Intermittent asthma in children

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1. Introduction: Preventer therapy is useful for chronic, but not intermittent asthma

It is important to recognise the place of inhaled steroids in childhood asthma before discussing management of intermittent asthma.

Childhood vs adult asthma

Childhood asthma differs from adult asthma on a number of grounds, even though they may be related.

Pathology

Bronchoscopic studies in children have documented that many children have neutrophilic rather than eosinophilic inflammation in the airways.

Prognosis

Asthma in childhood improves in many children at adolescence. This particularly applies to children with intermittent asthma and to boys.

Monitoring

Young children are observed and treated by adults, whereas adults observe and treat their own symptoms. This may lead to relative over-reporting or overtreatment of symptoms or peak flow by concerned parents. Adolescents, on the other hand, may want to normalise themselves and so be less likely to report symptoms, or to take treatment regularly. Peak flow is unreliable in children.[1]

Side effects

Children are vulnerable to the effects of inhaled steroids on bone metabolism during growth, and during rapid growth in adolescence.

The favourable prognosis, the possibility of overtreatment and the slightly increased side effect profile for inhaled steroids[2] mean that the balance of risks/benefits for treatment are different in children and adults. These differences should lead to caution in applying adult guidelines for asthma treatment to children.

The role of inhaled preventive treatment for asthma in childhood

What do preventers do and not do for asthma in childhood? Preventive treatment with inhaled steroids:

1. Does not alter the natural history of asthma in childhood. On ceasing prevention, benefits in lung function, exercise tolerance and sleep revert very quickly to resemble those of children who never had inhaled steroids.[3–5]
2. Does not alter the risk of airway remodelling. Airway remodelling has been demonstrated in very young pre-school children with asthma, but is not clearly associated with clinical asthma severity, nor prevented with treatment.[4,6]
3. Does not reduce the risk of intermittent virus-triggered exacerbations of asthma.[7]

The primary indication for inhaled steroid preventers for children is to control disabling chronic, or interval symptoms. Inhaled steroids should not be routinely prescribed in an attempt to prevent intermittent viral-triggered episodes, nor in the belief that they will reduce the risk of airway-remodelling or irreversible decline in lung function.

Family doctors need to be aware of this, as most children present to a family doctor during an acute attack, rather than with chronic symptoms, so the pressure to 'do something' will naturally focus round the attack. However the focus of regular preventive therapy is on the interval symptoms between attacks, rather than the attacks themselves.

Chronic disabling symptoms are recognised principally by:

- Reduced ability to participate in normal sports, fitness and play activities.
- Frequent interruption of sleep due to asthma, even in the intervals between respiratory infections.
- Very severe chronic symptoms can increase anxiety and impair coping, schoolwork and self-image. They can also slow height growth.

Other indicators of chronic asthma are not as robust in children.

- Frequent use of reliever medication, in the intervals between infections, suggests chronic symptoms, but some unfit and/or overweight children will use relievers as a face-saver to excuse their poor performance.
- Frequent time off school may be due to frequent infections, frequent chronic symptoms, or parental choice, and it is important to find out the main reason. Some parents will keep children home from school when it is cold, or when they are tired, even though the child has not had symptoms. In extreme cases parents may have anxiety about separation from their own child, and the child's 'severe' medical condition becomes a handle to keep them close.

Over time dosage adjustment may be necessary. Inhaled steroids show a plateau response above about 200µg fluticasone per day (=400µg budesonide/beclomethasone per day), so above these levels, addition of long-acting beta agonists may be more helpful than further increases in dose. Long acting beta agonists should not be prescribed without inhaled steroids.

2. Management of intermittent asthma in childhood (symptoms only with viral infections)
(See illustration)

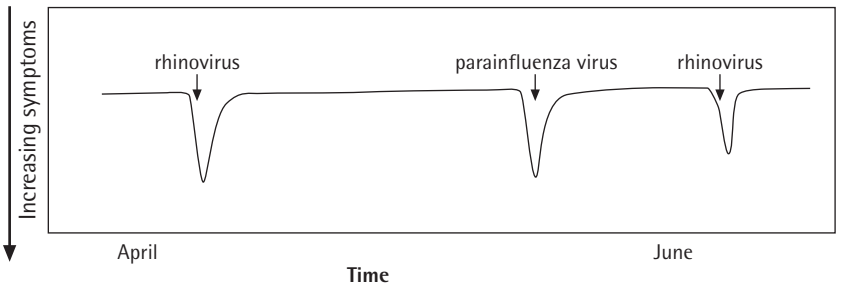
As many as 85% of acute asthma exacerbations in children are triggered by respiratory virus, *Mycoplasma pneumoniae*, or *Chlamydia pneumoniae* infection.[8] Two-thirds of these cases are due to rhinoviruses – the major common cold virus. The usual time course is onset of wheezing and breathlessness about 24 hours following the onset of URTI symptoms such as runny nose. Initial deterioration is rapid, followed by slow recovery. Often it takes 10–14 days to recover lung function and exercise tolerance. Typical bacterial infections (e.g. pneumonia due to *Strep pneumoniae*) have not been shown to trigger asthma attacks. Interestingly, increased exposure to virus infections in infancy increases the incidence of infant wheeze, but decreases the incidence of later atopic asthma.[8]

