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COMPARATIVE STUDY OF NEBIVOLOL VERSUS ATENOLOL IN THE TREATMENT OF MILD AND MODERATE ESSENTIAL HYPERTENSION.

V. SUSMITHA* AND Ch.V.NAGANJANI

Department of Pharmacology, KMC, Guntur, A.P, India

ABSTRACT

Nebivolol, β1 selective drug is a third generation β blocker with nitric oxide donating antiproliferative and antioxidant properties which are useful to maintain a proper metabolic profile compared to atenolol, a β1 selective drug most commonly used. A prospective randomized parallel double blind study was conducted in patients with essential hypertension. Group A received nebivolol and group B received atenolol for 12 weeks. Baseline investigations were carried out before and after the study. The data was statistically analysed using students 'T' test. Both atenolol and nebovolol showed significant reduction in both systolic blood pressure and diastolic blood pressure ($P<0.001$) after 12 weeks. Heart rate was significantly reduced ($P<0.001$) in the group that received atenolol. Blood sugar was significantly increased ($P<0.001$) in atenolol group after 12 weeks. It was concluded that nebivolol was better than atenolol in terms of improvement in blood sugar and heart rate.

KEY WORDS: Nebivolol, Atenolol, Hypertension, Blood sugar, Heart rate

V. SUSMITHA
Department of Pharmacology, KMC, Guntur, A.P, India

INTRODUCTION

Essential hypertension accounts to about 90% of all cases of hypertension. It has been accounted to 6% of deaths worldwide[1.] There are 31.5 million hypertensives in rural and 34 million in urban population and total of 70% of these would be stage I hypertension (SBP > 139mmHg DBP >85-89 mmHg) & stage I hypertension carries a significant cardiovascular risk and there is a need to reduce this blood pressure[2]. Hypertension is the major cause of stroke and other cardiovascular risk factors like CAD, MI, HF, renal insufficiency and dissecting aneurysm of aorta[3].The main aim of the treatment is to decrease cardiovascular risk[4] associated with HTN and risk from the coexisting cardiovascular risk factors[5] and improve the quality of life and encourage a healthy life style[6]. Over the past few years, the beta blockers have become some of the most widely prescribed drugs for the treatment of hypertension as well as for the other cardiovascular conditions. Now they are considered the first step antihypertensive drugs [7]. Nebivolol is a novel, potent, competitive and highly selective β1 blocker devoid of intrinsic sympathomimetic activity along with peripheral vasodilation and NO induced benefits such as antioxidant activity and reversal of endothelial dysfunction. Nebivolol facilitates better protection from the cardiovascular events[7,16]. Nebivolol has also been shown to improve the tolerability profile with respect to adverse effects such as bradycardia, blood sugar levels, and loss of libido, fatigue and insomnia[8].

MATERIALS AND METHODS

Patients both male and female aged 18 to 60 years attending medical outpatient department in the government general hospital were selected for the study. The protocol was approved and prior permission was also taken from the Institute of Ethics Committee. The study was a double blind randomized comparative parallel study of β1 blockers nebivolol and atenolol in the patients with mild to moderate hypertension classified according to JNC 7 classification[15]. The sample size was 100 patients. They were randomly allocated to two groups with 50 patients each. The criteria for selecting the patients included patients of either genders aged between 18 - 60 years with newly diagnosed hypertension, previously untreated, or who had responded poorly or were intolerable to previous treatments. Patients with mild (prehypertension 120-139/80-89 mmHg) to moderate(stage I 140-149/90-99 mmHg) classified according to JNC VII classification were selected by taking the average of three readings of blood pressure taken in sitting, standing and supine positions. The exclusion criteria included secondary hypertension or malignant hypertension, asthma or chronic obstructive diseases, bradycardia, atrial fibrillation or recurrent tachyarrythmias, insulin dependent diabetes, history of sensitivity or serious adverse reactions to β blockers, myocardial infarction or cerebrovascular accidents in the last 6 months, severe renal or hepatic diseases, pregnancy or nursing, any concurrent conditions like alcohol or drug abuse, disabling or terminal disease, personality or mental disorders, concurrent therapy with medications like tricyclic antidepressants, MAO inhibitors, corticosteroids, NSAIDS, and hormonal contraceptives.

A written informed consent was obtained from all the patients after a detailed explanation prior to enrolment. Tab. nebivolol 5 mg once daily was given to one group of patients and tab. atenolol 50 mg once daily was given to another study group before breakfast. Drugs used were identical in appearance and taste. The patients were treated for a period of 12 weeks. The patients were followed for every 2 weeks throughout the study period. Compliance regarding the medication consumption was assessed by the pill count method where 18 pills were given at each visit every 2 weeks. The patient has to show the remaining four pills. Laboratory investigations done were complete blood picture, blood glucose, blood urea, serum creatinine, serum cholesterol, serum electrolytes, and urine analysis: albumin, sugar, microscopy, chest x ray, and electrocardiogram. The blood pressure was measured in sitting, standing and supine

