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MODERN APPROACHES TO THE INHALATION THERAPY IN PULMONARY BRONCHO-OBSTRUCTIVE PATHOLOGY

Key words: *chronic obstructive pulmonary disease, Easyhaler, Bufomix, asthma*

Introduction.

International Congress of European Respiratory Society took place on 15-19 September 2018 in Paris, where specialists from all over the world discussed most relevant, controversial and discussable questions of the modern respiratory medicine. Issues of the respiratory diseases treatment at the level of primary care as well as specialized interventions, that were recently implemented in the medical practice, were highlighted in the poster sessions and presentations. A big number of presentations were devoted to the methods of treatment and diagnostics improvement of bronchial asthma, chronic obstructive pulmonary diseases, inhalers and education of the patient.

Scientists from Ukraine participated actively in the congress along with the scientists from all over the world. They presented 42 presentations on the issues of adult and pediatric respiratory medicine at the different congress sessions. 3 studies were presented at the congress by the Propedeutics of Internal Medicine Department of Vinnitsya National Pirogov Memorial Medical University under the guidance of professor Mostovoy Y.M. — “Role of the e-cigarettes in the smoking cessation” [7], “Role of the fat and muscle tissues in formation of the quality of life in COPD patients” [15], “Comparative laboratory evaluation of systemic inflammatory response in patients with opium drug addiction and community-acquired pneumonia” [18].

The only Ukrainian producer, that represents Ukrainian industry at the international level is Yuria Pharm, who presented own solutions for inhalation use Okistar Hyal 7, Lorde hyal, Nasisoft, that are used in patients with cystic fibrosis, bronchiectasis, cough, rhinitis.

This is not surprising that pharmaceutical firms were interested in such an event, which can be seen

from 58 sessions and more than 90 hours of lectures devoted to the issues of respiratory medicine, 20 of which were devoted to the problems of prevention, diagnostics, conservative and operative treatment of COPD and bronchial asthma. Most of the sessions discussed the role of the inhaler in the treatment of these nosologies, education of the patients and their comfort during the use of inhalers.

Such interest to the issues of bronchial asthma and COPD is understandable as according to the GINA 2018 data up to 18 % of population have bronchial asthma [9], and COPD affects 7.6 % of population [2]. Causes of asthma and COPD are not yet understandable [1], so adequate and individualized approach to the choice of acting molecule as well as inhaler can have a great impact on the treatment efficacy due to the direct action of the drug, as well as indirectly through the influence on the adherence to treatment [3].

We want to draw reader's attention to the session called: “Back to basics in Asthma and COPD: Optimising the Patient Journey”, where the following topics were highlighted: national programs of early diagnostics and treatment of asthma and COPD based in the national Finnish programs, factors, that influence the efficacy of inhalation therapy and personalized medicine in asthma and COPD.

Professor Mika Makela from Helsinki University have presented the results of the 10-year national program devoted to the treatment and prevention of asthma, which set the following goals:

- Early diagnostics and active treatment.
- Self-controlled treatment as the primary treatment method.
- Decrease of the respiratory irritants such as active and passive smoking.
- Introduction of education and rehabilitation of patients in the combination with the usual treatment and individual plan.
- Spread of knowledge among key group of medical workers.

- Spread of the scientific research.

This educational program involved 25 thousands of specialists throughout the country. Introduction of this program improved diagnostics of asthma, allowed to timely administer anti-inflammatory therapy, decreased number and duration of in-hospital stay and expenses of health system on the treatment of this group of patients [10, 11].

Similar program was introduced for the early diagnostics and treatment of chronic obstructive pulmonary disease, which allowed to decrease the number of smok-

aggregation. Turbulent flow is created inside the inhaler channel as the result of the interaction of inner inhaler resistance and inspiratory effort of the patient. The higher is the inner inhaler resistance is, the less efforts are necessary for the provision of turbulent flow [6].

Three features of aerosol influence the amount of active substance that reaches lungs: aerodynamic size of particles, speed of the aerosol cloud and its duration [4].

