

RESPIRATORY DISEASE IN CHILDHOOD AS A RISK FACTOR FOR THE DEVELOPMENT OF ASTHMA IN ADULTS

Rodolfo Matias de Melo

Eighth period medical student at
UNIGRANRIO-AFYA
Duque de caxias – RJ

Heloisa Griese Luciano dos Santos

Medical student eighth period at
UNIGRANRIO -AFYA
Duque de caxias – RJ

João Guilherme Moura Luciano dos Santos

Eighth period medical student at
UNIGRANRIO-AFYA
Barra da Tijuca – RJ

Priscila Perpetuo Almeida do Nascimento

Fifth Medical Academic at UNIFESO
Teresópolis - RJ

Shirlei de Oliveira Soares Araújo

Medical Student second period at
UNIGRANRIO -AFYA
Duque de caxias – RJ

Djeine Capocci Batista

Medical student eighth period at
UNIGRANRIO -AFYA
Duque de caxias – RJ

Paloma Aline Fernandes Santos

Seventh-year medical student at UNESA
Presidente Vargas - RJ

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Yvone Taube Maranhão

Medical Student sixth period at
UNIGRANRIO-AFYA
Barra da Tijuca – RJ

Dejanilton Melo da Silva

Academic of Medicine tenth period of
UNESA
Presidente Vargas - RJ

Luis Antonio Luciano dos Santos

Pediatrician. Post-graduation in Audit in
Health Systems by Universidade São Camilo.
Post-Graduation in Medical Law by UERJ.
MBA in people management from FGV.

Abstract: Wheezing in infants has been documented as a risk factor for asthma in childhood, adolescence and adulthood, and becomes important when it comes to recurrent wheezing (three or more episodes per year). The diagnosis of recurrent wheezing and asthma in infants and preschoolers is essentially clinical. With important risk factors such as viral infections, being male, prematurity, among others, after the need to rule out differential diagnoses such as primary immunodeficiency, cystic fibrosis, foreign body aspiration and gastroesophageal reflux disease. If an etiological diagnosis is not achieved, the treatment must be based on the same basis as the treatment of asthma. The lack of a gold standard for diagnosing asthma in the preschool period is an important gap in the prediction rules, therefore,

Keywords: Asthma, wheezing in infants, respiratory disease

INTRODUCTION

Wheezing in infants has been documented as a risk factor for asthma in childhood, adolescence and adulthood, and becomes important when it comes to recurrent wheezing (three or more episodes per year). (ABOUT 2019).

According to the Sociedade Brasileira de Pediatria update practical guide on recurrent wheezing in infants and preschoolers (2017), recurrent wheezing in infants (RLS), initially called wheezing baby syndrome, was characterized as the persistence of wheezing for 30 days or more, or the presence of three or more episodes of wheezing within a six-month period. SRL is the second most common obstructive pulmonary disease in humans, in chronological order throughout life, and the most frequent of all of them.

CHONG et al (2018) report in the Guideline of the Brazilian Association of Allergy and Immunology and Brazilian

Society of Pediatrics for wheezing and asthma in preschoolers, that there is a correlation with SRL and asthma. The latter begins in the first years of life and can be confused with other diseases that cause respiratory symptoms such as wheezing, short and rapid breathing, chest tightness and coughing. For some authors referring to recurrent wheezing, more than three episodes of wheezing per year have been defined as synonymous with asthma.

In view of the above, considering that wheezing is a recurrent and highly prevalent symptom in children with respiratory diseases, especially in infants, the choice of the clinical case of the patient SRA aged 3 years and 6 months in the medical practice internship at the PDC in the outpatient clinic of pneumopediatria under the guidance of Professor Dr Fernanda Guimarães, is justified by serving as a source of relevant information regarding the persistence of wheezing in infants and preschoolers as an indication of asthma in the future, bringing with it a theoretical and practical survey in the approach of these children.

DESCRIPTION OF THE HEALTH-ILLNESS PROCESS

A wheeze is a continuous, musical sound that originates from oscillations in a narrowed airway. Wheezing is heard mostly on expiration as a result of critical airway obstruction. (NELSON 2017).

Infants and preschoolers have different characteristics from the other groups of wheezers for several reasons, including: smaller airways in the first years of life, frequent infections by viral agents in a mature phase of the immune system, passive exposure to cigarette smoke and allergens, among others. (CHONG 2018).

Immunological and molecular influences may contribute to an infant's propensity to wheeze. Children in this age group tend to

have more lymphocytes and neutrophils rather than mast cells and eosinophils in the bronchoalveolar lavage fluid. A variety of inflammatory mediators have also been implicated in wheezing infants, such as histamine, leukotrienes, and interleukins. (NELSON 2017).

