Impact of the Tamsulosin in Alpha Adrenergic Receptor of Airways at Patients with Increased Bronchial Reactibility

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ABSTRACT

Objective: In this work, effect of tamsulosin as antagonist of alpha 1A and alpha1B adrenergic receptor and effect of agonists of beta2 adrenergic receptor – salbutamol in patients with increased bronchial reactibility was studied. Methods: Parameters of the lung function are determined with Body plethysmography six (6) hours after administration of tamsulosin. Raw and ITGV were registered and specific resistance (SRaw) was calculated as well. Tamsulosin was administered in per os manner as a preparation in the shape of the capsules with a brand name of “Prolosin”, produced by Niche Generics Limited, Hitchin, Herts. Results: After six (6) hours of administration of tamsulosin, results gained indicate that blockage of alpha1A and alpha1B-adrenergic receptor (0.8 mg per os) has not changed significantly (p > 0.1) the bronchomotor tonus of tracheo-bronchial tree in comparison to the check-up that has inhaled salbutamol agonist of adrenergic beta2 receptor (2 inh. x 0.2 mg), (p < 0.05). Blood pressure suffered no significant decrease following administration of the 0.8 mg dose of tamsulosin. Conclusion: This suggests that even after six hours of administration of tamsulosin, and determining of lung function parameters, the activity of alpha 1A and alpha1B-adrenergic receptor in the smooth bronchial musculature has not changed in patients with increased bronchial reactivity.

Key words: Tamsulosin hydrochloride, salbutamol.

1. INTRODUCTION

In the bronchial tree of a healthy person, we have equilibria of the activity of alpha-adrenergic and beta2-adrenergic system in favour of prevailing of the activity of beta2-receptor. Due to this fact, supposed that in case of hypo-activity of the beta2-adrenergic system dominates alpha-adrenergic system and this mechanism deemed to play key role in the bronchoconstriction at patients with bronchial asthma and bronchial reactibility (1).

Airways smooth musculature tonus is under the influence of different neurotransmitters, hormones, drugs and mediators, which manifest their action by connecting to the surface of the specific receptor in airways smooth musculature cells. All these factors are related to the tonus of airways smooth musculature and manifest their action through an excitatory (agonist) effect and inhibitory (antagonist) effect during connection to the respective receptor localized in airways musculature cells (2).

Researches in experimental animals and in isolated segments of human bronchi proved the presence of a small number of alpha-adrenergic receptor. These researches have also proved that the presence of this receptor in pulmonary diseases is increased. Some factor of the external environment such physical activity or exposure to cold air may initiate inflammatory processes and degranulation of mastocyte (3).

Actually, it is supposed that during the exposure to cold air, bronchoconstriction can be initiated through the increase of the alpha-adrenergic receptor activity. Therefore, this fact has placed in the focus the role of alpha-adrenergic receptor in the mechanism of asthma (4).

Ileen et al. consider that alpha 1 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 rare sympathetic innervations found in bronchial tree (5).

Objective of this work is to evaluate the importance of alpha-adrenergic system in the adjustment of bronchomotor tonus in patients with increased bronchial reactivity. Effect of the Tamsulosinas alpha 1A and alpha1B-adrenergic receptor antagonist in patients with increased bronchial reactivity studied here.

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2. MATERIAL AND METHODS

Examinations are done in six (6) patients with increased bronchial reactivity.

Selection of patients for this study done based on the records from anamnesis, clinical-laboratory findings, and functional examinations of respiratory tract. Study involved six (6) patients. Researched were informed regarding the aim of examination. At least 48 hours prior research commence, examined persons 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 (FEV), with Godart Company pneumoctest, and afterwards by metering of the resistance of the airflow in lung (Raw) and intratoracal volume of gases (ITGV) with the body plethysmography. From the gained Raw and ITGV results, specific resistance (SRaw) was calculated.

$$SRaw = \frac{Raw \times ITGV}{SRaw(n = 6; X \pm SEM)}$$

Basic features and those of the pulmonary function of researched are provided in the Table 1. In persons with bronchial asthma and increased bronchial reactivity (n=6) following the measurement of initial values, administered tamsulosin (alpha_1A and alpha_1B-adrenergic receptor antagonist) orally (0.8 mg), and after 6 hours, determined were lung function parameters Raw and ITGV. Afterwards, salbutamol as aerosol was applied in the end as a control (beta_2-adrenergic receptor agonist) in a dose of (2 inh. x 0.2 mg), and Raw and ITGV values were measured again and SRaw was calculated.

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

Results gained were grouped and analyzed. Statistic processing of records included the defining of the average values (X), standard deviation (SD), standard error of the mean (SEM), and testing of the significance of changes in between groups of patients treated with tamsulosin.

Results gained tested with a test (t-test) in order to conclude significant changes in between examined groups. Results were processed with a computer statistic software GraphPad InStat III.

