ABC of Asthma

JOHN REES

TREATMENT OF CHRONIC ASTHMA

 β Stimulants

The variety of devices available allows most patients to inhale their drugs

The mainstay of treatment of mild intermittent asthma is one of the selective β_2 stimulants taken by inhalation. Their onset of action is fast, and salbutamol, terbutaline, and fenoterol have an effect lasting for four to six hours. If more than occasional doses are required their regular use should be considered, with additional symptomatic use as necessary. It makes little sense rigidly to restrict the daily dose to two puffs four times a day when an initial nebuliser dose in hospital may be five to 10 times this total dose. The dose needed varies between patients, as does the dose producing side effects such as tremor. A maximum daily dose, perhaps 20 puffs, should be established so that the patient can seek help if he feels he needs to exceed this dose. Patients should be taught to monitor their inhaler use and understand that if this increases or its effects get less these are danger signals indicating deterioration in asthmatic control and of the need for further treatment.

In using a metered dose inhaler the patient should inhale slowly and deeply and then hold his breath for five to 10 seconds. This technique should be checked at each visit until the patient is competent. Some patients never manage to master the technique, but alternative devices, such as rotacaps and extension tubes, mean that few patients cannot inhale bronchodilators in some way.

Nebulisers owe most of their effect to the large doses used and are rarely necessary except in acute severe attacks of asthma. Oral treatment requires 20 times the inhaled dose for a similar effect, and consequently side effects (tachycardia, tremor, and cramps) are much more common. Sometimes longacting oral preparations may be used at night, but otherwise treatment by mouth should be reserved for the few patients who cannot cope with any of the available inhalation devices.

Anticholinergic bronchodilators

Inhaler technique should be checked at each visit until the patient can do it correctly. It should not simply be left to the pharmacist or written instructions

Ipratropium bromide blocks the cholinergic bronchoconstrictor effect of the vagus nerve. It is most effective in very young children and older patients and least effective in asthmatic patients in their teens and 20s. The present dose delivered by inhaler is probably too low, but a more suitable dose of three or four inhalations three times a day is inconvenient. Ipratropium bromide therefore takes second place as a bronchodilator unless tremor is troublesome with β stimulants. If the response to a β stimulant is inadequate then the technique of using the inhaler should be checked first. If this is satisfactory evidence of an extra anticholinergic effect should be sought by measuring peak flow before and after the β agonist and then 30 minutes after adding ipratropium. At these doses drying of secretions or interference with mucociliary clearance does not occur. Very occasional paradoxical bronchoconstrictor effects have been reported after inhalation of ipratropium bromide.

Methylxanthines

Theophylline is often used as a first line agent for asthma in North America. Its safety margin is low, however, and individual differences in the doses required are high, so that treatment is best monitored by measuring blood concentrations. Inhaled treatment with β agonists is much preferable, but some patients who respond to β agonists benefit from added theophylline, especially for symptoms at night. In these cases a slow release oral preparation containing theophylline or its ethylene diamine salt, aminophylline, should be used. Absorption of aminophylline from suppositories is much less predictable and they are best avoided.

The commonest side effects of theophylline are nausea, vomiting, and abdominal discomfort, but headache, malaise, fast pulse rates, and fits also occur, sometimes without warning from gastrointestinal symptoms. The dose of theophylline should start at around 7 mg/kg/day, in divided doses, doubling if no response occurs. If any side effects occur or if the dose rises above twice this starting dose the blood concentrations of theophylline must be measured. Ideally all patients taking theophylline should have their concentrations monitored and doses adjusted until there are between 10 and 20 mg/l (50-100 μ mol/l). Above 20 mg/l toxic effects are unacceptably high, although 15-30% of patients will have gastrointestinal effects below this level.

Disodium cromoglycate

Sodium cromoglycate is available in a metered dose inhaler or as dry powder for inhalation

Disodium cromoglycate has little or no bronchodilator action but blocks bronchoconstrictor responses to challenge by exercise and antigens. It is used as the first line prophylactic agent after failure to control asthma with occasional inhalation of a β agonist. Success is most likely with young atopic asthmatics but may occur at all ages. Disodium cromoglycate is usually given as plain spincaps containing 20 mg of the drug as a dry powder. Metered dose inhalers delivering 1 mg per inhalation are also available and seem to be just as effective. Occasionally patients develop reflex bronchoconstriction in response to the irritant effects of the dry powder. This can be treated by giving a β agonist just before, by switching to the metered dose inhaler, or by giving compound spincaps containing 0.1 mg isoprenaline in addition to the 20 mg of cromoglycate. The last alternative is the least satisfactory as patients recognise the immediate bronchodilator effect of the isoprenaline and then tend to use the preparation inappropriately.

