

Variations of Lung Function Status in Hypertension and Antihypertensive Medication

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Abstract

Introduction: Essential hypertension is associated with altered pulmonary function. Antihypertensive medication and lung function are also associated. Amlodipine (calcium channel blocker) and Atenolol (beta blocker) are commonly used antihypertensive drugs.

Objective: To evaluate the effects of antihypertensive drugs on lung function status in patients with essential hypertension.

Materials and Methods: This prospective observational study was carried out in the Department of Physiology of Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbag, Dhaka, from July 2012 to June 2013 on 100 newly diagnosed essential hypertensive patients. Based on prescribed treatment, these study subjects were divided into two groups - B1 and B2. B1 included 50 patients who received amlodipine 5mg daily and B2 included 50 patients who received atenolol 50mg daily. Lung function tests were done in both B1 and B2 groups before taking medication, after 3 months of medication and after 6 months of medication. For assessing lung function status, Forced Vital Capacity (FVC), Forced Expiratory Volume in 1st second (FEV₁) and Peak Expiratory Flow Rate (PEFR) were measured with a computer based Spirometer. Age, sex and BMI matched 50 apparently healthy normotensive subjects were also studied as control (group A). Data were compared among subjects of different groups. For statistical analysis independent sample 't' test and paired sample 't' test were performed.

Results: Mean FVC, FEV₁ and PEFR were significantly lower in newly diagnosed hypertensive patients in comparison with that of healthy normotensive subjects. Mean FVC, FEV₁ and PEFR were found significantly higher in the group taking amlodipine for 6 months when compared to newly diagnosed hypertensive patients but lower than those of controls. In addition mean FVC and FEV₁ were found significantly lower in the group taking atenolol for 6 months when compared to newly diagnosed hypertensive patients and those of controls.

Conclusion: Reduced lung function occurs in newly diagnosed essential hypertensive patients which improve by treatment with amlodipine but decreases after treatment with atenolol.

Key-words: Newly diagnosed essential hypertensive patients, lung function status, antihypertensive drugs.

Introduction

Hypertension is an increasingly important public health challenge throughout the world among the cardiovascular diseases¹. Essential hypertension is the most common form, accounts for 90-95% of all causes of hypertension². Although several studies observed that high blood pressure has link to multiple clinical outcomes including cardiac, cerebrovascular, renal and eye diseases³, a few studies found an association between lung function and hypertension⁴⁻¹⁰. All antihypertensive drugs lower high blood pressure, though drugs from different classes differ in their mechanisms of action. Therefore changes in pulmonary function with chronic

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antihypertensive drugs therapy would be expected to differ depending on the site and mechanism of action of the drugs. Several studies suggested that Calcium channel blockers have no adverse effects on resting airway function in patients with asthma^{11,12}. Some studies revealed no significant bronchodilatation 45 minutes after Calcium channel blocker administration in asymptomatic asthma patients¹³. On the other hand, another study observed improvement of airway resistance, peak expiratory flow rates and FEV₁ after one and two hours of Calcium channel blocker administration in patients with bronchial asthma¹⁴. Few studies revealed that relatively cardioselective agents has been considered contraindicated in patients with asthma or COPD, as it may produce bronchoconstriction and thereby worsen respiratory flows and symptoms in these patients^{15,16}. On the other hand, Two systematic reviews of randomized controlled trials revealed that the cardioselective beta blocker has no adverse effects on lung functions in patients with asthma or COPD^{17,18}.

Although several investigators observed the effect of amlodipine and atenolol on lung function separately no report compared the effect of amlodipine and atenolol on lung function in newly diagnosed hypertensive patients. Therefore this study aimed to evaluate the lung function in untreated hypertensive patients and compare the effect of amlodipine and atenolol on lung function.

Materials and Methods

This prospective observational study was carried out in the Department of Physiology of Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbag, Dhaka, from July 2012 to June 2013. Hundred newly diagnosed hypertensive patients aged 30-55 years were selected as study group. Age, sex and BMI matched 50 apparently healthy normotensive subjects were also studied as control (group A). Based on treatment, these study subjects were divided into two groups; B1 and B2. B1 included 50 patients who received amlodipine 5mg daily and B2 included 50 patients who received atenolol 50mg daily. Lung function tests were done in both B1 and B2 groups before taking medication, after 3 months of medication and after 6 months of medication. Basing on the duration of the treatment group B1 was named as B1_a (newly diagnosed hyper-

tensive patients before treatment), B1_b (after 3 months of medication with amlodipine) and B1_c (after 6 months of medication with amlodipine). Similarly subjects of group B2 were named as B2_a (newly diagnosed hypertensive patients before treatment), B2_b (after 3 months of medication with atenolol) and B2_c (after 6 months of medication with atenolol). These patients were selected from the Out Patient Department of Cardiology, BSMMU.

