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Case Study

Childhood Asthma: A Synopsis of the Advances in Care and Treatment

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Abstract

Background: Asthma is a heterogeneous chronic inflammatory disorder of the airways, associated with bronchial hyperresponsiveness that leads recurrent that results in recurrent, episodes of wheezing, breathlessness s, chest tightness coughing and bronchial obstruction. Although the disease can start at any age, the first symptoms occur during childhood in most cases.

The severity of asthma in early childhood determines the severity of the symptoms and loss of lung function in later years.

Aim/Objectives: To review and describe the current definition, diagnosis and management of childhood asthma in a summary form.

Methods: Conducted a literature search of all available articles om childhood asthma on PubMed between January 2012 and June 2019.These articles were reviewed for relevance and validity.

Results/Discussion: Typical wheezing patterns in infants or preschool children are short, recurrent exacerbations of cough and wheeze separated by symptom-free intervals. Inhaled corticosteroids are now recommended as the first-line prophylactic therapy in all age groups; however, these medications do not alter the underlying severity or progression of asthma symptoms and lung remodeling may still occur. Although asthma is a major cause of childhood disability and in rare cases causes premature death, asthma morbidity and mortality are largely preventable when patients and their families are adequately educated about the disease and have access to high-quality health care including biological therapy. That is, poor outcomes for childhood asthma, such as hospitalizations and deaths, are at least partially sensitive to the quality of ambulatory health care. With the advent of biomarkers and biological therapy, severe asthma in both children and adults can be effectively controlled.

Conclusion: Biomarkers and biological therapy for asthma should be made available in resource limited settings including those in Sub-Saharan Africa. Both urgent and scheduled asthma visits should include education regarding asthma medications, proper inhaler technique, and use of objective monitoring devices, as well as the creation of a written asthma action plan.

Keywords: *Childhood Asthma; Modified Asthma Predictive Index; Phenotype; Endo-types; The Pediatric Asthma Risk Score (PARS)*

Background

Asthma is a chronic inflammatory disorder of the airways associated with airway hyper responsiveness that leads to recurrent episodes of combination of wheezing breathlessness, chest tightness or coughing Usually this is associated with diffuse but variable airflow obstruction that is often reversible spontaneously or with treatment.

Asthma is a highly variable disease, in terms of presentation, disease progression over time, and response to therapy. As such, the diagnosis and treatment asthma in young children and adolescents is often challenging At any age, recurrent lower respiratory symptoms

associated with cough, wheezing evidence of lower airway obstruction, and response to bronchodilator support a diagnosis of asthma; however, there is no single historical feature that confirms the asthma) diagnosis [1,2]. Comorbid allergic conditions such as allergic rhinitis and eczema are often present. Cough without wheezing is rarely associated with asthma in children. Approximately 80% of asthmatic patients report disease onset before 6 years of age. However, of all young children who experience recurrent wheezing, only a minority will go on to have persistent asthma in later life. The most common form of recurrent wheezing in preschool children occurs primarily with viral infections. These 'transient wheezers' or 'wheezy bronchitis' are not at an increased risk of having asthma in later life. Transient wheezing is associated with airways viral infections, smaller airways and lung size, male gender, low birth weight, and prenatal environmental tobacco smoke (ETS) exposure.

The natural history of asthma is not well described. The relatively few cohort studies that initially examined this issue from childhood to early adulthood contained methodologic problems pertaining to subject selection (most were hospital or clinic based) and design (many were retrospective, did not incorporate a physiologic test for airway reactivity, and some did not examine the question of atopy). Within the past few years, however, more data have become available from ongoing, prospective studies [3,4]. Natural history studies of asthma have identified biologic, genetic and environmental risk factors for persistent asthma From the Tucson cohort respiratory study, a statistical optimization of the major risk factors for persistent childhood asthma provided 97% specificity and 77% positive predictive value for persistent asthma in later childhood.

Diagnosis

The diagnosis of Asthma usually requires documentation of reversible airway obstruction, however lung function tests can usually be done only in children ages six and older.

The Modified Asthma Predictive Index (mAPI) This score applies to paediatric patients ≤ 3 years old. The Modified Asthma Predictive Index (mAPI) provides a method for predicting likelihood of a later asthma diagnosis. It is only applicable in young children with 4 or more episodes of wheezing per year. The presence of one major criterion or two minor criteria indicates a high likelihood that the infant or child will have persistent asthma.

