

Management of asthma in pre-school children

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SUMMARY. *The management of asthma in pre-school children often presents physicians with challenging problems. This article addresses the diagnostic criteria by which the diagnosis may be made, discusses the prognosis of untreated asthma and states the principles underlying the treatment of asthma in this age group. The management according to a stepwise protocol is discussed with reference both to maintenance therapy, and the treatment of acute severe asthma. The methods by which appropriate medication may be delivered are also described.*

Keywords: *asthma; management of disease; pre-school children.*

Introduction

ASTHMA occurs in patients of all ages, but in no age group is it more difficult to manage than in young children. This paper concentrates on the special needs of the pre-school child and gives practical recommendations on management issues not specifically addressed in published guidelines.¹

Epidemiology

The prevalence of asthma, increasing in children in the United Kingdom, is between 10% and 20%, with a male to female ratio of approximately 1.5:1.²⁻⁴ Although mortality from asthma has also increased, this rise has not been seen in pre-school children (OPCS statistics, 1979-85). However, there has been an increase in hospital attendances in pre-school children.^{5,6} Since the 1970s, there has been a greater readiness to diagnose asthma, but there are differences of opinion as to whether the increased prevalence is related to diagnostic transfer⁷ or a true increase in prevalence.^{8,9}

The lack of an accepted definition for a disease with widely varying presenting symptoms makes the interpretation of an increased prevalence difficult.

Presentation

The symptoms of asthma include mild episodic wheezing, recurrent cough, and cough or wheeze following a viral illness, exposure to allergens, or exercise. These may result in sleep disturbance.

The likelihood of a child developing asthma or eczema is increased if one parent suffers from an allergic disease.¹⁰ A small number of young children have severe, persistent symptoms which are usually related to allergy, viral infections, a family history of asthma, or chronic lung disease following premature birth (bronchopulmonary dysplasia) (Landau L, personal communication).¹¹ Gastro-oesophageal reflux may also produce symptoms similar to those of asthma in infants.¹² More than

one of the above factors may coexist in the same child and a complex relationship exists between these factors and bronchial hyperreactivity.¹³⁻¹⁵

The most common factor which exacerbates asthma is thought to be viral upper respiratory tract infections, to which infants and children are often exposed.¹⁶ Viruses have a cytotoxic effect on the lungs and also increase their sensitivity to the asthmatic response: this is not an infective attack upon the lungs, but a virus induced toxic reaction.^{17,18}

Diagnostic criteria

The diagnostic criteria of asthma in pre-school children are different to those in older children as infants and small children cannot undertake exercise tests or perform reproducible peak flow recordings. One must rely on good history taking and careful physical examination. The family history may give useful clues of atopy. A previous history of bronchiolitis or croup may point to the likely diagnosis.^{19,20} A persistent night cough may also suggest asthma, as may the development of a cough on exercise, or the tendency to become 'chesty' following an upper respiratory tract infection. Retrospective analysis of patient notes may also reveal recurrent respiratory problems suggestive of asthma.²¹ Asthmatic symptoms are often associated with chronic rhinitis, and enlarged adenoids may be a feature of the condition.^{22,23}

In infancy other disorders mimicking 'the asthma syndrome' must be considered. Although less common the more likely are cystic fibrosis, gastro-oesophageal reflux, inhaled foreign body, whooping cough, congenital lobar emphysema or other congenital lung anomalies. A chest x-ray may be useful in eliminating the majority of these conditions.

Prognosis for untreated infants with asthma

The belief that the symptoms of asthma are self limiting and that children grow out of asthma before they become adults, is, in many cases, incorrect. Some patients may have years without symptoms, but long term studies show that 48% of children with infrequent wheezing and 80% with frequent wheezing will still have symptoms at the age of 21 years.²⁴

Untreated bronchial hyperreactivity may lead to persistent hyperresponsiveness, and perhaps to irreversible airways impairment.²⁵⁻²⁷ Failure to treat the inflammatory aspect of asthma may have long term effects on the child and cause reduced lung function in adulthood. Prophylactic medication such as an inhaled corticosteroid is the approach most likely to reduce or abolish this phenomenon.²⁸ It would therefore seem logical and in the best interest of the child to introduce prophylactic therapy at an early stage of treatment.

Principles

The aims of treatment are to improve the health of infants in the short term and to reduce the long term risk of recurrence of symptoms.