Although inhaled steroids used **acutely** in high doses seem to reduce the severity of intermittent asthma episodes,[9] their use in this way may cause confusion between preventers and relievers. This distinction has been one of the most helpful educative tools in asthma, and personally I am reluctant to confuse it by prescribing preventers as relievers. Montelukast at the onset of attacks has been shown to reduce symptoms and health care usage in young children,[10] but is not subsidised in New Zealand.

The priorities in children with intermittent asthma are to ensure:

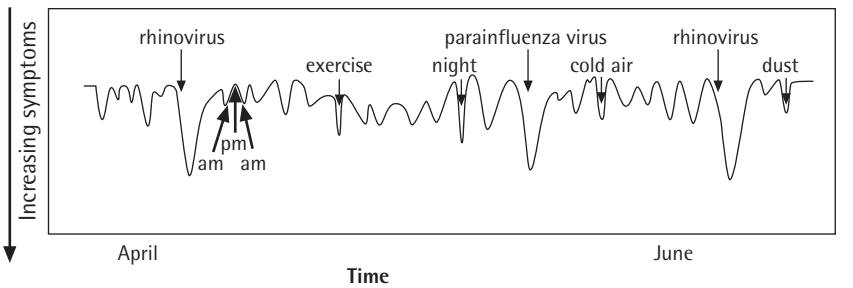
Two asthma phenotypes in childhood

Figure 1. Intermittent asthma. Virus-triggered episodes only.



This child will not benefit from inhaled steroid preventers, even if they see the family doctor during each episode.

Figure 2. Chronic (or persistent) asthma.



In the intervals between virus-triggered episodes various regular symptoms are shown for the purpose of illustration. These include diurnal variation (worse in mornings), wheeze with exercise, night time, cold air exposure and dust exposure. Note that these interval symptoms are much briefer (often measured in minutes) and generally milder than the acute virus-triggered exacerbations (measured in days). However, they adversely affect the child's sleep, exercise and education on a frequent basis. This child needs inhaled steroid preventers.

(a) That they and their parents or caregivers have a sensible stepwise protocol to guide their management of an acute episode, and reduce panic
(b) That parents and caregivers know when and whom to call for help, and are 'given permission' to do so
(c) That sensible precautions for reducing virus exposure, if necessary, be considered.

Spacer use

Current best practice for spacer use is as follows:

- Use a small volume spacer with a mask for children under two years and a large volume spacer without mask as soon as the child can use the mouthpiece effectively. Spacers used regularly should be replaced six-monthly.
- Wash the spacer in a mixture of dishwashing liquid and water in a clean bowl, once a week, and let it air dry without rubbing. In an acute situation a new spacer can be 'primed' with 10 waste puffs of reliever before use.

1. Shake the inhaler before each puff
2. Deliver one puff into the spacer at a time
3. Let the child breathe tidally through the spacer for three to four breaths after each puff.

- In an acute exacerbation six to 10 puffs can be given at a time, using steps 1–3 for each puff. [Some guidelines suggest six puffs for under–five-year-olds and 10 puffs for over-fives, but these are inevitably arbitrary doses.]
- *A nebuliser has no advantage over a spacer used correctly as above, except in the following situations:*
  - when the asthma is so severe the child cannot move the spacer valve (in practice these are children severe enough to require intensive care)
  - in some toddlers who tolerate one and not another form of delivery
  - in rare children with sensitivity to the aerosol propellant
    AND THEN ONLY if the nebuliser pump delivers adequate flow. If it takes longer than five minutes to deliver 2.5 ml of solution, the airflow is inadequate for good nebulisation. A nebuliser that is used regularly should be serviced every six months or so.

Action plan

A typical action plan I would write is for:

- Two puffs of reliever via spacer for mild symptoms not associated with chest tightness or breathlessness, e.g. symptoms on exertion, or at night.
- Six puffs via spacer (given one at a time, and shaking the aerosol before each puff) if the child is wheezy and having difficulty breathing. This can be repeated in two hours at home, or more often under medical supervision.
- If it is not working, or not lasting two hours, the family should seek medical assistance.
- If the child is extremely breathless and cannot speak or walk, an ambulance should be called and 10 puffs via the spacer can be given every 20–30 minutes.

