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Original Research Paper

Medicine

CARDIOVASCULAR OUTCOMES OF TENELIGLIPTIN IN PATIENTS OF TYPE 2 DIABETES MELLITUS IN RURAL POPULATION

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ABSTRACT

Aim: To evaluate the cardiovascular outcomes of teneligliptin treatment in case of Type-2 Diabetes Mellitus patients

Methods: A total number of 85 patients of type 2 diabetic mellitus were selected on the basis of ADA criteria . After exercising exclusion criteria the selected patients were subjected to thorough clinical examination and routine investigation like complete blood count, FBS, 2hr PPBS, HbA1c, lipid profile, renal function tests, liver function tests, urine routine/ microscopsy , urine microalbumin, ECG, Echocardiography (2D and Color Doppler),CIMT (Carotid intima media thickness) in all cases.Specialised investigation like X-ray chest, USG of abdomen and pelvis, CT/MRI of Brain etc. were done in selective cases as per requirement.

Patients with other oral antidiabetic agents were investigated with above tests on first visit and they were given teneligliptin 20mg OD along with the previous antidiabetic drugs. The tests were repeated after 3 months on next visit and the value were noted. Data collected from both the settings of the test were compared, analysed .

Results: Clinical parameters, including body mass index and blood pressure, did not show any difference before and after treatment. Biochemical parameters like FBS and 2hrPPBS, HbA1c were signifacantly reduced after treatment.(FBS 136±40.7 to 124±8.44 in males,and in females 127±35.9 to 111±7.9,2hrPPBS 302±73.5 mg/dl to 284±66.6 in males and 196±21.7 to 187±17.3 in females). Average HbA1c at onset in males was 8.4±1.5% and in females was 8.0±0.7%. After 3 months average HbA1c in males was 7.4±0.7% and in females was 7.3±0.5. The total cholesterol, LDL, TG has decreased significantly from baseline data in comparison to the results after 3 month.HDL also showed rise after treatment.Three months after treatment, there were improvements in LV systolic and diastolic function [LV ejection fraction, 66 ± 4.4 % to 67.5 ± 4.1 in males, 64.3 ± 4.2 % to 65.8 ± 4.1 in females, , $p < 0.01$; E-wave velocity/A-wave velocity (E/A) ratio, 0.86± 0.08 to o.85±0.05in males, 0.85 ± 0.08to 0.81±0.06, $p < 0.01$]. Moreover,CIMT also diminished after treatment(0.77±0.07 to 0.73±0.07 in males,0.75±0.07 to 0.72±0.06 in females $p < 0.01$).

Conclusion. DPP-4 inhibitors like teneligliptin has significant improvement of cardiovascular functions however more number of patients with longer duration of treatment require to conclude the above result .

KEYWORDS :

Introduction.

Cardiovascular system is one among the worst affected organ system in Diabetes Mellitus with increased incidence of Angina pectoris, Myocardial infarction and Congestive heart failure. In diabetic population congestive heart failure in absence of coronary artery disease, hypertension, valvular heart disease or alcoholism is now a well established clinical entity and adds to the spectrum of diabetic morbidity. This is mostly due to direct involvement of the myocardium (Cardiomyopathy). The existence of diabetic cardiomyopathy was first proposed by Rubler et al (1) in 1972, based on their experience with four adult diabetic patients who suffered from congestive heart failure in the absence coronary heart disease, valvular or congenital heart disease, hypertension or alcoholism. A wave of subsequent studies in 1970's and 1980's provided credence to this new disease entity.

Studies have found that Diabetes Mellitus produces functional, biochemical and morphological myocardial abnormalities independent of coronary atherosclerosis and hypertension. These abnormalities may result in impaired left ventricular diastolic function, contributing importantly to heart failure with normal systolic function(2). This points to a mechanism other than macrovascular damage as the pathogenesis process and probably the microvascular damage in myocardial vasculature in a similar manner as occurs in retina, kidney and peripheral nerves.

Dipeptidyl peptidase-4(DPP-4) inhibitors are a novel class of antidiabetic drugs that can help control fasting and post prandial glucose levels by increasing the Plasma concentrations of incretin hormones including glucagon-like peptide(GLP-1) and glucose-dependent insulinotropic polypeptide. DPP-4 inhibitors have been thought to have cardio-protective effects owing to increases in the incretin hormones levels and B-type natriuretic peptide(BNP) bioavailability in type-2 DM patients. Recent studies have reported the pleiotropic effects of DPP-4 inhibitors, including anti-inflammatoty effects, improvement of endothelial dysfunction and cardio-protective effects(3).

