Pediatric Pulmonology 3:83–85 (1987)

Effects of Nebulized Fenoterol, Associated With Ipratropium or Steroids, on the Heart Rate of Infants Under One Year of Age With Acute Wheezing

Javier Mallol, MD,[1] Ricardo Muñoz, PT,[2] Homero Puppo, PT,[3] Victor Ulloa, PT,[2] Olivia Toro, PhD,[3] Guido Girardi, MD,[1,4] and Luis Barrueto, MD,[1]

Summary. The main objective of this study was to evaluate the effect of fenoterol alone or associated with ipratropium bromide or steroid on the heart rate in young children. Ninety-four infants less than 1 year of age were randomly allocated to receive nebulized fenoterol alone, fenoterol plus ipratropium bromide, fenoterol plus corticosteroids, or normal saline solution. An increase in heart rate was observed in all four groups. The increases were statistically significant ($P < 0.001$) in all three treatment groups, and no difference between them was observed ($F = 0.65$, NS). However, the heart rate remained within clinically acceptable limits. We conclude that nebulized fenoterol alone or combined with ipratropium or steroids can be safely used in the treatment of wheezy infants. **Pediatr Pulmonol 1987;3:83–85.**

Key words: Separate vs combined medication; statistically incomparable effects; clinical safety.

INTRODUCTION

Several studies have shown that aerosolized β-adrenergic agonists are the initial treatment of choice in the management of acute wheezing in children.[1] Recently, it was reported that a β-agonist administered in combination with the cholinergic antagonist ipratropium bromide (IB) produces greater bronchodilatation than either drug alone.[2,3] The same feature, more bronchodilator effect, has been observed when a β-agonist and a corticosteroid were used together.[4] The combination of β-agonist and IB is of particular interest in young infrants, as previous studies have suggested that IB may be a more effective bronchodilator than β-agonists in this age group.

The present study was designed to evaluate the effect of nebulized fenoterol, nebulized fenoterol and IB, and fenoterol used in combination with corticosteroids on the heart rate of young infants being treated for acute wheezing.

MATERIALS AND METHODS

Ninety-four infants less than one year of age, admitted to the respiratory unit during the winter of 1984, were randomly allocated to one of four treatment groups after informed consent was obtained. Group 1 was given nebulized fenoterol plus IB, group 2 received fenoterol alone, group 3 received fenoterol plus corticosteroids, and group 4 served as a control group receiving nebulized saline. If the clinical score of patients in the control group deteriorated during the period of the study they were reassigned to an active treatment group.

All infants studied had hyperinflation, wheezing, and prolonged expiration. The scoring system of Tal et al[4] was used to provide an objective clinical evaluation. Only infants with moderate obstruction (clinical scores: 6–9) were included. No attempt was made to distinguish between asthma and bronchiolitis. Infants with preexisting cardiopulmonary disease or those who required mechanical ventilation or prolonged oxygen therapy in the neonatal period were excluded from the study.

The dose for fenoterol was 0.03 ml/kg of a 0.5% solution and for IB 1 ml of 0.025% solution (250 μg). Corticosteroids were given as either prednisone, 2 mg/kg/day in three divided doses orally, or parenteral dexamethasone, 0.3 mg/kg/day in three divided doses.

Nebulized medications were administered by a jet nebulizer, using a flow rate of 6 liters/min. Active medications were diluted to 4 ml with normal saline and nebulized over 10–12 minutes. Four treatments and heart rate counts were administered within 24 hours.

The humeral pulse (over the inside of the elbow joint) was recorded by the same observers immediately before

From the Bronchopulmonary Unit[1] and Physical Therapy Unit,[2] Ex. González Cortes Children's Hospital; Public Health Department, University of Chile, Southern Metropolitan Area;[3] and University of Chile, Department of Pediatrics,[4] Santiago, Chile.

Received January 31, 1976; (revision) accepted September 18, 1986.

Address correspondence and reprint requests to Dr. J. Mallol, Hospital Infantil Ex. González Cortes, Ramón Subercaseaux 1534, Santiago, Chile.

