Wheezing in infants: can we separate the wheat from the chaff?

Wheezing in the first years of life has a high prevalence worldwide and poses a major challenge. The management of wheezing is usually frustrating both for physicians and parents, who see the gradual increase in the therapeutic armamentarium that keeps adding to their children’s “preventive” treatment, usually with no changes perceived in episode frequency or severity. It should be noted that the term “preventive treatment” is not present in the international literature, where we will only find references to asthma “control treatment”.

Different studies have shown that wheezing occurs in up to 50% of children younger than 3 years old, and the most common cause of wheezing are respiratory infections, mainly of viral etiology. These children usually have risk factors for recurrent respiratory infections, such as having school age siblings or attending a daycare center, among other factors. However, many times nasopharyngeal secretion tests by indirect immunofluorescence are negative, thus the viral etiology is ruled out. The use of molecular techniques in Argentina has helped to identify the viral etiology of infections in over 60% of children seen as outpatients and in over 80% of hospitalized children with compatible symptoms.

In spite of the reasons already mentioned and clearly known by pediatricians, recurrent wheezing in infants results in a growing and indiscriminate use of steroidal anti-inflammatory drugs. Several studies have shown that low doses of inhaled corticosteroids have no impact on the development of the hypothalamic-pituitary-adrenal axis in these children; however, other studies have demonstrated that higher doses do have an effect on this axis, in addition to the fact that their younger age or lower weight significantly increase the adverse event rate. One study on the growth of infants and toddlers two years after discontinuation of inhaled fluticasone 100 mcg twice daily versus placebo found that those receiving the drug had grown 1.6 cm less compared to baseline values in 2 year old children with a weight of less than 17 kg.

More than 10 years ago, Castro Rodríguez published the Asthma Predictive Index (API) using the Tucson cohort children; this index was based on major and minor criteria. One criterion of particular interest is the presence of wheezing not associated with colds, which is the most common cause of wheezing in infants and toddlers, and of inadequate treatments, as already mentioned. In all publications making a reference to the API, Castro Rodriguez focuses on its strength to demonstrate which children will not present asthma (high negative predictive value), but points out that it is not strong enough as a predictor for those who will develop asthma. He was also part of a group that reproduced the index in Colombia and found much lower sensitivity and specificity values than those previously described.

For this reason it is necessary to have supportive methods to improve these indexes’ sensitivity or, in other words, find out who out of these infants and toddlers could actually develop asthma at school age and benefit from an anti-inflammatory treatment that will prevent the early narrowing of airways. It would also be important to be able to detect who of these infants and toddlers would actually benefit from an anti-inflammatory treatment, even if they do not develop asthma at a later stage, in order to reduce the indiscriminate use of these drugs. The prevention of early asthma in kids (PEAK) trial has shown that children with a positive API who received daily treatment with fluticasone had a significant clinical improvement versus those who received placebo. This study had two limitations: it was conducted in children with a mean age of 3 ± 0.6 years old, and children with a negative API had been excluded.

In this issue of the Archivos Argentinos de Pediatria, Balinotti, et al. evaluated the association between the API and the fraction of exhaled nitric oxide (FE\textsubscript{\text{NO}}) (see page 191). There is a clear correlation between this marker and the degree of eosinophilic airway inflammation, and it is known that patients with this kind of inflammation have a better response to anti-inflammatory treatment, especially to inhaled corticosteroids. Several studies have shown that children with recurrent wheezing and low FE\textsubscript{\text{NO}} levels may have a better response to leukotriene receptor antagonists than to inhaled corticosteroids.