Airways hyperresponsiveness exists in asthmatic adults and older children, but at present there is no conclusive evidence of this in young children. Respiratory triggers alter airways hyperresponsiveness and cause long term damage that influences the duration and severity of asthma.²⁹ Inflammation, one of the principal mechanisms underlying the symptoms of asthma, is seen in adults with mild and even subclinical asthma. Recurrent attacks cause lung damage with increased permeability and

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eventual thickening of the basement membrane together with deposition of fibrin. Airways hyperresponsiveness is reduced by oral and inhaled corticosteroids,^{30,32} and sodium cromoglycate,^{33,34} but not by beta-agonists or theophylline.^{34,36}

Infants might have a different physiological response to allergic stimuli from that of adults; a deficiency of beta-receptors could account for their failure to respond to beta-agonists. However, beta-receptors are present,³⁷⁻³⁹ and failure to respond may, in part, be related to the size of the airway — resistance to airflow is inversely proportional to the fourth power of the radius of the airway.⁴⁰ Submucosal oedema, the shedding of epithelium into the lumen, and the inflammatory exudate, may also account for the failure of beta-agonists to work effectively in many infants.

Although the 1990 British Thoracic Society guidelines for the management of asthma do not apply to children, they state that bronchodilator therapy alone is unlikely to be successful in all but the mildest cases of asthma, and should be used as required rather than regularly.⁴¹ Effective use of beta-agonists as sole medication is even less likely to be effective in infants and young children. The clinician should therefore be ready to prescribe early and effective prophylaxis for any child with frequent symptoms.

Education and information for parents and children

Many doctors are still reluctant to label an infant as asthmatic,^{42,43} and many parents are reluctant to accept the diagnosis.⁴⁴ This may lead to delay in starting appropriate treatment.⁴⁵ This reluctance may stem from the fact that in the past the asthmatic child was regarded as intellectually and physically inferior.^{46,47}

Acceptance of the diagnosis can be encouraged by pointing out examples of asthma sufferers who have excelled in their chosen field. There are many examples of famous athletes who suffer from asthma and these may help when presenting the diagnosis to the asthmatic child's family.

Family education is vital if treatment is to be accepted. Groups such as the National Asthma Campaign can offer support, advice and information for parents. The practice nurse can provide instruction and information for patients and follow patients up either individually or through the practice asthma clinic.

Management

Prevention

Specific allergens may play a part in infantile asthma, the more common of these being the house dust mite, pollens, animal dander, other airborne allergens and foods. The elimination of house dust mites is almost impossible, but where the patient is extremely sensitive, reduction of levels may be beneficial. Specific sources of animal allergens can be removed, but this may cause domestic stress.⁴⁸ Effective restriction of exposure to pollens and other airborne allergens such as agricultural sprays and aromas can also be difficult.

Allergens in foods can be difficult to identify, but a trial elimination of certain foods may be worthwhile.⁴⁹ If an infant's diet is altered, a dietitian's help should be sought to ensure that the child is still receiving a balanced diet.

Passive smoking is increasingly being shown to contribute to asthma and other paediatric respiratory symptoms. Paediatric respiratory disease has also been shown to be worse if the mother smokes in pregnancy,^{50,51} and smoking in pregnancy increases histamine responsiveness in infancy.⁵² Of the environmental problems which worsen childhood asthma, smoking is the most readily prevented. The importance of eliminating tobacco smoke

from the asthmatic child's environment cannot be over emphasized.

Medication delivery systems

Whether treating infants with bronchodilators or prophylactic drugs, getting the medication into the lungs can be a problem.⁵³ The use of syrups is commonplace but relatively large doses must be given with the consequent risk of side effects.

Metered dose inhalers. Despite the widespread use of metered dose inhalers, it is impossible to ensure that a child under the age of five years is receiving an appropriate dose of the prescribed medication.⁵⁴ Even with correct usage initially, patients can lapse into incorrect technique after a relatively short time.^{55,56} With so many better delivery systems now available, no pre-school child should use only a metered dose inhaler.

