Comparison Of Two Different Bronchodilators In The Treatment Of Acute Bronchiolitis

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Citation

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Abstract

Acute bronchiolitis is an acute inflammatory respiratory illness of children less than two years of age. Classically adequate hydration, supplementary oxygen, bronchodilators, and corticosteroids may be used in the treatment of acute bronchiolitis.

In this study, we aimed compare salbutamol to ipratropium bromide in the management of acute bronchiolitis. We enrolled 34 infants hospitalized for bronchiolitis to evaluate the efficacy of these two different bronchodilators. Thirty-four infants under 2 years of age were randomized to receive either nebulized salbutamol (group I) or nebulized ipratropium bromide (group II). Clinical severity was scored on admission and 12-hour intervals after the start of nebulization. The symptom score evaluated five items: respiratory rate, presence of wheezing, presence of recession, presence of nasal flaring and general appearance. No difference was observed in clinical improvement between the two groups on hospital admission and at 12, 24, 36 and 48 hours during treatment. The mean duration of hospital stay was not significantly different between two groups. Both groups showed a significant improvement following 48hours of treatment.

We conclude from our work on infant with acute bronchiolitis that there is no difference between the clinical scores of infants receiving ipratropium bromide or salbutamol. Because of the possible side effects of salbutamol, ipratropium bromide may be preferred as bronchodilator in infants with acute bronchiolitis.

INTRODUCTION

Bronchiolitis is the acute, infectious inflammation of the small airways. Clinical symptoms include fever, wheezing, tachypnoea, increased respiratory effort, and intercostal and subcostal retractions. Respiratory syncytial virus is the causative agent in approximately 70% of the cases, but many other pathogenic agents (parainfluenza virus, adenovirus, rhinovirus, influenza type A and B viruses and mycoplasma) may cause the same illness. . Bronchiolitis has a peak incidence in infants at 2-5 months of age, and in most cases the clinical picture improves within one weekHowever, in about 50% of the cases, recurrent episodes of wheezing and asthma develop within two years after the onset of infection. Bronchiolitis is the most important risk factor for asthma in children below two years of age. Oxygen supplementation and hydration make up the basis of the treatment of bronchiolitis because of decreased fluid intake, loss of fluid secondary to dyspnoea and tachypnoea, and hypoxaemia. Bronchodilator agents, corticosteroids, ribavirin and epinephrine are other agents used for treatment, either separately, or in combination ([1,2,3,4]).

In the past, anticholinergic agents had been the preferred treatment due to the belief that young infants possessed a paucity of beta-2 receptors. However, the use of anticholinergics has decreased due to changes in this theory ([5]). Ipratropium bromide, an anticholinergic agent, has its effects by inhibiting acetylcholine secretion from the vagus nerve. This inhibits the contraction of smooth muscles, mucous secretion in the airways and oedema of the airway mucosa (1).

Our purpose in this study was to investigate which of salbutamol or ipratropium bromide is better in comparison to each other in the management of acute bronchiolitis in infants.

MATERIALS AND METHODS

The efficacy of two different bronchodilator agents were

investigated in 42 infants with acute bronchiolitis between January 2000 and May 2001 in Deparment of Pediatrics at Abant Izzet Baysal University in Duzce Faculty of Medicine Hospital. This is a non-blinded, randomised prospective comparative study. Randomisation to two separate groups (Group I and II) was done according to file number at time of admission. We obtained written informed consent from the parents.

Each child with their first episode of expiratory wheezing, tachypnoea, retraction with or without fever, and cough was diagnosed as acute bronchiolitis. We included infants below 24 months of age who had moderate or severe degree of acute bronchiolitis to our study. We excluded all those who had received corticosteroids or bronchodilators within the last month, or had underlying lung and/or cardiac disease. Patients that we did not observe any clinical improvement within 48 hours according to the scoring criteria were excluded from the study. These patients were put on steroid treatment. In total, 8 infants with acute bronchiolitis were excluded. Thus, the remaining 34 infants who met our inclusion criteria were recruited.

Patients in group I (n:19) received 0,15 mg/kg salbutamol in nebulized form every 4 hours, whereas patients in group II (n:15) received 250 µg ipratropium bromide in nebulized form every 6 hours. In the first 24 hours, we started intravenous fluid and stopped oral intake of the patients to prevent aspiration. We also added oxygen therapy, when needed. No antibiotic therapy was administered.

To assess the clinical status of the patients, we used a clinical scoring system composed of respiratory rate, presence or absence of nasal flaring during inspiration, wheezing and the general status (Table I).

Figure 1

Table I: Clinical scoring system in bronchiolitis. The sum of the points gives the clinical score.