Subjects with history of acute or chronic lung and chest wall disease e.g. pneumonia, tuberculosis, asthma, COPD, malignancy etc, history of coronary heart disease, diabetes mellitus, alcohol/tobacco users and smokers were excluded from the study. After random selection of the subjects a detail personal, medical, family, socioeconomic, occupational and drug history were recorded in a preformed questionnaire and thorough physical examinations were done and documented. For the assessment of lung function FVC, FEV₁ and PEFR were measured with a computer based Spirometer.

Then all the patients were requested to attend the Department of Physiology of BSMMU, again after 3 months and after 6 months of antihypertensive medication, to have the assessment of the above mentioned study variables. For statistical analysis independent sample 't' test and paired sample 't' test were performed by using SPSS (Statistical Package for Social Sciences) for windows version 16.0 as applicable. P value <0.05 was accepted as level of significance.

Results

The mean of the percentages of predicted values of FVC, FEV₁ and PEFR were significantly lower in group B1_a, B1_b and B1_c respectively than those of control. In addition, the mean percentage of predicted values of FVC, FEV₁ and PEFR were significantly increased in group B1_b and B1_c in comparison to their corresponding base line values of group B1_a (Table-I).

Table-I: Percentages of predicted values of FVC, FEV₁ and PEFR in different groups (n=100)

Parameters	Group A (n=50)	B1 _a (n=50)	B1 _b	B1 _c
FVC (L)	88.9±0.827	73.9±1.037	76.28±0.960	78.12±0.
FEV ₁ (L)	90.62±0.772	79.38±1.157	81.08±1.151	83.3±1.0
PEFR (L/s)	78.38±1.373	72.96±1.289	73.5±1.235	75.6±1.3

Statistical analysis

Groups	p value		
	FVC	FEV ₁	PEFR
A vs B1 _a ^φ	0.000***	0.000***	0.005**
A vs B1 _b ^φ	0.000***	0.000***	0.010*
A vs B1 _c ^φ	0.000***	0.000***	0.150ns
B1 _a vs B1 _b ^Ω	0.000***	0.016*	0.465ns
B1 _b vs B1 _c ^Ω	0.000***	0.000***	0.055ns
B1 _a vs B1 _c ^Ω	0.000***	0.000***	0.033*

Data were expressed as mean±SD.

φ = independent sample 't' test, Ω = Paired sample 't' test

Group A: Apparently healthy subjects (control group)

Group B1_a: Newly diagnosed hypertensive patients before treatment

Group B1_b: After 3 month's treatment with amlodipine

Group B1_c: After 6 month's treatment with amlodipine

***:Significant (p≤0.001), **:Significant (p≤0.01), *:Significant (p≤0.05)

Ns:Nonsignificant, n:Number

The mean of the percentages of predicted values of FVC, FEV₁ and PEFR were significantly lower in group B2_a, B2_b and B2_c respectively than those of control. In addition, the mean percentage of predicted values of FVC and FEV₁ were significantly decreased in group B2_b and B2_c in comparison to their corresponding base line value B1_a. But the mean percentage of predicted value of PEFR was nonsignificantly increased in group B2_b and B2_c in comparison to their corresponding base line values of group B2_a (Table-II).

Table-II: Percentages of predicted values of FVC, FEV₁ and PEFR in different groups (n=100)

Parameters	A (n=50)	B2 _a (n=50)	B2 _b	B2 _c
FVC (L)	88.9±0.827	74.72±0.786	72.84±0.997	71.42±1.028
FEV1 (L)	90.62±0.772	79.04±1.079	76.88±1.248	75.62±1.298
PEFR (L/s)	78.38±1.373	74.36±1.444	75.28±1.353	76.6±1.302

Statistical analysis

Groups	p value		
	FVC	FEV ₁	PEFR
A vs B2 _a ^φ	0.000***	0.000***	0.046*
A vs B2 _b ^φ	0.000***	0.000***	0.111ns
A vs B2 _c ^φ	0.000***	0.000***	0.349ns
B2 _a vs B2 _b ^Ω	0.000***	0.000***	0.317ns
B2 _b vs B2 _c ^Ω	0.000***	0.042*	0.154ns
B2 _a vs B2 _c ^Ω	0.000***	0.000***	0.035*

Data were expressed as mean±SD.

