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Effect of Antihypertensive Drugs on Blood Sugar Level

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ABSTRACT

There is highly co-incidence between hypertension and insulin resistance which is the important causative factor to develop diabetes mellitus (DM). Our study was prospective study in effect of beta-blockers, angiotensin-converting enzyme inhibitor (ACEI) and calcium channel blocker (CCB) on blood glucose level in patients newly diagnosed with hypertension and without diabetes in MVJ hospital, Bangalore. Fasting blood glucose and post prandial blood glucose measured for patients prescribed antihypertensive for four months. In a nutshell, we observed that Beta blockers worsen the glycemic condition and it increased blood glucose level, beside that it increased incident of impaired glucose tolerance. In case of calcium channel blocker and ACEIs, blood glucose level slightly increased and decreased respectively after two months.

Keywords: Antihypertensive, Fasting blood glucose, Post prandial blood glucose, Impaired glucose tolerance

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INTRODUCTION

There is highly prevalence of insulin resistance with hypertension, which is a major risk factor to develop type 2 diabetes mellitus.¹ Because hypertension and diabetes mellitus act as two big risk factors for cardiovascular disease, the risk gives a boost to increase when both synchronizes generally as part of metabolic syndrome. Various theories about the mechanisms of antihypertensive-induced glycemic defects have been postulated. Few of these theories have been confirmed and some are conflicting. In general, postulated mechanisms can be classified into four categories: effects on peripheral blood flow, effects on the insulin receptor, effects on the liver and effects on insulin release. Improved peripheral blood flow to skeletal muscles is thought to facilitate glucose disposal to the tissues. In this way, medications such as alpha-blockers, which promote peripheral vasodilation, may improve insulin sensitivity and glucose uptake.² All major guidelines in the relevant specialty suggest the use of either ACE inhibitors or ARBs as the first line treatment in hypertensive patients with diabetes when cost is not a concern.^{3, 4, 5} It has been found in many trials that the incidence of new onset diabetes is incomparably deflated in patients treated with ARBs, ACE inhibitors.⁶ Additionally, many hypertensive patients with diabetes require other antihypertensive treatments in combination with renin-angiotensin system blockers to achieve appropriate control of blood pressure, but until now there has been no consensus about the choice of treatments for combination therapy.

MATERIALS AND METHOD

The study was carried out in Medical College and Research hospital, Bangalore. It was an observational study. Cross-sectional study of beta-blockers (Atenolol), angiotensin-converting enzyme inhibitor (Lisinopril) and calcium channel blocker (Amlodipine) on blood glucose level in patients of hypertension without diabetes. Protocol was approved by Institutional Human Ethics Committee (IHEC-KCP1/2013-14). All patients newly diagnosed with hypertension and those who were taking Atenolol, Lisinopril and Amlodipine which are most commonly used antihypertensive drugs in this hospital were included in the study during the time period of September 2013 to December 2013. The assessed parameters of study were; gender distribution, age distribution of subjects and blood glucose levels following chronic antihypertensive therapy. Hypertensive patients were interviewed through a predesigned questionnaire. If the participants could not understand the questions due to language problems, interview was carried out in the language of the patient (Telugu, Kannada and Hindi). Participation was voluntary and verbal consent was acquired from each participant before administering the questionnaire. The study

was based on the basic principles defined in US 21 CFR part 312.20 and ICH (09 May 1997) 'Guidance for Good Clinical Practice' and the principles enunciated in the Declaration of Helsinki (Edinburgh, October2000). The questions were designed to elicit details of age, gender, address and phone number of patient, their life style in detail, blood pressure levels, drug history. Other than questionnaire, Physician's prescribing records, Patients medication profile, and Pathology laboratory test, used as source of data. All patients with hypertension without diabetes, receiving antihypertensive therapy were included in the study. Patients who weren't treated with antihypertensive agents, mentally challenged, unconscious, drug addicts, and those who unable to comply were contemplated as exclusion criteria. Blood samples of hypertensive patients for oral glucose tolerance test were collected by laboratory technician. The collected samples were sent to the in-house pathology lab and the reports were collected and interpreted by the investigators/clinician and as the hospital is government hospital, blood sugar tests were free of charge. According to WHO 1999, fasting blood glucose level between 110 to 125 mg/dl and 2 hr blood glucose level, after giving 75 gm glucose through oral route in between 140-200 mg/dl were considered as impaired glucose tolerance. The patients were diabetic when the fasting blood glucose level was found to be more than 125 mg/dl and 2 hr post prandial blood glucose was more than 200 mg/dl. Data was analyzed using Statistical Package for Social Sciences 16 (SPSS, Inc., Chicago, IL, USA). All values are expressed as mean \pm Standard error of mean (SEM).