DPP-4 inhibitors are classified as peptidomimetic (i.e., vildagliptin, saxagliptin, anagliptin and teneligliptin) and non-peptidomimetic (i.e., sitagliptin, alogliptin, and linagliptin). These drugs improve glucose fluctuations in patients with type-2 DM(4).

Various studies have reported that compared to traditional antidiabetic treatment, DPP-4 inhibitors lead to improvement in LV function but its cardioprotective effect still remains controversial.

Teneligliptin, a novel peptidomimetic- chemotype prolylthiazolidine- based DPP-4 inhibitor, has been reported to be effective, safe and generally well tolerated in some studies.

MATERIAL AND METHODS

The study was carried out in P.G. Department of Medicine in collaboration with Department of Cardiology and Pharmacology, S.C.B Medical College & Hospital from January 2016 to December 2017.. After satisfying all the exclusion/inclusion criteria 85 cases were taken into study.

STUDY DESIGN

Selection of Cases

Inclusion Criteria (According to American Diabetes Association)

Fasting Blood Sugar (FBS) ≥ 126 mg/dl

Hemoglobin A1c (HbA1c) ≥ 7%

Exclusion Criteria

The following patients were excluded from the study:

Patients already on other incretin-based drugs prior to admission/consultation.

Patients on insulin therapy.

Patients with existing cardiovascular diseases like Atrial fibrillation, Coronary artery disease, Dilated cardiomyopathy, Symptomatic heart failure etc.

Patients already having microvascular /macrovascular complications of Diabetes.

Patients having hepatic, renal or gastrointestinal dysfunction.

Patients with other endocrinal disease.

Patients with malignancy
Patients of Type 1 DM

After exercising exclusion criteria the selected patients were subjected thorough clinical examination and routine investigation like complete blood count, FBS, 2hr PPBS, HbA1c, lipid profile, Renal function tests, liver function tests, urine routine/ microscopsy , urine microalbumin, ECG, Echocardiography (2D and Color Doppler),CIMT (Carotid intima media thickness) in all cases.

Specialised investigation like X-ray chest, USG of abdomen and pelvis, CT/MRI of Brain etc. were done in selective cases as per requirement.

Patients with other oral antidiabetic agents were investigated with above tests on first visit and they were given teneligliptin 20mg OD along with the previous antidiabetic drugs. The tests were repeated after 3 months on next visit and the value to be noted. Data collected from both the settings of the test were compared, analysed and opinion formed.

ECG

Single channel 12 lead electrocardiogram was obtained by conventional method by BPL, Cardiart 108T-MK-VI model ECG machine.

X-Ray Chest PA view : done to detect associated cardiac/lung pathology and cardiothoracic index.

USG Abdomen : To detect pancreatic calculi, kidney size and presence of stone.

Echocardiography

Echocardiograms were recorded in the Cardiology department with a commercially available ultrasound system (HDI 1500 Ultrasound System).

Subjects were examined in the left lateral decubitus position using standard parsternal, short-axis, and apical views. All recordings and measurements were obtained by the same observer according to the recommendations of the American Society of Echocardiography and were always performed at midday to avoid the influence of circardian rhythm on left ventricular function. Particular attention was given to record the LV size and systolic function and then the LV diastolic function by Doppler recording of the LV filling velocities. Isovolumic relaxation time (IVRT) i.e., the interval between the aortic valve closure and mitral valve opening, was recorded on the dual M-mode echo. Pulsed wave (PW) mitral Doppler velocities were recorded with cursor on the tips of the mitral valve on the Apical 4-chamber view. 'E' velocity and deceleration tme (DT) was noted and the heights of 'E' and 'A' velocities recorded.

Criteria of American Society of Echocardiography(5) were used for assessing LV systolic dysfunction viz.

LV Ejection fraction less than 50%,
Percentage Fractional shortening less than 36%,
E-point septal separation more than 7 mm and
Cardiac output less than 3 litres/min.

Mayo Clinic criteria(6) were used for detecting the LV diastolic dysfunction viz.,
'A' velocity higher than 'E' velocity on PW mitral Doppler.
E/A ratio less than 1.

Deceleration time more than 240 m.sec.

