Current issues in childhood asthma

Part 2: questions and answers

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Most childhood asthma can be managed by general practitioners. Last month, Part 1 of this article presented current concepts in the diagnosis and management of childhood asthma; here, in Part 2, specific clinical issues and situations are discussed in a user-friendly question and answer format.

What to do...

When therapy is initiated but the patient remains symptomatic

The first response should not be to increase the prescribed dose of medication. Instead, ask the following questions:

- Is the patient taking his or her medication?
- Is the patient using his or her inhaler device correctly?
- Could the diagnosis of asthma be incorrect?
- If a spacer is being used, has it been treated to reduce static electricity? Spacers should be washed in detergent every two to four weeks and left to drip-dry.

In this situation, it is often useful to obtain a chest x-ray to exclude other pathology. The possibility of an inhaled foreign body should always be considered in young children. As well, patients with asthma can develop other diseases such as whooping cough or mycoplasma infection.

Spirometry should be performed in children six to seven years of age and over.

IN SUMMARY

- **Not all persistent coughs in childhood are caused by asthma. In fact, a cough that does not respond within a week to appropriate asthma therapy is unlikely to be due to asthma.**
- **If a patient remains symptomatic on therapy, increasing the prescribed dose of medication may not be the most appropriate course of action. Review the diagnosis and whether medication has been taken correctly or at all.**
- **In general, inhaled corticosteroids should be reserved for children with frequent episodic asthma inadequately controlled by a nonsteroid medication or with persistent asthma. The risk of adverse effects from inhaled steroids can be rescued by back-titrating the dose to the lowest dose that maintains good control.**
- **Long acting β_2-agonists are useful as 'symptom controllers' in some children with asthma; Leukotriene antagonists may be useful as first line 'preventer' treatment for children with frequent episodic asthma and in some children with exercise-induced asthma.**
- **Referral to a specialist should be considered when children with asthma require increasing or continued treatment with oral or high doses of inhaled corticosteroids and when there is a failure to respond to appropriate therapy.**

When cough is persistent

Cough is a common symptom in childhood and while children with asthma will frequently have a cough, not all persistent coughs in childhood are caused by asthma. There is now significant concern that too many children with recurrent cough are being diagnosed as having asthma and treated inappropriately, often with high doses of inhaled steroid.

It is important to recognise that treatment for cough is not always required and a decision to treat depends on the severity and frequency of symptoms. A cough that does not respond within a week to appropriate asthma therapy is unlikely to be due to asthma.

As stated in Part 1 of this series, the diagnosis of asthma based on cough alone, in the absence of wheeze, should be made with caution. If asthma is suspected as the cause for a persistent cough, and treatment with anti-inflammatory medication is contemplated, then nonsteroid medication such as sodium cromoglycate or nedocromil sodium should be tried first.

If the cough is not relieved, inhaled steroids may be used for a trial period of two to four weeks. Prolonged use of high dose inhaled corti - costeroids for cough should be avoided.

Paediatric specialist referral is indicated if the cough is unresponsive to treatment or if continued inhaled corticosteroid treatment is required.

What is the role of inhaled corticosteroids?

There are a number of key issues related to the use of inhaled corticosteroids in childhood and adolescence. In general, inhaled steroids should be reserved for, and are the mainstay of treatment in, children with frequent episodic asthma inadequately controlled by a nonsteroid medication or for those with persistent asthma.

The maintenance dosage should be the lowest dose that gives good control of asthma symptoms.

Low dose or high dose?

In the majority of children and adolescents with asthma, satisfactory control can be achieved with low doses of inhaled steroid – for example, 400 μg per day of beclomethasone (Becotide, Respocort) or budesonide (Pulmicort) or 200 μg per day of fluticasone (Flixotide).

