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Bronchial asthma - what should every doctor know?

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Abstract

More than 235 million people worldwide suffer from asthma. Most of the patients have mild asthma, but in a large part of them asthma is not fully controlled and they are exposed to the occurrence of exacerbations. It is believed that the most important reason for poor asthma control is the patients' failure to comply with chronic treatment recommendations.
This article describes the symptoms and course of the disease. There is also contain information about the criteria of diagnosis and changes in therapeutic progress which were announced in 2019 by Global Organization for Asthma.

Keywords: asthma, dyspnoea, GINA 2019

Introduction

Asthma belongs to a group of heterogeneous diseases, usually characterized by chronic inflammation of the respiratory tract. Symptoms include wheezing, shortness of breath, chest tightness and coughing (vary in intensity and frequency) and difficulty in exhaled airflow of varying severity. Restriction of airflow is limited by contraction of smooth bronchial muscles, swelling of bronchial mucosa, formation of mucous membranes and over time reconstruction of bronchial wall (as a result of chronic inflammation) [5,10,13].

Asthma can be divided into allergic and non-allergic due to its etiology. Allergic asthma usually starts in childhood and often coexist with other atopic problems – e.g. positive history of atopic diseases, positive results of skin tests, specific IgE antibodies in blood, usually induced sputum eosinophilia and good response to inhaled ICS. The most important role in the pathomechanism of this type of asthma is played by subpopulations of helper lymphocytes Th2. Mast cells are activated by allergens and IgE. Then mediators responsible for bronchial obstruction are released such as: histamine, cysteinyl leukotrienes, prostaglandin D2.Non-allergic asthma usually occurs in adults and is characterized by a progressive course. Usually skin tests are negative, no specific IgE antibodies in the blood and worse response to inhaled ICS. The pathomechanism of non-allergic asthma is not well understood. There were also 3 asthma phenotypes: late onset, with persistent bronchial obstruction and coexisting with obesity [1,5,10,13].

Asthma can also be divided according to the type of inflammation in the airways (bronchi) assessed on the basis of the dominant type of inflammatory cells present in sputum induced by eosinophilic, neutrophilic and low-cellular asthma [5,10,13,17].

However, the most important division for a clinician is the classification according to the degree of control of symptoms. Asthma can be divided into:

- well-controlled asthma - symptoms during the day ≤ 2x/week, no awakening at night due to asthma symptoms, need for ad hoc treatment ≤ 2x/week (does not apply to preventive medication before exercise) and without limiting vital activity due to asthma
- partially controlled asthma - met 2 or 3 of the above criteria
- uncontrolled asthma – met ≤ 1 of the above criteria [5,10,13].

Risk factors

Factors causing asthma attacks and exacerbations or their persistence: allergens, respiratory infections (mainly viral), air pollution, cigarette smoke, physical exertion, strong emotions, weather changes, medications (B-blockers, NSAIDs), food and food additives [5,17].

Factors increasing the risk of asthma exacerbation: uncontrolled asthma symptoms (excessive consumption of short-acting B2-mimetic agents, consumption of over 1 pack containing 200 doses is associated with increased risk of death), non-use of inhaled ICS (non-observance of the intake, incorrect inhalation), low FEV1 value (especially below 60% of the due value), serious psychological and socio-economic problems, exposure to cigarette smoke, allergens in allergic patients, coexisting diseases (obesity, chronic rhinoconjunctivitis, food allergy), sputum or blood eosinophilia, pregnancy, at least 1 severe exacerbation of asthma in the last 12 months, previous intubation or treatment in the intensive care unit due to asthma, increased FE_{NO} concentration (in patients treated with inhaled ICS) [5,10,17].

Risk factors for chronic bronchial obstruction: no inhalation ICS, exposure to ciagarette smoke or other harmful substances, low initial FEV1, chronic excessive secretion in the airways, eosinophilia of sputum or blood, premature birth, low birth weight, high weight gain in childhood [5,10,13].