According to the Guidelines of the Brazilian Association of Allergy and Immunology and the Brazilian Society of Pediatrics for wheezing and asthma in preschool children, most wheezing in infants is caused by inflammation secondary to bronchiolitis, which is predominantly a viral disease caused in approximately 50% of cases by Respiratory Syncytial Virus (RSV). However, many other entities may present with wheezing, thus having some important differential diagnoses, including: structural abnormalities of the airways, foreign body aspiration, gastroesophageal reflux disease, cystic fibrosis, immunodeficiencies, bronchiectasis. (CHONG 2018).

The manual of routines for hospitalized pediatric patients of the Allergy, Immunology and Pneumology sector of UFRN (DANTAS, 2019) presents a table that suggests the investigation of alternative diagnoses of recurrent or persistent wheezing according to associated symptoms. This instrument didactically translates the main possible differential diagnoses for wheezing infants (Table 01).

Regarding treatment, according to the practical guide Sociedade Brasileira de Pediatria on recurrent wheezing in infants and preschoolers (SRLP) (2017), considering the multicausality of SRLP, treatment must be specific, however if a diagnosis is not achieved etiological, the treatment must be justified in the same way as the treatment of asthma.

Intermittent wheezers must use inhaled beta agonists in crises. Persistent wheezing

ASSOCIATED SYMPTOMS	SUGGEST INVESTIGATE
Neonatal problem and wheezing from birth	Congenital airway and tracheoesophageal abnormality
Wheezing or coughing associated with eating or vomiting, with or without regurgitation, unexplained crying	gastroesophageal reflux
History of choking, choking, especially associated with coughing or sudden onset of shortness of breath	Foreign body aspiration
Wheezing with little cough suggests an obstruction of mechanical cause	vascular ring
Symptoms that change with stridor position	Tracheomalacia, Bronchomalacia or Vascular Ring
Little weight gain, cough, and recurrent lung infection	Cystic fibrosis, ciliary dyskinesia
Repeated, slow-moving infections at multiple sites, poor weight gain	Immunodeficiency

Table 01: Alternative diagnoses of recurrent or persistent wheezing.

Source: Adapted from Almpi et al.(2009)

preschoolers must receive beta agonists in attacks and a leukotriene antagonist or inhaled corticosteroid continuously.

A recent review on the efficacy of leukotriene antagonists in preschool children as long-term monotherapy demonstrated that this type of drug can also be used in SRLP.

Short-acting beta 2 agonists and inhaled corticosteroids must preferably be used in the form of metered-dose inhalers with valved spacers. Powder inhalers cannot be used on children in this age group. Long-acting beta agonist agents are not recommended for children under four years of age. Leukotriene antagonists are recommended, the only one available in Brazil is montelukast.

As described in the clinical case, some tests are necessary to help confirm the diagnosis and/or rule out possible diagnostic hypotheses, as already mentioned.

According to the practical guide of the Brazilian Society of Pediatrics cited above, a chest X-ray must be requested to rule out congenital malformations, infections and other less common diseases.

Primary immunodeficiencies are an important differential diagnosis that must be ruled out. These may be present in several clinical specialties. In difficult-to-control asthma, a warning sign is IgA

immunodeficiency and immunodeficiencies associated with pneumonia and sinusitis, and IgG, IgA and IgM dosage must be investigated. In general, in infants at risk, it is important to assess the level of serum immunoglobulins: IgG, IgA, IgM and IgE. (DANTAS 2019).

The specific IgE against RSV is related to the severity of the acute illness as well as the levels of IL-2 and IL-10, being an indicator of the duration of respiratory failure and consequently greater morbidity of the post-discharge respiratory condition. (CHONG 2018).

Total serum IgE and peripheral blood eosinophilia have been associated with persistent wheezing. Medeiros et al. They concluded that total serum IgE can be influenced by the current or past presence of intestinal parasitosis. In this sense, the parasitological examination of feces must also be requested to rule out helminthosis with present or past infestation. Helminthosis could alter the eosinophil count in peripheral blood, the level of serum IgE. (SOUZA 2016).

In the case in question, the mother was instructed regarding the importance of carrying out the exams, being referred at the same place to arrange them and to return to the consultation for reassessment and follow-up.

CASE DISCUSSION

The diagnosis of recurrent wheezing and asthma in infants and preschoolers is essentially clinical, with the main findings being the presence of wheezing, coughing, respiratory distress and continuous or recurrent nocturnal awakenings. (CHONG 2018).

The same author reports that the diagnosis of asthma in preschoolers and younger children is difficult, since wheezing and coughing are common in children without asthma and complementary exams are not very useful. In this sense, it is often only possible to make a syndromic diagnosis of recurrent wheezing and only the follow-up until school age or later allows a more precise etiological definition.

According to ASBAI and SBP Guidelines for Wheezing and Asthma in Preschoolers, most predictive rules for asthma do not go beyond the creation phase. The lack of validation and analysis of predictive indices prevents these instruments from actually being used safely as a method of predicting asthma at the end of the school term. These indices became closely related, not only with the forms of expression of this disease and the probability of active asthma, but also, mistakenly, started to be adopted as diagnostic criteria for asthma in preschool age.