RESULTS AND DISCUSSION

With a response rate of 100%, all 90 patients participated in the study. Ninety Patients were assessed to receive antihypertensive therapy during four month; most of participants were male (68.42 %)(Figure 1). Hypertension was found more prevalent in patients of age group between 41-60 years (62.21 %) composed of 46.66% males and 15.55% females. (Figure 2)

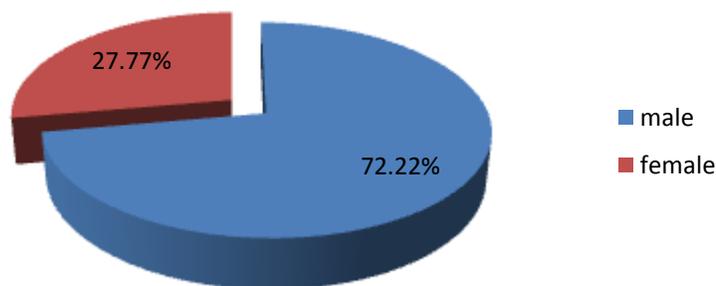


Figure 1. Gender distribution of subjects

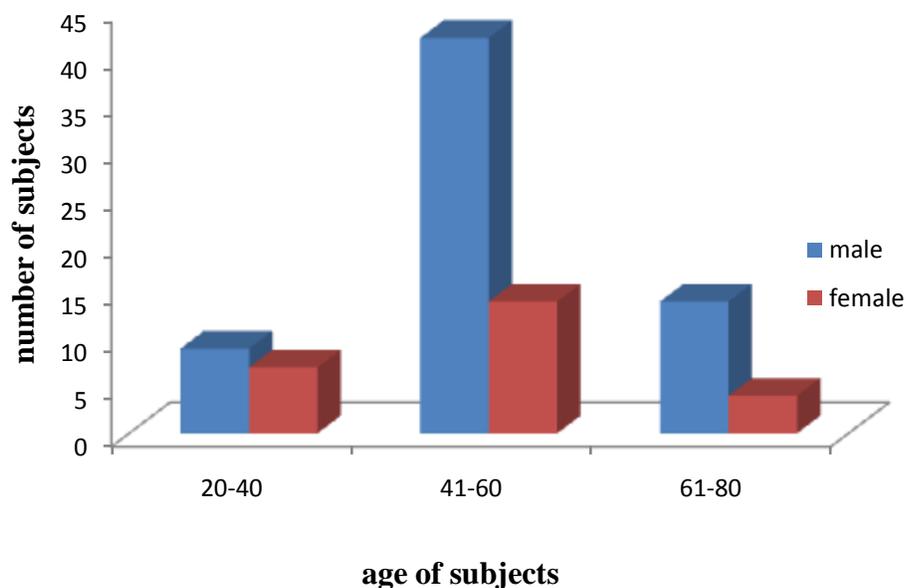


Figure 2. Age distribution of subjects

Out of 90 patients 32 patients prescribed calcium channel blocker (CCB), among these agents amlodipine was most commonly prescribed drug followed by nifedipine. In case of beta blocker drugs, atenolol was the most widely prescribed drug followed by metoprolol and carvedilol respectively and 40 patients prescribed by these agents. As compared to last two class of antihypertensive, fewer number of participants prescribed by angiotensin-converting enzyme inhibitors (ACEIs) (18 patients) and lisinopril was most common prescribed drug in this class of antihypertensive. Blood glucose level of patients taking beta blockers, calcium channel blockers and ACEIs as antihypertensive therapy was observed during each month. It was found that beta blockers produce impairment in postprandial glycemc control in time dependent manner. It was found that disturbance in blood glucose level increase on prolong therapy of beta blockers. After four months mean fasting blood glucose (FBG) was 117.19 mg/dl which was 91.84 mg/dl initially for patients prescribed beta blocker. It was believed that long-term treatment with β -blockers alters the first phase of insulin secretion, which plays an important role in controlling post load glycemia, so that more insulin is needed in the second phase⁷. Beta blockers also seem to attenuate insulin clearance in insulin-resistant patients^{7,8}, leading to >10% higher steady-state plasma insulin; the resulting hyper insulinemia could down regulate the insulin receptors and consequently, lower insulin sensitivity. In addition, β -blockers tend to increase total peripheral resistance, leading to a reduction in skeletal muscle blood flow and glucose uptake, which increases insulin resistance^{9,10,11,12,13}. In our study, blood glucose level for the patients prescribed beta blockers was not in normal range, this was clear even in first month of taking this drug and

