

DIAGNOSIS AND MANAGEMENT OF PRESCHOOL ASTHMA

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ABSTRACT

Asthma is the most common chronic disease in childhood and remains under-diagnosed despite reports of increasing prevalence in most countries. Improperly treated asthmatics may suffer from avoidable complications including chronic daily symptoms, frequent emergency visits and unnecessary hospital admissions. Diagnosing asthma in affected preschool children is particularly important, as this age group is the most at risk for having severe symptoms and frequent asthma exacerbations. However, establishing a diagnosis of asthma in younger children can be challenging. This article summarises key elements of current recommendations on the diagnosis and management of preschool asthma. The goal is to increase awareness of typical signs and symptoms of preschool asthma and to provide healthcare providers with guideline-based recommendations for maintenance therapy.

INTRODUCTION

Asthma is a heterogeneous disease, usually characterised by episodic respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, as well as chronic airway inflammation and reversible airflow limitation on pulmonary function testing.¹ Asthma is the most common chronic disease of childhood. The asthma prevalence in Africa is approximately 10% of children of 6–7 years of age and is increasing over time.²

Most children with asthma present with their first symptoms in the preschool years.³ This population is at greater risk, compared to other age groups, to experience emergency visits and hospital admissions for asthma.⁴ The diagnosis of asthma can be challenging in preschoolers, who are unable to perform conventional lung-function testing by spirometry. Asthma in toddlers was previously classified according to wheezing phenotypes (ie episodic or multi-trigger wheeze and transient, persistent or late-onset wheeze); however, the clinical usefulness of this phenotyping has not yet been demonstrated and is therefore no longer commonly used.¹ Nonetheless, early diagnosis and proper treatment of childhood asthma is important and may, in addition to symptom control, allow for maximum lung growth and function in later life. This article presents the current approach to diagnosis and management of asthma and wheezing in preschool children as recommended by national and international guidelines.

DIAGNOSTIC APPROACH

Episodic airways obstruction and reversibility of airflow limitation are the cornerstones of an asthma diagnosis. Pulmonary function testing before and after inhaled bronchodilator medication is therefore commonly used to confirm suspected asthma in older children and adults. In the absence of objective measures of reversible airways obstruction a diagnosis of asthma can be challenging. Caregivers may report symptoms of airways obstruction in preschool children as cough, wheezing, shortness of breath or limitation with physical activity. All these symptoms may occur intermittently. Wheezing is the most specific sign of airflow obstruction, particularly when triggered by exercise, laughing, crying or environmental exposure outside of a respiratory tract infection. Cough is more indicative of asthma when happening at night or, similar to wheezing, when triggered by exercise, laughing or crying.¹ If related to a viral infection, an asthmatic child will often have a prolonged cough for more than ten days, have more than three episodes of prolonged cough per year and may continue to cough in between viral episodes. Symptoms of asthma are frequently overlooked by caregivers or healthcare providers and may only present as exercise-induced. A thorough medical history is therefore of great importance.

The family history plays a crucial role when suspecting asthma in a child. A family history of atopy is the most important risk factor for asthma in children, the strongest association is in the presence of maternal atopy.⁴ Different international guidelines including the 2017 Global Initiative for Asthma (GINA) report

TABLE I: SIGNS AND SYMPTOMS OF PRESCHOOL ASTHMA (MODIFIED FROM BRITISH THORACIC SOCIETY, 2016)⁴

DESCRIPTION	PARAMETER	SENSITIVITY	SPECIFICITY	POSITIVE PREDICTIVE VALUE	NEGATIVE PREDICTIVE VALUE
Signs and symptoms	Cough	88%	7%	76%	15%
	Wheezing	54%	57%	80%	27%
	Shortness of breath	76%	52%	84%	40%
Combination of symptoms	Cough and wheezing	49%	59%	80%	51%
History of atopy	Personal history of rhinitis/eczema	47–62%	20–75%	72–86%	14–30%

have emphasised the importance of atopy among the diagnostic criteria for asthma in preschoolers,¹ whereas other guidelines put less emphasis on this.³ While it is important to raise awareness to signs and symptoms of obstruction of the airways, wheeze, cough, shortness of breath and atopy have low predictive values for the diagnosis of asthma in preschool children, as illustrated in Table I. Therefore, a treatment trial can be helpful to confirm a diagnosis of asthma by documenting improvement or resolution of symptoms with asthma therapy. Current guidelines including the South