Several prediction rules were developed to help the clinician in the diagnosis of asthma in preschool children, and the multiplicity of them reveals the difficulty in developing a widely accepted rule.

Among the prediction rules and predictive indexes of asthma for infants and preschoolers, there are three that have been used more widely, according to authors.

Castro-Rodrigues et al cited by SBP 2017 and SOUSA 2016, developed the Asthma Predictive Index (API) for infants, comprising diagnostic criteria:

Major Criteria: 1- Presence of asthma in the parents, 2 – Atopic dermatitis in the child.

Minor Criteria: 1 - Presence of allergic rhinitis; 2 - Wheezing in the absence of a cold; 3 – Blood eosinophilia greater than or equal to 4%.

The presence of one major and/or two minor criteria are predictive of asthma. However, sensitivity and positive predictive value were low, 41.6 and 59.1% respectively.

As an example of this aspect, Souza 2016, when using this predictive classification method in his research, in the results and discussion, observed that two recurrent wheezing infants studied, although with a positive skin test, presented negative API, which they indicated as a possible limitation of this index.

Another simpler classification made alternatively by the European Respiratory Society characterizes recurrent wheezing in infants and preschoolers as: 1 - Episodic viral: when it is usually triggered by viral infections and the child does not have cough or wheezing between episodes. 2 – Multiple triggers: in addition to colds, crying, laughing, climate change, dust, and other factors provoke crises. Episodic wheezing is predominantly transient and multiple trigger wheezing related to asthma.

Another widely used index is the “Prevention and Incidence of Asthma and Mite Allergy” (PIAMA) designed to predict asthma at school age before four years of age. It uses clinical parameters that are easy to obtain and has good discriminatory power.

The lack of a gold standard for diagnosing preschool asthma is an important gap in the prediction rules. The very fact that the definition of asthma differs between the aforementioned studies and the fact that a definition that really identifies the disease in this age group is unknown, hinders the comparison of the prediction rules among themselves.

According to SBP 2017, Most studies show a higher prevalence of wheezing in male infants. This is attributed to the smaller airway caliber at this age, higher prevalence of atopy and bronchial hyperresponsiveness. Prematurity and low birth weight are also risk factors for impaired lung function as well as gastroesophageal reflux disease (GERD). Although the association between wheezing and GERD is recognized, the exact meaning of this relationship and its clinical implications remain controversial. What is known is reflux disease can cause respiratory disease by aspiration of gastric contents, vagal reflex, increased bronchial reactivity, or release of tachykinins.

An interesting aspect described in the guideline on wheezing and asthma in preschoolers (CHONG 2018) is about the development of the respiratory microbiome. The authors portray that there is evidence that the development of this airway microbiome occurs very early in life and later in life can be influenced by environment, health status and age. Vaginal delivery, breastfeeding, environmental exposures during the first hours of life and the environment around the first 100 days seem to define respiratory formation with the potential to guarantee respiratory health conditions throughout life. The respiratory microbiome (upper airways and lung) is probably closely related to the development of respiratory diseases such as asthma, either in the early onset form, in wheezing in infants, or in its classic stabilized form, in adolescents and adults.

Many authors have studied the relationship between viral infection by RSV and the subsequent development of asthma, evaluating the fact that certain individuals have a genetic predisposition to virus-induced wheezing and the development of asthma. Epidemiological studies have used persistent wheezing or its recurrence (three

or more episodes, RS) in infants as a synonym for asthma. (CHONG 2018).

The SBP 2017 reports that the relationship between viral infections and the development of asthma is little known, but it is known that these are the main triggers for wheezing, especially (RSV). Viral infections in infants can induce wheezing or be protective against allergic asthma in older children.

The practical guide mentioned above (SBP 2017) brings the theory of hygiene in an interesting way. Nesta suggests that genetically atopic children when exposed in the first months of life (period of development of the immune system) to antigens of some bacteria and farm animals, they can reduce the probability of manifesting asthma due to the deviation in the differentiation of T lymphocytes from T helper 2 (TH2) to T helper 1 (TH1), which stimulate the production of IgG4, acting against infectious agents to the detriment of TH2, responsible for stimulating the production of IgE by B lymphocytes. Although the theory is contested, epidemiological studies corroborate their causal relationship.

SELF-REFLECTION

Respiratory disease in childhood, particularly wheezing in infants, has been studied due to the large number of hospitalizations and documented as a risk factor for asthma in childhood and adulthood. Although the subject is of great importance for public health, there are still gaps in the predilection of infants who may develop asthma in preschool age and adulthood. Therefore, the opportunity to carry out the portfolio with this theme brought me closer to the area of pediatric pediatrics, awakening my interest as a future doctor in the proposed theme.

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