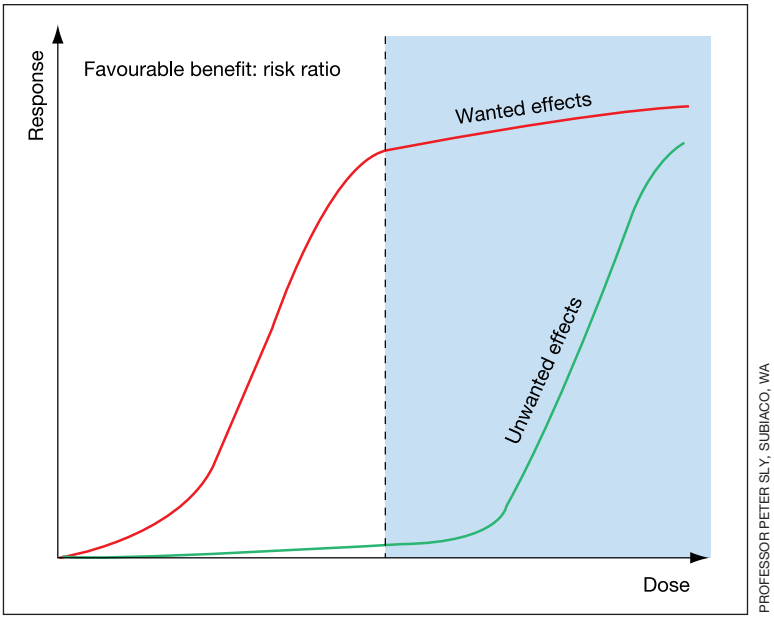

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Figure 1. As the dose of inhaled corticosteroid increases, there is a progressive rise in the risk of side effects.

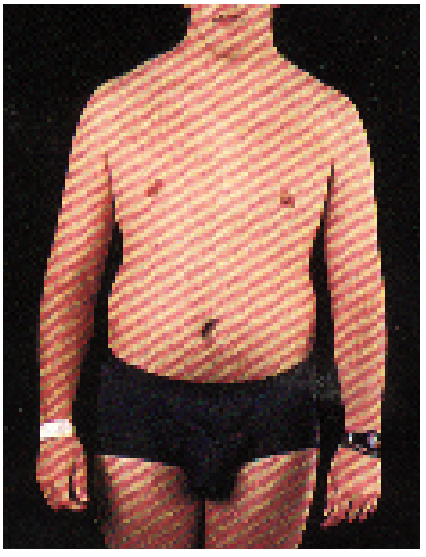
There is limited published evidence to support a progressive dose–response curve for inhaled steroids.[1] Most studies show little advantage in using doses in excess of 800 μg of beclomethasone or budesonide or 400 μg per day of fluticasone.

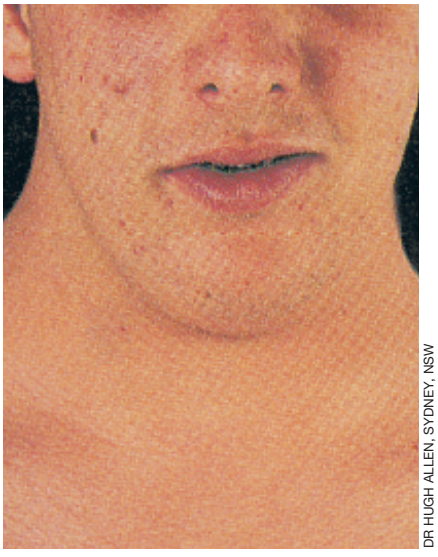
Occasional patients may require higher doses – for example, if not adequately controlled with 400 to 500 μg per day of beclomethasone or 200 to 250 μg per day of fluticasone in combination with a long acting β_2-agonist. But, as the dose of inhaled corticosteroid increases, there is a progressive rise in the risk of side effects (see Figure 1). Thus, a decision to use doses higher than those mentioned above for continuing maintenance treatment must be individualised after assessing the relative risks and benefits for that patient. Further, more complex treatment regimens increase problems with adherence.

Which agent has the least side effects?

Inhaled corticosteroids are, by and large, very safe in age-appropriate doses. However, all inhaled corticosteroids exhibit dose-related systemic effects.[2]

It is virtually impossible to make direct comparisons between the available drugs and, in particular, between budesonide and fluticasone. This is because most of the systemic effects of inhaled corticosteroids come from the fraction





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Figures 2a (left) and b (right). A 14-year old boy with asthma who was being treated with 800 μg inhaled steroid per day. Six months after commencing treatment, he developed a round face, buffalo hump, acne, hirsutism and striae, and a synacthen stimulation test showed adrenal suppression.

of the dose deposited in and absorbed from the lung, and the available drugs have different physicochemical properties and different deposition characteristics from their inhaler devices. Recent meta-analyses of the published literature have come to differing conclusions.[2,3]

However, the following guidelines can be offered:

- Data obtained from nonasthmatic subjects may not be applicable to asthmatics and data from subjects with mild asthma may not apply to subjects with more severe asthma.
- Short term studies of growth and markers of bone turnover may not reflect long term safety and thus need to be interpreted with caution. Large cohort studies measuring height over several years are required when comparing systemic effects of an individual drug or comparing the relative effects of two drugs.
- Markers of adrenal activity are sensitive to suppression by inhaled corticosteroids and although they may be a marker of systemic activity they may not be an accurate marker of adverse effects.