Children between two and three years of age and their parents can usually be taught to use a metered dose inhaler with a chamber device. The chamber device removes the need for coordination between actuation and inhalation.⁵⁷ The drug is delivered into the device and remains there in cloud form while the child breathes through the valve and mouthpiece. Although the manufacturers recommend that the breath is held after inhalation, the devices are effective when the child breathes normally. They increase lung deposition by threefold compared with metered dose inhalers alone. A large proportion of the drug not entering the child's airway remains in the chamber, as opposed to the situation when using metered dose inhalers alone where the oral and gastric deposition of the drug may be up to 90% of the total dose.⁵⁸ This factor reduces the side effects produced by systemic absorption, especially at high doses.

Some clinicians advocate the use of a metered dose inhaler inserted into a polystyrene coffee cup to deliver asthma therapy to infants but there seems little justification for this now that there are more effective means of delivering inhaled therapy. Masks can be fitted to chamber devices, and when gently applied to the infant's face, the metered dose inhaler can be activated.^{59,60} No seal need be enforced between the mask and the infants face so the dosage is not precise (as with nebulized therapy). Without a seal the valve is not actuated, but tilting the chamber so that the mouthpiece points down ensures that the drug will flow through the open valve.

Good control of symptoms can be achieved with these devices, and when the infant resists therapy, it can be administered effectively while the child is asleep.^{60,61} The chamber device can be decorated with stickers to make it more interesting to the child and, before starting treatment, a plaything can be put inside, so that the child becomes familiar with it and is less likely to resist treatment.

The Nebuhaler® (Astra) and Volumatic® (Allen and Hanburys) are both effective. An advantage of the Nebuhaler is that as well as receiving budesonide and terbutaline inhalers it can be used to administer ipratropium bromide and, with an adaptor, sodium cromoglycate.

Nebulizers. These are beneficial in the treatment of acute severe asthma,^{62,63} and can be used to administer high doses of beta-agonists or anticholinergic drugs, although administration should always take place under medical advice if not supervision. Paradoxical bronchoconstriction has been reported in infants following treatment with nebulized salbutamol so caution is needed when treating acute episodes of asthma.⁶⁴ The pH of the solution or the preservative used may play a part in this response.⁶⁵ During nebulization the concentration of oxygen in the blood may fall, and it is good practice to intersperse the treatment with oxygen given by mask where this is possible.

In severe persistent asthma, it may be necessary to institute

maintenance therapy via a nebulizer. Sodium cromoglycate and corticosteroids are available for nebulization. Nebulized beclomethasone has been found to be disappointing in this application, probably because the suspension for nebulization is relatively dilute — 2 ml of suspension contains 100 µg of active medication.^{66,67} There have been favourable reports of the use of budesonide suspension in children with severe asthma.^{68,69} In this case, 2 ml of suspension contains 0.5 mg or 1 mg of active medication. However, in view of this relatively high dose, budesonide suspension should be reserved for severe cases of asthma in young children and should be used only in consultation with a consultant paediatrician with an interest in asthma.

The use of nebulizers by pre-school children should decrease now that there are other effective means of administering inhaled drugs. However, if nebulizers are used at home, parents must be carefully instructed about their use, made aware of the possibility of toxic effects and of the importance of seeking immediate help if the child does not respond to treatment.^{70,71}

Dry powder inhalers. Over the age of three years most children can inhale therapy in powder form. The first dry powder inhaler was developed for use with sodium cromoglycate; an inhaler was then developed for salbutamol and beclomethasone. More recently multi-dose inhalers for beta-agonists and corticosteroids have become available.^{72,73} As well as being 'ozone friendly' these devices are relatively easy to use and their use can be easily taught. They should be the main delivery systems for children over three years of age.

Therapy for infants aged up to 18 months

Less is known about asthma in children aged up to 18 months than in other age groups and until recently few studies had been performed. Avoidance of known allergens should always be attempted as a first step, but increasingly general practitioners and hospital doctors are faced with the need to treat symptoms in children in this age group, and chamber and mask devices make inhaled therapy a practical option.

Intermittent mild asthma. In the case of mild non-persistent symptoms that do not interfere with the child's feeding or sleeping, providing reassurance for the parents will probably be sufficient, or at the most decongestant nose drops. Bronchodilator syrups are unlikely to produce appreciable improvement but can be tried.

