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ORIGINAL ARTICLE

Effect of Nebivolol on serum blood sugar and lipid profile in T2DM (Type 2 Diabetes Mellitus) patients with mild to moderate hypertension.

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ABSTRACT… Objective: To determine the effect of nebivolol on serum lipid profile and glycemic control in T2DM patients with mild to moderate hypertension. **Study Design:** Randomized Controlled Trial. **Setting:** Sheikh Zayed Medical College & Hospital Rahim Yar Khan. **Period:** November 2020 to January 2021. **Material & Methods:** T2DM patients with mild to moderate hypertension were randomly divided in to two groups to give nebivolol and atenolol. Blood pressure, fasting blood sugar and serum lipid profile were analyzed pre and post treatment by using SPSS 21. **Results:** After 12 weeks of treatment blood pressure was significantly reduced in both study group i.e nebivolol (SBP from 155±15 to 128±12 p=0.001 and DBP from 90±12.5 to 81±8.5 with p =0.004). Atenolol (SBP from 159±11.0 to 132±9.5 p=0.001 DBP from 92±8.0 to 79±9.5 p=0.002). However no significant changes were observed in SBP and DBP between two groups p=0.32 and p=0.72 respectively. No significant changes observed in glycemic control in both study groups. Nebivolol (HbA1c from 8.5±3.0 to 8.0 ±4.2 p=0.72) Atenolol (HbA1C from 8.2±4.2 to 8.5±3.5 p=0.72). However in comparison with nebivolol, atenolol significantly deteriorates blood sugar and HbA1c with p value 0.002 and 0.0016 respectively. There were no significant changes observed in terms of lipid profile in both study groups. However in comparison with nebivolol, atenolol deteriorates serum lipid profile with significant p values i.e total Cholesterol (0.004), triglycerides (0.006), LDL-Cholesterol (0.002) and HDL-Cholesterol (0.008). **Conclusion:** Nebivolol has a neutral effect on glycemic control and serum lipid profile in T2DM patients with mild to moderate hypertension.

Key words: Blood Pressure, Blood Sugar, Hypertension, Lipid Profile, Nebivolol.

INTRODUCTION

The number of diabetic's patients is increasing at an alarming rate all across globe. T2DM is one of the most prevalent forms (90%) of diabetes affecting one out of every 11 people. Diabetes mellitus is a mulifactorial disease and both traditional as well nontraditional risk factors play a vital role in its pathogenesis. Obesity, dyslipidemia, insulin resistance, subclinical inflammations are important cardiovascular risk factors in diabetic patients.[1]

The numbers of diabetic patients were increased drastically to 240 million worldwide in last 20 years. The numbers of diabetic patients are more in developing countries as compared to developed nations. In 2019, there were 19.4 million cases of diabetes in Pakistan. These cases will expect to reach 26.2 million in 2030. Pakistan also jumps from 8th to 4th position in world diabetes ranking in last two decades. There is strong need to control diabetes in developing countries in order to overcome social and economic burden.[2]

Diabetes has strong association with hypertension. A study conducted in T2DM revealed the prevalence of hypertension was about 40-60% patients. Similarly hypertensive patients are at increased risk to develop diabetes due to insulin resistance.[3] cardiovascular disease is twice common in diabetics as compared to non diabetics. A cardiovascular disease is foremost cause of death in diabetic patients. The co existence of obesity, insulin resistance,

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dyslipidemia, subclinical inflammation and endothelial dysfunction in T2DM and hypertensive patients are associated with increased risk of cardiovascular disease.[4]

Beta blockers are generally classified as cardio and non cardioselective. Nebivolol is classified as cardioselective beta blocker with vasodilating properties. In comparison with other beta blockers, nebivolol has a very good impact on hemodynamics parameters in hypertensive patients.[5] In comparison with other beta blockers, nebivolol improves central hemodynamics, erectile dysfunction, inflammation, oxidative stress, endothelial dysfunction and platelets function.[6]

Studies have shown that nebivolol has dual effects on glycemic control and lipid profile. Some studies demonstrated favorable effects while other studies did not show any significant effect on blood sugar and lipid profile in T2DM patients with hypertension.[7-9]

The main purpose of this study was to determine the effect of Nebivolol on serum lipid profile and glycemic control in T2DM patients with mild to moderate hypertension