For the provision of disaggregation patient should breath in deeply and rapidly from the beginning of the

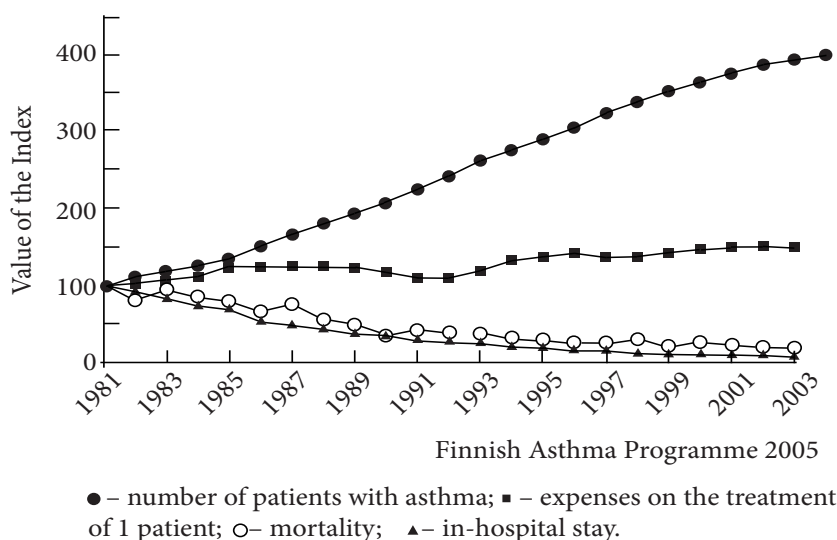


Fig. 1. State of morbidity, mortality and in-hospital stay after the national program onset in Finland [10].

ers, hospital admissions and treatment expenses for patients with COPD [13].

In the second presentation professor Henry Chrystyn analyzed principles of the inhalation therapy and importance of the patient's education, when this form of therapy is administered. It was mentioned, that during the inhaler manufacturing acting molecule is adsorbed on the lactose and turbulent flow is necessary for their dis-

inhalation. The relation between the peak inspiratory flow and clinical efficacy of inhalation therapy was established. Peak inspiratory flow (PIF) of ≥ 30 l/min is necessary for the provision of the sufficient effect of the inhalation. Most of the patients can reach this PIF. Children, patients with asthma and COPD especially during exacerbation could not reach sufficient inspiratory flow for the provision of adequate inhalation.

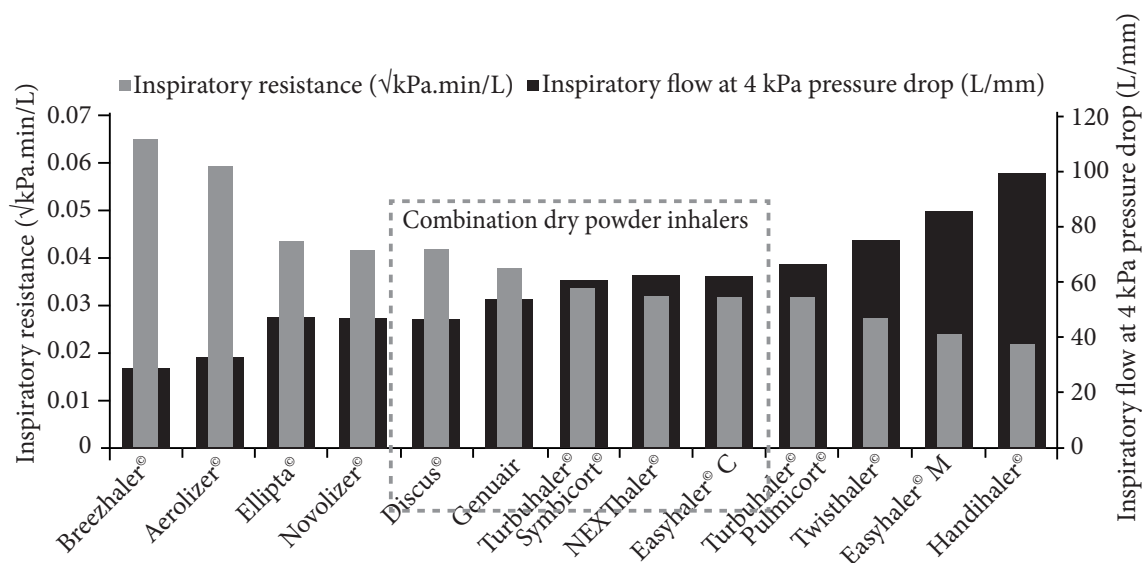


Fig. 2. Dependence of inner inhaler resistance and required PIF.

Inhalers, which demand the creation of high inspiratory flow, should not be used in these patients. Easyhaler M, Twisthaler, Handihaler demand higher PIF for the creation of turbulent air flow. Inner resistance of different combined inhalers is rather similar [14, 17].

But Easyhaler use allows to reach more stable dose deposition in lungs when compared to turbuhaler at different values of PIF (Fig. 2) [12].