The current literature supports the view that beclomethasone and budesonide at 400 μg per day or fluticasone at 200 μg per day are safe and free of significant side effects in long term studies. That is, fluticasone is as effective and just as safe as twice the dose of beclomethasone with a lower risk of systemic effects, particularly on growth and bone composition, at doses of up to 200 μg per day.[4] As indicated earlier, a decision to use doses in excess of these limits must be individualised after careful evaluation of the relative risks and benefits for the patient. (For a guide to the role of fluticasone in asthma management see 'What is the role of the new medications? Fluticasone' below.)

The risk of adverse effects from inhaled steroids can be reduced by back-titrating the dose to the lowest dose that maintains good symptom control. There is no definite formula for doing this. A generally safe approach is to wait until the patient has been largely symptom-free for about a month and then reduce the dose by about 25% increments every two to four weeks depending on the individual circumstances.

What about effects on growth?

High dose inhaled steroids can suppress growth (Figures 2a and b). But poorly controlled asthma can also delay puberty and cause short stature. This applies to all the available steroid products. Additionally, there appears to be an individual sensitivity to steroids, with some children experiencing side effects at relatively low doses. However, in children with severe persistent asthma, treatment with inhaled steroids may result in improved growth through better symptom control and a reduced use of oral steroids (see Figure 3).

What is the role of the new medications?

Long acting beta$_2$ agonists

As a drug class, the long acting β_2-agonists are now known as 'symptom controllers'. Their initial positioning in asthma treatment reflected the initial PBS authority restriction to use in severe nocturnal asthma. However, new evidence from studies in both adults and children has emerged which supports a broader role for symptom controllers in the treatment of asthma in children and the authority restriction has now been removed. Adding a symptom controller is now an alternative to increasing the dose of inhaled corticosteroid.[5]

The addition of a symptom controller should be considered for children with asthma who:

- have regular sleep disturbance due to asthma despite appropriate preventer therapy
- continue to have poor symptom control despite taking 400 to 500 μg per day of beclomethasone dipropionate or budesonide, or 200 to 250 μg per day of fluticasone propionate.

Symptom controllers are not recommended as monotherapy for children with asthma.

Salmeterol

Salmeterol xinafoate (Optrol, Serevent) has been approved for use in children aged four years of age and over. Salmeterol is available as both a pressurised metered dose inhaler (pMDI) and dry powder inhaler (see Part 1, 'Step 3. Selecting a delivery device').

Eformoterol

Eformoterol fumarate dihydrate (Foradile) has been approved for use in children aged five years and over. It is only available in a dry powder inhaler.

Eformoterol fumarate has a more rapid onset of action than salmeterol but given that symptom controllers are prescribed for maintenance treatment and not acute symptom relief, the importance of the more rapid onset of action of eformoterol is of uncertain benefit.

Leukotriene antagonists

Leukotriene antagonists are the newest available class of asthma medication and act by blocking leukotriene receptors.

Montelukast sodium (Singulair) has been approved for use in Australia in children six years of age and over. Other drugs are likely to be approved soon.

Montelukast has the advantage of being taken orally as a once daily dose. It has a good side-effect profile. Comparative studies in children have shown it to have a potency equivalent to 400 μg per day of beclomethasone dipropionate.

Montelukast is now an alternative first line 'preventer' treatment for children with frequent episodic asthma and for young children as a way of preventing exercise-induced asthma at school if they cannot be relied upon to take a β_2-agonist immediately before exercise. Montelukast provides protection against exercise induced asthma for many hours.[6] However, the overall role of these agents in the treatment of asthma in children is currently unclear as experience with their use has been limited.