MATERIAL & METHODS

In this 12 week randomized controlled trial 600 patients were recruited from medical unit, diabetic clinic and cardiology outdoor of Sheik Zayed Medical College/ Hospital Rahim Yar Khan from November 2020 to January 2021. Out of 600, 210 patients were enrolled in this study on the basis of following criteria. T2DM patients with mild to moderate hypertension according international society of hypertension criteria[10] and borderline serum lipid profile according to ATP III criteria.[11] Patients with history of smoking, cardiovascular disease, renal dysfunction, hepatic impairment, CNS disorders severe hypertension, high lipid profile and bradycardia were excluded from the study. Patients were also screened for other causes of dyslipidemia and diabetes by detailed clinical/drug history and medical records. An informed consent was taken from all participants. Study approval was got from the intuitional review board (IRB) of this institute (24-IRB/SZMC/SZH) dated 24-02-2020. Patients were allocated in to two groups by simple randomization. Patients in group A and group B were given tablet nebivolol and atenolol daily over a period of 03 months. The doses of both drugs were adjusted according to mean blood pressure. The desired blood pressure was less than 140/90mmHg. Patients were dropped from the study if hypertension was not controlled within 15 days of treatment.

Body weight was measured by digital weighing machine. Height was measured by microtoise. BMI was calculated as weight in kg/height in m^2. Blood pressure was measured by sphygmomanometer apparatus following standard protocols. A 5ml blood was collected through venipuncure after overnight fasting of 12 hours. Sample was used to analyze blood sugar and serum lipid profile. Blood sugar was analyzed by digital glucometer. Serum lipid profile was analyzed by automated analyzer (microlab 300)

Statistical Analysis

Data was analyzed by statistical package for social sciences (SPSS 2022) Numeric data was presented percentages as well as mean ± standard deviation. Continuous variables were analyzed by Kolomogorov-Smirnov test. A t-test was used to see any difference among baseline variables between two groups. Paired t-test was used to compare the difference within group and Mann-Whitney U-test between groups. A p-value < 0.05 was considered to be statistically significant.

RESULTS

Baseline study variable are shown in Table-I. There was no significant difference in anthropometric and metabolic parameters at start of research in both study groups. After 12 weeks of treatment blood pressure was significantly reduced in both study group i.e nebivolol (SBP from 155±15 to 128±12 p=0.001 and DBP from 90±12.5 to 81±8.5 with p =0.004). Atenolol (SBP from 159±11.0 to 132±9.5 p=0.001 DBP from 92±8.0 to 79±9.5 p=0.002). However no significant changes were observed in SBP and DBP between two groups p=0.32 and p=0.72 respectively. There were

no significant changes observed in glycemic control in both study group over a period of 12 weeks Nebivolol (BSF from 130±20 to 125±18.5 p=0.62 HbA1c from 8.5±3.0 to 8.0 ±4.2 p=0.72) Atenolol (BSF from 145±14.0 to 155±18.2 p=0.72 HbA1C from 8.2±4.2 to 8.5±3.5 p=0.72). However in comparison with nebivolol, atenolol significantly deteriorates blood sugar and HbA1c with p value 0.002 and 0.0016 respectively. There were no significant changes observed in terms of lipid profile in both study groups. Nebivolol (total cholesterol from 220±15.5 to 200±12.5 p=0.55 Triglycerides from 175±22.5 to 165±18.0 p=0.76 LDL-cholesterol from 145±15.5 to 142±12 p=0.82 HDL-cholesterol from 35±3.2 to 43±4.2 p=0.46). Atenolol (total cholesterol from 222±16.5 to 243±12.0 p=0.96 Triglycerides from 172±20.5 to 192±18.2 p=0.42 LDL-cholesterol from 142±17.5 to 152±22 p=0.35 HDL-cholesterol from 38±2.2 to 36±2.8 p=0.56). However in comparison with nebivolol, atenolol deteriorates serum lipid profile with significant p values total Cholesterol (0.004), triglycerides (0.006), LDL-Cholesterol (0.002) and HDL-Cholesterol (0.008) Table-II.

In our study both drugs showed excellent safety and tolerability profile. All patients are completed the study and no one dropped from study. No minor and major adverse effects were recorded in both study groups.