Score	Breath rate (respirations/ min.)	Retractions	Nasal flaring during Inspiration	Wheezing	General status
0	<30	No	No	No	Normal
1	30-45	Only intercostal	Mild and rarely	Heard only with stethoscope	Moderately uneasy and occasionally crying
2	45-60	Intercostal, subcostal and supraclavicular	Moderately severe And intermittently	Heard in both expiration and inspiration with stethoscope	Very uneasy, crying continuously
3	<60	Abdominal respiration accompanying	Severe and continuously	Heard in both expiration and inspiration without stethoscope	Lethargic

Patients who scored 4-8 points were considered to be moderately ill, and those that scored 9-12 as severely ill. Children were evaluated clinically before treatment and at 12, 24, 36 and 48 hours of treatment. They were assessed both asleep and awake. When they were awake, we prefer to evaluate the infants in their agitation free periods. Two physcians, who did not know which treatment was applied to the infant, performed the clinical assessment, and the overall clinical score was calculated as average of the two measurements. The two groups were compared according to their clinical scores and the duration of hospitalisation. Duration of hospitalisation was accepted as the time between the admission of the infant and actual discharge time.

Radiological and other laboratory results including viral analysis were not studied in every patient, because of technical difficulties.

We used Mann-Whitney U test to compare the clinical scores of group I against group II. We analysed differences between the clinical scores before, and at 12, 24, 36 and 48 hours of therapy in each group using Wilcoxon test. A value of $p<0.05$ was accepted as statistically significant.

RESULTS

Among 34 infants with acute bronchiolitis, 20 (58%) were male and 14 (42%) female. The mean age of the patients was 6.9 3.4 months standard deviation (age range 3-24 months). There were 29 (85%) infants below one year of age, and 15 (44%) younger than 6 months. When the two groups were compared according to age, no significant difference was found ($p>0.05$).

No significant difference was found between the two groups

regarding the clinical scores before the onset of treatment (8.37 1.34; 8.33 1.49; respectively) (p>0.05). After 12, 24, 36 and 48 hours of treatment, the clinical scores of group I, and group II are shown in Table 2.

Figure 2

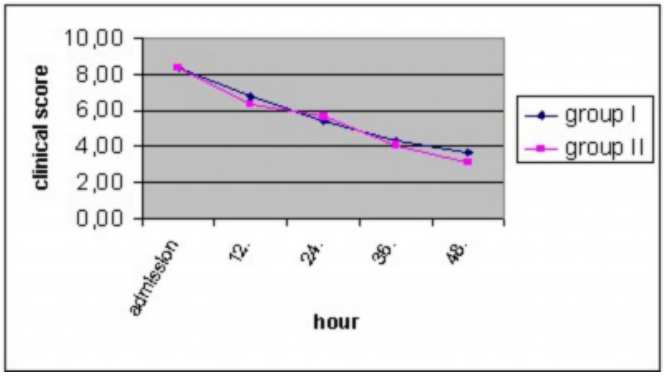
Table 2: Clinical scores following treatment

Time (hrs)	Group I mean±SD	Group II mean±SD
12	6.55±1.39	6.33±1.44
24	5.55±1.65	5.66±1.87
36	4.06±1.75	4.17±1.66
48	3.41±1.57	3.13±1.50

There was no statistically significant difference between the two groups regarding the clinical scores after the onset of treatment (p>0,05) (Figure I).

Figure 3

Figure I: Changes in the clinical scores of the patients in group I, and group II at the time of admission and during treatment.



When the difference in the duration of hospitalisation between Group I and II was analysed, no significant difference was found (3.52 1.02; 3.46 0.83; respectively) (p>0.05).

We observed a statistically significant clinical improvement at 48 hours of treatment in both Group I and Group II (p<0.001).

Except sinus tachycardia seen in 4 patients (4, 9, 9 and 11 months of age) of Group I as an adverse effect of salbutamol, no adverse effect was noted. Sinus tachycardia was detected on the first day of treatment. Heart rates of the infants increased above 150 beat / minute, and resolved within 6-10 hours.

DISCUSSION

Acute bronchiolitis is an important lower respiratory tract infection, especially in children younger than 6 months of age. Its clinical picture resembles asthma because of rhinorhoea, wheezing and tachypnoea. This similarity has affected the treatment modalities of acute bronchiolitis, and has caused bronchodilators and corticosteroids to be used commonly in its management (1-5). In children hospitalised in Canada with the diagnosis of bronchiolitis, bronchodilators were used with a rate of 78%, whereas in a study conducted together with pediatric allergists and pulmonologists in the United States bronchodilators were recommended in bronchiolitis with a rate of 86% ([6]). In spite of the common use of bronchodilators, no consensus has been achieved on the duration and dosage of the treatment, and whether to use the oral or nebulized form ([7]).