The modified asthma predictive index

Major criteria	Minor criteria
Parental History of Asthma.	Allergic sensitization to eggs, milk or peanuts.
Physician diagnosed atopic dermatitis.	Wheezing apart from viral illnesses.
Allergic sensitization to at least one aeroallergen.	Blood eosinophilia > 4%.

For children aged over five years, details of cough and wheeze and triggers of symptoms and signs of asthma can aid in the diagnosis. Spirometry, where available is useful in establishing an objective criteria for the presence of airway obstruction. In patients older than five to six tears.

Spirometry measurements include forced vital capacity (FVC) and Forced expiratory volume in one second (FEV1). Airflow obstruction is defined as FfEV1 less than 89% of the predicted airflow in healthy children.

There are reference tables based on age, height sex, and race.

The management of pediatric asthma differs from that of adult asthma in a number of ways. Primary care clinicians caring for children are essential to confirm the diagnosis and initiate future management of asthmas. However, the natural history of pediatric asthma is not fully understood, particularly with respect to the relationship between risk factors and the subsequent development of asthma in later

childhood and adult life. Second, because asthma is a heterogeneous disease with many phenotypic expressions during childhood, it is challenging to characterize as the clinical manifestations of asthma are non-specific.

Third, the evaluation of asthma in children can be complicated by difficulty in obtaining objective lung function measurements and the lack of definitive biomarkers. Fourth, multiple wheezing phenotypes are expressed in early childhood. Indeed, many children wheeze during the first few years of life, but approximately 60% are 'transient early wheezes' who outgrow their disease by the age of 6 years. As only 15% of wheezing infants develop persistent asthma in later childhood [5], many cross-sectional surveys may include these 'transient early wheezes' in the population defined as having persistent asthma. Many infants or preschool children can wheeze, usually in association with viral infections. Fifth, longitudinal data that follow the disease from birth to death or disease remission are lacking. Sixth, asthma may impact lung growth in the developing child, and anatomic differences in children such as smaller airway size and lower inspiratory flow rate may impact medication deposition in the airways. Finally, it is not clear which are the most effective therapies for a particular wheezing phenotype or whether early intervention can alter the course and outcome of this chronic disease.

Asthma and other wheezing disorders are among the most common causes of hospitalization and other health care use in young children representing a significant burden to the child, the family, the health care system, and society. These very common symptoms in the first years of life represent a heterogeneity of diseases with little to differentiate the clinical presentations, which is a cause of inadequate treatment. Asthma and other wheezy disorders are likely to embody several endotypes associated with distinct clinical features, divergent underlying molecular causes, and different treatment responses. Much of the information about phenotypes and endotypes in Childhood Asthma has been achieved through a radical breakthrough using computer software ice Machine learning or Big Data and cluster sampling i.e. eosinophilic versus Non eosinophilic asthma or Allergic versus non-allergic asthma phenotypes [6].

Users of PARS answer questions about early wheeze, difficulty breathing when healthy, previous allergy skin testing, race, and parental asthma. The tool then generates a score that indicates whether the risk for asthma is low, moderate, or high, and provides a percentage for the likelihood that the child will develop asthma by the age of 7.

The typical pattern of illness in preschool-aged children consists of short but recurrent exacerbations of cough and wheeze usually triggered by viral respiratory tract infections. Documenting reversible airflow obstruction on lung function, allergen sensitization, increased IgE levels, or blood eosinophilia is helpful in establishing a diagnosis of asthma in preschool-aged children, if present; however, the diagnosis is most often based on symptom patterns, presence of risk factors, and therapeutic responses. The preschool-aged asthmatic population tends to be characterized as exacerbation prone with relatively limited impairment, unlike older children and adolescents who have more impairment-dominant disease [7].

Classification of childhood asthma. Biologic therapies for asthma associated with type 2 inflammation

Asthma is the most common chronic lower respiratory disease in childhood throughout the world. Several program guidelines and/or consensus documents are available to support medical decisions on pediatric asthma e.g. the Global initiative for Asthma, (GINA), the Expert Panel Repot Thee of the National Asthma Education and Prevention Program (NAEPP) Coordinating Committee (CC), coordinated by the National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health [8,9] and the World Allergy Organization (WAO) [10]. The 2007 NAEPP guidelines use the severity of asthma classification with features of asthma severity divided into three charts to reflect classification in different age groups (0 - 4y, 5 - 11y and 12y and older). Classification includes (1) intermittent asthma, (2) mild persistent asthma, (3) moderate persistent asthma, (4) and severe persistent asthma.