IVRT more than 110 m sec on dual M-mode echo of aortic and mitral valve recorded simultaneously. Those having both systolic and diastolic dysfunction were considered to have global dysfunction.

STATISTICAL ANALYSIS

The recorded and calculated values of all the parameters in the study group were statistically analysed. Linear regression method was used to find out the correlation among variables. The significance between different groups and means were calculated by students' paired 't' test and 'p' values were ascertained with respective degree of freedom. Frequencies were calculated by using Chi square test. χ^2 value was observed and 'p' value calculated. The result was accepted to be statistically significant, when p value was <0.05. Microsoft Excel software was used to calculate these values and graphs.

CIMT (CAROTID INTIMA MEDIA THICKNESS)

In healthy middle-aged adults, CIMT values between 0.6 and 0.7 mm have been considered normal, while CIMT of 1 mm or more has been associated with significant increased absolute risk of CHD.

According to the ASE (American Society of Echocardiography) guidelines, patients at intermediate CVD risk, peripheral arterial disease, cerebrovascular disease, diabetes mellitus, or abdominal aortic aneurysm were the potential candidates for CIMT measurement.

CIMT testing was done in Radiodiagnosis department by B-mode vascular ultrasound system.

OBSERVATION

TABLE-1: AGE AND SEX DISTRIBUTION OF STUDY GROUP (N=85)

Age group(in years)	Male		Female		Total	
	N	%	N	%	N	%
0-20	0	0	0	0	0	0
21-40	11	13	6	7	17	20
41-60	29	34	16	19	45	53
> 60	15	18	8	9	23	27
Total	55	65	30	35	85	100

Table-1 shows: In the study group there are 55 males and 30 females in which males outnumber the females with M:F = 1.8: 1. There are maximum number of males and females are of middle age group i.e.41-60 years.

TABLE -2 COMPARISON OF CLINICAL PARAMETERS AT BASELINE AND AFTER 3 MONTHS

	BASELINE		3 MONTHS		P-value	
	Male	Female	Male	Female	Male	Female
BMI, Kg/m2	24.5±1.7	21.8±1.7	24.2±1.4	21.7±2	0.02	0.77
SBP, mm Hg	136±9.5	126±7.0	132±6.4	122±5.4	0.04	0.01
DBP, mm Hg	86±5.8	74±4.6	84±4.9	72±4.3	0.39	0.04

Table-2 shows comparison of clinical parameters at the starting of the study and after 3 months. The average BMI of male patients at

the onset was 24.5±1.7 Kg/m2 and the average BMI of female patients at the onset was 21.8±1.7 Kg/m2.After 3 months average BMI of male patients was 24.2±1.4 Kg/m2 that of female patients was 21.7±2Kg/m2. Average SBP at onset in males was 136±9.5 mmHg and in females was 126±7.0 mmHg. After 3 months average SBP in males was 132±6.4 mmHg and in females was 122±5.4 mmHg.

Average DBP at onset in males was 86±5.8 mmHg and in females was 74±4.6 mmHg. After 3 months average DBP in males was 85±4.9 mmHg and in females was 7.3±4.3 mmHg.

TABLE-3 COMPARISON OF BIOCHEMICAL PARAMETERS AT BASELINE AND AFTER 3 MONTHS

	BASELINE		3 MONTHS		P-value	
	Male	Female	Male	Female	Male	Female
FBS, mg/dl	136±21.7	127±15.9	124±8.44	111±7.9	<0.01	<0.01
2hr PPBS, mg/dl	302±73.5	284±66.6	196±21.7	187±17.3	<0.01	<0.01
HbA1c,%	8.4±1.5	8.0±0.7	7.4±0.7	7.3±0.5	<0.01	<0.01
TC, mg/dl	190±17	187±23	174±17	169±22.9	0.16	0.79
HDL, mg/dl	41±7.5	40±7	42±6.5	41±5.6	0.09	0.47
LDL, mg/dl	108±29	107±25	102±26	103±22	0.29	0.52
TG, mg/dl	168±60.4	165±27.7	156±36	162±24	0.10	0.30
Urine Micral, µg/L	19.8±2.2	19.3±2.1	19.6±1.7	19.4±1.9	0.27	0.62
CIMT, mm	0.77±0.07	0.75±0.07	0.73±0.07	0.72±0.06	<0.01	<0.01