DISCUSSION

The main aim of our study was to investigate the outcome of nebivolol on serum blood sugar and lipid profile in T2DM hypertensive patients. Our study demonstrated that a nebivolol significantly reduced blood pressure but showed neutral or no effect on blood sugar and lipid profile in T2DM patients with hypertension. Some studies revealed that non vasodilating beta blockers (atenolol, metoprolol, propanolol) significantly deranged blood sugar and lipid profile as compared to nebivolol.[12-14] A review studies over a period of 20 years also yield similar results.[15]

Variables	Group A Nebivolol (n=110)	Group B Atenolol (n=110)	P-Value
Age(years)	35±14	38±11	0.72
Gender (M/F)	75/35	78/32	0.32
Body weight(kg)	76±9.0	78 ±10.5	0.97
BMI (Body Mass index kg/m^2)	27±4.5	26 ±3.2	0.096
Blood pressure Systolic (mmhg)	155±15	159±11.0	0.62
Blood pressure Diastolic (mmhg)	90±12.5	92±8.0	0.41
Blood sugar fasting(mg/dl)	130±20	145±14.0	0.031
HbA1c	8.5±3.0	8.2±4.2	0.22
Duration of diabetes(yrs)	6.2±2.8	5.8±3.2	0.88

Table-I. Baseline study variables (N= 220) t-test between two groups

Variables	Group A Nebivolol (n=110)		P-Value*	Group B Atenolol (n=110)		P-Value*	P-Value$^+$
	0 week	12 Week		0 week	12 Week		
SBP	155±15	128±12	0.001*	159±11.0	132± 9.5	0.002*	0.32
DBP	90±12.5	81± 8.5	0.004*	92±8.0	79±9.5	0.001*	0.72
Blood Sugar(f)	130±20	125±18.5	0.62	145±14.0	155± 18.2	0.72	0.002$^+$
HbA1C	8.5±3.0	8.0± 4.2	0.72	8.2±4.2	8.5±3.5	0.65	0.0016$^+$
Total Cholesterol	220±15.5	200±12.5	0.55	222±16.5	243±12.0	0.96	0.004$^+$
Triglycerides	175±22.5	165± 18.0	0.76	172±20.5	192±18.2	0.42	0.006$^+$
LDL-Cholesterol	145±15.5	142±12	0.82	142±17.5	152±22.5	0.35	0.002$^+$
HDL-Cholesterol	35±3.2	43±4.2	0.46	38±2.2	36±2.8	0.56	0.008$^+$

Table-II. Comparison of the changes from 0 to 12 weeks within and between groups
*** Significantly (p<0.05) comparison within groups**
$^+$ Significantly (p<0.05) comparison of changes of each variable between the two groups.

However in our study both nebivolol showed neutral effects while atenolol showed delirious effects on glycemic control and lipid profile.

A 06 months study revealed that nebivolol significantly improved blood sugar and lipid profile in comparison with atenolol.[16] Similar results were attained in another study in which nebivolol and carvedilol not only improve glycemic control and lipid profile but also reduce insulin resistance.[17] In another study nebivolol significantly improved deranged serum lipid profile in type 2 diabetic hypertensive patients.[18] A study demonstrated the renoprotective effects of nebivolol in addition to improve blood sugar and lipid profile over a period of 12 weeks.[19] Our results were inconsistent with above mentioned studies, although nebivolol demonstrated neural effect on serum lipid profile and serum sugar but when comparison was done between nebivolol and atenolol significantly deteriorates serum lipid profile and serum sugar.

In a systematic review of eight randomized trials and three observational studies. Marketou et al, 2017[20] revealed that nebivolol has beneficial or neutral effect on glycemic control and lipid metabolism. The duration of these studies were from four weeks to six months. This review suggests that nebivolol can be safely used in hypertensive patients with deranged serum lipid profile and blood sugar. Similar studies pointed out that in comparison with other beta blockers, nebivolol have excellent safety and tolerability profile with favorable effects on glycemic control and lipid profile.[21-22] In our study nebivolol has better safety and tolerability profile with neutral effect on glycemic control and lipid metabolism.

In addition various studies have demonstrated additional beneficial effect of nebivolol in comparison with conventional beta blockers such as low risk of adverse effects, better safety profile, better clinical outcome, reduced microalbuminuria, anti-inflammatory effects, anti-oxidant and anti-proliferative properties.[23-27]

These studies suggest that nebivolol can be safely used in hypertensive patients with deranged serum glucose and lipid profile. Nebivolol could also prevent diabetes related cardiovascular complications in hypertensive patients.

CONCLUSION

Nebivolol has a neutral effect on glycemic control and serum lipid profile in T2DM patients with mild to moderate hypertension.

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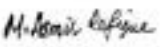
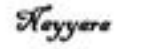
2	M. Aamir Rafique	Literature review, Data collector, collection of references and statistical work.	
3	Nayyara Tahir	Design of study, acquisition of data, analysis & interpretation of data, Drafting.	
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