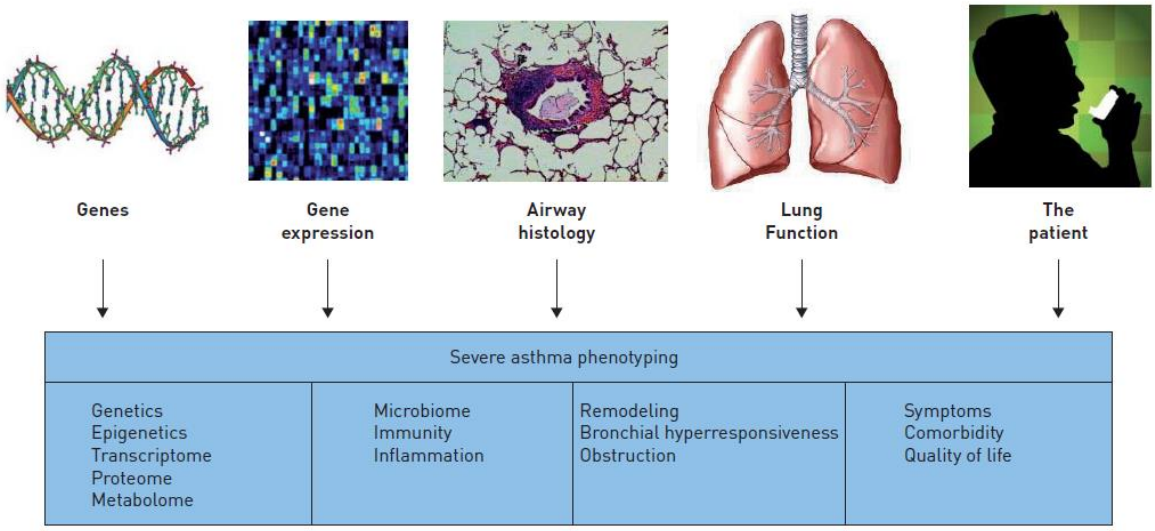

Fig 1. Integration of factors beginning with genetics, which may contribute to the ultimate phenotype of the severe asthma patient [3].

Clinical picture

Subjective symptoms:

- paroxysmal dyspnoea, mainly expiratory (sometimes felt as a squeeze in the chest, disappearing spontaneously or under the influence of treatment)
- wheezing
- dry, paroxysmal cough (usually accompanied by dyspnoea, however, it happens that it occurs as a single symptom, then we speak of the so-called cough variant of asthma)
- in the case of allergic asthma, symptoms of other allergic diseases, most often allergic rhinitis [5,13].

These symptoms are of variable intensity and, apart from asthma attacks and exacerbations, may not occur at all.

Physical symptoms:

- diffuse, bilateral whistles, mainly expiratory,
- rhonchi,
- extended exhaust,
- during exacerbations - work of additional respiratory muscles even with the intramural tension of the intercostal space [5].

In the case of very severe exacerbations, we can deal with a so-called silent chest, in which case there are no auscultatory symptoms.

Asthma can occur at any age, when it starts in adulthood has a more severe course. Asthma develops exacerbations, that can develop rapidly in a few minutes or may develop gradually over hours or days. Untreated seizures and exacerbations can lead to death. Uncontrolled asthma for many years leads to irreversible, progressive bronchial obstruction [5,13].

Diagnosis

Diagnosis of asthma according to GINA requires symptoms of the disease and a variable degree of bronchial obstruction depicted in functional tests [13].
Usually, there are a minimum of two types of respiratory symptoms, they are characterized by variability in occurrence and severity over time, often worse at night or after waking up. Very often they are caused by physical exertion, laughter, allergens, cold air. It intensifies or provokes viral infection [5,13].
Functional tests should confirm reduced pulmonary function and bronchial obstruction. Methods for the assessment of respiratory function:

1. The diastolic test - a positive result of (preferably when a patient who had already taken bronchial diastolic drugs discontinued them with SABA at least 4 hours before the examination and LABA at least 15 hours) is observed when:

- the increase in FEV1 in adults is > 12% and > 200 ml compared to the baseline value after 10-15 minute inhalation of 200-400 micrograms of salbutamol (more reliable diagnosis when the increase in FEV1 >15% and >400 ml),
- in children the increase in FEV1 >12% of the due value [1,5,13,14].

2. Excessive variability of PEF we observed when - in adults mean daily variability of PEF >10% and in children >13% in measurements performed 2 x days over 2 weeks [1,2].
3. Significant improvement in lung function after 4 weeks of anti-inflammatory treatment when FEV1 > 12% and > 200 ml or PEF > 20% in adults, compared to baseline value without respiratory tract infection during this period [1,2,13].
4. A challenge exercise- a positive result of test when:

- in adults FEV1 decreases by > 10% and > 200 ml compared to baseline,
- in children FEV decreases by > 12% of due value or PEF decreases by > 15% [1,2,13]

5. An inhalation provocative test- a positive result from:

- decreases FEV1 by ≥ 20% compared to the baseline after inhalation of a standard dose of metacholine or histamine
- or decreases FEV1 by ≥ 15% in a standard hyperventilation test using hypertonic NaCl or mannitol solution [1,2,13,14].