Other adverse reactions to disodium cromoglycate are rare, and this helps to explain the resistance to oral alternatives such as ketotifen, which produces drowsiness in about 10% of patients. Cromoglycate should not be dismissed as ineffective until it has been tried for at least four weeks, and its use must be regular. It has no place in acute exacerbations of asthma and may even increase narrowing of the airways by its irritant effect.

Corticosteroids

Many acute episodes of asthma are preceded by a period of poor control. Most patients can be taught to detect this deterioration and prevent a severe attack by starting themselves on a short course of oral corticosteroids

Occasional asthmatic patients end up taking long term oral corticosteroids but this should be only after failure of vigorous treatment with other drugs, and the symptoms or risks of the disease must be balanced against the adverse effects of long term treatment with oral corticosteroids. In contrast short courses of oral steroids for exacerbations of symptoms and inhaled steroids have few problems.

Inhaled steroids are given by metered dose inhaler or one of the other inhalation devices used for β agonists. The dose should be adjusted to produce optimum control. Inhaled steroids may be given twice daily with no problems apart from occasional oropharyngeal candidiasis or a husky

The dose of inhaled corticosteroid should be adjusted for each patient. Clinically important adrenal suppression does not occur below 1500 µg/day of beclomethasone dipropionate (or its equivalent)

voice until a daily dose above the equivalent of 1500 µg beclomethasone dipropionate is reached. At higher doses suppression of the hypothalamic-pituitary-adrenal axis may be found even with inhaled steroids. Inhaled steroids must be taken regularly to be effective and have no place in treating acute asthma. Once inhaled steroids are being taken there is no benefit to be gained from adding or continuing sodium cromoglycate.

Short courses of steroids—10-40 mg for one to three weeks—may be stopped abruptly or tailed off over a few days. Low cortisol and ACTH concentrations are found for two to three days after 40 mg prednisolone for three weeks, but clinical problems with responses to stress or exacerbations of asthma seem not to occur. Most asthmatic patients can be taught to keep such a supply of steroids at home and use them when predetermined signs of deteriorating control occur. If patients require long term oral corticosteroids, they should be stabilised on an alternate day regimen whenever possible, the goal always remaining to discontinue long term steroids in the future. They should be combined with inhaled steroids in moderately high doses to keep the dose of oral steroids as low as possible. Alternative preparations such as triamcinolone and ACTH are less flexible to use than prednisolone and have no advantages in terms of adrenal suppression.

Desensitisation and allergen avoidance

As discussed in the article on precipitating factors, the results of trials of desensitisation and allergen avoidance have been disappointing. Some patients have obvious precipitating factors—in particular, animals—and avoidance is helpful but usually leaves other unknown precipitating factors. More common are patients with sensitivity to pollens or house dust mites. Such stimuli are almost impossible to avoid in everyday life, although symptoms improve with rigorous measures such as admission to a dust free environment in hospital.

There is some evidence that desensitisation is beneficial in pollen asthma and that repeated courses increase the improvement. Controlled studies in adults sensitive to house dust mites have shown no benefit from desensitisation. Several studies in children have suggested some benefit, but these were all highly selected patients, and it is unusual to find asthmatics with a single sensitivity. The degree of control produced by desensitisation can usually be achieved with simple, safe inhaled therapy.

There is no sound evidence to support desensitisation to other agents in asthmatics. In particular, cocktails produced from the results of skin tests or radioallergen sorbent tests are not a valid form of treatment.

Combination therapy and other treatments

Many oral and inhaled combined preparations are available, but in a variable disease such as asthma they do not permit the necessary flexibility of treatment

In a variable disease such as asthma where treatment should be regularly tailored to the state of the disease it seems particularly illogical to use fixed dose combinations. Several such oral preparations are still available, often containing small doses of theophylline, ephedrine, and a barbiturate. Although some patients with mild asthma exist happily taking such preparations, there is no indication for prescribing them to new patients. Some inhaled combination preparations are available but these also restrict the flexibility of treatment.

Other drugs such as α stimulants, antihistamines, and calcium antagonists have occasionally been found to have some effect. Nevertheless, they have no great practical value in asthma.

Occasional dramatic claims for hypnosis and acupuncture have not been confirmed in controlled trials. Ionisation of inspired air may produce a small effect on lung function and may attenuate the response to exercise, but such effects are minimal.

Dr John Rees, MD, MRCP, is senior lecturer and consultant physician, Guy's and Lewisham Hospitals, London.