African Childhood Asthma Working Group (SACAWG) 2017 update for the management of chronic asthma in children⁵ recommend a three-month therapeutic trial with low-dose inhaled corticosteroid (see Table II). If feasible, it is recommended to arrange a follow-up as early as six weeks after starting the new therapy, in order to monitor inhalation technique and improve adherence. It may, however, take up to 3–4 months before the maximal therapeutic effect of inhaled corticosteroids can be seen.¹ Reversibility of airways obstruction is confirmed if there is improvement with the therapy and worsening of symptoms at its cessation.¹ Other guidelines also include a positive response to short-acting beta-agonist (SABA) as a sign of reversibility.³ Validated tools to measure the severity of airways obstruction using clinical observations have been developed for paediatric patients. The Paediatric Respiratory Assessment Measure (PRAM) score⁶ can also be used to measure treatment responses (see Table III). If the clinical history is atypical for asthma and/or there is no response to inhaled corticosteroids, alternative diagnosis needs to be considered (see Table IV).

TABLE II: PREFERRED LOW-DOSE ICS AS TOTAL DAILY DOSE (MCG) IN CHILDREN LESS THAN FIVE YEARS (SACAWG)⁵ AND CHILDREN 6–11 YEARS (GINA 2018 UPDATE)²¹

INHALED CORTICOSTEROID	LESS THAN 5 YEARS	6–11 YEARS
Beclomethasone dipropionate (HFA)	50–100	50–100
Budesonide (pMDI and spacer)***	100–200	100–200
Budesonide nebulised***	250–500	250–500
Fluticasone propionate (HFA)	50–100	100–200
Ciclesonide #	N/A	80–160

***Most preparations are registered for twice daily use except Budesonide which can also be administered once per day.

Not registered in South Africa for use in children less than 12 years of age

TABLE III: THE PRESCHOOL RESPIRATORY ASSESSMENT MEASURE (PRAM) SCORE²⁰

CRITERIONS	DESCRIPTIONS	SCORE
O ₂ SATURATION	≥95%	0
	92–4%	1
	<92%	2
SUPRASTERNAL RETRACTION	Absent	0
	Present	2
SCALENE MUSCLE CONTRACTION	Absent	0
	Present	2
AIR ENTRY	Normal	0
	Decreased at the base	1
	Decreased at the apex and the base	2
	Minimal or absent	3
WHEEZING	Absent	0
	Expiratory only	1
	Inspiratory (± expiratory)	2
	Audible without stethoscope or silent chest (minimal or no air entry)	3
PRAM SCORE (MAX 12):		
PRAM SCORE	0–3	4–7
SEVERITY	Mild	Moderate
		Severe

TABLE IV: DIFFERENTIAL DIAGNOSIS OF WHEEZE IN CHILDREN UNDER FIVE YEARS OF AGE (SACAWG)⁵

CATEGORY	DISEASE ENTITY
Congenital upper airways	Laryngomalacia Complete cartilage rings Cysts, webs Tracheomalacia Vocal-cord paresis Subglottic stenosis
Congenital lower airways	Vascular rings/sling Bronchomalacia
Aspiration 'syndromes'	Gastroesophageal reflux disease (GERD) Swallowing incoordination Laryngeal cleft Tracheoesophageal fistula
Bronchiectasis	Cystic fibrosis Primary ciliary dyskinesia Persistent bacterial bronchitis Immunodeficiency (primary/secondary to HIV)
Bronchial obstruction	Lymph nodes enlarged by tuberculosis (TB), HIV or lymphoma
Endobronchial lesions	Foreign body Tumours TB granuloma
Cardiac	Enlarged cardiac chambers Pulmonary oedema Congenital heart disease (left to right shunts)
Miscellaneous	Bronchopulmonary dysplasia

TABLE V: CHILDHOOD ASTHMA CONTROL TEST OF CHILDREN 4-11 YEARS OLD (ALLERGY AND ASTHMA NETWORK)¹⁶

Have your child complete these questions.

1. How is your asthma today? **SCORE**

				☐
Very bad ①	Bad ①	Good ②	Very good ③	

2. How much of a problem is your asthma when you run, exercise or play sports?

				☐
It's a big problem, I can't do what I want to do. ①	It's a problem and I don't like it. ①	It's a little problem, but it's okay. ②	It's not a problem. ③	

3. Do you cough because of your asthma?

				☐
Yes, all of the time. ①	Yes, most of the time. ①	Yes, some of the time. ②	No, none of the time. ③	

4. Do you wake up during the night because of your asthma?

				☐
Yes, all of the time. ①	Yes, most of the time. ①	Yes, some of the time. ②	No, none of the time. ③	