6. Excessive fluctuations in pulmonary function were found during subsequent medical visits without respiratory tract infections during this period (diagnosis less reliable), in adults FEV1 variability > 12% and > 200 ml, in children FEV1 variability > 12% or PEF > 15% [1,2,13].

These methods allow us to conclude that there is a variable degree of restriction of expiratory airflow through the respiratory tract, which, together with the occurrence of symptoms, enables us to diagnose asthma [13,14].

Treatment

Developing a partnership with the patient, involving him/her in the treatment process and following the recommendations are of great importance in the treatment and control of asthma. The patient's education should include information on:

- diagnosis and essence of the disease,
- available treatment methods,
- techniques for taking inhalation medication,
- possible side effects,
- ways to reduce exposure to factors that cause asthma attacks,
- monitoring disease control,
- methods of treatment in the event of aggravation and exacerbation of the disease (including information on when to seek medical help) [1,7,8,13].

The general rules for the use of medicines include:

- Controller medications (regular taken medication) – e.g. inhaled glucocorticosteroids (ICS), inhaled long-acting β_2 – agonist (LABA), long-acting anticholinergic agents, leukotriene receptor agonist (LTRA), theophylline in a prolonged-action form.

They are usted to reduce airway inflammation, control symptoms and reduce future risks such as exacerbations and decline in lung function.

- Reliever (rescue) medications (taken on an ad hoc basis) – e.g. inhaled short-acting β_2 – agonist (SABA), inhaled short-acting anticholinergic agents and oral glucocorticosteroids. They are provided to all patients for as-needed relief of breakthrough symptoms, including during worsening asthma or exacerbations.
- Add-on therapies for patients with severe asthma – e.g. oral glucocorticosteroids, anti-immmunoglobulin E (anti-IgE – omalizumab), anti-interleukin 5/5R (mepolizumab, reslizumab),

These may be considered when patients have persistent symptoms or/and exacerbations despite optimized treatment with high dose controller medications (high dose LABA or inhaled corticosteroids) and treatment of modifiable risk factors [1,4,13,12].

The choice of medications depends on the degree of asthma control and current treatment. According to the latest recommendations published in April 2019, GINA (Global Initiative for Asthma) recommends the use of small doses of inhaled glukocorticosteroid/formoterol as the preferred ad hoc treatment method (against dyspnea) in all stages of asthma treatment (GINA 1-5), and the previously used drugs from the group of short-acting beta2-mimetics agents (SABA), move to an alternative treatment site. This is a significant change because SABA has been recommended by GINA in the first place for the last 50 years [6,13,16].

There is strong epidemiological evidence that the use of SABA (short-acting β2-agonists) in monotherapy increases the risk of severe exacerbation and death from asthma, and the inclusion of inhaled low-dose glucocorticosteroid (Budesonide 200-400 μg/day) even in patients with sporadic symptoms (0-1 per week) reduces the risk of exacerbation by half (START study; Reddel et al.) [11,15].