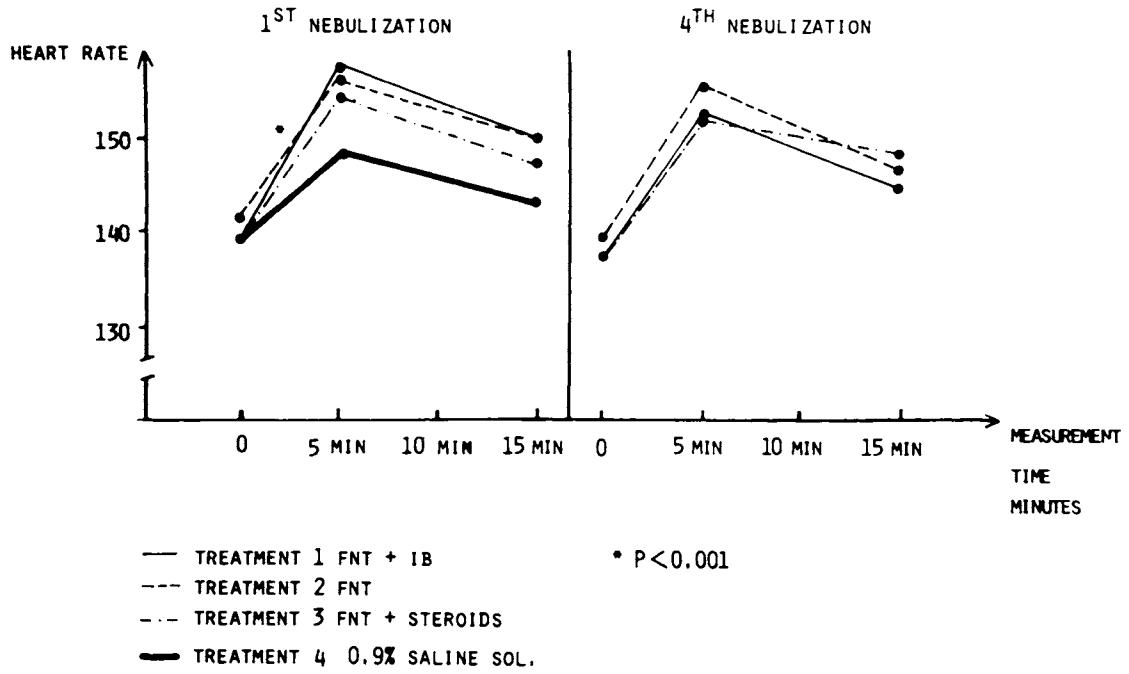

Fig. 1. Behavior of the mean heart rates recorded before nebulization (zero), 5 minutes later, and again at 15 minutes. The asterisk indicates a significant difference between baseline pulses and pulses at 5 minutes in the first and the fourth nebulizations.

TABLE 1 —Mean heart rate (± SD) for the treatment groups during the first and fourth nebulizations

	First nebulization			Fourth nebulization (at 24 hours)		
	Baseline (0 min)	5 min	15 min	Baseline (0 min)	5 min	15 min
FNT + IB	138.56 (9.44)	157.31 (14.36)	150.81 (13.85)	137.24 (10.27)	152.76 (8.59)	144.36 (11.35)
FNT	140.75 (13.36)	156.00 (11.46)	150.17 (14.95)	139.16 (12.04)	155.26 (11.53)	146.00 (9.23)
FNT + C	138.80 (10.94)	154.87 (10.04)	147.60 (9.53)	137.38 (5.79)	151.54 (10.89)	148.00 (14.19)
Control	139.00 (21.57)	148.75 (14.81)	143.00 (17.94)	—	—	—

FNT, fenoterol; FNT + IB, fenoterol plus ipratropium bromide; FNT + C, fenoterol plus corticosteroid.

nebulization (0 minute), 5 minutes later, and again at 15 minutes, ie 5 minutes after termination of nebulization. An open study design was employed.

Student's t test was used to analyze within-group differences in the heart rate at 0, 5, and 15 minutes. Between-group comparisons were made using analysis of variance (ANOVA).

RESULTS

The mean baseline heart rate was similar in the four groups ($P > 0.05$). The heart rate increased after nebulization in each of the four groups, but statistically significant differences ($P < 0.001$) from baseline were only found in groups 1, 2, and 3. The increase in heart rate was similar in each of the three groups (ANOVA F = 0,65, NS). There was no difference between the heart rate at 0 and 15 minutes in any of the groups. There was no difference in the baseline (zero) heart rate in groups 1, 2, and 3 when the first and fourth nebulizations were compared. By the fourth treatment no subject was left in the control group (Fig. 1; Table 1).

DISCUSSION

Although the bronchodilator effect of β-adrenergic agonists and ipratropium bromide have been described in detail in older children and adults, to the best of our

knowledge no studies have previously reported the hemodynamic effects of these drugs in infants. The doses of medications used in the present study were similar to those recommended in previous dose-response studies with the same drugs.[5-7]

We observed an increase in heart rate in the control group and in all three treatment groups, suggesting that it was a partly physiological effect of the stress of the nebulization procedure and partly of pharmacological origin. Clinical and experimental observations indicate that corticosteroids may enhance the β-agonists' effects by potentiating β-adrenergic responsiveness.[4, 7] Based on that information, we expected that the fenoterol plus steriod group would have a higher mean heart rate than the other treatment groups, but this did not occur.

The increase in heart rate was maximal at 5 minutes, it had returned to baseline levels by 15 minutes, and it was similar in all groups studied. We believe that fenoterol alone or combined with ipratropium or steroids can be used safely in the treatment of acute wheezing infants.

REFERENCES

1. Robertson D, Smith F, Beck R, Levison H. Response to frequent low doses of nebulized salbutamol in acute asthma. J Pediatr. 1985; 106:672-674.
2. Beck R, Robertson C, Galdés-Sebaldt M. Levison H. Combined salbutamol and ipratropium bromide by inhalation in the treatment of severe acute asthma. J Pediatr. 1985; 107:605-607.
3. Bryant DH. Nebulized ipratropium bromide in the treatment of acute asthma. Chest. 1985; 88:24-29.
4. Tal A, Bavilski Ch, Yohai D, et al. Dexamethasone and salbutamol in the treatment of acute wheezing in infants. Pediatrics. 1983; 71:13-18.
5. Reilly P, Yahav J. Mindorff C, et al. Dose-response characteristics of nebulized fenoterol in asthmatic children. J Pediatr. 1983; 103:121-126.
6. Davis A, Vickerson F, Worsley G, et al. Ddtermination of dose-response relationship for nebulized ipratropium in asthmatic children. J Pediatr. 1984; 105:1002-1005.
7. Kaliner M. Mechanisms of glucocorticosteroid action in bronchial asthma. J Allergy Clin Immunol. 1985; 76:321-329.