PECULIARITIES OF SEVERE ASTHMA IN CHILDHOOD

Doina Anca Plesca¹’², Eugenia Buzoianu¹’²

¹University of Medicine and Pharmacy „Carol Davila”, Bucharest, Romania
²Department of Pediatric and Pediatric Neurology „Dr.Victor Gomoiu” Children Clinical Hospital, Bucharest, Romania

Abstract

Asthma is the most common chronic disease in children and an important health problem worldwide. Asthma severity is the most important feature of asthma being related to its short and long term outcomes.

At first asthma severity was established according to the level of symptoms, the need for rescue medication and lung function tests.

Most recent guidelines for asthma management recommend that asthma severity should be determined according to the step of therapy needed to achieve asthma control.

Before deciding whether a patient has severe asthma or not, it is important to distinguish between severe asthma and difficult to treat asthma related to incorrect inhaler technique, improper adherence or incomplete controlled comorbidities.

Severe asthma in children has a series of distinctive features towards severe asthma in adults.

In children severe asthma is closely linked with atopy unlike severe asthma in adults.

Adolescents are at a highest prevalence of severe asthma and at the highest death risk through asthma do to poor treatment adherence and do to at risk behaviors (smoking).

In children with severe asthma lung function measurements are age dependent and might be between normal ranges despite the presence of symptoms at the time of the assessment.

Severe asthma in children has a multifactorial etiology. There are many molecular, genetic and epigenetic patterns related to severe asthma.

The main drivers of severe asthma management in children are therapy optimization and comorbidities treatment.

The perspectives in severe asthma management in children include individualized treatment and biological therapies.

Key words: chronic respiratory disease, severe asthma, child

Asthma represents an important health problem in the entire world. Asthma is thought to affect 350 millions people around the world and to cause 250.000 deaths each year ¹. At the same time asthma is the most common chronic disease in children².

Asthma prevalence among children is estimated to be around 9,3% in USA and between 5-27% in Europe and it follows an ascendant pattern in the entire world ³, 4, 5, 6. Furthermore, approximate two thirds of asthma cases in adults are thought to emerge before the age of 18 years old ⁷.

Asthma is a very heterogeneous disease. The heterogeneity of the disease is the result of the interaction between genetic factors and environmental factors, pathological mechanism underlying the disease, health care access, the pattern of treatment response, asthma severity, asthma comorbidities, short and long term outcomes of the disease and other factors ¹.

Asthma severity is the most important feature of asthma, being related to the short and long term outcomes of the disease.

In the early asthma guidelines asthma severity was established according to the level of symptoms, the need for rescue medication and lung function tests⁴. Recently it became more and more obvious that the assessment of asthma severity must include the assessment of asthma treatment responsiveness. That is due to the fact that a child who appear to have severe asthma based on his symptoms can gain a quick treatment response and, in reverse, a child who may appear to have mild or medium asthma may fail to achieve a good asthma control contrary to exception ⁵.

Asthma severity must be periodically reevaluated because asthma severity is not an unchangeable feature of the disease, but a feature that can vary over time ⁶.

Most recent guidelines for asthma management provide the recommendation that asthma severity must be determined according to the step of therapy needed to achieve asthma control ⁶. According to Global Strategy for Asthma Management and Prevention, asthma is considered moderate to severe if requires step 4 medication (medium/high dose of inhaled corticosteroids + long acting beta agonist) or step 5 medication (step 4 + oral corticosteroids or anti IgE therapy) resulting controlled asthma or still uncontrolled asthma, despite therapeutic interventions with step 4 or 5 medication⁷.

According to International ERS/ATS Guidelines on Definition, Evaluation and Treatment of Severe Asthma, severe asthma is asthma which requires treatment with high dose inhaled corticosteroids (ICS) plus a second controller (and/or systemic CS) to prevent it from becoming uncontrolled or which remains uncontrolled despite this therapy received for at least three months ⁸.
World Health Organization included also the category of untreated severe asthma in the definition of severe asthma. Untreated severe asthma is an asthma that is not receiving a proper controller therapy due to poor socioeconomic resources1. It is commonly accepted that, before deciding whether a patient has severe asthma or not, it is important to distinguish between severe asthma and difficult to treat asthma related to incorrect inhaler technique, to improper adherence or to incomplete controlled comorbidities (obesity, chronic rhinitis, etc) 2.

It is also important to distinguish between severe asthma and uncontrolled asthma due to persistent environmental exposure, untreated comorbidities or psychosocial factors 2.

Uncontrolled asthma is more often responsible for persistent symptoms and severe exacerbation than severe asthma. At the same time uncontrolled asthma is much easier to treat than a severe asthma 2.

Difficult to treat asthma is asthma which fails to become controlled do to comorbidities, poor adherence or persistent environmental allergen exposure 2.

Treatment resistant asthma or refractory asthma is asthma which fails to maintain a complete control of symptoms and exacerbation despite treatment with high dose ICS (inhaled corticosteroids) and a second controller (LABA – long acting beta agonist or OCS – oral corticosteroids) 2.