Third presentation of the session was presented by the professor Federico Lavorini, which was devoted to the use of inhalation therapy in the real life conditions. Large study CRITIKAL was mentioned during this presentations. Impact of different mistakes during the inhaler use, their types and frequency, relation with the asthma course were determined during the study. 5 000 patients were enrolled in the study. Skills of the inhaler use and manifestations of the bronchial asthma were determined in these patients. The following inhalers were compared during the study: symbicort turbuhaler, seretide diskus and seretide MDI. The main mistake during the Turbuhaler use was incorrect positioning and turns of the inhaler basis during the dose preparation, which made up to 50 % of the patients. Other widespread mistakes were the same among these inhalers:

- incorrect head positioning during inhalation;
- insufficient inspiratory effort;
- absence of the complete exhalation before the inhalation initiation;
- absence of the breath holding after inhalation (or breath holding < 3 sec).

These mistakes decreased the control of the asthma symptoms, increased risk of the asthma exacerbation. Some of the mistakes increased risk of the exacerbation by two times. But data on the cumulative influence of several mistakes on these risks is absent in this article [16].

Also relation between different types of mistakes and risk of the uncontrolled asthma was established.

Risk of the uncontrolled asthma during the symbicort turbuhaler use was increased by: insufficient inspiratory effort, incorrect head positioning during inhalation, absence of the complete exhalation before the inhalation initiation, absence of the breath holding after the inhalation, incorrect preparation of the second dose.

During the seretide diskus use these mistakes were the following: insufficient inspiratory effort, absence of the complete exhalation before the inhalation initiation, absence of the breath holding after the inhalation, incor-

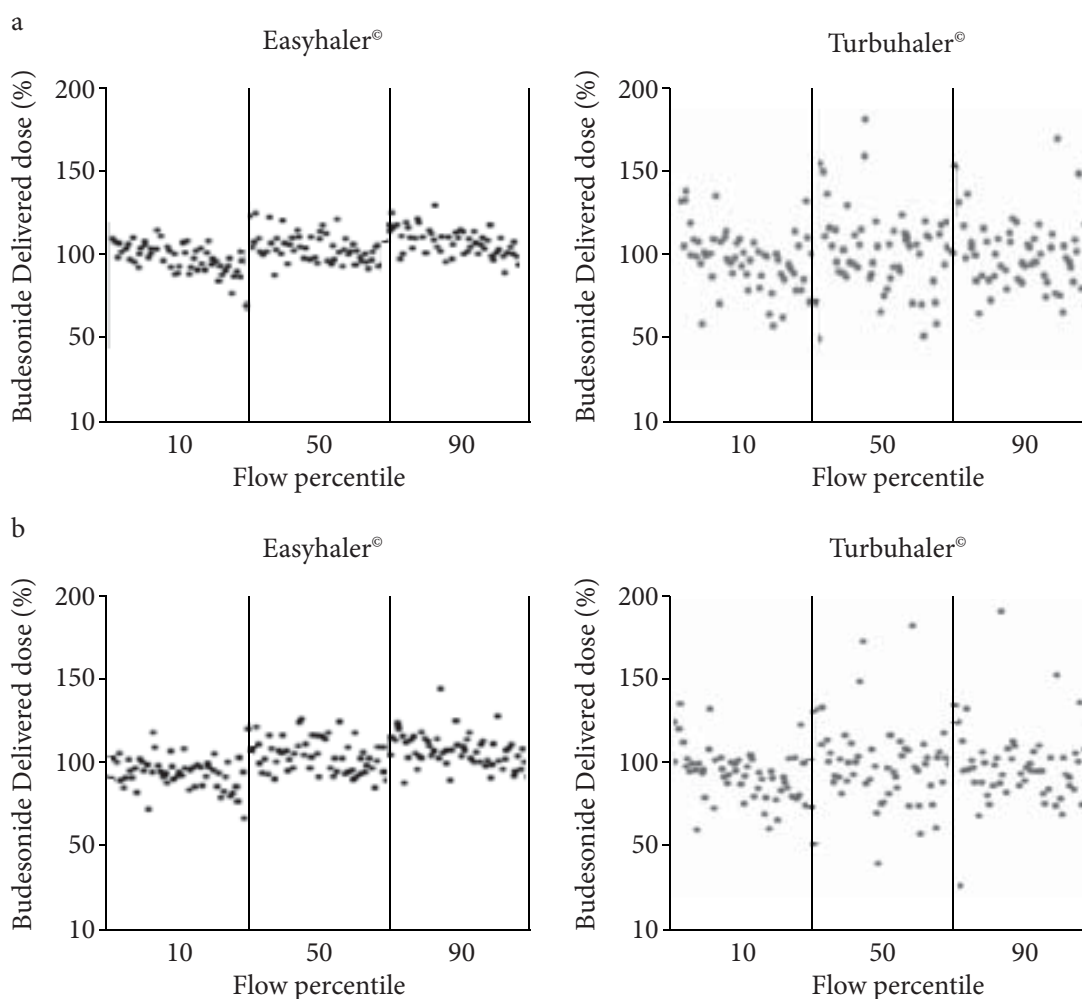


Fig. 3. Deposition of budesonide (a) and formoterol (b) in lungs after easyhaler and turbuhaler used at different PIF values [12].