3. RESULTS

The research, in patients with increased bronchial reactivity, indicate that blockage of alpha_1A and alpha_1B-adrenergic receptor with tamsulosin (0.8 mg orally), 6 hours after defining of lung function parameters, has not changed significantly (p > 0.1) the bronchomotor tonus of the tracheobronchial system, in comparison to the inhaled control–salbutamol (agonist of beta_2-adrenergic receptor), which is very effective in removal of increased bronchomotor tonus, by causing significant decrease of the resistance (Raw), respectively of specific resistance (SRaw), (p < 0.05) (Figure 1).

Tamsulosin, as a blocker of alpha_1A and alpha_1B-adrenergic receptor, in a dose of 0.8 mg after 6 hours decreases the arterial systolic and diastolic pressure (AP), but not in a significant manner (p > 0.1) (Figure 2).

<table>
<thead>
<tr>
<th>n</th>
<th>Age(y)</th>
<th>Height (cm)</th>
<th>Mass (kg)</th>
<th>VC (L)</th>
<th>FEV (L)</th>
<th>Raw (kPa L/s)</th>
<th>ITGV (L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>41 ± 1.30</td>
<td>175 ± 1.17</td>
<td>86 ± 0.78</td>
<td>3.52±3.2</td>
<td>2.60±3.46</td>
<td>0.32±0.01</td>
<td>4.04±0.14</td>
</tr>
</tbody>
</table>

Table 1. Basic characteristics and pulmonary function in examined.

4. DISCUSSION

In adjustment of the airways calibre, parasympathetic (cholinergic) nerve system plays a dominant role. In patients with asthma, it is supposed to manifest a hyper-activity of the cholinergic system because in these patients, anticholinergic drugs may cause emphasized bronchodilator effect, whilst this effect does not manifest in healthy people. Although, mechanism of this hyper-activity of this system not yet known entirely (6).

A huge number of studies, which deals with research of adjustment of the airways function and their mechanism, indicate the considerable role of relaxing effect of the beta, adrenergic receptor and constrictor effect of alpha-adrenergic receptor and interaction of neurohumoral factors in this adjustment.

Fact that after 6 hours of administration of tamsulosin provided no response of adrenergic-alpha_1A and alpha_1B receptor in the permeability of airways with reversible changes of the lung function. Results of this work indicate that blockage of alpha_1A and alpha_1B adrenergic receptor with Tamsulosin (0.8 mg per os) does not change the bronchomotor tonus in patients with increased bronchial hyper-reactivity(p > 0.1). Meantime, agonists of beta_2-adrenergic receptor (salbutamol) are very effective in removal of increased bronchomotor tonus (p < 0.05).

Similar results were gained by author Walden et al., who presented that the blockage of alpha adrenergic receptor through administration of phentolamine has no significant impact to the
reaction of the smooth musculature of airways towards histamine. Although in some of patients with asthma are registered improvements of lung functional tests (FEV_{1}) but without any significant impact (4).

In the past, discussed were three known mechanisms by which adrenergic and cholinergic drugs manifested bronchoconstriction effect in people: 1) drugs, which stimulate cholinergic system; 2) beta-adrenergic blockers, and 3) drugs, which alpha-adrenergic system (7).

Some author concluded that systemic administration of phentolamine causes increase of the incidence, rate, and amplitude of respiratory movement of sheep foetus in uteroduring hypoxia. This proves correlation of phentolamine with central respiratory mechanisms (8).

In favor of the facts related to the non-significant role of phentolamine in airways are also conclusions of some of the authors saying that alpha blockers does not cause the myorelaxant effect following the induction of bronchoconstriction from the inhalatory therapy with mechacholine and histamine in the experiment with apes. Meantime, atropine has manifested the partial bronchodilator effect only after inhalation of methacholine yet not after the inhalatory therapy with histamine (9).

Nonetheless, some authors have concluded that asthmatic patients included in the research have manifested heterogenic reaction of the smooth musculature of airways towards histamine yet not after the inhalatory therapy with histamine (9).

A question rises whether constriction of smooth respiratory musculature caused from two sub-types of alpha-adrenergic receptor (alpha subscripts 1A and alpha subscripts 2B). Regarding this, there are neither previous reports by which to prove two sub-types of alpha-adrenergic system (7).

Results suggest that effect of tamsulosin depends directly on the presence and structural extension of alpha adrenergic receptor, respectively from two sub-types of these receptors. Therefore, further researches of the configuration and sub-types of receptors would help in clearer definition of the role of receptors in the mechanism of bronchial reactivity.

5. CONCLUSION

Based on results gained, conclusion are as follows:

- 6 hour after definition of lung function parameters, administration of tamsulosin—blocker of adrenergic receptor (alpha subscripts 1A and alpha subscripts 2B) applied per os in a dose (0.8 mg) in patients with increased bronchial reactibility, does not cause significant decrease of specific resistance (SRaw) of airways (p > 0.1).
- Salbutamol as an agonist of the beta_{2}-adrenergic receptor applied inhalatory in patients with increased bronchial reactivity causes a significant decrease of specific resistance (SRaw) of airways (p < 0.05).
- Tamsulosin has caused decrease of the systolic and diastolic arterial pressure but not significantly (p > 0.1).

CONFLICT OF INTEREST: NONE DECLARED.

REFERENCES