



## EDITORIAL

# Identifying severe asthma in pediatrics: The glass half full or half empty



One of the main limitations in adequately identifying severe asthma (SA) in pediatric patients is undoubtedly the lack of consensus regarding its definition. The severity of underlying physiopathological alterations on one hand, and the lack of disease control on the other.<sup>1</sup>

In view of the existing terminological confusion, the World Health Organization (WHO) in 2009 established a task force with the aim of proposing a uniform definition of asthma severity,<sup>2</sup> which contemplated the level of treatment needed to achieve control of the disease. This initiative was also incorporated by the Global Initiative for Asthma (GINA) in its revision of 2014.<sup>3</sup> The term “problematic severe asthma” has been proposed in reference to patients who are unable to achieve control despite maximum treatment effort, and includes both difficult to control asthma and asthma resistant to treatment.<sup>4</sup>

*Why is it important to identify pediatric patients with SA?* A first reason could be its prevalence. Few studies have analyzed the prevalence of SA in the pediatric population. Lang et al. found the prevalence at 10 years of uncontrolled SA in a Norwegian cohort to be 0.5% for the general population and 4.5% among asthmatics.<sup>5</sup> Nordlund et al., using the definition proposed by the WHO and a different methodological approach, found the prevalence at 12 years in a cohort of Swedish children to be 0.23% (2.1% in asthmatics).<sup>6</sup> The article published in this issue of the journal by Plaza-Martín et al.<sup>7</sup> is the first study on the prevalence of SA in pediatric patients in Spain. During a period of three months, pediatric pneumology and allergy units from 30 Spanish hospitals analyzed 12,376 asthmatic patients and identified SA (according to medical criterion) in 8.8% of the cases (95% CI: 8.3–9.3%). Among these, difficult to control SA was diagnosed in 24.2% (95% CI: 21.7–26.8%) – representing 2.2% of the asthmatic subjects.

Another clear reason why it is important to identify SA in pediatric patients is its consequences. In effect, children with SA suffer important morbidity. In the mentioned study,<sup>7</sup> during the preceding year the patients with SA suffered  $6.0 \pm 5.0$  exacerbations, and in the previous 6 months

20% had been admitted to hospital, 63% required emergency care, and 40% had made four or more unscheduled visits to their doctor, with a strong impact upon quality of life. This situation evidently implies important social and healthcare costs associated to SA – the amount totaling about 5380 euros/year in Spain. This sum is more than 10 times the cost of mild asthma, without taking into account the indirect costs, which are not negligible.<sup>8</sup> On the other hand, SA in pediatric patients is not without mortality.<sup>9</sup> Another no less relevant aspect is the middle- to long-term sequelae of the disease. Fitzpatrick et al.,<sup>10</sup> during the follow-up of pediatric patients with SA enrolled in the National Heart, Lung, and Blood Institute Severe Asthma Research Program, recorded a post-bronchodilator test reduction in FEV1 in 46% of the cases, and in 29% of the patients the decrease was over 1% annually – this suggesting progressive airflow limitation. Tai et al.<sup>11</sup> in turn found 44% of the patients with SA in childhood to develop chronic obstructive pulmonary disease by 50 years of age, with an odds ratio (OR) of 31.9 (95% CI: 3.4–269).

*And how can we identify pediatric patients with SA?* We first need to know the characteristics of the disorder, which differ from those of adult SA.<sup>7,12–14</sup> Pediatric SA tends to be more common in males, in patients with several years of asthma, with atopic conditions (increased IgE titers and exhaled nitric oxide levels, and greater aeroallergen sensitization), with lung function, and relatively normal limits, and an improved bronchodilator response. On the other hand, adequate evaluation is required of each and every one of the dimensions of this complex and heterogeneous syndrome (symptoms, lung function, inflammation, and even quality of life), particularly taking into account that the association among them is weak and not substitutable but complementary.<sup>15</sup> The symptoms can be evaluated using previously validated questionnaires (though accepting their limitations), such as the CAN in Spain, which defines poor control as a score of  $\geq 8$ , with sensitivity and specificity performance in the range of 70%.<sup>16</sup> The gold standard for assessing lung function in asthma is FEV1, but the cut-off points used to define severity are based on expert

opinion and have not been duly validated. Furthermore, most children with SA have normal or almost normal FEV1 values (FEV1 >80% of the predicted value). Alteration of the FEV1/FVC ratio is more sensitive in this respect.<sup>17</sup> Serial pre- and post-bronchodilation measurements are needed in our patients, since bronchodilation is correlated to airway inflammation parameters and is a risk factor for the development of fixed airflow obstruction. Since the lungs of children are growing, the data should be presented graphically, as in the case of the body weight and height curves, using percentiles<sup>18</sup> that are available for this purpose (Global Lung Function Initiative; [www.lungfunction.org](http://www.lungfunction.org)). Although inflammatory parameters as such are not used for classifying the severity of asthma, increased exhaled nitric oxide levels are common in patients with SA, and are directly related to the risk of exacerbation, poor adherence and/or performance of the inhalatory technique and scant asthma control, and are predictive of the loss of lung function.<sup>19,20</sup> Regarding quality of life as the ultimate concern in asthma treatment, Nordlund et al.<sup>21</sup> found a PAQLQ (S) score of <6.2 to distinguish severe problematic asthma with a sensitivity of 85% and a specificity of 97%. This dimension of asthma probably should be included in the assessment of our patients.

A number of factors condition the correct identification of patients with SA, such as the existence of disagreement among specialists in classifying the severity of asthma, probably due to variability in interpretation of the symptoms and lung function, and even to variability in the attributed importance of the symptoms versus lung function<sup>22</sup>; heterogeneity in assessing asthma control among patients, parents and physicians<sup>23</sup>; the importance of adding objective measures – particularly those referred to lung function – to symptoms evaluation in order to better classify the severity of asthma and not underestimate the disease (which would lead to undertreatment)<sup>24,25</sup>; and the high percentage of pediatricians who do not routinely use lung function tests in evaluating their asthma patients.<sup>26</sup> We therefore need to develop and implement strategies such as adequate training of the healthcare professionals; therapeutic educational measures targeted to our patients and/or their caregivers; and structural and institutional improvements designed to overcome the existing problems and ensure better identification of SA in pediatric patients – with a view to offering optimum treatment capable of reducing morbidity and of avoiding deleterious effects upon lung growth and function. Let's fill the glass!

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