Importance of Alpha-adrenergic Receptor Subtypes in Regulating of Airways Tonus at Patients with Bronchial Asthma

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ABSTRACT

Background: In this work, effect of Tamsulosin hydrochloride as antagonist of alpha1A and alpha1B- adrenergic receptor and effect of Salbutamol as agonist of beta2- adrenergic receptor in patients with bronchial asthma and increased bronchial reactivity was studied. Methods: Parameters of the lung function are determined by Body plethysmography. Raw and ITGV were registered and specific resistance (SRaw) was also calculated. Tamsulosin was administered in per os way as a preparation in the form of the capsules with a brand name of “Prolosin”, producer: Niche Generics Limited, Hitchin, Herts. Results: Results gained from this research show that blockade of alpha1A and alpha1B- adrenergic receptor with Tamsulosin hydrochloride (0.4 mg and 0.8 mg in per os way) has not changed significantly (p > 0.1) the bronchomotor tonus of tracheobronchial tree in comparison to the inhalation of Salbutamol as agonist of beta2- adrenergic receptor (2 inh. x 0.2 mg), (p < 0.05). Arterial blood pressure showed no significant decrease following the administration of the dose of 0.8 mg Tamsulosin. Conclusion: This suggests that the activity of alpha1A and alpha1B- adrenergic receptor in the smooth musculature is not a primary mechanism which causes reaction in patients with increased bronchial reactivity, in comparison to agonists of beta2- adrenergic receptor which emphasizes their significant action in the reduction of specific resistance of airways.

Key words: Tamsulosin hydrochloride, Salbutamol.

1. INTRODUCTION

Effect of autonomic nervous system in the bronchomotor tonus of the airways was researched intensively last years. Particular care is paid to the adrenergic and cholinergic effects. Importance of adrenergic action in the regulation of bronchomotor tonus is not quite known. They can effect through alpha1 or beta2 – adrenergic receptor in the smooth musculature of airways and to modify their permeability (1).

Increased bronchial irritability of airways in asthmatics is caused also by the autonomic dis-balance, which derives from the decreased beta2-adrenergic function, which results in increase of cholinergic and alpha-adrenergic response to different stimulators (2). Many researchers emphasize that in the group of selected asthmatic patients, without effects from other medicaments, administration of alpha-adrenergic antagonist leads towards improvement of the airways function (3, 4). Alpha-adrenergic antagonist (e.g. indoramin) causes the bronchodilation due to the blocking of alpha-adrenergic receptor and can be useful therapeutics for a certain asthmatic population (5). Remains unclear whether these results are caused by the blockage of stimulation of alpha-adrenergic receptor of mastocytes, or airways smooth muscles (6).

Lately, experiments performed in vivo show that clonidine intermediates an inhibitory control over the existing activity of vagal excitation (7, 8). However, these results are not verified by other researchers. Some authors have verified that in the group of asthmatics, agonist of alpha1-adrenergic receptor, inhaled phenylephrine does not affect in the airways resistance (9).

Airways smooth musculature tonus is under the effect of different neurotransmitters, hormones, drugs, and mediators which do manifest their action by connecting to the surface of the specific receptor in airways smooth musculature cells. All these factors, related to the tonus of airways musculature, manifest their action by excitatory effect (agonist) and inhibitory effect (antagonist) during the connection to respective receptor localized in airways musculature cells (10).

Researches “in vivo” in experimental animals and in isolated segments of human bronchi has proved the presence of a small number of alpha-adrenergic...
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2. MATERIAL AND METHODS

This study project was approved by the Ethic Committee of the Medical Faculty in Prishtina.

Examinations were done on 31 patients with bronchial asthma and increased bronchial reactivity. Selection of patients for this study was done based on the data from anamnesis, clinical-laboratory ascertainment, and functional examinations of respiratory system. Study involved 31 patients. At least 48 hours prior research of bronchial reactivity response, patients has not administered any of the bronchodilator substances. Examined were informed respecting the role of alpha adrenergic receptor in the mechanism of asthma (13).

Ileen et al. consider that alpha, adrenergic receptors in the smooth bronchial musculature may be stimulated only with a direct action of catecholamine in circulation, and only in physiologic doses because of very weeded-out sympathetic innervations found on bronchial tree (14).

Work aims the assessment of the importance of alpha-adrenergic system in the regulation of bronchomotor tonus in patients with bronchial asthma and bronchial increased reactivity. Effect of the Tamsulosin hydrochloride as the alpha1A and alpha1B adrenergic receptor antagonist in patients with increased bronchial reactivity in comparison to the effect of beta2 adrenergic agonists (Salbutamol) was studied in this work.

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Table 1. Basic characteristics and pulmonary function in examined.

<table>
<thead>
<tr>
<th>n</th>
<th>Age (v)</th>
<th>Height (cm)</th>
<th>Mass (kg)</th>
<th>VC (%)</th>
<th>FEV₁ (%)</th>
<th>Raw (kPa L/s)</th>
<th>ITGV (L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>31</td>
<td>45.11 ± 1,20</td>
<td>178.18 ± 1.13</td>
<td>71.91 ± 0.67</td>
<td>103.33±3.3</td>
<td>104.44±2.46</td>
<td>0.12±0.05</td>
<td>4.08±0.13</td>
</tr>
</tbody>
</table>

and the SRaw were taken for analyses. Research of the bronchial response to different substances was done with the measurement of Raw and the SRaw as very sensitive indicators, compared to the parameters calculated from the MEF curve, and therefore they are very important in the research of the bronchoconstriction and bronchodilatation. Realized values of MEF₁₅₀, MEF₂₀₀ show that calculated parameters from the curve flow-volume during the volumes in small parts of the lung are more sensitive than classic indicators of the measured obstruction with the spirometric examinations (FEV₁, 100 x FEV₁/FVK). Comparison of direct variables obtained from Raw, and SRaw and indirect indicators of the airways obstruction (FEV₁, 100 x FEV₁/FVK, RME₂₅ and RME₅₀) is very important in patients with bronchial asthma and lung obstructive diseases.

