

# Comparison of Initial Response of Nebulized Salbutamol and Adrenaline in Infants and young Children Admitted with Acute Bronchiolitis.

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## ABSTRACT

### Background

Acute bronchiolitis is common cause of hospitalization in infants and young children. There are widespread variations in the diagnosis and management. Despite the use of bronchodilators for decades, there is lack of consensus for the benefit of one above another.

### Objective

To compare initial response of nebulized adrenaline and salbutamol.

### Method

Children aged two months to two years admitted with acute bronchiolitis in the department of Paediatrics of Manipal teaching hospital, Pokhara, Nepal, from 1<sup>st</sup> March 2014 to 28<sup>th</sup> February 2015 were enrolled. Patients fulfilling inclusion criteria received either adrenaline or salbutamol nebulization. Data were collected in a predesigned proforma. Respiratory distress assessment instrument (RDAI) scores were considered primary outcome measure and respiratory rate at 48 hours, duration of hospital stay, requirement of supplemental oxygen and intravenous fluid were considered secondary outcome measure.

### Result

A total of 40 patients were enrolled in each study group. Mean RDAI scores at admission was in 9.75 with (CI- 9.01, 10.49) in adrenaline and 9.77 (CI- 9.05, 10.50) in salbutamol group. There was gradual decline in mean RDAI scores in both the groups over 48 hours to 4.15 (CI- 3.57,4.73) and 4.13 (CI- 3.69,4.56) in adrenaline and salbutamol group respectively. Hospital stay was 5.32 days in adrenaline and 5.68 days in salbutamol group. Patients nebulized with adrenaline required oxygen for 33.30 hours compared with 36.45 hours in salbutamol. Intravenous fluid duration was also less in adrenaline group compared to salbutamol group (33.15 vs 37.80 hours).

### Conclusion

Patients of acute bronchiolitis nebulized with either salbutamol or adrenaline experienced similar decline in RDAI scores in the first 48 hours. Duration of supplementary oxygen and intravenous fluid was less in adrenaline group compared with salbutamol group.

## KEY WORDS

*Acute bronchiolitis, adrenaline nebulization, salbutamol nebulization*

## INTRODUCTION

Acute bronchiolitis is a common lower respiratory tract infection in infants and young children aged two months to two years. It causes significant morbidity and health care cost in young infants.<sup>1</sup> It has been associated with viral infections most commonly respiratory syncytial virus (RSV). Majority of the infants have mild self-limiting illness while others can have severe disease requiring inpatient treatment and admission in pediatric intensive care units. There are limited therapeutic options due to the lack of clear diagnostic test or definition.<sup>2</sup> Widespread variations exist in the proportion of patients who receive diagnostic testing and medications or interventions.<sup>3</sup> Diagnosis is mostly established based on clinical findings and there is limited role of laboratory investigations.<sup>4</sup> Respiratory distress assessment instrument (RDAI) based retractions and wheezing help in deciding need for hospitalization and treatment interventions.<sup>5</sup> Other parameters like respiratory rate (RR) and oxygen saturation (SO<sub>2</sub>) are also monitored in all infants seeking medical facilities.

Supportive treatment and use of humidified oxygen are established mainstay therapy. Despite widespread use of inhaled bronchodilators for decades, there is lack of evidence for beneficial action of one over another.<sup>6,7</sup> Walsh et al. have suggested that racemic albuterol, rather than racemic epinephrine, should be the initial agent chosen, as doing so modestly increases the rate of successful discharge.<sup>8</sup>

Nebulized epinephrine has been demonstrated to offer short term benefits with decreased risk of hospitalization and length of hospital stay.<sup>9-12</sup> Other studies indicate no statistically significant difference between adrenaline and salbutamol nebulization for treatment of moderately ill infants.<sup>13,14</sup> Skjerven et al. have observed that racemic adrenaline inhalation on demand appears to be superior to inhalation on a fixed schedule.<sup>15</sup>

Treatments of acute bronchiolitis with use of bronchodilator either adrenaline or salbutamol is still a matter of debate. We have limited studies regarding treatment options of acute bronchiolitis from developing countries like ours. Current study aims to find if there is any difference in outcome of patients with bronchiolitis treated with either adrenaline or salbutamol.

## METHODS

Hospital based observational study was conducted in department of paediatrics of Manipal teaching hospital; Pokhara, Nepal from 1<sup>st</sup> March 2014 to 28<sup>th</sup> February 2015. Study was conducted after obtaining clearance from ethical review board of the institution.

All infants and young children aged two months to two years admitted to the department of paediatrics of Manipal teaching hospital were considered eligible for study. Written

informed consent was taken from parents before enrolling in the study. Those who didn't provide written consent were excluded from the study. Other exclusion criteria were: i) history of prematurity ii) underlying congenital heart disease iii) chronic respiratory disease iv) presence of gross congenital malformation and (v) referred cases who were already receiving other treatment.

