

Alpha and beta adrenergic stimulants in bronchiolitis and wheezy bronchitis in children under 18 months of age

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SUMMARY Total respiratory resistance was measured before and after nebulised phenylephrine in 5 babies (age range 7 to 17 months) with wheezy bronchitis, and in 2 babies (aged 2 and 6 months) with bronchiolitis. None showed a change in resistance after treatment. Total respiratory resistance was measured before and after nebulised adrenaline in another 14 babies (age range 4 to 13 months) with bronchiolitis. No fall in resistance was noted in any baby after treatment whether or not it was given by a conventional or an ultrasonic nebuliser. We conclude that α - and β -adrenergic stimulants are ineffective in bronchiolitis and wheezy bronchitis in children under 18 months of age.

Bronchiolitis generally occurs in epidemics in the winter. It usually affects infants and occasionally produces severe symptoms requiring admission to hospital. Many drugs have been used in these severely ill infants but the only therapeutic agent that is of unquestionable benefit is oxygen. Corticosteroids have no significant effect on the duration or severity of the clinical state (American Academy of Pediatrics Committee on Drugs, 1970). β -Adrenergic stimulants, such as isoprenaline and salbutamol, are ineffective in reducing pulmonary and total respiratory resistance (R_T) in infants with bronchiolitis or wheezy bronchitis (Phelan and Williams, 1969; Rutter *et al.*, 1975).

We have recently shown that nebulised phenylephrine reduces total respiratory resistance and improves the clinical state in children with acute viral croup (Lenney and Milner, 1978c), presumably because the α -adrenergic stimulant reduces mucosal oedema. The pathological features of acute bronchiolitis include necrosis of bronchiolar epithelium, lymphocytic infiltration, and oedema of the submucosa and adventitial tissues, and we considered it possible that this oedema might also respond to α -adrenergic stimulants.

The purpose of this study was to examine the ability of nebulised α -adrenergic stimulants to reduce airways obstruction in bronchiolitis and wheezy bronchitis.

Subjects

Twenty-one babies were studied as inpatients (13 boys and 8 girls), their ages ranged from 2 to 17 months (mean 7 months). Apart from their acute respiratory illness they were well. Three babies with wheezy bronchitis had had two previous wheezing episodes. Two babies with wheezy bronchitis and 3 with bronchiolitis had a family history of asthma, eczema, or hay fever in first-degree relatives. At the time of testing all the babies were in the recovery phase of the illness but on examination they still had increased respiratory efforts, prolonged expiration, expiratory rhonchi and, in 7 with bronchiolitis, occasional basal crepitations. Permission for testing was obtained from at least one parent of each child and 16 of the 21 babies had one of their parents present throughout the test. The study had been passed in advance by the Nottingham Ethical Committee.

Method

Total respiratory resistance (R_T) was measured using a modification of the forced oscillation technique (DuBois *et al.*, 1956; Cogswell, 1973). This technique depends on the fact that when an oscillating sine-wave airflow is applied to the respiratory tract the transthoracic pressure changes induced are related to the total impedance of the system. The total impedance comprises R_T , elastic impedance,

and inertial impedance. At six cycles/second, the resonant frequency of the respiratory system, elastic and inertial impedance are of equal magnitude and opposite in sign, therefore cancelling out and allowing R_T to be calculated directly.

The apparatus and technique have been described (Lenney and Milner, 1978a, b). Each child was given 80 mg/kg chloral hydrate as sedation. When sleeping the child was placed supine on a couch and the face mask was slowly lowered over the mouth and nose using gentle pressure until an airtight seal was obtained. Traces were obtained from five or six breaths. R_T was expressed as the mean of at least 6 readings. R_T measurements were repeated 10 minutes later. The children were then given either 2 ml sterile water and 2 ml 0.25% phenylephrine or 2 ml 0.4% adrenaline hydrochloride solution using a conventional nebuliser (Pari) or an ultrasonic nebuliser (Moynahan 675). R_T measurements were repeated 10 and 20 minutes after nebulised therapy. The children who received water were then given 2 ml 0.25% phenylephrine and the measurements repeated. The water and phenylephrine were delivered by Pari nebuliser on 6 occasions and by the Moynahan ultrasonic nebuliser on one. Of the remaining 14 children with bronchiolitis 8 were given adrenaline by the Pari nebuliser and 6 by the Moynahan ultrasonic nebuliser. Pulse rate was measured before and 10 minutes after each inhalation and blood pressure was measured before and after the phenylephrine inhalation using the Doppler technique.

Results

Although no data of R_T in normal children under 18 months old have been published, all 21 children in this study had initial R_T values considerably higher than expected from extrapolation of available data (Cogswell, 1973). R_T measurements 10 minutes later were similar to the initial reading. The coefficient of variation between the two readings was 6.7% giving a correlation coefficient (r) of 0.97 ($P < 0.001$). The 5 children with wheezy bronchitis and 2 children with bronchiolitis showed no significant change in R_T after either nebulised water or nebulised phenylephrine. Mean percentage change in R_T 10 minutes after water was +4.6% (range +23% to -16%) and the mean percentage change 10 minutes after phenylephrine was +6.41% (range +11.1% to +1.6%). This pattern was also seen in the one child with wheezy bronchitis who was given phenylephrine by the ultrasonic nebuliser (Fig. 1). There was no significant difference in values between treatment after 10 and 20 minutes in any child. There was no improvement clinically in any child after either treatment. After inhalation of adrenaline the mean

percentage change in R_T 10 minutes after therapy was +4.4% (range +15.4% to -5.7%) in the ultrasonic nebuliser group and -1.4% (range +17.6% to -11.1%) in the Pari nebuliser group (Fig. 2). Once again there was no significant difference between