What can the family doctor do when asked for assistance at step 3 above?

If the parents are using a spacer effectively, and a nebuliser is no more effective, what can the family doctor add? The most important aids are oxygen and safe monitoring.

1. Provide a reassuring and calming environment to reduce anxiety
2. Measure oxygen saturation and give oxygen if S_aO_2 is less than 92%
3. Give six puffs of reliever (salbutamol or combined salbutamol-ipratropium in more severe cases) via spacer every 20 minutes for an hour
4. Give prednisone tablets or prednisolone liquid 1mg/kg stat [during recovery the same dose is given *mane* for up to three days]
5. Monitor oxygen saturation and check progress in one hour (and hourly if a supervised observation area is available)
6. Refer to paediatric care if not improving rapidly. Arrange ambulance transport if requiring oxygen.

Reducing the risk of virus-triggered asthma attacks

- Reducing risk of infections. Although it is normal for young children to get frequent infections, there are certain factors that significantly increase the incidence. These are tobacco smoke exposure,[11] day care, and older siblings.
  - Complete avoidance of cigarette smoking at home or in the car. Compared to children in non-smoking homes, smoking outside the home and inside respectively increased children's smoke exposure 5-fold and 11-fold.[12] Thus we should be advising that complete cessation is best for the child, and not just smoking outside
  - Avoidance of active smoking in older children
  - Avoidance of day care, or choosing a smaller or home-based day care in young children
  - Frequent hand washing with soap by all at home, particularly when one of the family has a respiratory infection
  - Annual influenza vaccine.
- Becoming a supporter of St John's Ambulance (sensible for children with frequent or severe attacks as it reduces the anxiety about calling an ambulance, and the cost involved) http://www.stjohn.org.nz/donate/supporters.aspx

Measures with unproven benefit, and some studies failing to show benefit

- Starting a dose of prednisone or prednisolone at home at onset of episode (seems sensible but little evidence of efficacy[13])
- Use of reliever early during an infection
- Regular use of a low dose inhaled steroid (e.g. fluticasone 50µg i bd via spacer) over the respiratory

Key Points

- Childhood asthma, although sharing some features with adult asthma, has important differences in phenotype, natural history, treatment and side effects.
- Preventer therapy is directed at controlling the chronic symptoms (especially those causing exercise limitation or sleep disturbance) in the intervals between asthma exacerbations, rather than preventing intermittent attacks.
- Intermittent asthma (without interval symptoms) requires a different approach.
- Asthma exacerbations are mostly triggered by respiratory virus infections.
- Management of intermittent asthma focuses on the exacerbations: education about spacer use, the action plan, and minimisation of infection risk, especially that due to tobacco smoke.
- In rare instances (very frequent or severe seasonal exacerbations, or life-threatening exacerbations) there is justification for using preventive therapy with inhaled steroids over a season or period of risk.

virus season. It may be appropriate to trial this in some children with frequent severe winter episodes, but be prepared to discontinue it if it makes no difference.

Life-threatening acute asthma

Deaths from asthma are very rare in childhood. New Zealand total mortality data for the three years 2002 to 2004 showed three deaths in children, all of them in the age range 10–15 years. Often these deaths are sudden and anaphylactic-like, occuring before medical assistance arrives. However there is a small group of children who have had a life-threatening episode of asthma, for instance a respiratory arrest, an ICU admission, or threatened ICU admission. These children are at risk of further life-threatening episodes of asthma. Attacks like this may occur in children with chronic asthma, but just as often occur out of the blue in children with mild, intermittent or no previous asthma. In some children an anaphylactic-type response to a rarely encountered allergen may be responsible. These children will normally see a paediatrician in hospital. Apart from the measures listed above, my approach for these children is as follows:

- Try to identify the trigger on history and on skin tests for inhaled allergens (it may be infectious, allergic, irritant or unknown), in case there is an avoidable trigger
- Make sure the child has a working spacer and family know how to use it
- Go over the action plan carefully, and suggest immediate prednisone and paediatric assessment in any asthma attack that is more than trivial
- Prescribe a low dose inhaled steroid for two to three years after their last severe attack.

The reason for the last line, which is contrary to the advice for most children with intermittent attacks, is that there is circumstantial evidence, from a large state-wide population study of asthma in Saskatchewan, that inhaled steroids reduce the risk of a life-threatening attack. The evidence is thin, but the stakes are high.

Competing interests

The author has, in the past five years, received funding to attend symposia from companies that have an interest in medications for asthma, which is dealt with in this paper.

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