The primary outcome measure for current study was predetermined to be difference in RDAI score. Duration of hospital stay, RR (respiratory rate) and HR (heart rate) at 48 hours, requirement of supplemental O<sub>2</sub> and IVF (intravenous fluids) were considered to be secondary outcome measures.

All cases that were enrolled in the study were categorized in the two groups. Children in the first group were patients treated with adrenaline nebulization 0.1 ml/kg of 1:1000 dilutions with 3 ml normal saline every six hourly. Children in the second group had received salbutamol nebulization 0.15 mg/kg with 3 ml normal saline every six hourly. Supportive treatment including oxygen therapy, intravenous fluids, and antipyretics were same for both the groups.

Data were collected from each case in pre designed proforma. Baseline characteristics, heart rate, respiratory rate, duration of symptoms, oxygen saturation on room air and RDAI score was noted at the time of admission and HR, RR, SpO<sub>2</sub> (oxygen saturation) in room air, RDAI score were recorded for each child again at six hours, 24 hours and 48 hours. Duration of hospitalization along with requirement for supplementary O<sub>2</sub> and IVF was also recorded for all cases.

Data were entered into predictive and analytical software (PASW) version 18.0. Primary outcome and secondary outcome measures were expressed as mean ± S.D. (standard deviation) and 95% Confidence Interval for mean (CI).

## RESULTS

During the specified study period a total of 110 cases of bronchiolitis were admitted in the study site. Out of them 12 were excluded because of refusal to provide consent. 18 were excluded from the study because they met exclusion criteria. Hence remaining 80 cases were enrolled in current study, who were then alternately allocated to receive either adrenaline (n=40) or salbutamol (n=40). The baseline characteristics of study participants are presented in table 1.

RDAI scores between salbutamol group and adrenaline group are calculated over four different time periods (at admission, 6 hours, 24 hours and 48 hours) are presented in table 2. Mean RDAI scores at admission was in 9.75 (CI- 9.01, 10.49) in adrenaline and 9.77 (CI- 9.05, 10.50) in salbutamol group. There was gradual decline in mean RDAI

**Table 1. Baseline characteristics:**

Variables	Adrenaline group Mean(SD)	Salbutamol group Mean(SD)
Age ( Months)	7.70±2.32	7.03±4.11
Sex (Male %)	52.50	47.50
Duration of symptoms (Days)	3.28±1.36	3.3±1.30
Respiratory rate	49.0±11.0	47.0±8.0
Heart rate	130±13.0	129±13.0
RAO <sub>2</sub>	89.2±4.7	88.37±3.7
RDAI	9.75±2.31	9.77±2.28

RAO<sub>2</sub>: Room air oxygen saturation

RDAI: Respiratory distress assessment instrument

scores in both the groups over 48 hours to 4.15 (CI- 3.57, 4.73) and 4.13 (CI- 3.69, 4.56) in adrenaline and salbutamol group respectively.

Secondary outcome measures are shown in table 3. There were no significant differences in duration of hospital stay and respiratory rate between these two groups. Hospital stay was 5.32 days in adrenaline and 5.68 days in salbutamol group. Duration of supplementary oxygen was less in adrenaline group compared to salbutamol group (33.30 vs 36.45 hours). Intravenous fluid duration was also less in adrenaline group compared to salbutamol group (33.15 vs 37.80 hours).

## DISCUSSION

Baseline characteristics were similar in both the study groups with mean age of presentation 7.7±2.32 months in adrenaline group and 7.0±4.11 months in salbutamol group. Mean duration of symptoms was 3.3 month in both the groups and mean ± SD admission RDAI was 9.7±2.3. Infants with history of prematurity, underlying congenital heart disease, major congenital malformations, and chronic lung disease might present severe disease requiring prolonged hospitalization and additional medications. We have excluded infants with high risk group from our study.

Current study done in infants hospitalized with acute bronchiolitis treated with nebulized adrenaline experienced the similar degree of improvement in RDAI till 48 hours as those receiving salbutamol. There were no significant differences in duration of hospital stay, respiratory rate between these two groups. Requirement of supplementary oxygen and intravenous fluids was slightly less in adrenaline group compared to salbutamol group.

Most patients of either group had significant improvement of RDAI and other parameters over 48 hours. Infants in both groups had similar supportive therapy with added normal saline nebulization with either therapy. Most of the infants in both the groups were discharged before five days of admission. Children with longer duration of hospital stay had persistent clinical features and hospital acquired infections. Though mild tachycardia was noted in all children at initial stage of therapy none had significant tachycardia and adverse effects of nebulized drugs.