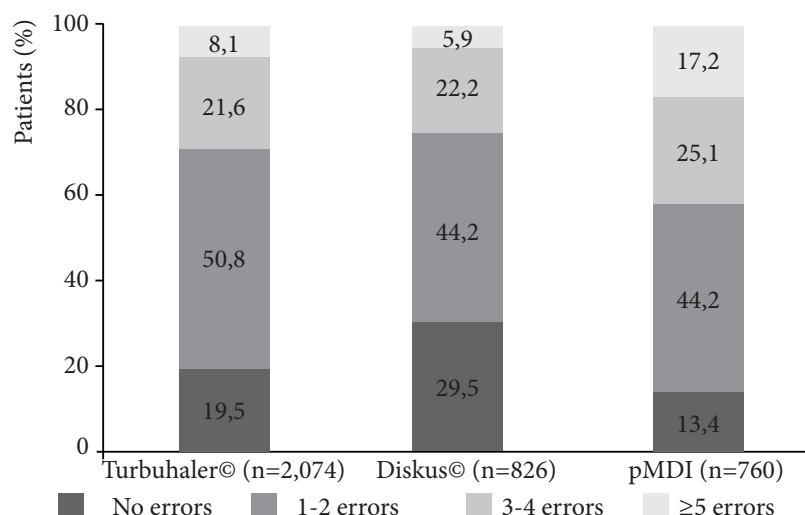


Fig. 4. Number of mistakes during the different inhalers use.

rect preparation of the second dose.

These mistakes decrease the control over the asthma symptoms, increased risk of the asthma exacerbation. Some of the mistakes increased risk of the exacerbation in two times. But data on the cumulative influence of several mistakes on these risk is absent in this article [16].

But, as we can see on the diagram, only 20-30 % of patients use inhaler without mistakes and the same amount make 3 and more mistakes during the inhaler use. This can be explained by the difficulty of the patient's education to perform correctly all the stages of the first and second doses preparation.

Results of multicenter study devoted to the correct use and feasibility of the Easyhaler use have showed that 77.5 % of patients with COPD and 61.9 % of children with asthma demonstrated correct inhalation technique after the one demonstration by a doctor. This percent was 89.2 % and 83.5 % correspondingly at the second visit [8]. This was also accompanied by the improvement of spirometry parameters (fig. 5).

In our study under the guidance of professor Mostovoy Y.M., we studied clinical efficacy and adherence to treatment in patients with partially controlled bronchial asthma. We assessed parameters of the quality of life, pulmonary function and initial adherence to treatment, after that we educated patient to use easyhaler with stepwise printed instruction, demonstration of the educative video and technique of the inhaler use by the investigator. After the treatment initiation 33 % performed inhalation correctly and 96.7 % at the end. Adherence to treatment increased from 50.5 % to 78.7 %, FEV1 increased from 54.5 % to 63.7 % over the period of 8 weeks [19].

So, it is necessary to follow these steps when administering inhaler to the patient:

1. Choose most feasible inhaler.
2. Analyze available treatment options, their costs and abilities of the patient.

3. If there're several available options, ask patient to participate in the inhaler choice.

4. Consider, that spacer use for DPI increases drug delivery and decreases adverse events risk.

5. Ensure, that there are no physical barriers, that can limit the inhaler use by the patient.

6. Avoid use of different inhalers, whereas possible [5].

In the fourth presentation professor Giorgia Walter Canonica analyzed issues of personalized medicine in the treatment of asthma, which were devoted to the choice and change of inhalers in patients with asthma and COPD. Personalized medicine is focused on the needs of the patients rather than mechanisms of the disease development. Individual approach to the choice of inhaler is one of the elements of the personalized medicine, that can improve adherence to treatment and control of the asthma symptoms. Education of the patient should be the key element during the contact of the doctor and patient. Doctor should explain reasons for the inhaler administration, explain how to use it and also regularly check the correctness of its use. Such approach improves adherence to treatment and the course of respiratory diseases.