Table-3 shows comparison of biochemical parameters at onset and after 3 months.. After 3 months average FBS and 2hrPPBS in males was 124±8.44 mg/dl and 196±21.7 mg/dl respectively . In females average FBS and 2h rPPBS was111±7.9 mg/dl and187±17.3 mg/dl respectively . Similarly Average HbA1c at onset in males was 8.4±1.5% and in females was 8.0±0.7%. After 3 months average HbA1c in males was 7.4±0.7% and in females was 7.3±0.5.Average TC at onset in males was 190±17 mg/dl and in females 187±23 mg/dl. After 3 months average TC in males was 174±17 mg/dl and in females was 169±22.9 mg/dl. Average HDL at onset in males was 41±7.5 mg/dl and in females was 40±7 mg/dl. After 3 months average HDL in males was 42±6.5 mg/dl and in females was 41±5.6 mg/dl. Average LDL at onset in males was 108±29 mg/dl and in females was 107±25 mg/dl. After 3 months average LDL in males was 102±26 mg/dl and in females was 103±22 mg/dl. Average TG at onset in males was 168±60.4 mg/dl and in females was 165±27.7 mg/dl. After 3 months average TG in males was 156±36 mg/dl and in females was 162±24 mg/dl. Average urine micral at onset in males was 19.8±2.2 µg/L and in females was 19.3±2.1 µg/L. After 3 months average urine micral in males was 19.6±1.7 µg/mL and in females was 19.4±1.9 µg/L. Average CIMT at onset in males was 0.77±0.07 mm and in females was 0.75±0.07 mm. After 3 months average CIMT in males was 0.73± 0.07 mm and in females was 0.72±0.06 mm.

TABLE-4 COMPARISON OF CARDIAC PARAMETERS ASSESSED BY ECHOCARDIOGRAPHY AT BASELINE AND AFTER 3 MONTHS

N=85	BASELINE		3MONTHS		P-value	
	Male	Female	Male	Female	Male	Female
Left atrial diameter, mm	37.9 ± 3.0	38.4±2.8	38.8 ± 2.8	39.2±2.7	<0.01	0.29
LV systolic diameter, mm	26.6 ± 1.8	26.4±1.0	26.1 ± 1.9	25.9±1.1	<0.01	<0.01
LV diastolic diameter, mm	38.3 ± 3.0	37.5±2.6	37.6 ± 3.1	37.4±2.5	0.01	0.72
LV ejection fraction,%	66 ± 4.4	64.3±4.2	67.5 ± 4.1	65.8±4.1	<0.01	<0.01
E-wave velocity, cm/s	60.1± 4.5	60.5±5.2	63.3± 4.6	62.2±5.1	<0.01	<0.01
A-wave velocity, cm/s	68.4± 5.3	67.8±5.9	68.8± 5.5	67.3±5.3	<0.01	<0.01
E/A ratio	0.86 ± 0.08	0.85±0.08	0.82 ± 0.05	0.81±0.06	<0.01	<0.01
Deceleration time,ms	233 ± 11.8	236±12.4	238 ± 10.2	240±11.6	<0.01	<0.01

Table-4 shows comparison of cardiac parameters assessed by echocardiography at onset and after 3 months. The average LAD at onset in males was 37.9±3 mm and in females was 38.4±2.8 mm. After 3 months average LAD in males was 38.8±2.8 mm and in females was 39.2±2.7 mm. Average LVIDs at onset in males was 26.6±1.8 mm and in females was 26.4±1.0 mm. After 3 months average LVIDs in males was 26.1±1.9 mm and in females was 25.9±1.1 mm. Average LVIDd at onset in males was 38.3±3.0 mm and in females was 37.5±2.6 mm. After 3 months average LVIDd in males was 37.6±3.1 and in females was 37.4±2.5 mm. Average LVEF at onset in males was 66±4.4% and in females was 64.3±4.2%. After 3 months average LVEF in males was 67.5±4.1% and in females was 65.8±4.1%. Average E-wave velocity at onset in males was 60.1±4.5 cm/s and in females was 60.5±5.2 cm/s. After 3 months average E-wave velocity in males was 63.3±4.6 cm/s and in females was 62.2±5.1. Average A-wave velocity at onset in males was 68.4±5.3 cm/s and in females was 67.8±5.9 cm/s. After 3 months average A-wave velocity in males was 68.8±5.5 cm/s and in females was 67.3±5.3 cm/s. Average E/A ratio at onset in males was 0.86±0.08 and in females was 0.85±0.08. After 3 months average E/A ratio in males was 0.82±0.05 and in females was 0.81±0.06. Average DT at onset in males was 233±11.8 ms and in females was 236±12.4 ms. After 3 months average DT in males was 238±10.2 ms ms and in females was 240±11.6 ms.

