Management of problematic severe asthma in children

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Abstract

The majority of children with asthma are classified as mild or moderate and can be successfully managed with regular inhaled corticosteroids and bronchodilators. However, 5–10% of asthmatic children continue to have sub-optimal control despite apparent appropriate therapy. These children suffer significant morbidity including poor school attendance, adverse effects on family life and consume disproportionate healthcare 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 problematic severe asthma requires a multidisciplinary approach and should be undertaken by professionals with appropriate skills. Symptomatic children on high dose therapy, those who require continuous or frequent use of oral steroids or in whom diagnostic uncertainty persists should be referred to the local severe asthma services which have a range of enhanced diagnostic tools and can access newer biologic therapies and funding for alternative treatments. This article outlines the scale of the problem and offers guidance on initial diagnostic work-up and criteria for referral.

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

Introduction

Asthma is a chronic inflammatory disease characterized by airway hyperresponsiveness 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 the UK has a diagnosis of asthma with the vast majority controlled by low doses of medication including inhaled bronchodilators and corticosteroids. The majority are managed successfully in Primary or sometimes Secondary care. A small proportion of asthmatic children has 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)."

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There is no universally agreed definition of difficult asthma in children and specifically at what level of treatment prescription or asthma attack frequency, the term difficult asthma should apply. Previous consensus studies suggested failure to achieve symptom control despite prescribed high dose inhaled corticosteroids as a minimum requirement, whilst more recent work stipulated a treatment level equivalent to at least British Thoracic Society Guidelines high-dose therapies (short-acting β_2 agonist as required, medium-dose inhaled corticosteroid and an additional drug, usually a long-acting β_2 agonist).

Despite effective therapies and evidence-based guidelines many children and adults with asthma fail to achieve satisfactory control of their symptoms. The Environment and Childbirth cohort study from Norway estimate 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 a consensus that severe asthma in children requires a multidisciplinary, stepwise approach involving considerable healthcare time and resource. This frequently involves the use of high doses of anti-asthma medications and polypharmacy 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. According to the National Review of Asthma Deaths in the UK, in 2014 there were 18 asthma-related deaths in patients aged less than 19 years in the UK and whilst deaths occur in children with varying degrees of asthma severity confidential enquiries continue to highlight the increased risk amongst those classified as severe. 20% of asthma deaths in the UK occurred in patients who should have been referred to the specialist centre for management of severe asthma.

Problematic severe asthma classification

Asthma severity classifications are utilised in the stepwise approach advocated in the various national and international guidelines. The updated version of BTS asthma guidelines in 2016 provides a simple diagnostic algorithm of asthma. The goal of such guidelines is to ensure that individuals with asthma have no or minimal symptoms, remain free from exacerbations and have the opportunity to lead a normal lifestyle with no impairment to activity. This should be 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 problematic severe asthma

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

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Classification of severe asthma

1. Problematic severe asthma	Umbrella term describing poorly controlled asthma despite treatment with high dose steroids
2. Difficult to treat asthma	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

Is the diagnosis right?

Asthma is a clinical diagnosis. It is characterised by episodic respiratory symptoms predominantly wheeze which can be associated with cough, breathlessness and chest tightness in the absence of an alternative explanation. Children are often atopic and symptoms improve with adequate treatment. The BTS/SIGN guideline recommends grading the diagnosis of asthma by high, intermediate and low probability. A thorough history and examination is key to the diagnosis of asthma. Spirometry, bronchodilator reversibility and fractional exhaled nitric oxide (FeNO) 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 diagnoses should be carried out in children with 'low probability' of asthma or with poor response to standard asthma management (Table 2). 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 an alternative diagnosis.

Isolated cough is *not* a feature of paediatric asthma and asthma medication should not be prescribed for these children. A prospective review of 81 children with a 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 severe adult 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, sub-optimal inhaler technique or continued exposure to allergens are included under the umbrella term "difficult to treat asthma." Children should not have an escalation of asthma medication until associated conditions have been thoroughly addressed. In general, it helps to consider 10 things prior to initiation of biological therapies.

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 and the 2016 BTS asthma guideline recommend checking

Alternative diagnosis

Symptom/sign	Possible diagnosis	Investigation
Wet cough	Cystic fibrosis	Sweat test
	Immunodeficiency	Immunoglobulins, vaccine response
	Primary ciliary dyskinesia	antibodies, T cell subsets
	Bronchiectasis	Nasal ciliary biopsy, nasal nitric oxide
		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, Psychogenic	X-ray chest
Symptoms from infancy	Cystic fibrosis, PCD	Appropriate investigations
	Chronic lung disease	
Developmental delay	Recurrent aspiration	Barium studies, pH study
	GORD	

Table 2

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