Please complete the following questions on your own

5. During the last 4 weeks, how many days did your child have any daytime asthma symptoms?

⑤	④	③	②	①	①
Not at all	1-3 days	4-10 days	11-18 days	19-24 days	Everyday

6. During the last 4 weeks, how many days did your child wheeze during the day because of asthma?

⑤	④	③	②	①	①
Not at all	1-3 days	4-10 days	11-18 days	19-24 days	Everyday

7. During the last 4 weeks, how many days did your child wake up during the night because of asthma?

⑤	④	③	②	①	①
Not at all	1-3 days	4-10 days	11-18 days	19-24 days	Everyday

TOTAL ☐

MANAGEMENT

The goals of asthma management are to:

- achieve good control of symptoms;
- maintain normal activity;
- minimise future risk of flare-ups (asthma attacks), and
- minimise medication side-effects.¹

These goals are reached in partnership with the caregiver, the affected child and healthcare providers through monitoring the symptoms and providing education, skills training for effective use of inhaler, encouragement for good adherence and a written asthma action plan.

Inhaled corticosteroids (ICS) remain the treatment of choice for asthma management. The lowest ICS dose possible should be used to achieve symptom control. Medium-dose ICS, when taken properly, will decrease the number of

exacerbations requiring treatment with oral steroids by 50%, shorten duration of exacerbations and cause less symptoms between episodes.⁷ Preferably, inhaled medication should be given through a valved holding chamber or spacer. Chambers with face masks are used in younger children. Children that show a proper seal technique, sometimes as early as four years of age, should use a mouth piece for inhalation.¹ A pressurised metered dose inhaler (pMDI) with a valved holding chamber is the preferred method of drug delivery.⁸ Use of a nebuliser is an alternative delivery method but should be reserved for children unable to adequately use a spacer device. Different from SABA, the effect of anti-inflammatories is not immediate. ICS start to have recognisable effects after 1–4 weeks and may not reach maximal efficacy before 3–6 months of use.⁹

A step-wise approach to achieve symptom control is generally recommended in asthma management:^{1,3,5}

Step 1 – As-needed inhaled short-acting beta₂-agonist (SABA) or low-dose ICS:

Preferred option: As needed short-acting beta₂-agonists (SABA)

For mild and infrequent symptoms of wheezing, SABA monotherapy as needed is generally recommended as the preferred treatment.^{1,3,5}

Other option: Low-dose ICS

GINA guidelines now consider ICS as an alternative for treatment of children with intermittent viral-induced wheeze and no interval symptoms, in whom inhaled SABA is not sufficient.^{1,10} Oral bronchodilator therapy is not recommended due to slower onset of action and higher rate of side-effects compared to SABA.

Step 2 – Initial controller treatment plus as-needed SABA

Preferred option: Daily low-dose ICS, plus as-needed SABA

Persistent (ie more than eight days per month) or severe symptoms (requiring oral steroids or hospital admission) should be treated with daily low-dose ICS as preferred controller choice. This treatment should be given for at least three months to establish its effectiveness in managing asthma symptoms.^{1,10}

Other option: Leukotriene receptor antagonist (LTRA)

LTRA (Montelukast™) is an alternative treatment for step 2, although proven less effective in reducing symptoms than ICS.⁵ It should be considered for children who are unable or refuse to receive ICS therapy, who have significant side-effects with ICS or those with allergic rhinitis (AR).¹

Step 3 – Additional controller treatment, plus as needed SABA

Preferred option: Medium dose ICS (doubling low dose ICS)

When symptoms remain uncontrolled with low-dose ICS, doubling the initial low daily dose ICS is the preferred option in the preschool population¹.

Other option: LTRA with low-dose ICS.

Step 4 – Continue controller treatment and refer for specialist assessment

Preferred option: Refer for expert advice and further investigation

If a child fails to achieve and maintain good asthma control after three months on medium-dose ICS, with proper adherence, technique and in the absence of treatable comorbidities, international guidelines such as GINA recommend to refer to a specialist.¹

Other options: High-dose ICS (perhaps combined with more frequent dosing) or low-dose ICS (for a few weeks only) or add LTRA or theophylline or add intermittent ICS to the regular daily ICS during exacerbations.

The best treatment of preschool asthma when step 3 is insufficient has not yet been established. Although not approved in this age group, inhaled ICS/LABA fixed combination therapy is now widely used as off-label medication in children five years of age and younger. In older patients, adding a LABA to a low-dose ICS provides additional control symptoms with a reduced risk of exacerbations.¹

Similarly, other frequently prescribed ICS medications may also not be approved for the preschool age and therefore be used off-label. Beclomethasone dipropionate, a prodrug that is rapidly activated by hydrolysis to the active monoester 17-beclomethasone monopropionate, is an ultra-fine particle compound with better lung deposition compared to larger particle ICS.¹¹ However, whether this results in superior efficacy remains to be proven.¹² Ciclesonide is an inactive prodrug that is converted to its active metabolite desisobutylciclesonide in the airways, and due to low oral bioavailability, has potentially less systemic side-effects. It is used once daily which may result in improved adherence.