Many randomised placebo-controlled studies have been carried out to investigate the efficacy of bronchodilators (especially sympathomimetics), but different results have been obtained regarding their effects on wheezing, retractions, oxygen saturation and respiratory rate ([3,8,9,10,11,12,13,14,15,16]). In a study conducted by Lugo et al, on 68 children with bronchiolitis receiving albuterol treatment, wheezing, retractions, oxygen saturation, respiratory effort and respiratory rate were evaluated. They reported that in 50% of children there was no clinical improvement (15). In another randomised placebo-controlled study, Dobson et al looked at 52 children younger than 2 years of age with the diagnosis of bronchiolitis of moderate severity presenting with their first attack. Nebulized albuterol was used and comparisons were made at the time of admission and at 24, 48, and 72 hours of treatment regarding oxygen saturation, the general status of the patient and the use of accessory respiratory muscles. No significant effect of the therapy was noted (3). Totapally and colleagues used tidal breathing flow-volume loops to assess the effect of albuterol on infants with bronchiolitis, and they found no significant change (16).

As a bronchodilator, the effect of ipratropium bromide (either alone or in combination with salbutamol or albuterol) on bronchiolitis has been evaluated and conflicting results has been obtained (1, 8, 11, [17,18,19,20]). In the studies of Sammartino et al, ipratropium bromide was reported to have desirable effects on oxygen saturation and respiratory effort (17). The same investigators administered inhaled ipratropium bromide in appropriate doses and the nebulized form of the drug to 23 children with bronchiolitis younger than 12 months. They found no significant difference

between the two groups. However, they reported the aerosol form of the drug to have been tolerated better. The oxygen saturation values of the two groups were significantly different when compared to the values of the control groups (1). Stokes et al noted improvement in respiratory effort with ipratropium bromide (18), whereas Henry et al did not observe this effect (19).

It has been suggested that heterogenous results regarding the effects of sympathomimetic or anticholinergic bronchodilators obtained in these studies may be due to several reasons. The clinical picture of bronchiolitis is due primarily to pathology such as mucosal oedema, exaggerated mucous secretion and the inflammation of small airways rather than the constriction (bronchospasm) of the smooth muscles of the airways. The observation that drugs that are both alpha and beta receptor agonists such as epinephrine are clinically useful, supports this (5, [21]). Barr et al found a beneficial effect of inhaled adrenaline in an infant with RSV bronchiolitis who was also receiving beta-adrenergic receptor blockade with propranolol. They pointed out that it was most probably the alfa-adrenergic stimulation improving airway obstruction by arteriolar vasoconstriction in the airway mucosa and hence reducing bronchial mucosal thickness ([22]). Whether the patients included in the studies were suffering with their first attack or recurrent attacks is another factor influencing the results. The patients with recurrent wheezing who better respond to bronchodilators may be asthmatic children, and this will falsely increase their level of efficacy in bronchiolitis ([23]). The young age of patients and RSV as the etiological agent also influence response to bronchodilators negatively (3). In our study, about half of the patients were younger than 6 months, thus the effect of age on the clinical response was not supported. In addition, as no viral serological studies were made, we could not evaluate the effect of RSV on the clinical response.

Several clinical scoring systems have been used for the clinical picture of bronchiolitis. For their modified scoring system Cengizlier et al used respiratory rate, wheezing, retraction and general condition (10), whereas Goh et al. included respiratory rate, subcostal retraction, wheezing, crepitations, oxygen requirement, nebulization, intravenous infusion in their scoring system (11). Kristjansson et al. formed a scoring system composed of respiratory rate, the presence or absence of intercostal retractions, findings on respiratory auscultation, the skin colour and general status of the patient ([24]), whereas the scoring system of Chowdhury et al. included wheezing, retraction, respiratory rate (8). Furthermore, Bertrand et al. used respiratory rate, wheezing, retractions and the necessity for oxygen supplementation (while they were keeping the oxygen saturation of the patients between 94% and 97%) in their scoring system ([25]).

Decreased oxygen saturation, tremor, flushing, hyperactivity and hypokalemia are the adverse effects seen with the use of sypathomimetic drugs. Cardiovascular adverse effects such as hypokalemia-induced supraventricular tachycardia, sinus tachycardia, premature ventricular contractions, palpitation, atrial fibrillation, and increased blood pressure may be observed (3, 6, 12, 21, 24, [26]). As an adverse effect, we detected sinus tachycardia in four infants of group I. The tachycardia resolved spontaneously within 6-10 hours.

In the literature, no adverse effect has been reported with the use of ipratropium bromide ([27,28]) except for the decrease in the heart rate caused by the cumulative dose of the drug ([29]).

The efficacy of sympathomimetics and anticholinergics in the treatment of acute bronchiolitis is still being discussed. In this study, we have found that there is no difference between the clinical scores of infants with acute bronchiolitis receiving ipratropium bromide or salbutamol. If a bronchodilator is used in the treatment of acute bronchiolitis, ipratropium bromide may be preferred because of the possible side effects of salbutamol.

Conflict of interest: None

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