As with the introduction of pulmonary function tests in infants, this group is once more using a novel technique in the country, which consists of detecting levels of exhaled nitric oxide in very small infants during tidal breathing while the child is asleep or in a calm, awake state. It is worth mentioning that these patients are signi-
Assessment of infants with respiratory distress

Acute lower respiratory tract infections (ALRTIs) represent a heavy burden on health systems each winter when they are faced with providing care to thousands of affected children. The burden of disease was estimated at 94,037,000 “DALYs” (disability-adjusted life years) and 3,900,000 deaths in 2001. The implementation of healthcare programs based on simple components that allow to classify patients according to the seriousness of their condition and, from this, to follow standardized measures can be an effective response to this situation.

Respiratory distress is related to the severity of the clinical condition, and such severity may lead to a cardiorespiratory dysfunction and death. In the case of infants with ALRTI, one of the top priorities is to maintain adequate levels of blood oxygen, so that hypoxemia can be avoided and treated on a timely manner.

In scenarios when it is not possible to measure oxygen saturation (O₂ sat), it is very important to assess respiratory distress using scores based on simple clinical elements (respiratory rate, wheezing, cyanosis, heart rate, intercostal retraction, etc.).

It is not easy to establish when or where this practice was first implemented. It is quite likely that the Silverman-Andersen score was one of the first approaches to standardize the assessment of respiratory distress syndrome. It is of little importance if it started in a study aimed at assessing the impact of the use of “mist” on the mortality of premature newborn infants. Its publication in textbooks of pediatrics led to a rapid dissemination of the score. Moreover, a decade later Dabbous included the Silverman-Andersen score in his “Bronchiolitis Score”, a complex assessment scheme of respiratory distress (made up of 9 components) designed to evaluate the effect of corticosteroids on the treatment of bronchiolitis; thus, this practice was extended to be used in infants up to 18 months old.

In 1974 Pierson, Bierman, and Kelley simplified the “Bronchiolitis Score” by developing what they called the “Pulmonary Index.” This scoring system was initially developed to assess the response to corticosteroid therapy in children aged 5 to 18 years old with status asthmaticus, but it has been more commonly used given its simplicity. In 1983, Tal, et al. used the Pulmonary Index to assess the efficacy of salbutamol and dexamethasone in infants with wheezing, and in order to make patients assessment even easier, they decided to modify one of the elements of the score developed by Pierson, et al.: they replaced...
the inspiratory-expiratory ratio by the presence of cyanosis.

Soon after, Lowell, et al. designed an even simpler tool to objectively evaluate the response of wheezing infants to adrenalin: the Respiratory Distress Assessment Instrument (RDAI). This scale only considers wheezing and chest retractions and it has become a widely used tool in the Northern Hemisphere.

All these instruments were initially developed to assess treatment effectiveness in pilot studies, not to be used in daily practice to decide on the approach of patients with respiratory distress syndrome. Probably because of this, it had not been expected that the score developed by Tal, et al. would have had such a wide dissemination in South America with its inclusion in the program implemented by Chile to face the high infant mortality rates due to ALRTIs. It is likely that the fact of being cited in a well-known textbook of pediatrics has probably resulted in other countries also including this score in their ALRTI programs. It should be noted that Tal’s score was also subject to adaptations and amendments. In this context, Chile and Peru decided to include the respiratory rate in a different manner (stratified by age) and, in addition, Argentina replaced the cyanosis assessment by the heart rate assessment.

More recently, Destino, et al. published a paper comparing the performance of the highly complex “Children’s Hospital of Wisconsin score” with the highly simple modified respiratory distress assessment instrument (RDAI). It is not surprising that no differences were found between both instruments, especially given the evidence that indicates that chest retraction is the most valid indicator of an O$_2$ saturation drop.

Undoubtedly, the best tool to be used in standardized healthcare programs is the one that can be easily applied with objectivity and accuracy. The numerous attempts to do so that have been described in the literature show that this has not always been easy.

There is probably not one unique way to assess respiratory distress in infants, but the elements of the different scores (alone or in combination) can certainly help identify warning signs regarding a possible risk of cardiorespiratory dysfunction or death in this type of patients highly susceptible to hypoxemia.

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