TABLE-5 COMPARISON OF E/A RATIO AT BASELINE AND AFTER 3 MONTHS

Age in years	E/A ratio, Baseline		E/A ratio,3months	
	Male	Female	Male	Female
0-20	0	0	0	0
21-40	0.85± 0.08	0.86 ±0.05	0.82± 0.06	0.84± 0.04
41-60	0.89±0.07	0.87±0.1	0.85±0.04	0.83±0.07
>60	0.87± 0.09	0.86± 0.06	0.83 ±0.06	0.84 ±0.06

Table-5 shows comparison of E/A ratio at baseline and after 3 months with age and sex distribution. The average E/A ratio was decreased after 3 months compared with baseline values in both males and females and in all age groups. There are no patients in < 20 years age group.

In 21-40 years group the E/A ratio was decreased in male from 0.85±0.08 to 0.82±0.06 and in female from 0.86±0.05 to 0.84±0.04.In 41-60 years group the E/A ratio was decreased in male from 0.89±0.07 to 0.85±0.04 and in female from o.87±0.1 to 0.83±0.07.In >60 years group the E/A ratio was decreased in male from 0.87±0.09 to 0.83±0.06 and in female from 0.86±0.06 to 0.84±0.06.

TABLE-6 COMPARISON OF EF % AT BASELINE AND AFTER 3 MONTHS

Age in years	EF%, Baseline		EF %, 3months	
	Male	Female	Male	Female
0-20	0	0	0	0
21-40	64.5 ±2.6	63.9±3.1	66.3± 2.6	65.3±2.6
41-60	66.4±4.6	64.6±4.3	67.8±4.4	66.2±4.4
>60	66.7± 3.7	63.6±4.9	68.2 ±3.4	65±3.4

Table-6 shows comparison of EF% at baseline and after 3 months with age and sex distribution. The average EF% after 3 months was increased compared with baseline values in both males and females and in all age groups. There are no patients in < 20 years age group.
In 21-40 years group EF was increased in male from 64.5±2.6% to 66.3±2.6% and in female from 63.9±3.1 to 65.3±2.6. In 41-60 years group the EF was increased in male from 66.4±4.6% to 67.8±4.4% and in female from 64.6±4.3 to 66.2±4.4%. In >60 years group the EF was increased in male from 66.7±3.7 to 68.2±3.4 and in female from 63.6±4.9 to 65±3.4.

TABLE-7COMPARISON OF CIMT AT BASELINE AND AFTER 3 MONTHS

Age in years	CIMT, Baseline		CIMT, 3months	
	Male	Female	Male	Female
0-20	0	0	0	0
21-40	0.72± 0.08	0.70 ±0.08	0.69± 0.08	0.67± 0.09
41-60	0.76±0.06	0.76±0.06	0.73±0.06	0.74±0.05
>60	0.81± 0.06	0.75± 0.06	0.77 ±0.05	0.71 ±0.05

Table-7 shows comparison of CIMT at baseline and after 3 months with age and sex distribution. The average CIMT was decreased after 3 months compared with baseline values in both males and females and in all age groups. There are no patients in < 20 years age group.
In 21-40 years group the CIMT was decreased in male from 0.72±0.08mm to o.69±0.08mm and in female from 0.70±0.08mm to 0.67±0.09mm. In 41-60 years group CIMT was decreased in male from 0.76±0.06mm to 0.73±0.06mm and in female from 0.76±0.06mm to 0.74±0.05mm. In >60 years group CIMT was decreased in male from 0.81±0.06mm to 0.77±0.05mm and in female from 0.75±0.06mm to 0.71±0.05mm.

TABLE-8 COMPARISON OF HbA1c AT BASELINE AND AFTER 3 MONTHS

Age in years	HbA1c, Baseline		HbA1c , 3months	
	Male	Female	Male	Female
0-20	0	0	0	0
21-40	7.9± 0.6	8.1 ±1.3	7.1± 0.4	7.2± 0.6
41-60	8.2±1.6	7.9±0.6	7.3±0.6	7.3±0.5
>60	9.1± 1.5	8.0± 0.5	8.2 ±0.8	7.2 ±0.4

Table-8 shows comparison of HbA1c at baseline and after 3 months with age and sex distribution. The average HbA1c was decreased after 3 months compared with baseline values in both males and females and in all age groups. There are no patients in < 20 years age group.