φ = independent sample 't' test, Ω = Paired sample 't' test

Group A: Apparently healthy subjects (control group)

Group B2_a: Newly diagnosed hypertensive patients before treatment

Group B2_b: After 3 month's treatment with atenolol

Group B2_c: After 6 month's treatment with atenolol

***:Significant (p≤0.001), **:Significant (p≤0.01), *:Significant (p≤0.05)

Ns:Nonsignificant, n:Number

Discussion

In the present study, values of the lung function parameters FVC (L) 88.9±0.827, FEV₁ (L) 90.62±0.772 and PEFR (L/s) 78.38±1.373 in healthy normotensive group were almost similar with the study of Selby et al⁵. The mean of the percentages of predicted values of FVC (73.9±1.037, 74.72±0.786), FEV₁ (79.38±1.157, 79.04±1.079) and PEFR (72.96±1.289, 74.36±1.444) were significantly (p≤0.001) lower in newly diagnosed hypertensive patients than those of apparently healthy subjects. Lingarde and Schroeder et al^{19,20} found significantly (p≤0.01) lower FVC in hypertensive patients. Again in this study the lower values of the mean percentages of predicted values of FVC and FEV₁ were significantly (p≤0.01) improved after 3 months (FVC-76.28±0.960, FEV₁-81.08±1.151) and 6 months (FVC-78.12±0.970, FEV₁-83.3±1.041) treatment with amlodipine. The lower values of these two parameters were further reduced after 3 months (FVC-72.84±0.997, FEV₁-76.88±1.248) and 6 months (FVC-71.42±1.028, FEV₁-75.62±1.298) treatment with atenolol. Van Zyl and Lawrence et al have revealed lower FVC (72.49) and FEV₁ (76.26) in hypertensive patients after using cardioselective beta blocker^{16,21}. In addition the lower values of PEFR was non-significantly improved after 3 months and significantly improved after 6 months treatment with amlodipine and atenolol.

Researchers suggested that the decrement of different ventilatory variables in essential hypertension may be associated with early left ventricular hypertrophy and moderately left ventricular dysfunction which may increase left atrial pressure. As a consequence, an elevation of pulmonary arterial pressure and interstitial oedema in the lung leading to decreased compliance of the lung and mild restrictive disease^{4,5,10}.

Different studies suggested various mechanisms for the improvement of lung function status in hypertensive patients after treatment with amlodipine. Calcium causes smooth muscle contraction, degranulation of mast cells and secretion of mucous from different cells in the airway epithelium²². Calcium channel blockers are vasodilators and in hypertension it inhibits calcium influx into arterial smooth muscle cells²³. It has been suggested that Calcium channel blocker may reduce bronchoconstriction by inhibition of contraction of bronchial smooth muscle and release of mediators from mast cells or polymorphonuclear neutrophils in asthma patients¹³.

Different researchers suggested various mechanisms for the decrement of lung function status in hypertensive patients after treatment with atenolol. In the respiratory system, Beta 2 adrenergic receptors (β_2 -ARs) represent the 70% of all Beta Adrenergic Receptor (β -AR), with the Beta 1 Adrenergic Receptors (β_1 -ARs) accounting for the remainder. As a consequence, the use of a selective β_1 -AR antagonist may not involve only for vascular effect²⁴. It has been suggested that bronchodilatation is mediated by autonomic beta-adrenoceptors, the dominant subtype²⁵ being β_2 . Beta-blocker cardio-selectivity is dose dependent, with competitive antagonism of both β_1 and β_2 adrenoceptors at higher plasma concentrations. Therefore with higher doses of cardioselective beta-blockers, β_2 receptor blockade may cause minor increases in airflow obstruction possibly through unopposed parasympathetic bronchoconstriction²⁶. Furthermore, beta-agonist improved the performance of skeletal muscles and also positively affect respiratory muscle strength^{27,28,29}. Therefore Beta blocker medication may result in a slight reduction of expiratory muscle strength causing a proportional decrease of FEV₁ and FVC¹⁰. The exact mechanisms involved for the decrement of lung functions in hypertension and improvement after treatment with amlodipine but not with atenolol in hypertensive groups of present study could not be elucidated from this type of study. However, it is assumed that all the above mentioned mechanisms may influence the degree of deterioration of these variables in hypertension patients and improvement after treatment with amlodipine but not with atenolol.

Conclusion

The ventilatory variables decrease in newly diagnosed patients with hypertension and lung function status improves after treatment with amlodipine but further decreases after treatment with atenolol. Apart from the suggested mechanism by several researchers these decrement may be associated with silent pulmonary disorders without presenting any pulmonary symptoms.

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