Properly severe asthma refers to refractory asthma and to asthma in which the comorbidities are only partially treated 2.

Before establishing the diagnosis of severe asthma we must exclude: poor inhaler technique (encountered in up to 80% patients), poor treatment adherence, incorrect diagnosis of asthma (which explains lack of response to specific asthma therapy), comorbidities (obesity, rhinosinusities, gastroesophageal reflux, depression and obstructive sleep apnea), persistent environmental exposure to allergens and irritants 2.

Statistically, 12-50% of the patients considered to have severe asthma, in reality, have a completely different diagnosis 2. The prevalence of severe asthma in children is estimated to be 0.5% among general pediatric population and 4.5% among children with asthma 10. Severe asthma in children has a series of distinctive features towards severe asthma in adults. Severe asthma in childhood is closely linked with atopy, unlike severe asthma in adult. In children, severe asthma is associated with atopy in 93.5% of cases 10. In children, as in adults, risk factors for severe asthma are obesity, air pollution, smoking, genetic and epigenetic factors 9. Adolescents are at the highest prevalence of severe asthma and death risk due to poorly adherence to treatment and at risk behaviors (smoking) 11.

The onset of symptoms in children with severe asthma occurs often in the first 3 years of life 11.

Children with severe asthma have higher serum IgE levels, higher serum and sputum eosinophils levels, higher exhaled nitric oxide than the children with mild and moderate asthma 11.

Nevertheless the use of sputum eosinophils or exhaled nitric oxide for guiding asthma treatment in children is not yet accepted 9.

Unlike severe asthma in adults, which tends to follow a persistent pattern, in children, severe asthma often follows a pattern with rapid evolving, frequent and severe exacerbations triggered by viral infections or/and allergens. 11

An important particularity of severe asthma in children is that they are often asymptomatic between exacerbations. 11 In children with severe asthma we can find a series of clinical and inflammatory phenotypes very different from those found in adults. Furthermore, these phenotypes change in time with age, unlike severe asthma in adults. 11 Also, in this category of children with severe asthma, lung function measurements are age dependent and might be between normal ranges despite the presence of symptoms at the time of assessment. 11

In severe asthma the small distal airways are more affected than the large proximal airways. This fact explains why FEV1 (forced expiratory volume in one second) is often normal in children. For these reason, in children, FEV1/CV (vital capacity) may be better correlated with asthma severity than FEV1 alone. 11

Four clinical phenotypes of severe asthma in children have been described: late onset with normal lung function, atopic early onset with normal lung function, atopic early onset with mild air flow limitation and early onset with important air flow limitation. 12

Three inflammatory phenotypes of severe asthma in children have been described: eosinophilic inflammation (more corticosteroid responsive), paucigranulocytic inflammation and neutrophilic inflammation (poor corticosteroid response). 10 Severe asthma in children has a multifactorial etiology and there are many molecular, genetic and epigenetic pattern related to severe asthma (IL4 receptor polymorphism, IL6 receptor polymorphism, etc). 9

The evaluation of an asthmatic patient suspected to have severe asthma must include: watching the patient using his inhaler, showing him the correct inhaler technique and recheck up to three times and again at each visit, discussing treatment adherence and the impediments of proper adherence, confirming the diagnosis of asthma, managing the comorbidities, identifying and exclusion of risk factors (environmental exposure, smoking, using of non steroidal anti inflammatory drugs), treatment stepping up and reevaluating after three to six months. 8

Severe asthma in children requires regular medical check-up, but also a careful follow-up at home. This condition often requires long term peak expiratory flow (PEF) monitoring. 8

The main drivers of severe asthma management in children are therapy optimization and comorbidities treatment.

Fortunately, only a very small group of patients with severe asthma is completely resistant to corticosteroid therapy, therefore ICS are the first line treatment for patients with severe asthma. 1
Severe asthma management in children includes, as additional therapeutic options, optimization of ICS/LABA dose, addition of OCS, add-on treatments without phenotyping, sputum guided treatment, phenotype guided add-on treatment (anti IgE antibodies), non pharmacological interventions and comorbidities treatment.  

To minimize the risk of severe outcomes patients with severe asthma need to undergo influenza vaccination each year. The perspectives of severe asthma treatment in children include individualized treatment based on the clinical and molecular phenotype pattern and biological therapies addressed to specific molecular particularities of each patient.

Conclusions

Severe asthma treatment in children involves the optimization of ICS/LABA dose and association with other controller therapies. Severe asthma management in children must include comorbidities treatment. The additional use of approved biological therapy (anti IgE antibody) provides an improvement in severe asthma control. The perspectives of severe asthma treatment in children include individualized treatment and biological therapies.

References


Correspondence to:
Doina Plesca, MD, PhD
Professor of Pediatrics,
Department of Pediatric and Pediatric Neurology „Dr.Victor Gomoiu” Children Clinical Hospital, Bucharest, 21, Basarabia B-ul, Bucharest, Romania
E-mail : doinaplesca@yahoo.com