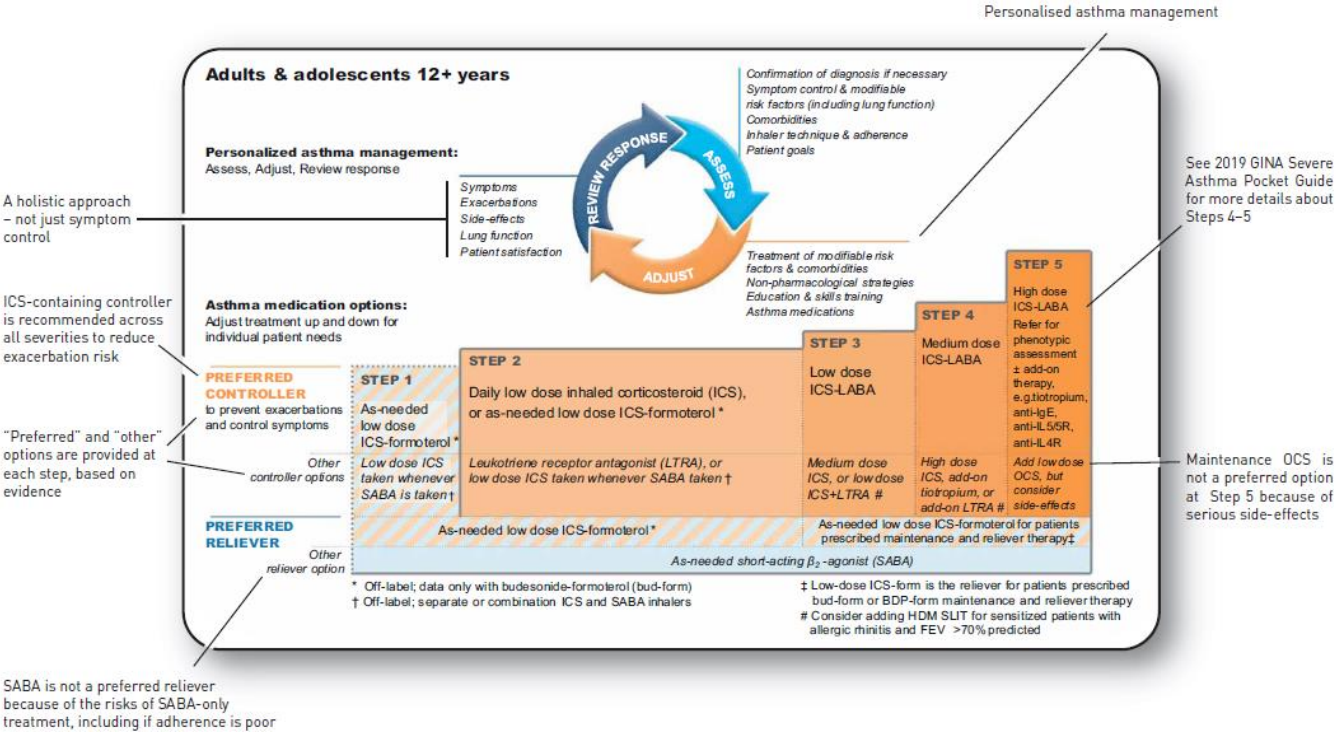

Fig.2 The 2019 Global Initiative for Asthma (GINA) treatment strategy figure for adults and adolescents, annotated to highlight key features.
ICS: inhaled glucocorticosteroids; SABA: short-acting β2-agonists; LTRA: leukotriene receptor antagonists; LABA: long-acting β2-agonists; OCS: oral glucocorticosteroids; BDP: beclometasone dipropionate; HDM: house dust mite; SLIT: sublingual immunotherapy; FEV1: forced expiratory volume in 1 s; IL: interleukin. Modified with permission of the Global Initiative for Asthma (www.ginasthma.org) [16].

Step 1

For safety reasons, GINA 2019 no longer recommends treatment with SABA alone even at the 1st step of therapy (patients with symptoms less than twice a month, no night-time symptoms, no exacerbation risk factors, normal lung function).

It is recommended that patients at 1st step of treatment should use low dose inhaled ICS/formoterol as-needed. Alternatively, a low dose of ICS when SABA is taken. [4,11].

Step 2

The recommended treatment for step 2 - low dose of ICS or ad-hoc low dose of ICS/formoterol (that is continuation of treatment in step 1 only with higher intensity in terms of necessity). The alternative is leukotriene receptor agonist (LTRA) or low dose ICS taken with SABA [4,11].

Step 3

The preferred treatment for this step is a low dose of ICS/LABA and alternatively a medium dose ICS or a low dose ICS with LTRA [4,11].

Step 4

Asthma is controlled using medium dose of ICS/LABA or using high dose of ICS alternatively adding tiotropium or LTRA [4,11].

Step 5

The highest degree of disease we treat with high doses of ICS/LABA, assess the phenotype, and use additional therapies with tiotropium, anti-IgE, anti-Il5/5R, anti-Il4R [4,11].

As the preferred option for an emergency drug, experts recommend a low dose of the ICS in combination with a formoterol from the 1st to the 5th degree of therapy.
Classical emergency medications considered to be SABA are only an additional option for all those who cannot use low-dose ICS with formoterol in one inhaler due to their availability or other medical conditions [11].

Summary:

Asthma is a leading problem of modern medicine and according to the estimates of the World Health Organization the number of patients will gradually increase, which forces us to analyze the problem and take action to reduce the incidence of the disease. We also need to focus on deriving such treatment regimens that will allow us to control asthma symptoms so that patients do not feel the reduction in life activity caused by asthma symptoms [9].

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