Management of severe asthma in children

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Abstract

The majority of children with asthma are classified as mild/moderate and can be successfully managed with regular inhaled corticosteroids and bronchodilators. However, more than 5% of asthmatic children continue to have sub-optimal control despite apparently appropriate therapy. These children suffer significant morbidity including poor school attendance, adverse effects on family life and consume disproportionate health care resources. True therapy resistant asthma is rare in children and paediatricians should focus on ensuring the correct diagnosis, identifying and managing modifiable risk factors for difficult to control asthma before using the label severe asthma. Management of severe asthma requires a multidisciplinary approach. Symptomatic children on Step 4 (less than 5 years) or Step 5 (more than 5 years) of British Thoracic Society/SIGN Asthma Guideline or in children with diagnostic uncertainty should be referred to the local tertiary paediatric respiratory service.

Keywords adherence; allergy; asthma; children; difficult; severe

Introduction

Asthma is a chronic inflammatory disease characterized by airway hyper-responsiveness and variable airflow obstruction manifesting as recurrent episodes of wheeze, breathlessness, cough and chest tightness. Asthma remains a clinical diagnosis. One in 11 children in UK has a diagnosis of asthma with the vast majority controlled by low doses of medication including inhaled bronchodilators and corticosteroids. They are managed successfully in Primary or sometimes Secondary care. A small proportion of asthmatic children have poorly controlled disease despite treatment with high dose inhaled steroids. The World Health Organization (WHO) defines severe asthma as: "Uncontrolled asthma which can result in the risk of frequent severe exacerbations (or death) and/or adverse reactions to medications and/or chronic morbidity (including impaired lung function or reduced lung growth in children)".

The British Thoracic Society (BTS) and Scottish Intercollegiate Guidelines Network (SIGN) guidelines define difficult asthma as persistent and/or frequent symptoms despite treatment with 400 mcg/day budesonide or equivalent of inhaled corticosteroids (ICS) in children less than 5 years or 800 mcg/day (500 mcg fluticasone) of ICS in children more than 5 years. Despite effective therapies and such evidence based guidelines many children and adults with asthma fail to achieve satisfactory control of their symptoms. The Environment and Child birth cohort study from Norway estimates 4.5% of children with asthma have severe disease. Although evidence for the management of children with severe asthma is sparse and, current practice is based on extrapolation of data from adult studies and research in children with mild to moderate asthma, there is consensus that severe asthma in children requires a multidisciplinary, stepwise approach involving considerable health care time and resource. This frequently involves the use of high doses of anti-asthma medications and of poly-pharmacy exposing these children to adverse drug effects. Paediatric asthma deaths in the UK peaked in the mid-1960s but children with poorly controlled asthma remain at risk of fatal exacerbations. In 2010 there were 16 asthma related deaths in children aged less than 14 years in UK and confidential enquires continue to highlight the increased risk amongst those classified as severe.

Severe asthma classification

Asthma severity classifications are utilized in the stepwise approach advocated in the various national and international guidelines. The goal of such guidelines is no or minimal symptoms, without exacerbations and the opportunity to lead a normal lifestyle with no impairment to activity accompanied by normal or near normal lung function in the face of little or no use of rescue bronchodilator therapy. However, the evidence base is insecure and differentiates poorly between the various levels of severity. There is a poor correlation between symptoms and measures of lung function and asthma severity. Such classifications are open to the criticism that they reflect the concept of asthma control rather than measure the severity of the underlying disease.

Approach to the patient with severe asthma

Table 1 highlights three groupings commonly utilized in evaluating children referred with 'severe asthma'. Terms including 'chaotic asthma', 'refractory asthma' 'brittle asthma' are best avoided.

Is the diagnosis right?

Asthma is a clinical diagnosis. It is characterized by episodic respiratory symptoms predominantly wheeze which can be associated with cough, breathlessness and chest tightness in absence of an alternative explanation. Children are often atopic and symptoms improve with adequate treatment. The BTS/SIGN guideline recommends diagnosis of asthma on the basis of high, intermediate and low probability. A thorough history and examination is key to the diagnosis of asthma. Spirometry and bronchodilator reversibility should be performed in children older than 6 years. Spirometry demonstrates small-medium airway obstruction in asthma. However, it may be normal even in patients with severe asthma. A detailed Peak flow dairy is useful in some children to provide longitudinal trends.