In 21-40 years group the HbA1c was decreased in male from 7.9±0.6% to 7.1±0.4% and in female from 8.1±1.3% to 7.2±0.6%.In 41-60 years group HbA1c was decreased in male from 8.2±1.6% to 7.3±0.6% and in female from 7.9±0.6% to 7.3±0.5%.In >60 years group HbA1c decreased in male from 9.1±1.5% to 8.2±0.8% and in female from 8.0±0.5% to 7.2±0.4%.

TABLE-9 COMPARISON OF FBS AT BASELINE AND AFTER 3 MONTHS

Age in years	FBS, Baseline		FBS , 3months	
	Male	Female	Male	Female
0-20	0	0	0	0
21-40	147± 27.0	127 ±16.7	133± 5.9	112± 8.4
41-60	132±23.2	129±18.8	119±10.3	115±6.6
>60	151± 28.1	121± 20.5	136 ±7.3	101 ±10.3

Table-9 shows comparison of FBS at baseline and after 3 months with age and sex distribution. The average FBS was decreased after 3 months compared with baseline values in both males and females and in all age groups. There are no patients in < 20 years age group.

In 21-40 years group the FBS was decreased in male from 147±27mg/dl to 133±5.9mg/dl and in female from 127±16.7mg/dl to 112±8.4mg/dl. In 41-60 years group FBS was decreased in male from 132±23.2mg/dl to 119±10.3mg/dl and in female from 129±18.8mg/dl to 115±6.6mg/dl. In > 6o years group FBS was decreased in males from 151±28.1mg/dl to 136±7.3mg/dl and in females from 121±20.5mg/dl to 101±10.3mg/dl.

DISCUSSION

Out 85 patients were finally selected for study in which males were 65% and females were 35%. Maximum number of male and female were in the age group between 41-60 years indicates that males have high incidence of Type 2 Diabetes Mellitus. This may be due to various influences like dietary habits, stressful life,sedentary life style and indiscriminate use of diabetogenic drugs. There was no single incidence of young diabetic (< 20 years).

This was in contrast with the study done by Sagara et al(8), in which they have found more cases of diabetes in age > 70 years. In our case M: F is 1.8:1 but Sagara et al, has found the M: F as 1:1.2. This may be due to regional variation of incidence in different age and sex groups.

Obesity is one of the risk factor of Type 2 DM. Fukuda-Tsuru et al(9), have recently examined the effect of teneligliptin on obese related factors. The BMI plays an important role in the effect of drugs. In our study the BMI in male was 24.5±1.7 Kg/m^2 and in females was 21.8±1.7 Kg/m^2. The results after 3 months was not much changed with BMI in male was 24.2±1.4 Kg/m^2 and in females was 21.7±2 Kg/m^2 with p value 0.02 in male and 0.77 in female. Use of teneligliptin did not show significant difference in status of BMI both in males and females indicating that the drug has no significant effect on obesity and other measures may play important role in reducing the BMI.

In our study some patients are hypertensive (both male and female) but majority were normotensive (with or without drugs) during the study period. The average SBP in male was 136±9.5 mmHg which decreased to 132±6.4 mmHg after 3 months similarly in females average SBP was 126±7.0 mmHg which decreased to 122±5.4 mmHg with p-value 0.04 in male and 0.01 in female. This signifies the teneligliptin has some effect in lowering the blood pressure.

The potential vasoprotective effects of DPP-4 inhibitors (Teneligliptin) substrate such as stromal cell derived factor-1α, chemokine that promotes homing of endothelial progenitor cells to areas of cellular injury(10). The average DBP in males was 86±5.8 mmHg which decreased to 84±4.9 mmHg after 3 months and similarly in females average DBP was 74±4.6 mmHg which decreased to 72±4.3 mmHg with p-value 0.39 in male and 0.04 in female.

The effect of teneligliptin in improving vascular endothelial function has already been studied by R. Morishita & H. Nakagami and Sagara et al. They have established the improvement in the peripheral arterial tonometry and flow mediated dilatation of the artery. However in our study it needs exploration of the effect of teneligliptin in improving the endothelial function. The blood pressure lowering effect in both SBP and DBP was not significant though there was a slight decrease in both the groups.

