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Efficacy of Bronchodilators in the Treatment of Bronchiolitis

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ABSTRACT

Bronchiolitis is a common respiratory infection affecting young children. Much controversy revolves around the efficacy of bronchodilators in the treatment of bronchiolitis. This study was conducted to address this issue.

Aim: To determine the efficacy of bronchodilators in the treatment of bronchiolitis.

Method: All children less than 2 years old with bronchiolitis were randomly assigned to receive nebulisations of Salbutamol, Ipratropium bromide or normal saline. A fourth group given only humidified oxygen without nebulisation were used as a control.

Results: Data were obtained for 120 patients. Fifty-one(42%) had respiratory syncytial virus (RSV) isolated from their nasopharyngeal aspirates. The demographic characteristics of the 4 groups were similar. There was no significant difference between the groups in terms of severity score, number of nebulisations required in the nebulised groups and the outcome as measured by the length of hospitalisation.

Conclusion: The use of bronchodilators did not alter the course of the disease and is therefore not effective in the treatment of bronchiolitis.

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INTRODUCTION

Bronchiolitis is a common respiratory infection affecting infants resulting in admissions to hospitals. The majority of the children have mild bronchiolitis while only about 30% have severe infection[1]. However, there has been much controversy in the literature on the use of bronchodilators in the treatment of bronchiolitis with some studies suggesting a positive response to bronchodilators[2-5]. Other studies have shown them to be ineffective[6] and even to cause a deterioration in lung function following nebulised salbutamol[7,8].

This study was conducted to determine the efficacy of inhaled bronchodilators in children admitted with bronchiolitis using a severity score and also to compare the effectiveness of ipratropium bromide and salbutamol as compared to a placebo(normal saline), as some studies suggest a difference in efficacy between these two bronchodilators in bronchiolitis[9-10]. A fourth group given only humidified oxygen was used as a control.

PATIENTS AND METHODS

The study was carried out at the Paediatric Department, Tan Tock Seng Hospital between August 1992 and July 1993. All children less than 2 years old admitted for signs and symptoms consistent with a clinical diagnosis of bronchiolitis such as tachypnoea, crepitations and wheeze with no past history of a previous wheeze, were entered into the study. Excluded from the study were those with congenital heart disease, immunocompromised patients and those requiring mechanical ventilation.

Patients were randomly assigned to be nebulised with one of the three solutions; they are salbutamol (2.5 mg/mL), ipratropium bromide (250 μg/mL) or normal saline as placebo. All the treatment were administered over 10 to 15 minutes by face mask driven by oxygen at a flow rate of 6-8 L/min. Children aged 6 months and below were nebulised with 0.3 mL of the solution while children above the age of 6 months were given 0.6 mL of the solution made up to 2 mLs with normal saline for nebulisation. The nebulisations were given at 4 to 6 hourly intervals. The study solutions were dispensed to the ward by the pharmacy in 2 mLs aliquots and therefore the attending physicians were unaware of the contents of the nebulising solutions. A fourth group consisted of patients that did not receive any nebulisation but had humidified oxygen during their hospital stay.

The following parameters: oxygen saturation, respiratory rate, presence of subcostal retractions, crepitations and wheeze, were assessed on admission and also daily for the duration of the hospital stay. The oxygen saturation was measured on admission and once a day pre-nebulisation. The value was determined after monitoring the child in an awake, non-crying state for 10 minutes using pulse oximetry (Ohmeda Bioux 3700e). The severity of the patient's condition was assessed with a score with respect to respiratory rate, presence of subcostal retractions, crepitations and wheeze, and the need for oxygen nebulisation or intravenous infusion (Table I). The patients were assessed by selected study personnel who were blinded to the treatment allocation. A severity score was determined by the total score of the above parameters for the day.

Nasopharyngeal aspirates were sent for culture, immunofluorescence for viral antigen detection and also chlamydia culture in those less than 6 months of age. A questionnaire was completed in relation to family history of asthma or atopy in the study population.

