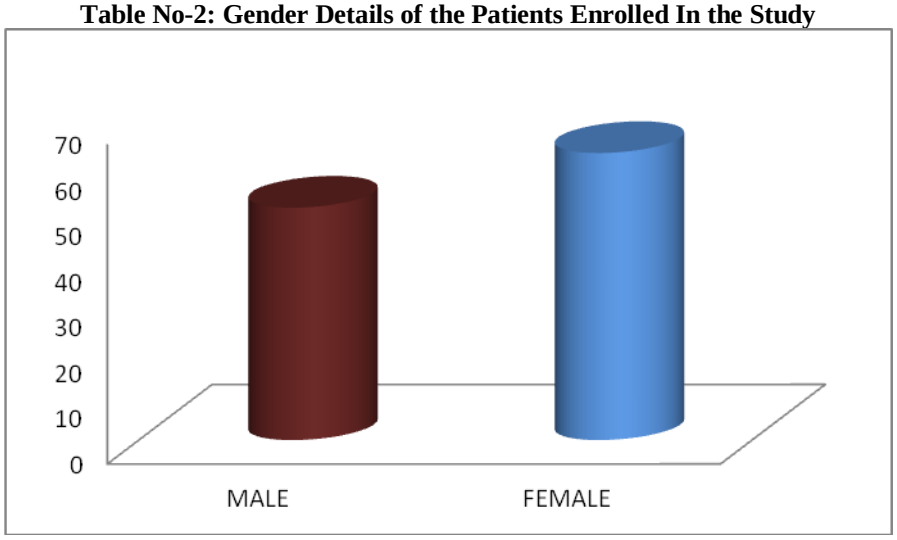

Figure No-1: Gender Details of the Patients Enrolled In the Study

4.2 Age Distribution of the Patients

Out of 114 patients 2(2%) patients were in the age range between 18-25 years, 29(25%) patients were in the age range between 26-40, 50(44%) patients were in the age range between 41-55, 26(23%) patients were in the age range between 56-70, 7(6%) patients were in the age range between 71-85.Among these 41-55 age range patients were high in number, 18-25 age range patients were low.

Figure No-2: Age Distribution of the Patients

S NO	AGE RANGE	NUMBEROFPATIENTS(n=114)	PERCENTAGE (%)
1	18-25	2	2%
2	26-40	29	25%
3	41-55	50	44%
4	56-70	26	23%
5	71-85	7	6%

4.3 Body Mass Index of the Patients

Out of 114 patients 2(2%) patients were under weight, 40(35%) patients were normal weight, 46(40%) patients were overweight, and 26 (23%) patients were obese.

Table No-3: Body Mass Index of the Patients

SNO	BMI	WEIGHT STATUS	NUMBER OF PATIENTS	PERCENTAGE (%)
1	BELOW 18.5	UNDER WEIGHT	2	2%
2	18.5-24.9	NORMAL AND HEALTHY WEIGHT	40	35%
3	25.0-29.9	OVERWEIGHT	46	40%
4	ABOVE 30	OBESE	26	23%

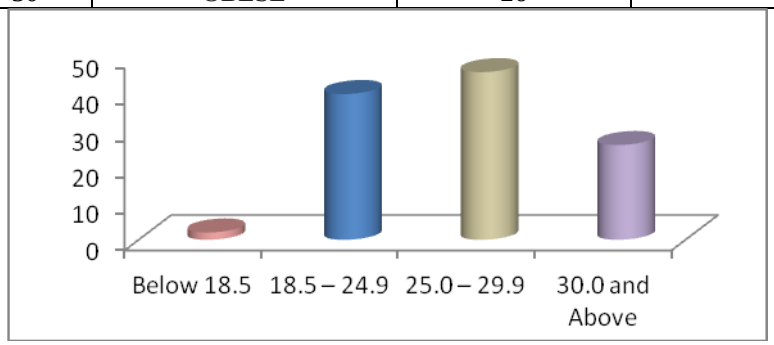

Figure No-3: Body Mass Index of the Patients

4.4 Duration of the Disease

Out of 114 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 No-4: Duration of Disease of the Patients

