Effect of bronchodilators on respiratory resistance in infants and young children with bronchiolitis and wheezy bronchitis

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Rutter, N., Milner, A. D., and Hiller, E. J. (1975). *Archives of Disease in Childhood*, 50, 719. **Effect of bronchodilators on respiratory resistance in infants and young children with bronchiolitis and wheezy bronchitis.** Respiratory resistance was measured using a forced oscillation technique in 16 infants and young children with bronchiolitis and wheezy bronchitis. Measurements were made before and after administration of nebulized salbutamol or isoprenaline. No significant change in resistance was found.

Acute obstructive airways disease in infancy and early childhood, diagnosed as bronchiolitis or wheezy bronchitis, is a common reason for hospital admission and is occasionally fatal. Phelan, Williams, and Freeman (1968) and Phelan and Williams (1969a) have shown that the major physiological abnormality is an increase in airways resistance, similar to that found in older children and adults with asthma. Since bronchodilators such as salbutamol and isoprenaline, which act by stimulating the β receptors of bronchial muscle, are effective in lowering the high airways resistance of older children with asthma, their use in the younger age group is obviously attractive.

There has been uncertainty concerning the clinical benefit of bronchodilators in the younger age group, though many authors consider that they are of little therapeutic value (Buffum, 1959; Reynolds and Cook, 1963). Objective assessment of the effect of bronchodilators has been reported in bronchiolitis (Phelan and Williams, 1969b) and wheezy bronchitis (Phelan and Williams, 1969a; Radford, 1974) in which the infants studied were less than 6 months of age. In none of these studies were bronchodilators shown to lower airways resistance.

The aim of our study was to assess the effect of salbutamol on airways resistance in older infants and young children with acute obstructive airways disease.

Material

Sixteen patients were examined whose ages ranged from 3 months to 3 years (Table). They were all

TABLE

Age distribution of patients studied

Age (m)	No.
3-6	7
6-12	6
>12	3
Total	16

recovering from bronchiolitis or wheezy bronchitis and were relatively well at the time of the study. Each patient had increased respiratory efforts with prolonged expiration and an audible wheeze. Diagnosis was made according to the clinical definition of Court (1973).

Method

Respiratory resistance was measured using the forced oscillation technique (Cogswell, 1973). This method is noninvasive and requires no co-operation from the patient.

A sine wave of airflow, generated by a loud speaker, is conducted to the infant's nose and mouth via a wide bore tube and face mask (Fig. 1). If the frequency of the applied airflow is at the natural resonant frequency of the respiratory system, changes in pressure as a result of that flow are a reflection only of the resistance of the respiratory tract. The frequency used in this study was 6 Hz and the apparatus was calibrated on each occasion with resistances of known value.

FIG. 1.—Schematic representation of apparatus.

Measurements of pressure and flow were made at the infant's mouth with a pneumotachograph and pressure transducer, and recorded simultaneously on an ultra-violet recorder. Resistance was calculated by dividing the maximum pressure oscillation by the flow change (Fig. 2). A mean resistance value was derived from 6

FIG. 2.—Measurement of resistance from simultaneous recordings of pressure and airflow.

measurements on the same trace, in expiration and where possible in inspiration.

Measurements of resistance were made in the resting state, again after inhalation of nebulized water (1.0 ml) and then 5 and 10 minutes after administration of nebulized salbutamol (1.0 ml of a 0.25% solution). Administration was achieved using a Wright's nebulizer and face mask, with a flow rate of approximately 8 l/min. All the 16 patients were sedated with chloral hydrate (75 ml/kg body weight) 30 minutes before application of the face mask, since recordings in crying infants are valueless. Recordings of pulse and respiratory rates

were made immediately before each resistance measurement. 3 infants received isoprenaline instead of salbutamol.

Results

Of the 16 patients studied, 13 were diagnosed as wheezy bronchitis and 3 as bronchiolitis. The average length of history before admission was 4 days, and the average hospital stay 8 days. All the patients were presumed to have a virus infection on the basis of a normal white cell count or mild lymphocytosis; virus isolation studies were not performed. A chest x-ray was performed on each patient. This showed overinflation of the lungs, sometimes with the presence of patchy atelectasis. Of the 13 patients diagnosed as wheezy bronchitis, 7 have had recurrent, similar attacks, 5 have a strong family history of atopic disease, and 2 have eczema.