Table I - Definition of categories for clinical assessment

	Scores				
	0	1	2	3	4
Respiratory rate/min	≤30	31-40	41-50	51-60	>60
Subcostal retractions	None	Mild	Moderate	Severe	-
Presence of crepitations	No	Yes	-	-	-
Presence of wheeze	None	Stethoscope	Quiet breathing	Use of accessory muscle	Obvious distress
Oxygen requirement	No	Yes	-	-	-
Nebulisation	No	Yes	-	-	-
Intravenous infusion	No	Yes	-	-	-

Severity Score = Sum of score for respiratory rate, subcostal retractions, presence of crepitations and wheeze, oxygen requirements, nebulisations and intravenous infusion.

Table II - Comparison of groups for demographic characteristics, viral isolation and oxygen saturation

	Normal saline	Salbutamol	Ipratropium bromide	Humidified oxygen
Number in each group	29	30	30	31
Sex M : F	20:9	24:6	20:10	22:8
Age (mths)	7.4 ± 0.89	5.7 ± 0.77	5.2 ± 0.67	5.9 ± 0.71
Family history of asthma	8	10	8	10
Family history of atopy	6	4	7	8
Positive RSV isolation	12	15	10	14
Oxygen saturation on arrival (mean)	94.5 ± 2.1	94.2 ± 2.8	94.7 ± 2.0	94.5 ± 2.2

RESULTS

Between August 1992 and July 1993, 99 patients admitted for bronchiolitis were included in the study. Of these, only 89 were analysed and 10 were excluded, of which 4 had a past history of wheeze, 2 were misdiagnosed as bronchiolitis and 4 had incomplete data. A fourth study arm was done from November 1993 to April 1994, and 31 patients were included. This group was only studied much later as at the completion of the first study, there were reservations that nebulising normal saline could also have an adverse effect on the airway and therefore may not be an adequate control group.

Respiratory syncytial virus was identified by immunofluorescence from 51 patients (42%). Parainfluenzae virus was isolated in 4 patients.

There was no difference between groups for gender or age distribution, the frequency of family history of asthma or atopy, isolation of a causative organism or oxygen saturation on arrival (Table II).

The severity scores between the groups were not significant when measured on the day of arrival, and over days 1, 2 and 3 of illness, using Kruskal-Wallis analysis ($p>0.5$) (Table III). The average length of hospital stay was about 4 days.

Comparison of the length of hospitalisation and the number of nebulisations required as an indication of effectiveness of therapy again showed no difference between the 3 groups ($p>0.5$). The group given only humidified oxygen had a comparable length of hospitalisation. A comparison done in those less than 6 months old also revealed no statistical difference. In fact, they did not stay longer or require more nebulisations than their older counterparts.

DISCUSSION

Controversy still surrounds the use of bronchodilators in the management of bronchiolitis. Although current textbooks do not recommend its use and evidence show that they may be ineffective[10,12,13], yet some authors still recommend its use in the treatment of this disease[5] and it is still a common practice in many paediatric departments. The proponents of the use of bronchodilators have criticised the earlier studies, which failed to confirm any therapeutic effect of bronchodilators, on methodologic problems such as loss of randomisation, single or infrequent drug administration and the need for sedation when measuring pulmonary function tests in these young children. This study is based on clinical observations made by an attending physician who is blinded to the type of solution used for therapy and we demonstrated no benefit in using bronchodilators. Similar results were observed in the study by Wang et al[6].