S NO	DISEASE DURATION	NUMBER OF PATIENTS(n=114)	PERCENTAGE (%)
1	BELOW 1	12	10%
2	1-10	93	82%
3	11-20	8	7%
4	21-30	1	1%

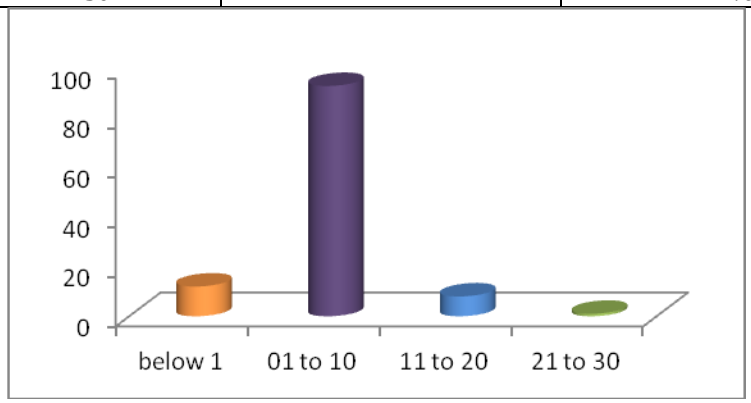

Figure No-4: Duration of the Disease of Patients

4.5 Combination of Oral Hypoglycaemic

Out of 114 patients 26 (23%) patients were on sulfonulureas and teneligliptin combination, 24(21%) patients were on biguanides and teneligliptin combination, 52(46%) patient were on sulfonylureas,biguanides. and teneligliptin combination and 12(10%) patients were on teneligliptin monotherapy.

Table No-5: Combinational Therapy in Patients

S NO	COMBINATION DRUGS	NUMBER OF PATIENTS (n=114)	PERCENTAGE (%)
1	SULFONYLUREAS+TENELIGLIPTIN	26	23%
2	BIGUANIDES+TENELIGLIPTIN	24	21%
3	SULFONYLUREAS+BIGUANIDES +TENELIGLIPTIN	52	46%
4	TENELIGLIPTIN	12	10%

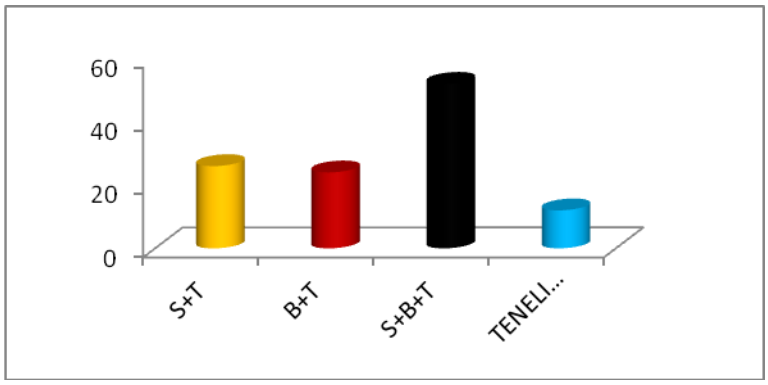

Figure No-5: Combinational Therapy in Patients

4.6 Adverse Drug Reactions

Out of 114 patients 89(78%) patients were reported with mild range of side effects,5(4%) patients were reported with moderate range of side effects and none of the patients shown severe range of side effects.

Table No-6: Adverse Drug Reactions of the Patients

S NO	CATEGORY	NO OF PATIENTS	PERCENTAGE
1	MILD	89	78%
2	MODERATE	5	4%
3	SEVERE	0	0%

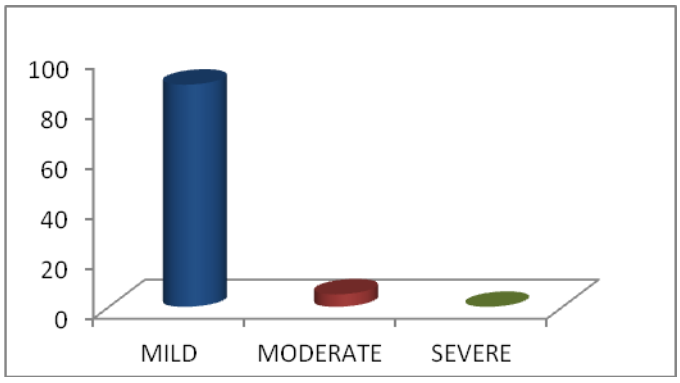

Figure No-6: Adverse Drug Reactions of the Patients

4.7 Glycemic and Non Glycemic Parameters Before and After the Treatment of Teneligliptin with Combination with Sulfonylurea's.