Careful evaluation for alternate diagnosis should be carried out in children with 'low probability' of asthma or in children with poor response to standard asthma management (Table 2).

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1. Not asthma	*The diagnosis is wrong*
2. Difficult to treat asthma	*Mild asthma exacerbated by one or more co-morbidities (asthma plus) and those with reversible factors such as poor adherence poor inhaler technique or excessive allergen exposure*
3. Severe therapy resistant asthma	*Continued symptoms despite trial of various medications and addressing reversible factors*

Table 1

The term 'wheeze' is often used by parents to describe other respiratory sounds including stridor and rattly breathing. Alternative diagnosis should be sought particularly in non-atopic children with a diagnosis of poorly controlled asthma and in young patients. In a study of 102 children investigated for problematic severe asthma, 10 out of 14 non-atopic children had alternative diagnosis.

Isolated cough is not a feature of paediatric asthma (cough variant asthma) and asthma medication should not be prescribed in these children. A prospective review of 81 children with chronic cough showed none of these children had asthma as their sole final diagnosis. Studies have also shown that in children with isolated cough, airway inflammation is not consistent with asthma.

CT chest is a useful biomarker in adult severe asthma but evidence of its value in paediatric severe asthma is poor and should be arranged only if a diagnosis other than asthma is suspected.

Difficult to treat asthma

Why is there poor symptom control?

Children with asthma of varying severity accompanied by other co-morbid conditions (asthma plus) such as obesity, chronic rhino-sinusitis, gastroesophageal reflux, psychological factors or potentially reversible factors including poor adherence, inhaler technique or continued exposure to allergens are included under the umbrella term "difficult to treat asthma". Children should not have escalation of asthma medication until associated conditions have been thoroughly addressed.

Is there a co-morbid condition? – Asthma plus

Asthmatic children often have conditions which escalate the severity of their asthma termed 'asthma plus'.

Is the child receiving/taking their medication?

Poor adherence to daily medication is the commonest cause for poor symptom control. Children are surprisingly frequently left to administer their own medication without adequate supervision. Inability to see immediate effect of daily medications is thought to be the major contributing factor for poor adherence. Adherence to treatment should be checked at every possible opportunity and difficulties encountered by children or carers in remembering and administering medications should be addressed with repeated education and practical tips and incorporated into a clear Asthma Management Plan. Prescription uptake should be assessed by contacting the General Practitioner and a home visit by the asthma or respiratory nurse is of immense value. The accessibility, use by date, dose and type of medications can all be assessed during such visits. Home visit by asthma/respiratory nurse should be considered in all poorly controlled patients. Education represents a significant component in children's lives and regular interaction with the school nurse is useful. Use of social media sites, email etc. to advocate adherence should be explored. The patient and parents should be involved at every stage and medications/delivery systems should be 'personalized' as far as possible to improve concordance to treatment. Chan et al. reported improved compliance, less health utilization and better symptom control in 60 children managed by Web based case management and education compared to 60 children whose asthma was managed by standard outpatient based education and management.

Alternative diagnosis

Symptom/sign	Possible diagnosis	Investigation
Wet cough	Cystic fibrosis	Sweat test
	Immunodeficiency	Immunoglobulins, vaccine response antibodies, T cell subsets
	Primary ciliary dyskinesia	Nasal ciliary biopsy, nasal nitric oxide
	Bronchiectasis	CT chest
Stridor	Tracheo-bronchomalacia	CT chest with contrast, bronchoscopy
	Vascular rings, mediastinal mass, foreign body	
Wheeze	Foreign body, aspiration	Bronchoscopy, barium studies
Breathlessness	Dysfunctional breathing	Psychology assessment
	Pulmonary hypertension	Cardiology assessment
Dry cough	Post viral, infection	X-ray chest
	Psychogenic	
Symptoms from infancy	Cystic fibrosis, PCD	Appropriate investigations
	Chronic lung disease	
Developmental delay	Recurrent aspiration	Barium studies, pH study
	GORD	

Table 2

Psychological and behavioural factors

Psychological dysfunction is associated with fatal and near fatal asthma and more than half of the children referred for evaluation of poorly controlled asthma have evidence of psychological distress. Psychological factors such as anxiety and depression are common in severe asthmatics. The extent to which persistent symptoms of asthma result in psychological morbidity or pre-existing psychological factors contribute to severity of asthma is not clear. Airway eosinophilic response to allergens is amplified by stress. Psychological factors influence asthma by neuro-