Maintenance therapy. If symptoms persist maintenance therapy can be administered in the form of sodium cromoglycate or a corticosteroid, inhaled through a chamber device and mask. Sodium cromoglycate has an outstanding safety record but it may take up to six weeks to achieve its full effect.⁷⁴ Parents should be told that any form of preventive therapy may take some time to be effective. Sodium cromoglycate should be used initially, in a dose of 10 mg (two puffs) four times a day. If the response to this is unsatisfactory one of the inhaled corticosteroids should be tried. These have been available for about 20 years and in normal therapeutic doses have a good safety record in children.⁷⁵⁻⁷⁷ They are increasingly being used as first line therapy.⁷⁸ The lowest effective dose of beclomethasone or budesonide should be used initially — 50–100 µg twice daily. Salbutamol (100 µg) or terbutaline (250 µg) can be given in addition as relief medication through a chamber device and mask on an as required basis. Some infants improve when ipratropium bromide (20 µg twice daily) is administered.^{79,80} Some children may become hyperactive when taking beta-agonists, and in this case ipratropium bromide should be tried instead.^{81,82}

Exacerbation of asthma. Parents should be advised to double the dose of prophylactic and relief therapy at the first sign of

an upper respiratory tract infection in an infant in this age group, or if the infant is exposed to a known allergen. In this way exacerbation of the condition can often be avoided or aborted in the early stages.

Parents should be advised to contact their doctor if the asthma is exacerbated and the child does not respond to treatment.

Acute asthma attacks. In acute severe attacks oxygen should be administered if available.⁸³ Soluble prednisolone can be tried in a dose of 1 mg per kg per day, the course lasting from one to five days depending on the response. However, there is as yet no good evidence of its efficacy in this age group. Terbutaline delivered using a large volume spacer device may be used in acute asthma attacks with the same effect as nebulized terbutaline if an equivalent dose of drug is used;⁸⁴ with more severe or acute symptoms terbutaline (10 puffs = 2.5 mg) or salbutamol (10 puffs = 1.0 mg) inhaled through a chamber device and mask should be tried. This provides a cheap, convenient and portable means of administering high doses of beta-agonists and other therapies and can replace, to a large extent, nebulized drugs. It is also possible that therapy is better administered through a chamber device to infants as this technique has not been shown to produce the paradoxical responses seen on occasion following treatment with a nebulizer.⁶⁴

If the child cannot inhale the medications satisfactorily, salbutamol or terbutaline should be given via a nebulizer in a dose of 2.5 mg. If there is no improvement then ipratropium bromide may be tried through a chamber device and mask or using a nebulizer (60–80 µg). If the child does not respond to any of these treatments admission to hospital should be arranged.

Theophyllines have not been shown to produce significant effects on lung function in this young age group, their side effects can be dangerous (vomiting and arrhythmias), and their therapeutic window is narrow.⁸⁵

In younger patients inhaled corticosteroids may act in a shorter time than the accepted four to six hours;⁸⁶ infants and children have shown dose-related responses in 10 to 20 minutes.^{87,88} This is consistent with investigations at the cellular level of the airway responses to glucocorticosteroids;^{89,90} peak plasma levels are seen five to 10 minutes after administration of inhaled steroids. Corticosteroids may thus have a 'hit and run' effect in the airways.^{91,92} If clinical trials support this, high doses of inhaled corticosteroids may provide a means of treating the acute severe asthma attack effectively, but at present the use of high dose inhaled corticosteroids cannot be recommended for general use.

In summary, the steps involved in the management of asthma in children aged up to 18 months are as follows:

1. Avoidance/prevention.
2. Symptomatic treatment with oral bronchodilators on an as required basis.
3. Inhaled sodium cromoglycate through a chamber device and mask plus inhaled beta-agonists or ipratropium bromide on an as required basis.
4. Inhaled steroid through a chamber device and mask plus inhaled beta-agonists or ipratropium bromide on an as required basis.
5. Refer to specialist.

Therapy for children aged 18 months to five years

Intermittent mild asthma. If symptoms are not controlled by avoiding known allergens, then treatment with a beta-agonist should be tried. This should be on an as required basis, as there may be hazards associated with the regular administration of

beta-agonists.⁹³ For a child who has only infrequent symptoms this may be the only treatment required. The beta-agonist should be administered using an inhaler where possible as the dose is small and by using this method it is delivered directly to the airways.

Maintenance therapy. If a beta-agonist is needed frequently or on a daily basis, inhaled prophylactic treatment should be instituted. The options are sodium cromoglycate or corticosteroids. If sodium cromoglycate does not achieve a response in four to six weeks, the child should be prescribed an inhaled corticosteroid. It may be possible to achieve a swifter response by using a double dose of the corticosteroid for the first week.