Table No-7: Statistical Analysis of Patients with Teneligliptin Along With Sulfonylurea's

S no	Characteristics	Before	After	Mean±standard
1	Systolic	140.38±29.5	131.92±18.1	8.46±13.76
2	Diastolic	89.23±12.9	85.38±8.1	3.84±6.37
3	FBS	196.0385±81.8	141.7308±52.5	54.30±45.60
4	PPBS	289.6923±80.7	218.0000±66.2	71.692±45.35
5	HBA1C	7.2308±0.8	6.7423±0.7	0.488±0.233
6	LDL	141.4615±22.7	142.2308±22.5	-0.769±1.861
7	HDL	32.7692±6.8	33.4231±6.6	-0.653±2.189
8	TRIGLYCERIDES	153.5769±20.2	161.0769±19.5	-7.5±1.555

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 to 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).

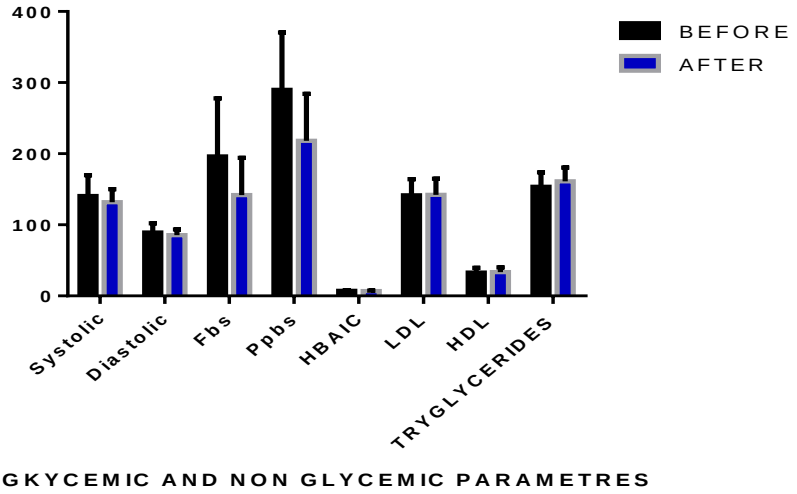

Figure No-7: Statistical Analysis of Patients with Teneligliptin Along With Sulfonylurea's

4.8 Glycemic and Non Glycemic Parameters Before and After the Treatment of Teneligliptin with Combination with Biguanides

Table No-8: Statistical Analysis of Patients with Teneligliptin Along With Biguanides

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

Out of 114 patients 24(21%) were administered with teneligliptin as a combination therapy to biguanides 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).

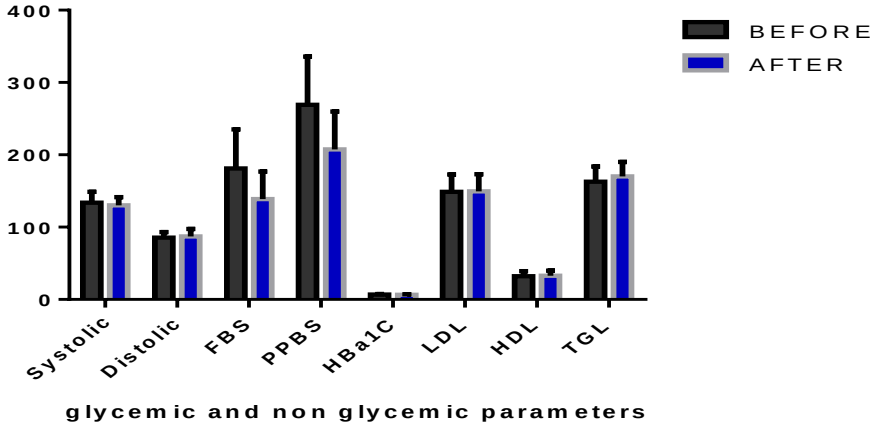

Figure No-8: Statistical Analysis of Patients with Teneligliptin Along With Biguanides

4.9 Glycemic And Non Glycemic Parameters Before And After The Treatment Of Teneligliptin With Combination With Sulfonylurea's And Biguanides.

