Research Article

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In order to evaluate the importance of the alpha-adrenergic system in the regulation of the bronchomotor tonus in patients with middle and severe bronchial reactibility, e ects of the Oxedrine (stimulator of alpha$_1$-adrenergic receptor) and Tolazoline (blocker of alpha$_2$ adrenergic receptor) in this adjustment were researched, in comparison to the e ects of the beta$_2$-adrenergic receptor (Hexoprenaline) and anticholinergic substances (Ipratropium bromide).

Material and Methods

is study project was approved by the Ethic Committee of the Medical Faculty in Prishtina. Selection of patients for this study was done based on the data from anamnesis, clinical-laboratory ascertainments, and functional pulmonary examinations. Study involved overall 21 patients. At least 48 hours prior research of bronchial reactibility response, patients has not administered any of the bronchodilatory substances. Examined were informed regarding manner of the functional pulmonary examinations. Patients were su ering from asthma, with or without being followed by bronchitis. Average of the disease lasting was 11 ± 6 years (from 4-20 years). Average of their age was 44 ± 7 years (from 29 - 45 years), whereas average of relative weight was 70 ± 7% (from 65 - 72%). e aim of the examination was explained to each of the patients in advance. Pulmonary function was de ned at the rest, which was composed of measurement of vital capacity (VC), forced expiratory volume (FEV$_1$), resistance in the airways (Raw) and intrathoracic gas volume (ITGV).

In addition to the measurement of these parameters of the pulmonary ventilator function, Maximum Expiratory Flow-Volume Curve (MEF) was also de ned. Curve (MEF) was registered in a seating position with same breathing action as the forced vital capacity. Person breathed with mouth (closed nose), through a muzzle of the pneumotachograph.

Air ow was measured with the help of the pneumotachograph, whereas the volume through a volume-integrator. MEF curve was registered in the X-Y writer (Hewlett-Packard).

Flow was registered in the ordinate, and the volume in abscissa. Several parameters were calculated, whereas Maximum Expiratory Flow was taken for analyses a er it has expirated 25, 50 and 75% of VC (MEF_{25}, MEF_{50}, and MEF_{75} - l/s.).

ese parameters were analyzed since they are situated in the part of the curve which primarily depends on mechanic features of the lungs and not from the expiratory force and also because of being more sensitive than FEV$_1$ in measurement of bronchial reactibility. Prior to the provoking of bronchoconstriction, at least two reproducible MEF curves, blood pressure, and pulse were measured as well.

General resistance of the air ow in the airways (Raw) and the volume of the intrathoracic gas (ITGV) were researched in patients. e patient was placed in the cabin of the plethysmograph that was closed in a hermetic manner, and was connected to the pneumotachograph through an oral mask in order to breathe the air. During the inspirium, with an expansion of the sternum, air in the cabin compresses; whereas, it decompresses in the lung, namely it comes to the decrease of the intrathoracic pressure with the proportional increase of the pressure in the cabin. During the expirium, the opposite situation appears: increase

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pressure, and pulse were measured and similarly were repeated a er 15, 30 and 60 minutes.

In order to observe changes in the airways permeability a er inhaling of aerosol of Oxedrine, Tolazoline, and Hexoprenaline or Ipratropium, index of changes in percentage was calculated, namely Raw, ITGV and SRaw (%P) values were calculated as follows:

$$\text{Ind. of decrease} = \frac{\text{Initial values - minimal value a er the inhaling of certain substance}}{\text{Initial values - minimal value a er the inhaling of certain substance}} \times 100$$

Bronchial tree of a healthy person have equilibrium of the alpha-adrenergic and beta$_2$-adrenergic system activity in the favor of domination of beta$_2$-receptor activity. Due to this fact, it is assumed that in case of hypoactivity of the beta$_2$-adrenergic system dominates alpha-adrenergic system, thus it was supposed that this mechanism plays the main role in the bronchoconstriction in patients with bronchial asthma [17].