In all the patients studied, a rise in pulse rate was noted after administration of the bronchodilator—no change was seen after water had been given. The mean rise was 9% in the 13 who received salbutamol and 17% in the 3 who received isoprenaline, with an overall mean increase of 10%. There was no significant alteration in respiratory rates after water or bronchodilators.

Mean normal values of resistance using the forced oscillation technique are 50 cm H₂O/l per s $\pm$ 25 (2 SD) at 3 months of age, falling to 25 cm H₂O/l per s $\pm$ 12 at 2 years of age (B. Taylor, unpublished, 1974). All 16 patients in the study had resting expiratory resistance values which were 2 SD or more above the mean value for their age. In no patient was an appreciable fall in expiratory resistance shown after administration of broncho-

FIG. 3.—Respiratory resistance values at rest, after water, and after bronchodilator in all 16 patients studied.

FIG. 5.—Mean respiratory resistance on inspiration, after administration of water and bronchodilator, expressed as a percentage of the mean resting value.

FIG. 4.—Mean respiratory resistance on expiration, after administration of water and bronchodilator, expressed as a percentage of the mean resting value. SD shown by vertical bars.

dilator (Fig. 3). The mean expiratory resistances after water and bronchodilator were almost identical to the mean resting resistance (Fig. 4). Inspiratory resistance could only be measured in half the patients, and values are widely scattered, but again no significant effect of bronchodilator was found (Fig. 5).

Discussion

The results show that salbutamol and isoprenaline do not lower the high respiratory resistance of older infants with acute obstructive airways disease and support the clinical impression that they are of little therapeutic value. The consistent increase in pulse rate produced by administration of nebulized bronchodilator suggests that significant amounts of the drug are being absorbed using this route, and therefore any bronchodilator effect should be apparent.

There are a number of explanations for the failure of bronchodilators. The upper airways in infants make a significant contribution to the total respiratory resistance and a degree of upper airways obstruction is commonly seen in association with chest disease. β -Stimulants (salbutamol and isoprenaline) have no effect on mucosal oedema and mucus production in the upper airways.

Pathological studies on infants and young children who have died with bronchiolitis and wheezy bronchitis have shown mucosal swelling and the presence of thick secretions in the bronchi and bronchioles. It is likely that this is responsible for the high airways resistance in wheezing infants, rather than constriction of bronchial muscle, which is poorly developed at this age (Engel, 1962). Further work is required to study the effect of bronchodilators in preschool children, in order to determine the age at which they become effective.

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REFERENCES

- Buffum, W. P. (1959). Asthma in infancy. *Pediatric Clinics of North America*, **6**, 683.
- Cogswell, J. J. (1973). Forced oscillation technique for determination of resistance to breathing in children. *Archives of Disease in Childhood*, **48**, 259.
- Court, S. D. M. (1973). The definition of acute respiratory illnesses in children. *Postgraduate Medical Journal*, **49**, 771.
- Engel, S. (1962). *Lung Structure*, p. 26. Thomas, Springfield, Ill.
- Phelan, P. D., and Williams, H. E. (1969a). Studies of respiratory function in infants with recurrent asthmatic bronchitis. *Australian Paediatric Journal*, **5**, 187.
- Phelan, P. D., and Williams, H. E. (1969b). Sympathomimetic drugs in acute viral bronchiolitis. *Pediatrics*, **44**, 493.
- Phelan, P. D., Williams, H. E., and Freeman, M. (1968). The disturbance of ventilation in acute viral bronchiolitis. *Australian Paediatric Journal*, **4**, 96.
- Radford, M. (1974). Effect of nebulized salbutamol in infants with wheezy bronchitis. *Archives of Disease in Childhood*, **49**, 243.
- Reynolds, E. O. R., and Cook, C. D. (1963). The treatment of bronchiolitis. *Journal of Pediatrics*, **63**, 1205.

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