All the patients in this study had mild to moderate bronchiolitis as demonstrated by their severity scores and oxygen saturation on admission. The table defining the categories for assessment of severity was based on that of Wang et al[6]. The severity score was the sum of the scores for respiratory rate, subcostal retractions, presence of crepitations and wheeze, oxygen requirement, nebulisations and the need for intravenous infusion. As all the patients received oxygen therapy and nebulisations with the exception of the group receiving humidified oxygen alone, the differences in the scores would imply differences in the other parameters. The use of accessory muscles, that is the degree of subcostal retraction, and the respiratory rate provide useful information on the degree of bronchospasm in infants with hyperactive airways[14]. Oxygen saturation was not included in the severity score due to the shortage of oximeters, therefore continuous monitoring was not possible. However, the oxygen saturations done once a day did not differ in the study groups. There was no significant difference in terms of improvement of the severity score and the duration of hospital stay when comparing the groups receiving nebulisations, to those only on humidified oxygen. The deterioration of severity scores on Day 1 of hospitalisation and subsequent improvement over Days 2 and 3 were observed in all 4 groups, thereby reflecting the natural course of the disease. Thus, the use of bronchodilators did not alter the course of the disease.

Lenney and Milner (1978)[15] suggest that infants less than 18 months old do not respond to

Table III - Comparison of severity score (mean) between the 4 groups

	Normal saline	Salbutamol	Ipratropium bromide	Humidified oxygen
Severity score (mean) on arrival	7.0 ± 1.8	6.5 ± 1.7	6.4 ± 1.7	6.8 ± 1.8
Day 1	8.0 ± 2.5	7.5 ± 2.1	7.3 ± 1.9	7.6 ± 2.2
Day 2	4.4 ± 2.4	4.7 ± 2.2	4.6 ± 1.9	4.6 ± 2.2
Day 3	3.1 ± 1.8	3.0 ± 1.5	3.4 ± 1.8	3.2 ± 1.6

Table IV - Comparison of the 4 groups for hospitalisation days and number of nebulisations

	Normal saline	Salbutamol	Ipratropium bromide	Humidified oxygen
Age > 6 months				
Hospital days (mean)	4.4	4.3	3.9	4.1
No. of nebulisations (mean)	13.6	14.6	12.8	nil
Age < 6 months				
Hospital days (mean)	4.7	4.3	3.9	4.3
No. of nebulisations (mean)	13.5	14.9	11.3	nil

bronchodilators. There have been some questions as to whether infants below the age of 6 months have enough smooth muscles in their airways to respond to bronchodilators. Matsuba and Thulbeck[16] have done morphometric studies of bronchial and bronchiolar walls in children and have reported the presence of adequate smooth muscles in young infants' airway. However, our study did not demonstrate any difference in response in those less than 6 months old and the older children. They did not require a longer period of hospitalisation nor need more frequent nebulisations. As again, there was no difference between the groups given bronchodilators and those that were not, we would conclude that bronchodilators are not efficacious in the management of bronchiolitis.

Although the small size of the study may have limited its ability to detect differences, the small magnitude of the differences observed in the study makes it highly unlikely that bronchodilators are effective in the patient population studied. Furthermore, studies done by Henry et al have also shown no benefit with the use of ipratropium bromide compared with normal saline[9] thereby supporting our findings, as well as the study done by Wang et al who showed no benefit from salbutamol and ipratropium bromide when used alone as compared to normal saline[6].

The use of bronchodilators is not without its hazards as demonstrated by the studies done by Prendiville et al[7] and O'Callaghan et al[8]. They showed that hypoxaemia and deterioration in lung functions can occur after inhaling nebulised salbutamol. Wang et al[6] also demonstrated that a drop in oxygen saturation occurred in those patients who were given bronchodilators. In view of the possible hazards of giving bronchodilators against the short-term benefit of improving the accessory muscle score and oxygen saturation by a mere 2%[5] in a disease where its effectiveness is doubtful, we advocate that based on our results, bronchodilators are not effective and therefore should not be used in the treatment of bronchiolitis. Furthermore, we found that parents accepted humidified oxygen alone as a mode of therapy well, and this therefore does not necessitate the use of bronchodilators in the management of bronchiolitis.

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