The prevalence of Type 2 DM is increasing rapidly worldwide. Intensive glycemic control in Type 2 DM significantly reduced the primary composite outcome of microvascular events. DPP-4 inhibitor (Teneligliptin) is a novel class of antidiabetic drug that can help control fasting and post prandial glucose level by increasing the plasma concentration of incretin hormones. In our study the average FBS level in male was significantly decreased after 3 months from 136±21.7 mg/dl to 124±8.4 mg/dl and in female decreased from 127±15.9 mg/dl to 111±7.9 mg/dl with p-value < 0.01 in both male and female compared with the baseline values. The average 2hrPPBS level in male was significantly decreased after 3 months from 302±73.5 mg/dl to 196±21.7 mg/dl and in female decreased from 284±66.6 mg/dl to 187±17.3 mg/dl with p-value < 0.01 in both male and female compared with the baseline values.

Teneligliptin has also shown significant improvement in HbA1c both alone and with other antihyperglycemic drugs. In our study HbA1c was reduced after 3 months from 8.4±1.5% to 7.4±0.7% in male and from 8.0±0.7% to 7.3±0.5% in female with p-value < 0.01 in both male and female compared with the baseline values. This result is similar to that of R. Morishita & H. Nakagami. The incidence of adverse events (hypoglycaemia) was not detected in any case. Teneligliptin has also been shown to stabilise the blood glucose level throughout the day with a little variation in night.

The total cholesterol, LDL, TG has decreased significantly from baseline data in comparison to the results after 3 months indicating that teneligliptin has direct effect on improvement of lipid profile.HDL also showed rise after 3 months of teneligliptin treatment. This is similar to the study done by Sagara et al (8).

There was no much changes in the value of urinary microalbuminuria in both male and female at baseline value and that of after 3 months. In our study the average MIcral changed after 3 months from 19.8±2.2 µg/L to 19.6±1.7 µg/L in male and from 19.3±2.1 µg/L to 19.4±1.9µg/L in female with p-value 0.27 in male and 0.62 in female compared with the baseline values.

The CIMT showed reduction in value after 3 months in both male and female patients with p-value < 0.01. The CIMT in our study has decreased significantly in all age groups after treatment with teneligliptin for 3 months.

Results of teneligliptin on various echocardiographic parameters showed that there was significant improvement in cardiac function. In our study the average Left atrial diameter in male 37.9±3.0 mm changed to 38.8±2.8 mm and in female 38.4±2.8 mm changed to 39.2±2.7 mm after 3 months of teneligliptin therapy. The LV systolic diameter and LV diastolic diameter also showed improvement after 3 months. The above results are similar to the observation made by T. Hashikata & M. Yamaoka-Tojo. The E-wave velocity showed improvement in function after 3 months of therapy with p-value < 0.01 but there was no significant change in A-wave velocity.

The E/A ratio was improved from 0.86±0.08 in male to 0.82±0.05 and in female from 0.85±0.08 to 0.81±0.06 with p-value < 0.01 which is significant. The improvement in E/A ratio was much marked in the elderly patients than in young patients. There was increase in Deceleration time in both male and female from baseline study to the results after 3 months.

The Ejection fraction and the Cardiac output depends on the thickness of the arterial wall and contractility of the LV muscle mass. In our study there was increase in EF in all age groups both in male and female. This may be due to the fact that the teneligliptin significantly improves the endothelial function and improves the myocardial contractility. The results are in comparison with the study done by Gemma Pujadas et al(11).

Conclusion

DPP-4 inhibitors (Teneligliptin) are a novel class of antidiabetic drugs.

There was significant reduction in both fasting and post prandial blood glucose without any side effects and without any incidence of hypoglycaemia.Teneligliptin significantly improves the endothelial function resulting in decrease in CIMT and decrease in both systolic and diastolic blood pressure.

Teneligliptin has significant effect on the cardiac parameters as monitored by echocardiography.

There was increase in Left atrial diameter and decrease in both LV systolic diameter and LV diastolic diameter.Teneligliptin increases the LV Ejection Fraction and E-wave velocity.

There was no significant change in A-wave velocity but there was decrease in E/A ratio in both male and female by teneligliptin therapy.The Deceleration time of heart was decreased after using teneligliptin.

DPP-4 inhibitors like teneligliptin has significant improvement of cardiovascular functions however more number of patients with longer duration of treatment require to conclude the above result.

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