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A STUDY OF PULMONARY PROFILE OF HYPERTENSIVE PATIENTS – COMPARISON OF ATENOLOL VS AMLODIPINE

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Abstract : Two groups of drugs commonly used for the treatment of hypertension are atenolol and amlodipine. These drugs are reported to have conflicting changes on pulmonary responses. In order to study the effect of hypertension and antihypertensive treatment on pulmonary responses, 40 patients with essential hypertension having diastolic blood pressure between 90–114 mmHg on three consecutive weekly visits were taken. Pulmonary responses were tested at the end of 2 weeks of placebo washout period and then at the end of 6 weeks of treatment with either atenolol or amodipine. Using a computerized autospiror along with the weekly recordings of heart rate and blood pressure, the various pulmonary and cardiac parameters were taken. Analysis of the result showed that atenolol treatment resulted in significant decline of forced vital capacity (FVC), % forced vital capacity (%FVC), and forced expiratory volume in first second (FEV1) whereas amlodipine did not show any significant change on pulmonary parameters.

Key words : hypertension betablockers calcium channel blockers

INTRODUCTION

Recent years have brought to light increasing evidence of hypertension in the pathogenesis of cardio vascular diseases and stroke (1, 2). According to 5th Joint National Committee on detection, evaluation and treatment of hypertension, it is defined as blood pressure equal to or greater than 140/90 mmHg recorded at more than two occasions (3). Percentage prevalence of hypertensions increases with age (4). The hypertensives when compared to normotensives, develop twice as much peripheral arterial disease, three times as much as coronary artery disease, four times congestive heart failure and seven times as much stroke (6). Early and appropriate treatment can reduce the risk related to these diseases. Atenolol and amlodipine are the two groups of drugs commonly in use for the treatment of hypertension. Pulmonary responses of atenolol and amlodipine studied in the past, give a conflicting view. Few studies have shown respiratory dipressant effect of atenolol specially in hypertensive asthmatics. Whereas others have reported no significant

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impairment of respiratory function. Regarding amlodipine the reports have pointed towards bronchodilation and its effectiveness in inducing protection against cold induced bronchoconstiction. As studies related to these drugs on pulmonary system are few and give inconsistent view, an attempt was made to ascertain pulmonary responses in hypertension to these drugs by conducting such experimental study.

METHODS

Selection of subjects

Forty hypertensive patients of both sexes in the age group 30–60 yrs, having diastolic blood pressure between 90–114 mg Hg on three consecutive weekly visits were included in this study. The selection criteria was on the classification of 5th National Committee on detection evaluation and treatment of hypertension. Subjects with chronic obstuctive lung diseases, myocardial infarction, diabetes mellitus, smokers and alcoholics were excluded from the study. All subjects were taken from Medical OPD of Guru Teg Bahadur Hospital. Twenty healthy normotensive age matched adults were taken up as controls. The subjects were briefed about the study and the consent was taken from all the subjects before the start of study.

Methodology

All who were already worked out to be as essential hypertensives were put on 2 weeks of placebo washout period which was taken as pretreatment period and then they were assigned in a randomized double blind manner to receive either atenolol or amlodipine for a period of 6 weeks which was taken as post treatment period. The duration taken was according to standard protocol. Pulmonary responses were performed on both controls as well as hypertensive subjects. In case of hypertensive subjects testing was done at the end of placebo wash out period and then at the end of 6 weeks of treatment with the two drugs. Pulmonary function testing was done with computerized H–1498 Autospiror. Parameters measured included forced vital capacity (FCV), percentage forced vital capacity (%FVC), forced expiratory volume in first second (FEV1), peak flow (PF) and peak flow at 75%. Heart rate measurement was done by examining the pulse and the blood pressure was taken with help of Sphygmomanometer.

Statistical analysis was done using analysis of variance (ANOVA) with Turkey test at 5% level of significance and paired t-test at 1% level of significance.

RESULTS

Table I A and B shows the values of mean resting systolic blood pressure (SBP) and diastolic blood pressure (DBP) readings in hypertensive receiving atenolol and amolodipine therapy respectively. It can be seen that there was a significant decline in the values of both systolic and diastolic blood pressure following treatment with atenolol as well as amlodipine. Comparison of the values of pulmonary parameters between controls and hypertensives receiving placebo is shown in Table IIA. Normotensives controls had significantly higher values of FVC, FEV1 and %FVC. Atenolol treatement resulted in the

TABLE IA : Cardiovascular parameters in pretreatment (Placebo) and post treatment group of atenolol.

Parameters	*Pretreatment (Mean ± SD)*	*Posttreatment (Mean ± SD)*	*P value*
Heart rate/(min.)	83.40±6.52	78.75±6.68	*<0.001
Systolic B.P. (mm Hg)	156.1±18.60	130.00±10.07	*<0.0001
Diastolic B.P. (mm Hg)	95.70±6.39	83.40±4.98	*<0.0001

*Significant P-value <0.01

TABLE IB : Cardiovascular parameters in pretreatment (Placebo) and posttreatment group of amlodipine.

Parameters	*Pretreatment (mean±SD)*	*Posttreatment (mean±SD)*	*P value*
Heart rate/(min.)	87.70±8.24	83.70±4.98	0.088
Systolic B.P. (mm Hg)	154.50±12.76	130.30±8.41	*<0.0001
Diastolic B.P. (mm Hg)	96.90±5.36	81.70±4.86	*<0.0001

*Singificant P value <0.01

TABLE IIA : Pulmonary parameter in control (normotensive) and pretreatment (Placebo) group of atenolol and amlodipine.