as we can see in result in second, third and fourth month, the value significantly increased respectively.

We observed slight increase in mean FBG (94.56 mg/dl) after three months which was 92.08 mg/dl originally for participants on calcium channel blocker, mean FBG and Post Prandial (PP) were negligible in first two months for these patients. By contrast, mean FBG and PP slightly decreased on third and fourth month for patients taking ACEIs however there was no major disturbance of blood glucose level in first two months of taking drugs belong to this class of antihypertensive agent (Table 1). Several clinical studies have shown that the administration of ACE inhibitors results in increased insulin-stimulated glucose disposal in diabetics or hypertensive individuals.¹⁴ The mechanisms of this action were initially thought to be exclusively related to an improvement in capillary blood flow. ACE inhibitors increase bradykinin levels through the inhibition of kininase II, which causes vasodilation and augmented capillary blood flow¹⁵ and thereby increases the delivery of insulin and glucose to skeletal muscle^{16, 17}. Likewise, we have seen reduction in blood glucose level after three months in participant taking ACEIs. However change in blood glucose level is not significant before two months for participants prescribed this class of antihypertensive.

Table 1. Blood glucose levels (mg/dl) of patients receiving antihypertensive therapy

Category of drug	At first		First month		Second month		Third month		Fourth month	
	FBG	PP	FBG	PP	FBG	PP	FBG	PP	FBG	PP
Amlodipine	92.08 + 1.13	118+ 1.1	92.1+ 1.4	118+ 1.15	92.18+ 1.45	119.6+ 0.91	94.56+ 2.2	121.8+ 3.98	95.86+ 2.56	123.76+ 3.2
Atenolol	91.84 +1.15	119+ 1.65	93.19+ 3.54	124+ 4.34	98.54+ 8.11	131.6+ 9.23	113.1+ 6.14	137.1+ 11.67	117.1+ 5.15	149.43+ 12.17
Lisinopril	93.45 +1.12	118+ 0.98	93.29+ 1.1	124+ 0.96	93.27+ 1.12	124.1+ 1.5	92.86+ 1.19	123.1+ 1.45	91.32+ 1.87	121.22+ 4.97

Values were represented as mean \pm SEM. FBG = Fasting blood glucose level; PP=Blood glucose level after two hours glucose.

It is well known that renin-angiotensin system-related agents such as ACE inhibitors and ARBs have potential for preventing new-onset of DM^{17, 18}. However, the effect of CCBs on glucose tolerance and insulin sensitivity has not been clearly elucidated, particularly in the clinical setting. There are a few study demonstrated that azelnidipine administration rather than amlodipine administration significantly ameliorated glucose intolerance in non-diabetic patients with essential hypertension. In addition, the number of circulating hematopoietic progenitor cells was significantly higher after azelnidipine administration than those after amlodipine administration^{19, 20}. In our study, blood sample taken from participant prescribed calcium channel

blocker on first and second month of therapy did not show significant change in blood glucose level instead the blood glucose (postprandial and fasting blood glucose) level slightly rose in third and fourth month after blood sample analyzed for its sugar level.

During of four months study, we found that 12.5% incidence of impaired glucose tolerance (IGT) in the group of patients who were using beta blockers as antihypertensive therapy whereas incident of IGT was zero in patients taking calcium channel blocker and ACEIs.

CONCLUSION

Beta blockers worsen the glycemic condition and it increased blood glucose level. It may be the risk factor to develop diabetes mellitus type 2 on long term use as an antihypertensive therapy, in addition it increased incident of impaired glucose tolerance. In case of calcium channel blocker and ACEIs, blood glucose level slightly increased and decreased respectively after two months, beside that, negligible changes of blood glucose observed in first two months of taking this class of antihypertensive

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