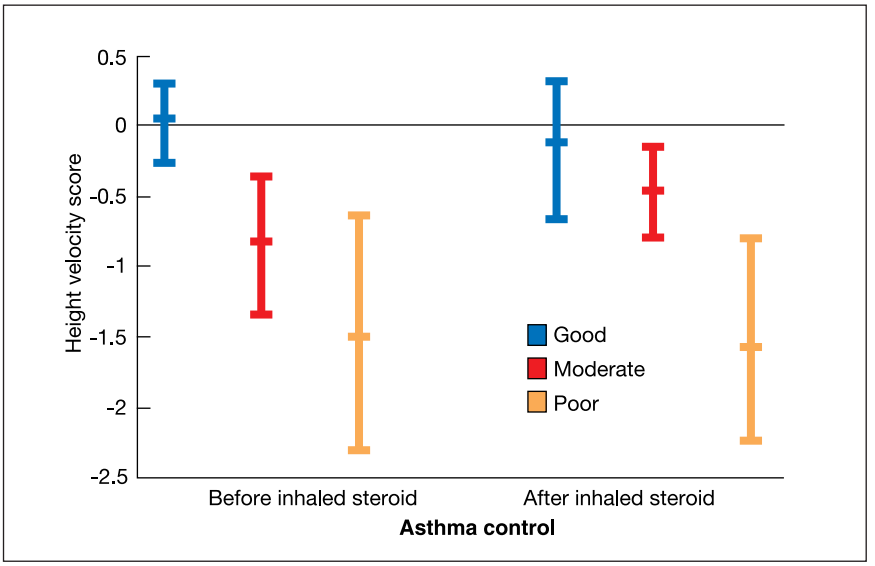

Figure 3. Effect of asthma control on height velocity score, before and after treatment with inhaled corticosteroid treatment. Children whose asthma is poorly controlled grow poorly, regardless of treatment.

ADAPTED FROM: NINAN TK, RUSSELL G. ASTHMA, INHALED CORTICOSTEROID TREATMENT, AND GROWTH. ARCH DIS CHILD 1992; 67: 703-705.

Fluticasone

Fluticasone propionate (Flixotide) is an inhaled corticosteroid with a topical potency approximately twice that of beclomethasone dipropionate when given via comparable devices. It has negligible oral bioavailability but absorption does occur from the lung, and systemic effects including adrenal suppression and growth suppression have been described with high doses. It is approved for use in children one year of age and over.

In Australia, the initial positioning of fluticasone again reflected a PBS authority restriction that specified use only in children and young people with severe asthma. The authority restriction has recently been removed and it is now available as a general PBS benefit. It is now a first line option when inhaled steroids are indicated – that is, in frequent episodic asthma unresponsive to a non-steroidal preventer or in persistent asthma.

As indicated earlier, low doses (200 μg per day or less) are effective for most children and, in this dose range, fluticasone has a favourable efficacy to side effect ratio. The dose used should always be the lowest dose that provides good symptom control as all inhaled corticosteroids exhibit dose-related systemic effects. As with other inhaled steroids, the decision to prescribe fluticasone in higher doses for a child must be made after an assessment of the relative benefit–risk ratio in that individual.

What is the role of peak flow measurement?

Measurement of peak flow is frequently recommended for monitoring asthma in adults, but the role peak flow in childhood asthma is less certain.

Monitoring peak flow is generally unreliable in children younger than six years of age. It can be used to indicate when older children should increase

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Figure 4. Peak flow measurement may be used to indicate when children older than six years should increase their drug treatment. It may also be helpful in the occasional child with asthma who cannot subjectively perceive severe airways obstruction.

their drug treatment and it may be helpful in the occasional child with asthma who is unable to subjectively perceive severe airways obstruction (Figure 4). However, concerns have been raised about the accuracy of home peak flow monitoring and the ability to detect significant asthma events using peak expiratory flow measurements.

The role of peak expiratory flow monitoring in children has been formally evaluated and found to add little to recording of symptoms and bronchodilator use in children with severe asthma, and to be too insensitive to register meaningful clinical changes in those with milder asthma.

A child who is using home peak flow measurement should be encouraged to bring the device to a consultation so that technique can be assessed.

Single measurements of peak flow in the surgery are of limited value due to the wide normal range. However, clinically useful information can be derived from the pattern of peak flow readings over a two-week period. When peak expiratory flow is used, changes from 'personal best' should be used rather than percentage of predicted normal values.

When to refer

Most childhood asthma can be managed by general practitioners. Indications for considering referral to a specialist paediatrician include:

- children and adolescents with asthma requiring frequent courses of oral steroids
- children five years and younger requiring continuing treatment with 600 μg per day or more of beclomethasone or budesonide or 250 μg per day of fluticasone
- older children and adolescents requiring continuing treatment with 1000 μg per day or more of beclomethasone or budesonide or 500 μg per day of fluticasone
- unacceptable side effects from medication, such as Cushingoid appearance or growth suppression
- children with persistent cough despite treatment with inhaled steroids
- patients with additional risk factors, such as a history of premature birth or symptoms that have not responded to adequate therapy, or with other symptoms such as stridor
- if there is doubt about the diagnosis (e.g. if symptoms continue despite apparently appropriate therapy)
- failure to respond to appropriate therapy.

Conclusion

Effective management of asthma in general practice requires knowledge of specific issues and clinical circumstances. General practitioners need to be aware that not all persistent childhood cough is caused by asthma. Further, if a patient remains symptomatic on therapy, increasing the prescribed dose of medication may not be the most appropriate course of action. In selecting agents from the range of medications available, an accurate assessment of the patient's condition and an appreciation of which agent gives the best results in a given situation is required. MT

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