Since ciclesonide is a relatively new medication, there are fewer studies on its long-term safety and efficacy.¹³ Fluticasone propionate is a large-particle steroid with the highest binding receptor affinity.¹⁴ Therefore, it is considered the most efficient ICS. A comparison of fluticasone with budesonide and beclomethasone in adults and children in a recent Cochrane review, concluded that at comparable doses, fluticasone was slightly more effective than budesonide or beclomethasone but with concurrent higher risks of unwanted side-effects.¹⁵ The availability and the relative costs of different treatment options need to be considered for controller choices in younger children.¹⁰

At every visit, the healthcare provider should attempt to quantify asthma control by asking about daytime symptoms, limitations of activity and night-time awakenings from cough, recent exacerbations (asthma attacks or flare ups) that may have caused an emergency visit, a hospital admission, prescription of oral steroid courses or repeated use of SABA. Reassurance of good adherence with the prescribed medication dose and adequate technique (watch patient using their inhaler and correct errors), as well as screening for potential side-effects of therapy, modifiable risks factor (eg environmental exposures) and comorbidities (eg AR) and alternative diagnoses should be assessed before considering to step up the treatment.¹ Routine follow-up is recommended every 3–4 months. Validated tools, for instance the Childhood Asthma Control Test (see Table V)¹⁶ can be used to quantify symptoms and asthma control in preschool children. Other tools are also available such as the TRACK score, Primary Care Asthma Control Screen (PACS) and the 30-second asthma test.¹ The lowest possible dose of medications should be used to achieve asthma control with normal activity level and very few symptoms and exacerbations. Healthcare providers should consider stepping down on medication at every visit, if symptoms are well controlled for at least three months. ICS can be stopped from a low dose in the presence of minimal symptoms during the season when the child is usually the most symptomatic.³

When prescribing corticosteroids, caregivers need to be informed of the potential risks for unwanted effects and the expected benefits of the medication. Patients should be monitored for common side-effects including growth retardation and adrenal suppression routinely on follow-up, specifically when using higher ICS doses or systemic corticosteroids. The child's height should be measured at least yearly. Growth velocity can be affected by ICS in the first 1–2 years of treatment in the prepubertal children. Nonetheless, a meta-analysis study concluded that ICS users had only a slight reduction in their adult final height of about 1 cm or 0.7%.¹⁷

EVOLUTION OF PRESCHOOL ASTHMA

The earlier the onset of wheezing, the better the prognosis. In 60% of affected preschoolers, the asthma will have resolved by age six years.¹⁸ Risk factors for persistence of asthma into later childhood include a family history of atopy with or without asthma. Female sex is a risk factor for the persistence of asthma into adulthood. The severity of asthma

during preschool years, according to the number of wheezing episodes and the trajectory of symptoms over time, are also associated with recurrent wheeze that can persist during adolescence.¹⁸

MANAGEMENT OF EXACERBATIONS

Poorly controlled asthma is a risk factor for future exacerbations. These are defined as an acute or sub-acute worsening of symptoms sufficient to cause distress or risk for health and necessitating an unscheduled visit to a healthcare provider or emergency room, requiring treatment with oral corticosteroids.¹ Strong predictors of an imminent exacerbation are increased daytime cough and wheeze as well as night-time use of beta-agonists.¹⁹

Cornerstones of the management of an exacerbation are frequent administration of SABA, systemic (oral or injected) corticosteroids and supplemental oxygen in patients with desaturations.¹ Healthcare providers and caregivers need to be familiar with recognising and treating asthma exacerbations.

CONCLUSION

Asthma in preschool children is important to recognise as the first symptoms of asthma usually present early in life. This population is more at risk of experiencing emergency

visits and hospital admissions due to asthma, compared to older children and adults. Even without spirometry testing, healthcare providers should be able to suspect and establish a clinical diagnosis in preschoolers with a positive history of airway obstruction and reversibility. A personal or family history of atopy and symptoms of airflow obstruction that occur outside of a viral episode make a diagnosis of asthma more likely.

Alternative diagnoses should be considered in the presence of atypical symptoms or unresponsiveness to asthma therapy. The cornerstones in the management of asthma in preschoolers are family education and ICS with different add-on medications in case of poor symptom control. The healthcare providers should arrange regular follow-up visits ideally every 3–4 months to assess for symptoms, adherence with prescribed medication dose, inhalation technique and side-effects of the medication. In the future, more accessible objective measurements of the lung function in this age group might become widely available to ensure an easier diagnosis and monitoring.

DECLARATION OF CONFLICT OF INTEREST

The authors declare no conflict of interest.

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