Table No-9: Statistical Analysis of Patients with Teneligliptin Along With Sulfonylureas and Biguanides

S no	Characteristics	Before	After	Mean±standard
1	Systolic	132.11±15.25	125.38±7.530	6.730±10.976
2	Diastolic	83.46±7.640	83.84±5.991	-.384±8.39
3	FBS	180.28±48.005	135.65±35.700	44.63±32.88
4	PPBS	276.26±60.07	205.65±49.37	70.61±44.52
5	HBA1C	7.15±766	6.67±.650	.480±.378
6	LDL	148.75±21.838	149.38±21.669	-.634±1.57
7	HDL	31.57±6.353	32.51±5.866	-.94231±2.57
8	TRIGLYCERICES	161.98±16.920	169.17±16.411	-7.192±1.81

Out of 114 patients 52(46%) were administered with teneligliptin as a combination therapy to biguanides and 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(44.634±32. 884), PPBS (70. 615±44.521), HBA1C . (480±. 378) and an increase in triglyceride levels (mean± SD) from base line was(-7.192±1. 815). HBA1C ,FBS,PPBS were statistically significantly lower at 24 week than at base line (p value<0.0001).

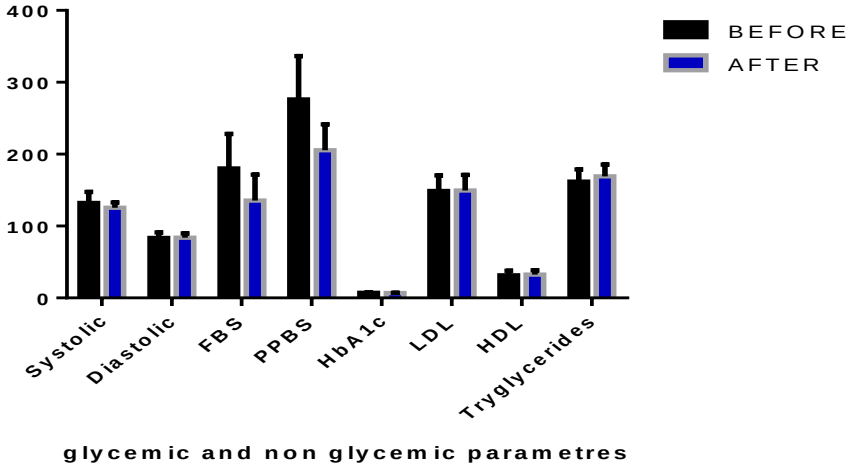

Figure No-9: Statistical Analysis of Patients with Teneligliptin Along With Sulfonylureas and Biguanides

4.10 Glycemic and Non Glycemic Parameters Before and After the Treatment with Teneligliptin.

Table No-10: 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

Out of 114 patients 12(10%) 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 evels (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).

