Bronchodilators in infancy

The clinical problem of the wheezy infant is becoming more common, hospital admissions for wheeze in children up to the age of four years having increased fourfold in the United Kingdom over the last two decades. The financial implications of this rising morbidity in an overburdened health service is considerable, and the paucity of evidence from controlled treatment trials on these children is a continuing source of frustration.

A long standing controversy in paediatric respiratory medicine is whether or not the airways of infants contain functional $\beta_{2}$ adrenergic receptors. Although data from studies spanning more than 20 years show that $\beta_{2}$ adrenoceptor agonists do not produce a clinically significant improvement in lung function in wheezy infants,\textsuperscript{1,4} it is now becoming clear that this finding cannot be explained by the absence of $\beta_{2}$ receptors. In early studies there were two possible confounding reasons why the infants studied failed to respond to inhaled salbutamol. Firstly, the acidic and hypo-osmolar nature of the form of salbutamol used (Ventolin Respirator Solution, Allen and Hanburys, UK) could have induced an element of bronchoconstriction.\textsuperscript{9} Perhaps more importantly the infants studied suffered from recurrent wheeze and therefore reversible bronchoconstriction was unlikely to be the only cause of airflow obstruction. The airways of wheezy infants differ from those of normal infants in several ways; there is evidence to suggest that they are smaller than those of age matched non-wheezy controls\textsuperscript{10} and that they are more likely to show fixed obstruction as a result of mucosal oedema and excessive mucus production secondary to an inflammatory process.\textsuperscript{11} These factors, in conjunction with the increased dynamic compression secondary to reduced airway tone which can occur during forced expiration in subjects with airways inflammation, make the interpretation of studies on the effects of $\beta_{2}$ adrenoceptor agonists difficult in subjects with existing disease of the airways.

Three previous studies have attempted to address these problems. Prendiville et al.\textsuperscript{1} showed that pretreatment with salbutamol protected the airway from histamine induced bronchoconstriction in recurrent wheezy infants, although baseline lung function did not improve. Similarly, O'Callaghan et al\textsuperscript{2} showed that salbutamol could protect the airways of wheezy infants from bronchoconstriction induced by nebulised water. Tepper\textsuperscript{3} was the first to report that infants with no history of airways disease showed orciprenaline reversible methacholine induced bronchoconstriction. The study by Henderson et al reported in this issue of Thorax takes these studies to their logical conclusion and examines the ability of salbutamol to hasten the recovery of histamine induced bronchoconstriction in infants with no history of airways disease.\textsuperscript{14} Although bronchoconstriction produced by the inhalation of histamine has different underlying mechanisms from those occurring in the naturally wheezy infant, it provides a useful model for the investigation of narrowing of airways in the absence of chronic airways inflammation. These authors found that salbutamol was responsible for a significantly faster rate of recovery than saline and suggest that this finding provides further evidence for the presence of functional $\beta_{2}$ adrenergic receptors in infant airways.

Salbutamol remains of unpredictable and often restricted immediate benefit in the wheezy infant and has been shown to improve baseline lung function only in conjunction with treatment with dexamethasone.\textsuperscript{12} If, however, we accept the work of Henderson et al as further proof for the existence of functional $\beta_{2}$ adrenoceptors in the infant airway, the failure of salbutamol to improve airflow obstruction in both bronchiolitis and asthma in this age group can no longer be attributed to the absence of these receptors and the alternative explanation—that the airflow limitation is predominantly due to oedema and excess mucus production secondary to inflammation—becomes more credible. It seems logical, however, to administer $\beta_{2}$ adrenoceptor agonists to these wheezy infants during their acute attacks of wheeze since, although there may be no immediate improvement in their clinical state and care must be taken to minimise the fall in oxygen saturation that can occur during nebulisation of salbutamol, further irritation of the already inflamed airway might be reduced.

More direct evidence of the role of inflammation in airways obstruction in the very young will only be forthcoming if fibroptic bronchoscopy and biopsy become more acceptable in this age group. In the meantime, perhaps we should refocus our attention on the potential for the use of anti-inflammatory agents in the treatment of wheeze in the infant.

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