**Table 2. Descriptive statistics for RDAI scores at different times (n=40)**

Time	Adrenaline group Mean±SD (CI)	Salbutamol group Mean±SD (CI)
Admission	9.75 ± 2.32 (9.01,10.49)	9.77±2.29 (9.05,10.50)
6 hours	8.15±2.37 (7.39,8.91)	8.03±2.19 (7.32,8.73)
24 hours	6.30±2.24 (5.58,7.02)	6.68±.36 (5.92,7.43)
48 hours	4.15±1.82 (3.57,4.73)	4.1±31.36 (3.69,4.56)

**Table 3. Secondary outcome measures**

Time	Adrenaline group Mean±SD (CI)	Salbutamol group Mean±SD (CI)
Respiratory rate at 48 hrs	37.0±6.0 (CI-34.62, 38.48)	36.0±5.0 (34.52,37.88)
Hospital stay (Days)	5.32±2.14 (4.64,6.01)	5.67±2.25 (4.95,6.40)
O <sub>2</sub> requirement hours	33.30±22.40 (26.13,40.17)	36.45±18.90(30.38,42.52)
Intravenous fluid requirement hours	33.15 ± 21.95 (26.13,40.17)	37.80±17.67 (32.15,42.45)

Mull et al. in a study of infants treated with epinephrine reported earlier emergency department discharge than the patients treated with albuterol. Epinephrine was not found to be more efficacious than albuterol in treating moderately ill infants with bronchiolitis.<sup>14</sup> However double-blind controlled trial by Langley et al., racemic epinephrine resulted in significant improvement in wheezing and the total RDAI score on day 2 and over the entire stay ( $p < 0.05$ ). Mean length of hospital stay in epinephrine arm was 2.6 days and 3.4 days in those in the salbutamol group was not statistically significant.<sup>11</sup>

Modaressi et al. have concluded that using epinephrine instead of salbutamol could be more effective on reduction of hospitalization duration and RDAI.<sup>12</sup> Marginal short term benefit of adrenaline over salbutamol has been found by various researchers.<sup>9-11</sup> Skjerven et al. in a study involving 404 infants found that though adrenaline relieved respiratory distress in hospitalized children but didn't decrease hospital stay in comparison to normal saline nebulization.<sup>15</sup>

In contrast, Gadomski and Scribani concluded that salbutamol is safe and effective for the initial treatment of young children with acute bronchiolitis.<sup>6</sup> Similarly Walsh et al. found that emergency department treatment of bronchiolitis with nebulized racemic albuterol led to more successful discharges than nebulized epinephrine.<sup>8</sup> Atopic children benefited from salbutamol/Normal saline combination whereas non-atopic children improved with hypertonic saline and normal saline nebulization in a study done by Ipek et al.<sup>13</sup>

Wainwright et al. had conducted a randomized, double-blind, controlled trial comparing nebulized single isomer

epinephrine with placebo in 194 infants admitted to four hospitals in Queens-land, Australia with a clinical diagnosis of bronchiolitis.<sup>16</sup> Although the respiratory effort score was significantly lower in the epinephrine group after the three treatments, the difference between the groups was small and clinically trivial, and it was not associated with a shorter time to readiness for discharge or a shorter hospital stay. The need for supplemental oxygen at admission had the greatest influence on the score for severity of illness and strongly predicted the length of the hospital stay and the time until the infant was ready for discharge. In contrast to other studies they also noticed significant tachycardia was noticed in epinephrine treated group compared to placebo.

Ray and Singh had enrolled 91 infants and young children with the clinical diagnosis of acute bronchiolitis who presented with wheeze associated respiratory tract infection. They concluded bronchodilators both L-adrenaline and salbutamol are useful in relieving mean symptom score and improving oxygenation in wheezy infants. Among the two drugs, L-adrenaline was found to have better efficacy in terms of relieving distress and improving oxygenation as well as decreasing the need for admission.<sup>17</sup>

Simşek-Kiper et al. studied seventy-five patients with mild to moderate acute bronchiolitis. Among these 39 (52%) received salbutamol and 36 (48%) received epinephrine.<sup>18</sup> Patients in both study groups had significant improvement in terms of clinical effects, including mean respiratory rate, mean oxygen saturation and severity score in the

emergency room management of acute bronchiolitis over the time. Both the study groups had experienced a similar pattern of clinical improvement similar with our results. However, it was also found that salbutamol had lower hospitalization and relapse rates compared to epinephrine and can therefore be a drug of choice in the emergency room management of acute bronchiolitis.

Infants and young children should receive supportive therapy and bronchodilators should be used based on clinical parameters. This study fails to draw any advantage of one over another when bronchodilators are tried in hospitalized infants with the clinical diagnosis of acute bronchiolitis.

Potential limitation of the study was small sample size and lack of placebo arm. Other limitations of the study include short follow up due to which long term outcome among two groups couldn't be analyzed. Future studies in this area should try to overcome these limitations.

## CONCLUSION

Patients with acute bronchiolitis nebulized with either salbutamol or adrenaline experienced decline in RDAI scores in the initial 48 hours. However, there was no significant variation in RDAI scores between the groups at each time intervals. Duration of supplementary oxygen and intravenous fluid was less in adrenaline group compared with salbutamol group.

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