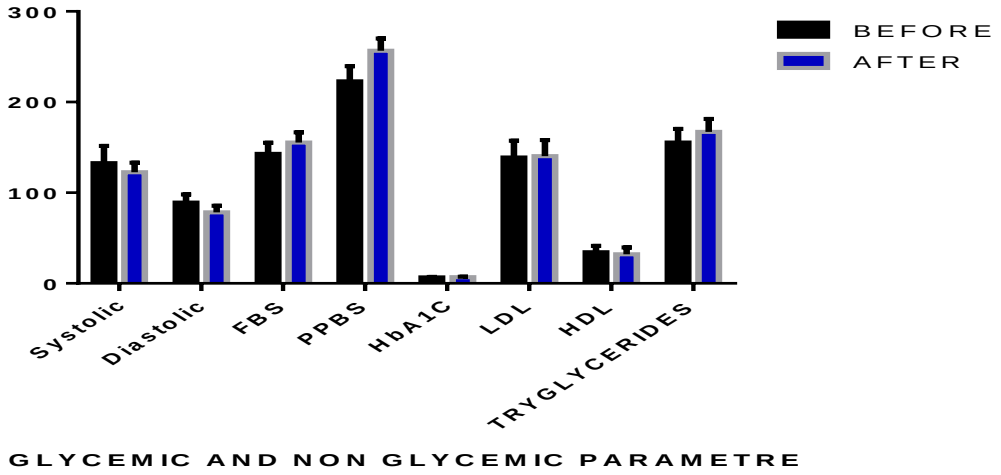

Figure No-10: Statistical Analysis of Patients with Teneligliptin Monotherapy

5.0 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. Out of 114 patients, 51 (45%) were male patients and 63 (55%) were female patients. This indicates that there were, more number of female patients having type-II diabetes mellitus when compared to male patients. Out of 114 patients 2 (2%) patients were in the age range between 18-25 years, 29 (25%) patients were in the age range between 26-40, 50 (44%) patients were in the age range between 41-55, 26 (23%) patients were in the age range between 56-70, 7 (6%) 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 41-55 age range patients were high in number, 18-25 age range patients were low.

Out of 114 patients 2 (2%) patients were under weight, 40 (35%) patients were normal weight, 46

(40%) patients were overweight, and 26 (23%) patients were obese. The above study shows that 40% patients were with highest BMI and 2% of patients were with low BMI.

Out of 114 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. 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 114 patients 26 (23%) patients were on sulfonulureas and teneligliptin combination, 24 (21%) patients were on biguanides and teneligliptin combination, 52 (46%) patient were on sulfonylureas, biguanides. and teneligliptin combination and 12 (10%) patients were on teneligliptin monotherapy. The study indicates that majority of patients (46%) were under the prescription of sulfonyl ureas , biguanides and teneligliptin and the lowest (10%) were on teneligliptin monotherapy.Out of 114 patients 89 (78%) patients were reported with mild range of side effects,5 (4%) 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).

Out of 114 patients 24 (21%) were administered with teneligliptin as a combination therapy to biguanides 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 (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).

Out of 114 patients 52 (46%) were administered with teneligliptin as a combination therapy to biguanides and 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 (44.634±32.884), PPBS (70.615±44.521), HbA1C .480±.378) and an increase in triglyceride levels (mean± SD) from base line was (-7.192±1.815). HbA1C ,FBS,PPBS were statistically significantly lower at 24 week than at base line (p- value<0.0001).Out of 114 patients 12 (10%) 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 was (-11.91±4.96). HbA1C, FBS, PPBS were statistically significantly lower at 24 week than at base line (p-value<0.0001).

5.1 Safety and Tolerability

Current study of 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 having high fiber food in their diet which can also lowers the cardio vascular events by maintaining the lipid profile. Very low number of patients was reported with moderate to severe adverse effects which gives clear information on teneligliptin use as appropriate.

6.0 CONCLUSION:

The combination of teneligliptin with other oral hypoglycaemic agents have been shown to improve glycaemic control efficient when compare with the monotherapy shown inadequate glycaemic control. In Our study has concluded that the addition of teneligliptin to the sulfonyl ureas shown heighest efficacy in reducing FBS and PPBS when compared to the combination with biguanides and teniligliptin monotherapy, Teneligliptin combination with sulfonyl ureas biguanides has demonstrated that reduction in HbA1c in a 24 week study. Teneligliptin may show benefits with hypoglcemia and had chances of increase in triglycerides, monitoring of triglycerides along with teneligliptin therapy is more safe and effective.In addition to effective glycemic control results of our study suggested that teneligliptin as add on therapy is well tolerated in type –II diabetis mellitus along with triglycerides monitoring. Current study on 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.

Finally the authors conclude that that the addition of teneligliptin to the sulfonyl ureas shown heighest efficacy in reducing FBS and PPBS when compared to the combination with biguanides and teniligliptin monotherapy and further research work can be enhanced by comparing the disease prevalence over a

group of population in various zones of state and geographic conditions.

7.0 Conflict Of Interest

The authors do not have any conflicts of interest.

8.0 Acknowledgements

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