Effect of Losartan and Amlodipine on Lung Function Status in Hypertensive Patients: A Randomized Control Trial
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Abstract

Introduction: Essential hypertension is associated with altered pulmonary function. Antihypertensive medication and lung function are also associated. Losartan (angiotensin II receptor blocker) and amlodipine (calcium channel blocker) are commonly used antihypertensive drugs.

Objectives: 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 hypertensive patients without any antihypertensive medication (group B, age 30-55 years). They were selected from the Out Patient Department (OPD) of Cardiology, BSMMU, Dhaka. 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). Group B1 included 50 patients received losartan 50 mg daily and B2 included 50 patients received amlodipine 5 mg daily. They were observed once before the treatment (B1a and B2a), after 3 months of medication (B1b and B2b) and after 6 months of medication (B1c and B2c). 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 RMS computer based Spriometer.

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

Conclusion: Reduced lung function occurs in newly diagnosed hypertensive patients which was improved by treatment with losartan and amlodipine.

Key-words: Hypertensive patients, Lung function test.

Introduction
Hypertension is a sustained elevation of systemic arterial pressure1. Essential hypertension accounts for 90-95% of all cases of hypertension. Now a day's hypertension becomes a significant public health challenge throughout the world because of its high prevalence2. In Bangladesh the prevalence rate of hypertension is also very high and more than 20% of the adults have hypertension3. Hypertension has been linked to multiple other diseases including cardiac, cerebrovascular, renal and eye diseases4. Several studies showed that hypertension and lung function are also associated5-11. In addition, a wide variety of antihypertensive drugs are now available with different mechanism of action and certain antihypertensive drugs can affect pulmonary function. A randomized controlled trial have shown that angiotensin II receptor blocker have no effects on FEV1 or airway resistance in COPD patients12.

Another study revealed that angiotensin II receptor blocker slightly reduced bronchial hyperresponsiveness to methacholine in patients with bronchial asthma13. Several studies suggested that Calcium channel blockers have no adverse effects on resting airway function in patients with asthma14,15. Some studies revealed no significant broncho-dilatation 45 minutes after Calcium channel blocker administration in asymptomatic asthma patients16. 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 asthma17. Although several investigators observed the effect of losartan and amlodipine on lung function separately no report compared the effect of losartan and amlodipine 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 losartan and amlodipine on lung function.

Materials and Methods
This prospective randomized control trial was carried out in the Department of Physiology of Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbag, Dhaka from July 2012 to June 2013. 100 newly diagnosed hypertensive patients aged 30-55 years were selected as study group (group B). 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). Group B1 included 50 patients received losartan 50mg daily and B2 included 50 patients received amlodipine 5 mg daily. They were observed once before treatment (B1a and B2a), after 3 months of medication (B1b and B2b) and after 6 months of medication (B1c and B2c). 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 RMS computer based Spriometer.

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Results

The mean of the percentages of predicted values of FVC, FEV1 and PEFR were significantly lower in group B1a, B1b and B1c respectively than those of control. In addition, the mean percentage of predicted values of FVC, FEV1 and PEFR were significantly increased in group B1b and B1c in comparison to their corresponding base line value of group B1a (Table-I). The mean of the percentages of predicted values of FVC, FEV1 and PEFR were significantly lower in group B2a, B2b and B2c respectively than those of control. In addition, the mean percentage of predicted values of FVC and FEV1 were significantly decreased in group B2b and B2c in comparison to their corresponding base line value B1a. The mean percentage of predicted value of PEFR was non significantly increased in group B2b and B2c in comparison to their corresponding base line values of group B2a (Table-II).

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

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Groups</th>
<th>FVC (L)</th>
<th>FEV1 (L)</th>
<th>PEFR (L/s)</th>
</tr>
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<tr>
<td></td>
<td>A (n=50)</td>
<td>86.9±0.827</td>
<td>90.62±0.772</td>
<td>78.38±1.373</td>
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<tr>
<td></td>
<td>B1a (n=50)</td>
<td>75.46±1.171</td>
<td>79.38±1.157</td>
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<tr>
<td></td>
<td>B1b (n=50)</td>
<td>76.84±0.999</td>
<td>81.08±1.151</td>
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<tr>
<td></td>
<td>B1c (n=50)</td>
<td>79.68±1.144</td>
<td>83.96±1.198</td>
<td>75.6±1.338</td>
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</table>

Statistical analysis

<table>
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<th>p value</th>
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<tr>
<td></td>
<td>FVC</td>
</tr>
<tr>
<td>A vs B1a</td>
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</tr>
<tr>
<td>A vs B1b</td>
<td>0.000***</td>
</tr>
<tr>
<td>A vs B1c</td>
<td>0.000***</td>
</tr>
<tr>
<td>B1a vs B1b</td>
<td>0.04*</td>
</tr>
<tr>
<td>B1b vs B1c</td>
<td>0.000***</td>
</tr>
<tr>
<td>B1a vs B1c</td>
<td>0.000***</td>
</tr>
</tbody>
</table>

Note: Data were expressed as mean±SE. φ = independent sample ‘t’ test, Ω = Paired sample ‘t’ test. Group A: Apparently healthy subjects (control group), Group B1a: Newly diagnosed hypertensive patients before treatment, Group B1b: After 3 months treatment with losartan, Group B1c: After 6 months treatment with losartan. ***: 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 in healthy normotensive group were almost similar to other investigators. The mean of the percentages of predicted values of FVC, FEV1 and PEFR were significantly lower in newly diagnosed hypertensive patients before treatment, Group B2a: Newly diagnosed hypertensive patients before treatment, Group B2b: After 3 months treatment with amlodipine, Group B2c: After 6 months treatment with amlodipine. ***: Significant (p≤0.001), **: Significant (p≤0.01), *: Significant (p≤0.05), Ns: Nonsignificant, n: Number.

Note: Data were expressed as mean±SE. φ = independent sample ‘t’ test, Ω = Paired sample ‘t’ test. Group A: Apparently healthy subjects (control group), Group B2a: Newly diagnosed hypertensive patients before treatment, Group B2b: After 3 months treatment with losartan, Group B2c: After 6 months treatment with losartan. Angiotensin II causes contraction of smooth muscle
in pulmonary arteries and veins\(^1\). It has been suggested that angiotensin II causes bronchoconstriction in mildly asthmatic patients possibly by a direct effect on airway smooth muscle or by release of bronchoconstrictor mediators such as endothelin\(^2\). Therefore Angiotensin II receptor blocker may reduce bronchoconstriction in symptomatic asthma patients\(^21\).

Different investigators 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 epithelium\(^23\). Calcium channel blockers are vasodilators and in hypertension it inhibits calcium influx into arterial smooth muscle cells\(^24\). 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 patients\(^19\). The exact mechanisms involved for the decrement of lung functions in hypertension and improvement after treatment with losartan and amlodipine 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 losartan and amlodipine.

**Conclusion**

The ventilatory variables decrease in newly diagnosed hypertensive patients and lung function status improves after treatment with losartan and amlodipine. This decrement may be associated with silent pulmonary disorders without presenting any pulmonary symptoms.

**References**