Sl. No.	*Parameter*	*Control (Mean±SD)*	*Pretreatment atenolol (Mean±SD)*	*Control (Mean±SD)*	*Pretreatment amlodipine (Mean±SD)*	*P value*
1.	FVC (ml)	*2945.50 ±798.4	2706.00 ±970.49	2945 ± 798.46	20.24.50 ± 642.80	*0.0021
2.	FEV1 (ml)	**2128.60 ±749.80	1801.00 ±769.51	2182.60 ± 749.80	1517 ± 558	*0.0145
3.	%FVC	84.98 ±15.85	85.45 ± 15.69	84.98 ± 15.85	73.07 ± 17.07	*0.0298
4.	%FEV1	75.42 ±9.63	***67.46 ± 12.02	75.42 ± 9.63	72.57 ± 14.71	0.1260
5.	PF (Lit/Sec)	4.47 ±2.03	3.69 ± 1.93	4.47 ± 2.03	6.07 ± 11.43	0.5332
6.	P75 (Lit/Sec)	4.04 ±2.11	3.14 ± 1.72	4.04 ± 2.11	3.28 ± 1.58	0.2498

*Significant P value <0.05

TABLE IIB : Pulmonary parameter in pretreatment (Placebo) and posttreatment group of atenolol.

Parameter	*Pretreatment (Mean ± SD)*	*Posttreatment (Mean ± SD)*	*P value*
FVC (ml)	2706.00±970.49	2285.50±769.95	*<0.001
FEV1 (ml)	1801±769.51	1625±705.79	*0.021
%FVC	85.45±15.69	70.46±13.64	*<0.001
%FEV1	67.46±12.02	62.76±18.65	0.145
PF (Lit/Sec.)	3.69±1.93	3.16±2.11	0.016
P75 (Lit/Sec)	3.14±1.72	2.63±2.08	0.019

*Significant P value <0.01)

TABLE IIC : Pulmonary parameter in pretreatment (Placebo) and post treatment group of amlodipine.

Parameter	*Pretreatment (Mean±SD)*	*Posttreatment (Mean±SD)*	*P value*
FVC (ml)	2024.50±642.80	2155.50±654.01	0.161
FEV1 (ml)	1517±558	1612±615.94	0.082
%FVC	73.07±17.07	78.60±16.98	0.126
%FEV1	72.57±14.71	78.21±11.75	0.093
PF (Lit/Sec)	6.07±11.43	3.91±2.11	0.378
P75 (Lit/Sec)	3.28±11.58	3.66±1.74	0.152

*Singnificant P value <0.01

significant decline in values of FVC, FEV1 and % FVC (Table IIB) whereas following amlodipine treatment, the values of all pulmonary parameters showed a trend of improvement but this rise was not statistically significant (Table IIC).

DISCUSSION

The study has attempted to find out the effect of hypertension and antihypertensive treatment on pulmonary responses. It has shown that hypertension *per se* has deleterious effects on ventilatory functions as FVC, FEV1, %PVC values were significantly lower in hypertensive on placebo as compared to normotensive controls (Table IIA). The exact mechanism of how raised blood pressure suppresses ventilatory functions is not known. It might be due to various interactions between vasomotor and respiratory centres either through peripheral sinoaortic mechanism or chemosensitive one in the centre, during hypertensive millieu. The result also included the effect of both atenolol as well as amlodipine in controlling both SBP and DBP of hypertensive (Table IA and IB). These findings are consistent with previous comparison of atenolol and amlodipine by Bruijn et al (7). Mechanism of action of beta blockers is not known but they may reduce BP through their effect of reducing cardiac output and inhibition of renin secretion (8). The antihypertensive effect of amlodipine is due to its relaxant effect on cardiac and vascular smooth muscles, mainly by blockade of L–type 'voltage operated' calcium channels (9, 10).

Regarding pulmonary responses atenolol treatment resulted in significant decline in the values of parameters i.e. FVC, FEV1, %FVC reported also by Heel et al (11), who noted that cardioselective betablockers like atenolol cause impairment of respiratory functions. Lawrence et al (12), Doshan et al (13) and Dorow et al (14) reported similar findings in hypertensive asthmatics. Desche et al (15) found atenolol had similar respiratory effect as that of propranolol. Whereas Fogari et al (16) and Krauss et al (17) reported no adverse respiratory effect of atenolol. Bronchoconstricting effect of atenolol may be due to B2 receptor blocking property as cardio-selectivity of atenolol is relative rather than absolute. Role of blockade of B1 receptor in airway smooth muscle is still controversial though it is well accepted fact that B1 receptor exist in

airway smooth muscle along with B2 though later predominate (18).

An increase in values of all respiratory parameters was noticed in patients receiving amlodipine (Table IIC). Löfdhal et al (18) stated that calcium channel blockers through their smooth muscle relaxant action are safe for the treatment of hypertensive asthmatics. It is well known that calcium plays a crucial role in smooth muscle contraction, degranulation of mast cells and sercetion of mucus from epithelial cells of respiratory tract (20). Therefore, calcium channel blockade might also influence the airway functions, the manner in which it would be useful for the asthmatics. Therefore, our study has shown an inclination of atenolol causing impairment of respiratory functions whereas amlodipine was shown to be having no adverse effect on the airways. Hence the use of later drugs i.e. calcium channel blockers in hypertensive or hypertensive asthmatics would be more beneficial and a better choiced regimen.

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