positions after taking prior precautions like no caffeine for the preceding one hour, no smoking for the preceding 15 minutes, no exogenous adrenergic stimulants, no urinary bladder distension and should be quiet and relaxed before the measurement. The sphygmomanometer used was mercury sphygmomanometer with cuff size 12-13 cm x 35 cm. The cuff was applied firmly so as to cover 75-80% circumference of the arm and 2/3rd length of the bare arm. All the measurements were made by the same member in the same room with the same BP apparatus and at the same time of day, preferably in the morning. The right arm was always employed for the recording. Sitting BP was taken after the patient has rested for 5 minutes, Standing BP was taken after standing for 2 minutes and supine was taken after lying supine for 2 minutes. The average of three readings were taken before starting trial and continued likewise. The method of measuring the blood pressure involved tying the cuff to the arm firmly. The cuff was inflated till the radial pulse is not palpable. The cuff was reinflated to 30 mm Hg higher than the pressure at which the radial pulse is not felt. The diaphragm of the stethoscope was place over the brachial artery. The cuff was placed at the level of the heart. The cuff was deflated at the rate of 2-3 mmHg/sec while auscultating the Koratkoff sounds. Koratkoff sounds phase I (appearance of sounds) was regarded as systolic pressure and phase IV (disappearance of sounds) was regarded as diastolic pressure. The blood glucose levels were estimated by drawing the blood sample under aseptic conditions in fasting state. Estimation was done using a semiauto analyser at the central laboratory GGH, by using glucose oxidase and peroxidase method to estimate fasting blood glucose levels. The patients were followed up for 12 weeks at 2 weeks interval. At each visit the blood pressure, heart rate and blood sugar level were estimated.

RESULTS AND DISCUSSION

The patients who completed the study out of 100 are 92.Eight patients lost follow up. Out of 92 patients 62% were males and the remaining 38% were females. 75% of the total patients were in the age group 31-50 years with mean age of 49.2±1.3 years in atenolol group and 46.3±1.2 years in nebivolol group. There was significant (P<0.001) reduction in systolic BP, diastolic BP, and heart rate in both the study groups as compared to the baseline recordings (Table 1).There was no change in the blood sugar level in the patients treated with nebivolol and there was a significant (P<0.001) increase in the blood glucose levels in the group treated with atenolol at the end of the study period. The mean changes in the heart rate and blood sugar from the baseline were significant(P<0.001) in atenolol group as compared to the nebivolol group(Table 2).Both the drugs were equally tolerated and common adverse effects like headache, bradycardia, dizziness, nausea and vomiting were seen.. Statistical analysis was done using paired “t” test (Table 1) and unpaired “t” test (Table 2) with confidence interval of 95%. P<0.05 was considered significant statistically.

Table 1

Comparison of effects of atenolol and nebivolol on blood pressure, heart rate and blood sugar in the patients of essential hypertension

Parameter	Group A - Atenolol 50 mg/day		Group B - Nebivolol 5 mg/day	
	Baseline	12 weeks	Baseline	12 weeks
SBP	141.28±1.2	132.92±8.33	142.68±1.3	127.92±8.3
DBP	89.48±1.73	82.2±3.95	90.2±1.62	81.2±4.41
HR	84.2±4	68±2	82.2±6	72±7
BS(mg/dl)	88.6±1.7	105.8±1.5	87.6±3.2	88.4±1.2

SBP – Systolic blood pressure, DBP – Diastolic blood pressure, HR – Heart rate, BS – Blood sugar

Table 2
Comparison of mean differences in blood pressure, heart rate & blood sugar in patients of essential hypertension treated with atenolol and nebivolol

parameters	Mean differences from baseline at 12 weeks	
	Atenolol	Nebivolol
SBP	8.8±4.03	14.52±2.68
DBP	6.88±2.21	8.92±3.73
HR	-16.8±0.2	-10.8±0.7
BS(mg/dl)	17.4±1.5	1.02±1.2

SBP - Systolic blood pressure, DBP – Diastolic blood pressure, HR – Heart rate, BS – Blood sugar

The principal aim of the present study was to establish the efficacy, tolerability and safety of nebivolol in comparison with the well-established cardioselective beta-blocker atenolol in the treatment of essential hypertension. Both active drugs were well tolerated. Heart rate is lowered similarly by nebivolol and atenolol. Nebivolol possesses several properties which are potentially attractive in the treatment of hypertension. It acts partly through the L-arginine/nitric oxide pathway, that has vasodilating effects[10,11]. In the present study, 100 patients with mild and moderate hypertension were randomized to two groups and were given the study drugs one for each group. The mean reduction of SBP & DBP in the nebivolol group is better than that in atenolol group. The heart rate reduction is less with the nebivolol group because nebivolol though decreases the sympathetic tone but causes less vagal activity compared to atenolol[12, 13]. The blood sugar levels are increased in the group that received atenolol because atenolol will decrease insulin sensitivity while nebivolol, with it's vasodilating properties will increase insulin sensitivity[14] .

CONCLUSION

Essential hypertension represents a global health public challenge. The impact on highly vascular organs like kidneys is highly devastating. Beta blockers are considered as safe and the first line drugs in the management of hypertension. According to National Institute for Health and Clinical Excellence (NICE) and the British Hypertension Society (BHS) recommended that "*β blockers should no longer be used as first line drugs for the treatment of uncomplicated hypertension."*This recommendation is based on the evidence of various studies of atenolol alone or with diuretics, increases the risk of new onset diabetes mellitus than other medicines such as ACE Inhibitors, angiotensin receptor blockers and calcium channel blockers, due to its adverse effects on carbohydrate and lipid metabolism. Now beta blockers are third or fourth choice drugs in the management of hypertension[9]. The result of this study showed that both atenolol and nebivolol showed similar potency in decreasing the blood pressure. The reduction in heart rate and increase in blood sugar levels is more with atenolol compared to nebivolol. Nebivolol should be a valuable addition to the antihypertensive therapeutic repertoire for the patients receiving β blockers, especially with cardiac impairment and diabetes.

CONFLICT OF INTEREST

Conflict of interest declared none

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