

# Effect of salbutamol in infants with wheezy bronchitis

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**Radford, M. (1975).** *Archives of Disease in Childhood*, **50**, 535. **Effect of salbutamol in infants with wheezy bronchitis.** Using the technique of whole body plethysmography, lung mechanics were measured in a group of infants with wheezy bronchitis. Compared with a group of normal infants previously studied, airway resistance and thoracic gas volume were found to be raised. Nebulized salbutamol was then administered and measurements were repeated when it was found that there was no objective improvement. It is concluded that salbutamol may not be an effective form of treatment of wheezy bronchitis in young infants and the reasons for this are discussed.

Wheezy bronchitis in infancy, defined as respiratory distress with generalized expiratory rhonchi, is common in general paediatric practice, but the treatment of this condition varies widely from one centre to another (Elderkin *et al.*, 1965; Wright and Beem, 1965). In particular, bronchodilator therapy is commonly given, but there is no good evidence that it is effective. In a previous communication (Radford, 1974) it was shown that airway resistance and lung volume can be reliably measured in infancy, and this makes it possible to assess the effect of various forms of treatment in an objective manner. The purpose of the present study was to test the effect of a commonly used bronchodilator, salbutamol, in infants with wheezy bronchitis.

## Subjects and methods

Airway resistance and thoracic gas volume were measured in 10 infants with wheezy bronchitis. This was purely a clinical diagnosis based on a combination of tachypnoea, respiratory distress, and generalized expiratory rhonchi in infants weighing less than 10 kg, and no attempt was made to subdivide the subjects on an aetiological basis. Most of them were only moderately sick and were studied at any convenient time during their illness. Others were more severely ill, requiring oxygen and intravenous fluids at the height of their illness, and were studied as soon as they were well enough to be nursed out of oxygen. Several had been treated with antibiotics, and some had received oral bronchodilator therapy, but not within the 6 hours preceding the study. Clinical and radiological features of the 10 infants are given in Table I.

The infants were sedated with chloral hydrate, 60 mg/kg, and airway resistance and thoracic gas volume were measured in a whole body plethysmograph as previously described (Radford, 1974). Salbutamol was then administered by blowing oxygen at 7 l/min through a Wright's nebulizer containing 10 ml 0.5% salbutamol solution. The outlet of the nebulizer was connected to an open-ended nasal adaptor which was fitted into the infant's nose using silicone putty to make an airtight seal. The tubing from the nebulizer was of thick-walled rubber and kept as short as possible to minimize droplet deposition on its walls. The nebulization was continued for two minutes, and the radial pulse counted before and after. With practice it was found that this procedure could be carried out without waking the infant, and the measurements of airway resistance and lung volume were repeated about 20 min later. Mean values were calculated from three separate measurements before and after nebulization.

## Results

Table II shows the results of airway resistance and thoracic gas volume in the 10 infants studied before giving salbutamol and compared with a group of 16 normal infants previously studied who fell into the same age range of 8–43 weeks. There was no significant difference between the mean age or weight of these two groups. Thoracic gas volume is expressed in relation to body weight, since it has been shown that there is a constant relation between these two parameters in normal infants (Howlett, 1972). Both airway resistance and thoracic gas volume were significantly higher in the group with wheezy bronchitis.

The effect of nebulization with salbutamol is

TABLE I  
*Clinical details of infants with wheezy bronchitis*

Case no.	Sex	Age (w)	Weight (kg)	Family history of asthma	Past history of eczema	Previous wheezing attacks	Chest x-ray
1	F	14	6.15	+	+	—	Patchy opacities
2	F	12	5.03	—	—	—	both lower lobes
3	M	20	7.95	—	—	—	Patchy opacities
4	M	13	5.82	—	—	—	both lower lobes
5	F	43	8.52	—	+	+	Normal
6	M	26	7.78	—	—	—	Patchy opacity
7	M	33	8.20	—	—	—	R upper lobe
8	F	13	6.00	—	—	—	Normal
9	F	8	4.87	—	—	+	Patchy opacity
10	F	12	5.49	—	—	+	L lower lobe

TABLE II  
*Lung mechanics in normal infants and infants with wheezy bronchitis*

	Normal (no. = 16)		Wheezy bronchitis (no. = 10)		Difference
	Mean	SD	Mean	SD	
Age (wk)	16.6	8.9	19.4	11.2	NS P 0.503
Weight (kg)	5.924	1.674	6.581	1.387	NS P 0.310
Thoracic gas volume (ml)	210.4	73.8	306.4	77.3	HS P 0.004
Thoracic gas volume/kg body weight (ml)	35.2	6.3	47.1	10.3	HS P 0.001
Airway resistance (cm H <sub>2</sub> O/l per s)	20.9	8.7	33.2	10.0	HS P 0.003

NS, not significant; HS, highly significant.

TABLE III  
*Effect of nebulized salbutamol in 10 infants with wheezy bronchitis*

	Before treatment		After treatment		Difference
	Mean	SD	Mean	SD	
Pulse/min	149	13	148	12	NS P 0.59
Thoracic gas volume (ml)	306.4	77.3	309.0	84.3	NS P 0.83
Thoracic gas volume/kg body weight (ml)	47.1	10.3	47.7	13.3	NS P 0.76
Airway resistance (cm H <sub>2</sub> O/l per s)	33.2	10.1	35.2	7.6	NS P 0.32

shown in Table III. There was no significant change in thoracic gas volume, airway resistance, or pulse rate after this treatment.