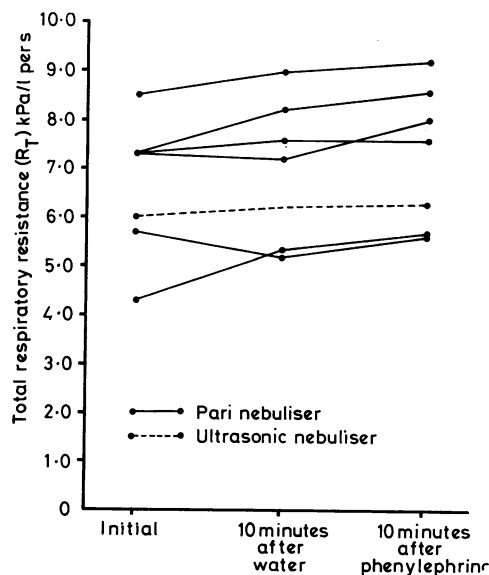


Fig. 1 Total respiratory resistance (R_T) in 5 children with wheezy bronchitis and 2 children with bronchiolitis, measured before and 10 minutes after nebulised water and 10 minutes after nebulised phenylephrine.

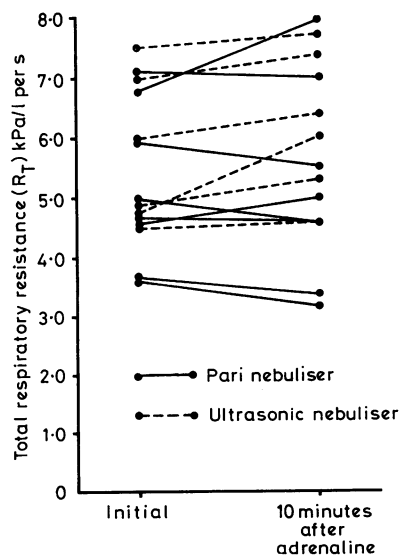


Fig. 2 Total respiratory resistance (R_T) in 14 children with bronchiolitis measured before and 10 minutes after nebulised adrenaline.

R_T values 10 and 20 minutes after therapy. No child showed any clinical improvement after therapy.

Pulse rate and blood pressure measurements were unchanged in the 7 children after phenylephrine inhalations. Pulse rate increased after adrenaline inhalation in 13 out of the 14 children tested. Mean initial pulse rate was 124 beats/min and the mean pulse rate after adrenaline was 142 beats/min. In the remaining child pulse rate was unchanged after adrenaline. Pulse rate was also unchanged after administration of water.

Immunofluorescence studies were performed in the 14 children with bronchiolitis who received adrenaline, and positive results for respiratory syncytial virus were obtained in 9 children.

Discussion

Nasal decongestant drops and sprays containing α -adrenergic stimulants are clinically effective in infective oedema of the nasal mucosa and we have shown that nebulised phenylephrine improves lung function in acute viral croup, albeit for the disappointingly short time of approximately 20 minutes (Lenney and Milner, 1978c). As oedema in the region of the small airways seems an important feature in the pathogenesis of bronchiolitis we considered it worthwhile to study the effect of treatment with nebulised α -adrenergic stimulants in this condition. It is probable that the pathological changes in infants and young children with wheezy bronchitis are similar to those seen in bronchiolitis and we have therefore studied children with both illnesses.

We initially chose phenylephrine as this is predominantly an α -adrenergic stimulant. We elected to use 2 ml 0.25% phenylephrine solution because this amount had proved effective in relieving obstruction in acute viral croup and was 25% of the dose previously used in treating asthmatic attacks in adults. When we failed to show improvement with this drug or with water we changed to adrenaline as we considered it possible that a combination of α - and β -adrenergic stimulants might be synergistic in this situation. However, none of the children showed any improvement in lung function or in clinical state after inhaled adrenaline whether the medication was given by a conventional or an ultrasonic nebuliser. Bronchiolitis is considered to be an infection acting mainly on the small airways and it is possible that medication given by conventional nebuliser would not penetrate sufficiently far down the airways because of the large droplet size of the mist. It was for this reason that we used the ultrasonic nebuliser which produces a mist predominantly of droplet size 1–3 μ m. It has been calculated that even in newborn babies most droplets of 1 μ m

or less can penetrate beyond the terminal bronchioli (Reid, 1977). The increase in pulse rate after the inhalation of adrenaline indicated that the drug was being absorbed. It still remains possible however that sufficient quantities of the drug did not reach the affected airways.

It has been claimed that the forced oscillation technique is sensitive to upper rather than lower airway changes. However, in a recent study using nebulised salbutamol we have found that in the first 3 years of life changes in R_T using the oscillator correlate well with changes in airways resistance using the body plethysmograph (Lenney and Milner, 1978a). In the present study the initial R_T s were strikingly raised in all patients, and in two children tested subsequently normal values were obtained, supporting our contention that the forced oscillation technique is reliable in this situation.

Sedation may have influenced the baseline R_T data but is most unlikely to have masked any changes produced by the treatments.

Our conclusion is that neither nebulised phenylephrine nor adrenaline has any part to play in the management of bronchiolitis.

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