Basic features and those of the pulmonary function of researched are provided in Table 1.

Researched were informed regarding the aim of examination. At least 48 hours prior research commence, examined patients has not administered any of the drugs or substances which to affect the results of the examination. Lung function was determined in the silence condition. This determination is composed of the measurement of the slowed vital capacity (VC), forced expiratory volume (FEV₁) with Godardt Company pneumo test, and afterwards by metering of the resistance of the air flow in lung (Raw) and intrathoracic volume of gases (ITGV) with the body plethysmography. From the gained Raw and ITGV results, specific resistance (SRaw) was calculated.

$$\text{SRaw} = \text{Raw} \times \text{ITGV}$$

In patients with bronchial asthma and increased bronchial reactivity (n=31) following the measurement of initial values, Tamsulosin hydrochloride was applied (alpha₁A and alpha₁B-adrenergic antagonist) with per os way (0.4 mg and 0.8 mg), and after 60 and 120 minutes, Raw and ITGV were measured, and afterwards salbutamol as aerosol was applied in the end (beta₂-adrenergic agonist) in a dose of (2 inh. x 0,2 mg), Raw and ITGV values were measured again and SRaw was calculated.

Hypothesis was used that changes in the adrenergic system are not important and not related to the development of bronchial asthma or other obstructive diseases and are not related to allergic manifestation.

Acquired results were grouped and analysed. Statistic data processing included definition of the average values (X), standard deviation (SD), standard mistake (SEM), and testing of significance of changes in between groups of patient treated with Tamsulosin.

Acquired results were tested with a test (t-test) by which significant changes can be ascertained in between examined groups. Records were processed by using the computer statistic software GraphPad InStat III.

3. RESULTS

Results of this research, in patients with bronchial asthma, show that blockage of alpha₁A and alpha₁B-adrenergic receptor with Tamsulosin hydrochloride (0.4 mg and 0.8 mg with per os way) does not change sig-
not be totally eliminated due to the fact that some authors have concluded that systemic administration of phenolamine causes the increase of the incidence, rate and amplitude of respiratory movements of sheep’s fetus in utero during hypoxia. This proves regarding relation of phenolamine in the central mechanisms of breathing, also (16).

In favor of the facts related to the non-significant role of phenolamine in airways are also conclusions of some of the authors which speaks about alpha blockers not causing the myorelaxant effect following the induction of bronchoconstriction from the inhalatory therapy with methacholine and histamine in the experiment with apes. Isoprenaline has manifested direct myorelaxant effect following the induction of bronchoconstriction with aerosol therapy with methacholine and histamine. Meantime, atropine has manifested the partial bronchodilator effect only after inhalation of methacholine yet not after the inhalatory therapy with histamine (17).

Nonetheless, some authors have concluded that asthmatic patients included in the research have manifested heterogenic response to phenolamine by categorizing these patients with positive reaction, patients with negative reaction and patients without reaction to phenolamine. This author assumes that this different reaction to phenolamine is as a result of the different relation of the activity of beta adrenergic receptor, alpha adrenergic and cholinergic receptor at the bronchial tree (18).

A question appears whether constriction of smooth respiratory musculature is caused by two sub-types of alpha adrenergic receptors (alpha_{1A} and alpha_{1B})? Regarding this, there are neither earlier reports by which to prove two sub-types of alpha adrenergic receptors in the airways musculature nor reports over effects of clonidine in the receptors of smooth musculature (19). Previous researches have not demonstrated any of the alpha_{2} adrenergic receptor in the respiratory epithelial surface (19). 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asthma and patients with increased bronchial reactivity.

5. CONCLUSION

Based on gained results, it can be concluded as follows:

- Application of Tamsulosin hydrochloride-blocker of receptor (alpha1A and alpha1B–adrenergic) applied with per os way in doses of (0.4 mg and 0.8 mg) in patients with bronchial asthma and increased bronchial reactivity, does not cause significant decrease of specific resistance (SRaw) of airways (p > 0.1).
- Salbutamol as an agonist of the beta2-adrenergic receptor applied inhalatory in patients with increased bronchial hyper-reactibility causes a significant decrease of specific resistance (SRaw) of airways (p < 0.05).
- Tamsulosina has caused decrease of systolic and diastolic arterial pressure but not in a significant (p > 0.1).
- This suggests that the activity of alpha1A and alpha1B adrenergic receptor in the smooth bronchial musculature is not a primary mechanism which will cause reaction in patients with increased bronchial reactivity. There is a possibility that sub-types of alpha1A and alpha1B adrenergic receptors persist, yet in insufficient way to react significantly with antagonist alpha-adrenergic substances.

CONFLICT OF INTEREST: NONE DECLARED.

REFERENCES