Conclusion. Nowadays there is a big amount of inhalers for the treatment of bronchial asthma and chronic obstructive pulmonary disease. Not only the acting molecule, but also a type of the inhaler should be taken into account when choosing inhaler, as the complexity of the inhaler use can lead to the mistakes during its use. Mistakes during the inhaler use cause worsening in the asthma course and increase risk of the exacerbations.

Pharmaco-economical, cognitive and other features of every patient should be taken into account when choosing the inhaler. Approach to the inhalation therapy choice should be personalized.

According to the data of many investigations, Easyhaler is easy in use, does not require synchronization with inhalation, its efficacy is low-dependent on the inspiratory effort, most of the patients use inhaler correctly after the education, which provides sufficient dose

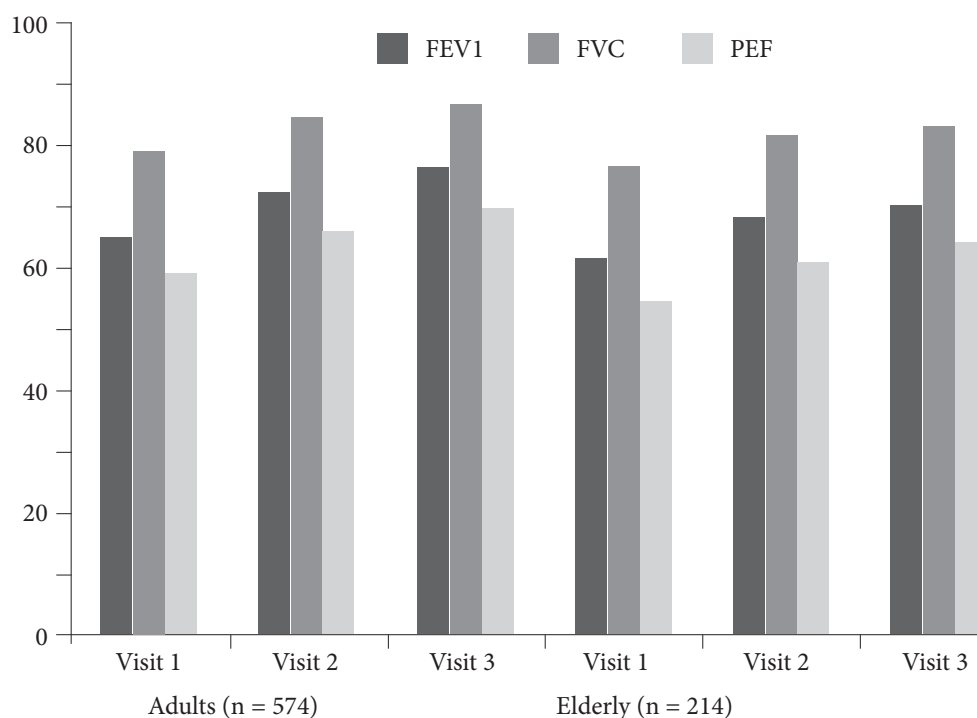


Fig. 5. Change of FEV1, FVC and PEF values after the study onset [8].

deposition in airways and, according to the available data, improves course of the bronchial asthma.

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Abstract

Introduction. Problems of the inhalation therapy of obstructive lung diseases are relevant and were discussed actively at the congress of European Respiratory Society. In this article we review one of the sessions devoted to the therapy of bronchial asthma and chronic obstructive pulmonary disease (COPD).

Materials and methods. We analyzed data of the session "Back to Basics in Asthma and COPD: Optimizing the Patient Journey" and corresponding data of national studies.

Discussion. National program of early diagnostics and treatment of asthma and COPD improved early diagnostics of diseases, decreased the number of exacerbations, hospitalizations and mortality from these diseases.

For the disaggregation of the active molecule the creation of turbulent flow is necessary, which depends on the inhaler resistance and peak inspiratory flow. It can influence the degree of active substance deposition in lungs.

Number of mistakes during the inhaler use impact the control of asthma, increases the exacerbation risk. Only 20-30 % of patients use their inhalers correctly. Individual features and cognitive abilities should be taken into account during the inhaler choice.

Conclusions. Systemic approach is necessary in asthma treatment. Government provision of the diagnostic and treatment programs for asthma decrease risk of hospitalizations. Correct choice of the inhaler and systemic education of the patient for the inhaler use improve symptoms and lung function.

Key words: chronic obstructive pulmonary disease, Easyhaler, Bufomix, asthma.

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