According to Szentivan, increased bronchial irritability of airways in asthmatics is caused by the autonomous disbalance, which derives from the decreased beta-adrenergic function, and which results with an increase of cholinergic and alpha-adrenergic response towards di erent stimulators [18].

Despite the theory of Szentivany, which considers that the adrenergic system activity is decreased, our results show that the activity of the beta$_2$-adrenergic receptor is increased in order to contra pose cholinergic constrictor impulses in patients with increased bronchial reactibility. Meanwhile, the activity of alpha-adrenergic receptor is not important in this mechanism.

Research on e ect of the phentolamine in patients with bronchial asthma has not registered any changes of lung functional tests parameters (FEV$_1$ GAV/WL; V$_{25}$ and V ERV$_2$) by ascertaining that the increased activity of alpha-adrenergic receptor is not the central mechanism in causing of the asthma disease and by emphasizing the dominant role of beta$_2$-receptor agonists [19]. Nonetheless, this author presents that asthmatic patients included in the research have manifested heterogenic response to phentolamine by categorizing these patients with positive reaction, patients with negative reaction and patients without reaction to phentolamine. is author assumes that this di erent reaction to phentolamine is as a result of the di erent relation of the activity of beta adrenergic receptor, alpha adrenergic and cholinergic receptor at the bronchial tree [19]. Blockage of alpha-adrenergic receptor through the application of phentolamine has no signi cant impact to the reaction of the airways smooth musculature to histamine. Although, in some of patients with asthma are registered improvements of lung functional tests (FEV$_1$ but without any signi cant impact [20]. Role of the phentolamine in the airways tonus should not be totally eliminated because systemic administration of phentolamine causes the increase of the incidence, rate and amplitude of respiratory movements of sheep fetus in utero during hypoxia. is proves regarding relation of phentolamine in the central mechanisms of breathing, also [21]. Phentolamine dose not cause the myorelaxant e ect following the induction of bronchoconstriction from the inhalatory therapy with metakolin and histamine in the experiment with apes. Isoprenaline has manifested direct myorelaxant e ect following the induction of bronchoconstriction with aerosol therapy with metakolin and histamine. Meantime, atropine has manifested the partial bronchodilator e ect only a eor o2e metakoli2e ye36ect nhe

functional test values in patients with asthma and chronic obstructive diseases [22].

All of these results suggest that role of Oxedrine and Tolazoline depends directly on the presence and structural extension of alpha adrenergic receptor, respectively from two sub-types of these receptors. erefore, further researches of the con guration and sub-types of these receptors would help out in a clearer de ning of the role of these receptors in the pathophysiologic mechanism of asthma and pulmonary obstructive diseases.

Conclusion

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

- Inhalation of Oxedrine (120 mg-aerosol), stimulator of alpha$_1$-adrenergic receptor applied to the patients with middle and severe bronchial reactibility does not change the increase of the speci c resistance (SRaw) of airways ($p > 0.1$).
- Application of Tolazoline (20 mg-aerosol), as blocker of alpha$_2$-adrenergic receptor applied to the patients with middle and severe bronchial reactibility also does not change the decrease of the speci c resistance (SRaw) of airways ($p > 0.1$).
- Application of Hexoprenaline through inhalation to the patients with middle and severe bronchial reactibility causes signi cant decrease of speci c resistance (SRaw) of airways ($p < 0.01$).
- Ipratropium as antagonist of the cholinergic system applied as aerosol in patients with middle and severe bronchial reactibility also causes signi cant decrease of speci c resistance (SRaw) of airways ($p < 0.01$).
- T is suggests that the application of agonists and antagonists in patients with middle and severe bronchial reactibility does not change the activity of alpha$_1$and alpha$_2$ adrenergic receptor in the smooth bronchial musculature and it is not a primary mechanism which causes reaction in patients with middle and severe bronchial reactibility. ere is a possibility that sub-types of alpha$_1$and alpha$_2$ adrenergic receptors persist, yet in insu cient size to react signi cantly with agonist and antagonist alpha-adrenergic substances.

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