### Discussion

The clinical condition of wheezy bronchitis described here is one which is familiar to all paediatricians, and frequently divided into viral bronchiolitis and asthmatic bronchitis. In viral bronchiolitis this clinical picture follows a short period of

fever and coryza, and is usually caused by the respiratory syncytial virus. In asthmatic bronchitis the condition is recurrent, often with no preceding symptoms or systemic upset, and frequently develops into childhood asthma. However, clinically it is often difficult to place an infant into one or other of these categories, and there is increasing evidence that these two conditions form part of a continuous spectrum of disease. Rooney and Williams (1971) followed up a series of infants with

viral bronchiolitis, in whom respiratory syncytial virus had been isolated, and showed a high incidence of recurrent wheezing, which is known to be associated with a high incidence of asthma in later childhood (Williams and McNicol, 1969). Similar results were obtained by Eisen and Bacall (1963) and König, Godfrey, and Abrahamov (1972), though these authors did not perform viral studies. It seemed reasonable, therefore, to treat the clinical syndrome of wheezy bronchitis as a single entity for the purposes of this study.

The observed increase in airway resistance and thoracic gas volume in these infants is consistent with lower airways obstruction. Hyperinflation probably results from early closure of airways whose internal diameter is compromised by oedema or bronchospasm. Similar results are found in other forms of lower obstructive airways disease studied by plethysmography, such as asthma or fibrocystic disease (Dubois, Botelho, and Comroe, 1956; Cook *et al.*, 1959; Meisner and Hugh-Jones, 1968). However, these are all studies on adults or older children. Comparable information on lung mechanics in infancy is very scanty and variable.

Phelan, Williams, and Freeman (1967) measured total pulmonary resistance and thoracic gas volume in infants with viral bronchiolitis, and found them both to be raised. They used an oesophageal balloon to measure intrapleural pressure and a pneumotachygraph to measure air flow at the nose and mouth, and measured thoracic gas volume in a plethysmograph. Wohl, Stigol, and Mead (1969) measured inspiratory and expiratory resistance in infants with bronchiolitis using the forced oscillatory technique of Dubois *et al.* (1955). They found a marked rise of expiratory resistance, but only a slight increase in inspiratory resistance, and did not measure lung volume.

The results of the present study clearly show that salbutamol, given in the manner described, has no beneficial effect on airways obstruction in wheezy bronchitis in infancy. The possible interpretations of this are that either it is genuinely ineffective, or it was not given in an effective manner. There has been a great deal of debate concerning the efficacy of aerosol administration of drugs. Bau *et al.* (1971) administered radioactively labelled nebulized water to subjects in a mist tent and scanned them immediately after. They found that though some radioactive water was deposited in the lungs, 90% of the radioactivity was localized in the stomach, presumably due to swallowing of droplets deposited in the posterior pharynx.

Nevertheless, bronchodilators given by aerosol are undoubtedly effective in asthma (Choo-Kang,

Parker, and Grant, 1970; Riding, Chatterjee, and Dinda, 1969). In the paediatric department of the Brompton Hospital, nebulized salbutamol is given to children aged 4 and over in an almost identical manner to that described here, and it is rapidly effective as judged by clinical improvement and increased peak flow (personal observation). Moreover, it has been shown that nebulized isoprenaline, when given to infants via a face mask, causes a brisk increase in heart rate, showing at least that it enters the systemic circulation (Phelan and Williams, 1969). For these reasons, it was concluded that salbutamol was given in an effective manner in this study, and therefore that it has no beneficial effect on airway obstruction in infancy.

These results tend to confirm a clinical impression, but there is very little published information on the effect of bronchodilators in wheezing conditions in infancy. Holland, Colley, and Barraclough (1960) found respiratory effort, as measured by intraoesophageal pressure swings, to be decreased in some cases of bronchiolitis and bronchopneumonia after injection of adrenaline. However, the number of subjects was small, the distinction between bronchiolitis and bronchopneumonia was not clear, and they made no attempt to measure airflow in and out of the lungs. Reynolds and Cook (1963) state that 'an occasional infant may improve with the administration of bronchodilator drugs', but publish no data to support this opinion. Phelan and Williams (1969) approached the problem more objectively; they studied 10 infants with viral bronchiolitis and measured total pulmonary resistance using an oesophageal balloon and a pneumotachygraph. They found no decrease of resistance after administration of nebulized isoprenaline or orciprenaline, and concluded that these drugs were ineffective in this condition. They were, however, unable to measure thoracic gas volume in these infants, which is an important index of the severity of obstructive airways disease.

Thus, it appears that there is some fundamental difference between the airways obstruction in this group of infants and in older children or adults with asthma. The pathology of lower airway obstruction in wheezy bronchitis is not clear. Studies in infants dying of viral bronchiolitis show the most severe lesions in bronchioles of calibre 75–300  $\mu\text{m}$ , with oedema of the bronchiolar wall, epithelial necrosis, and excess secretion of mucous associated with plugs of debris obstructing the lumen (Aherne *et al.*, 1970). However, these represent the severe cases and pathological studies in mild cases are of course not available. It is

therefore difficult to assess the relative importance of oedema of the bronchiolar wall and true bronchospasm, if such an entity exists.

Phelan and Williams (1969) state that in infants under the age of 12 months bronchial and bronchiolar muscle is thin and poorly developed and probably could not significantly narrow the lumen of the airway by contraction. It is true that bronchiolar muscle is less predominant in small airways and infants, but it does exist. Matsuba and Thurlbeck (1972) measured this and found that 6.5% of the bronchiolar wall of small infants in infancy was composed of smooth muscle compared with 14.2% in adults. It does not necessarily follow, however, that this decreased amount of muscle is not capable of effective contraction.

In conclusion, it seems very likely that the structural basis of obstructive airways disease in infancy differs from that in older children with asthma, but the nature of the obstruction is poorly defined. Further study is required to assess the effect of bronchodilator and other forms of therapy so that rational treatment may be given in this very common condition.

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