In contrast, the 2016 Global Initiative for Asthma (GINA) guidelines categorize asthma severity as mild, moderate, or severe. Severity is assessed retrospectively from the level of treatment required to control symptoms and exacerbations, as follows:

- **Mild asthma:** Well controlled with as-needed reliever medication alone or with low-intensity controller treatment such as low-dose inhaled corticosteroids (ICSs), leukotriene receptor antagonists, or chromones.
- **Moderate asthma**: Well controlled with low-dose ICS/long-acting beta2-agonists (LABA).
- **Severe asthma:** Requires high-dose ICS/LABA to prevent it from becoming uncontrolled, or asthma that remains uncontrolled despite this treatment.

Asthma severity is determined best at the time of diagnosis, before initiation of therapy. There are four categories of asthma severity, intermittent, mild persistent, moderate persistent and severe persistent.

The severity assessment comprises of symptoms and level of impairment.

In addition, a risk assessment should be performed based on the number of previous exacerbations requiring oral steroid intervention.

Although there is no doubt that the use of common systematic approaches for management can considerably improve outcomes, dissemination and implementation of these are still major challenges. Current treatment centers on guideline-directed care and consists of a stepwise approach with increasing doses of medications, primarily ICS, often in conjunction with a second controller medication to achieve disease control. In general asthma medications are classified into rescue (relievers and controller's). Controller Medications- These are usually taken every day, even if you feel well. They help prevent asthma symptoms and asthma attacks. However, they do NOT help quickly during an asthma attack.

All patients need access to quick-relief bronchodilators (short acting Beta agonists).

Asthma relievers (rescue medications- These are usually only taken when needed for quick relief or for an asthma attack. They help open up your lungs by relaxing the muscles that surround the airways. Reliever medications are sometimes called "rescue" medications or "quick relief" medications, since they start working quickly (usually within a few minutes). This is the inhaler you use when you have an asthma attack.

Inhaled drug delivery technique is important. To avoid frequent errors, check regularly.

Spacer (valve holding chamber) with Metered Dose Inhalation improves lower airway delivery at all ages (including adult's) and reduces side effects (thrush with inhaled corticosteroids).

However, management of persistent disease is based largely on expert opinion and extrapolation from studies in older children given the relative lack of data in this age group. Strategies used to manage intermittent disease include daily and intermittent controller therapy. Management strategies for persistent asthma include daily inhaled corticosteroids, daily leukotriene receptor antagonists, and combination therapies. Current asthma management relies on inhaled corticosteroids, but some asthma is not well controlled with inhaled steroids alone or in combination with long-acting bronchodilators or leukotriene pathway inhibitors. Of recent monoclonal antibodies/ biological therapy i.e. Omalizumab, Mepolizumab, Reslizumab, Benralizumab and Dupilumab have been approved for treatment of severe Asthma i.e. Global Asthma Initiative (GINA). step four disease. Asthma severity is defined as intermittent or persistent, with persistent asthma subdivided into mild, moderate, and severe. These categories are defined by the frequency of symptoms, lung function, and frequency of exacerbations requiring Oral Corticosteroids (OCS). Severe asthma is defined as asthma that requires either OCS for > 50% of the year or the combination of high dose Inhaled corticosteroids (ICS) and a Long Acting Beta Agonist (LABA) or other medication (leukotriene inhibitor/theophylline) to maintain control. Patients with severe asthma commonly have daily symptoms, awaken at night due to symptoms, have significant limitations in normal activities and an FEV1 < 60% of the normal predicted volume. Omalizumab is a monoclonal antibody to IgE, which is indicated for the treatment of patients with moderate to severe asthma with the allergic phenotype described above. Mepolizumab, reslizumab, and benralizumab target the IL-5 pathway either with monoclonal antibodies to IL-5 itself

(mepolizumab, reslizumab) or to the IL-5 receptor (benralizumab). Dupilumab is a monoclonal antibody to the IL-4 receptor, which modulates both the IL-4 and IL-13 pathways.

Conclusion

Finally, regular monitoring of symptom control and medication side effects is important along with titrating controllers to the minimally effective dose [8].

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