Bronchodilator drugs in childhood asthma

During the last 20 years there has been a striking proliferation in the number of bronchodilator formulations; each, the manufacturers would have us believe, is better than the rest. The aim of this annotation is to make a didactic statement attempting to put the various drugs into some sort of perspective for the clinician.

The pattern of prescribing is inevitably age-related, and so children over age 7 years, between ages 3 and 7 years, and those under 3 years are considered separately.

Children aged over 7 years

Most clinical trials have been on children over age 7 and so our knowledge is at its strongest here. This is fortunate since the treatment patterns available for the older child are at their most prolific.

The oral route is undoubtedly the most convenient as far as the patient is concerned. There is little to choose between the tablet and syrup formulations except the tendency for some of the latter to rot the teeth at an alarming rate. The main disadvantages are the relatively slow onset, with little response in the first 15 or 20 minutes, often not reaching peak effect for 45 to 90 minutes, and the relatively large systemic dose that is required in order to achieve adequate lung tissue concentrations. There seems little to choose between the drugs available. Of the newer beta-2 selective drugs: salbutamol, orciprenaline, and terbutaline, terbutaline has a longer half-life, so that thrice-daily rather than 6-hourly administration is adequate,¹ but whether this makes any difference in clinical practice has not been established. There seems little point in prescribing older bronchodilator preparations based on ephedrine, which are more likely to cause tachycardia and exhibit tachyphylaxis. The most appropriate pattern of administration has yet to be resolved. One study² suggests that some children with frequent or chronic asthma get fewer symptoms and more improvement in lung function by taking beta-2 stimulants on a regular rather than a prn basis. For those with only occasional symptoms, intermittent therapy still seems adequate. Slow-release salbutamol (salbutamol Spandets) is well worth considering for asthmatic children with irritating and persistent nocturnal coughs. This fairly large dose (8 mg) provides useful bronchodilatation overnight.

The remaining oral bronchodilators are in the

xanthine group. Their mode of action is in doubt, as the suggestion that these are phosphodiesterase inhibitors, preventing breakdown of cyclic-AMP, has not been proved.³ These drugs are not generally recommended for intermittent use but are undoubtedly an interesting and useful group if prescribed appropriately. One of the problems has been the very considerable person-to-person variation in blood level, due to wide variation in the rate of metabolic breakdown. Most proponents of theophylline recommend that blood levels should be measured after the child has been stabilised on 20 to 24 mg/kg body weight a day and dosage adjusted to ensure blood levels of 12 to 20 µg/ml.⁴ Measurements should then be repeated at 6-monthly intervals. Used in this manner theophyllines seem to have a useful prophylactic effect, equivalent to that of Intal,⁵ and breakthrough attacks can be treated by adding beta-2 stimulant therapy. Whether the addition of a beta-2 stimulant is additive or synergistic remains speculative. The main disadvantage of the theophylline drugs is their relatively low toxic/therapeutic index, so that nausea and vomiting are common. The popularity of theophyllines is likely to increase since the introduction of slow-release preparations which produce adequate blood levels on a twice-daily regimen.⁶

In recent years there has been a progressive swing to the use of inhalant devices which deliver beta-2 stimulant directly to the respiratory tract. The advantages of this route are the rapid onset, generally within 3 minutes, and the low incidence of side effects. Although it is now considered unlikely that isoprenaline and adrenaline were directly responsible for the increase in mortality in young asthmatic adults in the 1960s, these drugs do produce striking tachycardia and have been replaced by the more selective and longer-acting beta-2 stimulants. All are available in fluorocarbon-containing aerosol systems and, again, there are no studies to show that in clinical practice one has any great advantage over the others. Remiterol is a little different, with a more rapid onset and shorter duration, but this is not necessarily a major advantage. These preparations can be taken either as part of routine therapy in those with chronic symptoms, or intermittently for those less severely affected. All are very effective in preventing exercise-induced bronchospasm. The swing to inhaled drugs was to some extent due to the claim that orally-administered beta-2 stimulant had

little effect in inhibiting exercise-induced bronchoconstriction. A recent study indicates that this is purely a drug-related phenomenon and good inhibition can be obtained, provided generous doses (salbutamol 0.15 mg/kg body weight) are used.⁷ Doses of up to 12 puffs a day seem quite safe, but it is obviously essential to warn children and their parents to obtain immediate medical advice if the response to the inhaler is greatly reduced or lasts only for a short period.

Ipratropium bromide, an atropine derivative, is also available in aerosol form. This appears to have its maximal effect on the larger airways and is probably not as effective a bronchodilator agent as the beta-2 stimulants. It is undoubtedly less effective in blocking exercise-induced bronchoconstriction. Nevertheless there may be a place for this drug in combination with others in the management of chronic asthma.

Children aged 4–7 years

The options open for treating this group are more restricted. Oral therapy with beta-2 stimulants, possibly combined with oral theophylline, often provide adequate control, particularly in those with mild to moderately severe symptoms. Nocturnal cough can be helped by taking half a salbutamol Spandet tablet on retiring. Few children under age 7 years can use the aerosol devices adequately, although interface units such as Aerospacer may help some. The introduction of salbutamol in powder form has to a large extent filled this gap,⁸ and although more time-consuming, it is undoubtedly as effective as aerosol in achieving bronchodilatation. The doses generally recommended, 200 µg 4- to 6-hourly, can certainly be doubled without fear of adverse effects other than transient tremor.

Children below age 3 years

These children pose a greater problem. The attacks of wheezing are generally precipitated by viral upper respiratory tract infection and respond less strikingly to oral therapy with either beta-2 stimulant drugs or xanthine derivatives. There is no evidence that such

oral therapy is worth prescribing in the first year of life. The alternative is to provide the child and his parents with a compressor and nebuliser for use at home, or allow free access to hospital services. The child can then be given salbutamol respirator solution (0.5 ml with 2 ml of water) on either a regular or prn basis.⁹ This form of therapy is usually striking in the child over age 18 months.¹⁰ There are undoubtedly a few children between ages 12 and 18 months who obtain benefit, but there is no evidence that inhaled beta-2 stimulant drugs have anything to offer the wheezy child in the first year of life.

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