Children can often be well maintained on preventive therapy with only the occasional use of beta-agonists. Once control is achieved the dose of the preventive therapy should be reduced to the minimum needed to keep the child symptom free. If control is not achieved, as judged by increased symptoms or beta-agonist use, the child's compliance with medication and delivery technique should be checked. If the delivery technique is inadequate the means of delivery should be reassessed. The dose of inhaled corticosteroids should then be increased to a maximum of 400 µg daily. If adequate control is not achieved with this dose of corticosteroids together with standard doses of beta-agonists, the child should be referred to a paediatrician with a special interest in asthma.

Some children with nocturnal symptoms of asthma benefit from salbutamol or terbutaline in slow release form, but the tablets must be swallowed whole.

Bronchodilators which have a long lasting effect such as salmeterol may well improve asthma control but there is no clinical evidence that they have any anti-inflammatory effect. Studies in pre-school children are only just beginning and their results are awaited.

In some countries ketotifen and theophyllines are still used in large amounts. Studies have demonstrated the successful use of ketotifen in children under five years of age,^{94,95} but it has not been widely adopted in the UK. Although theophyllines are still frequently used in the UK they have unacceptable side effects and have little place in the treatment of young children as other therapies are more effective.⁹⁶

Exacerbation of asthma. Doses of both prophylactic and relief therapy can be doubled as for the younger age group, and parents should be advised to see their general practitioner if necessary.

Acute asthma attacks. Oxygen should be administered if available. Inhaled beta-agonists should be administered in high dose, as described for the younger age group. If a nebulizer is used the suggested dose of salbutamol or terbutaline is 5.0 mg in this age group. Subcutaneous terbutaline or salbutamol in a dose of 0.05–0.25 mg can be administered to produce effective bronchodilation. Oral corticosteroids should be started as soon as possible. A suggested dose of soluble prednisolone is 1–2 mg per kg given as a once daily dose. Continuation of the treatment should be assessed daily and should be response dependent; there is no need to taper off this treatment when given for less than seven days.⁹⁷

Once again if the child does not respond, admission to hospital should be arranged.

In summary, the steps involved in the management of asthma in children aged 18 months to five years are as follows:

1. Avoidance/prevention.
2. Symptomatic treatment with inhaled bronchodilators on an as required basis.
3. Inhaled sodium cromoglycate through an appropriate device plus inhaled beta-agonists on an as required basis.

4. Inhaled steroid through an appropriate device plus inhaled beta-agonists on an as required basis.

5. Increase dose of inhaled steroids and beta-agonists through chamber device; add ipratropium bromide or slow release beta-agonists.

6. Refer to specialist.

Conclusion

The management of pre-school children with asthma should be reviewed on a regular basis and the treatment adjusted to the patient's needs. If a child is free of symptoms for six months, reduction or even cessation of treatment can be considered. If a child does not respond to treatment, he or she should be referred to a hospital specialist, either as an acute admission or as an outpatient.

In using any device, medication or management plan, both the child and parents must be involved to ensure that they can use them effectively. It is important that the appropriate therapy is chosen for each patient.^{98,99} This places a considerable burden on the general practitioner and the practice team. However, the availability of nurses with additional training in asthma care is a great advance and should help improve the care of children with asthma in the general practice setting.^{100,101} Protocols are needed to ensure that all members of the primary care team follow the same procedures, and to act as a standard when carrying out audit. The development of an asthma protocol must be left to each practice but is most important, because regular contact with patients and education and follow up of patients are essential.

Untreated or undertreated moderate asthma in children affects their growth and development,⁸ and home and school life.¹⁰² If asthma is not diagnosed the child may be given many unnecessary courses of antibiotics and antitussives following a diagnosis of chest infection or upper respiratory tract infection. Prompt recognition of asthma, appropriate treatment and management advice, will usually ensure the child can grow and develop normally. The majority of problems associated with asthma can be avoided by effective prophylaxis. There must be a greater readiness to prescribe inhaled corticosteroids, to understand the problems involved with compliance, to reduce the use of oral bronchodilator syrups and to educate families and colleagues to form a team in the basic care of asthmatic children.

Asthma in pre-school children is common. Its management is more difficult than in older children and adults, but can be rewarding. Appropriate use of the available inhalation devices and therapies should result in a considerable reduction in morbidity in both the short and long term.

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