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Original Research Article

Study of therapeutic effects of nebulized adrenaline alone, nebulized adrenaline plus injectable dexamethasone (in combination) and nebulized 3% hypertonic saline alone in clinically diagnosed cases of bronchiolitis

Ishwari Prasad Verma*, Pukhraj Garg, B. S. Karnawat, Anil Jain, Pradeep Verma, Rakesh Kumawat

Department of Pediatrics, Jawaharlal Nehru Medical College, Ajmer, Rajasthan, India

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***Correspondence:**
Dr. Ishwari Prasad Verma,
E-mail: dripverma@gmail.com

ABSTRACT

Background: Bronchiolitis is a common respiratory tract infection in young children. Respiratory Syncytial Virus (RSV) is the common etiological agent, with highest incidence occurring between December and March. 90% of children are infected in the first 2 years of life. Infants hospitalized are more likely to have respiratory problems as older children, especially recurrent wheezing. The treatment is mainly supportive. Mild cases are managed with antipyretics, hydration and home remedies/cough formulas. Moderate cases may require humidified oxygen, parenteral fluids to maintain hydration and nebulization with bronchodilators. Nebulization with adrenaline along with IV dexamethasone more effective in terms of reduction in the duration of the symptoms and length of hospital stay.

Methods: This prospective study was done for 1 year from May 2015 onwards.120 clinically diagnosed cases of bronchiolitis were included. cases were classified into 2 groups on the basis of RDAI score, Mild cases with score of 4-15 &Severe cases with score of >15. All cases were divided in 3 therapeutic groups, A- nebulized with adrenaline alone, B- single dose of IV dexamethasone and nebulized adrenaline, C- nebulized with 3% hypertonic saline alone. Nebulization was done at 0,30,60 minutes interval and then 4 hourly till improvement of symptoms.

Results: Out of total 120 cases,74(61.66%) belonged to age group of 2-6 months. Males were more affected than females with ratio of 2.15:1. Most of patients (83.3%) had hyperinflated lung field in X-ray finding. Children with preterm birth had severe disease. The mean RDAI score was found to be reduced highest in adrenaline plus dexamethasone group that is 2.37±0.80 within 24 hours of admission with 26.24% reduction in the length of hospital stay as compared to group A and 20.61% as compared to group C.

Conclusions: combination of nebulized adrenaline and dexamethasone is better in terms of reducing clinical severity, length of hospital stay in children with moderate severity of acute bronchiolitis in comparison to adrenaline alone and 3% hypertonic saline alone.

Keywords: Respiratory distress assessment instrument**,** Respiratory syncytial virus

INTRODUCTION

Bronchiolitis is one of the common respiratory tract infections in young children. Respiratory Syncytial Virus (RSV) is the common etiological agent responsible for more than 50% of cases, although many other viruses are implicated. It has been estimated that about 6,00,000 infants and young children die from RSV annually.[1]

Bronchiolitis is a disorder most commonly caused in infants by viral lower respiratory tract infection (LRTI). It is the most common lower respiratory infection in this age group. It is characterized by acute inflammation, edema and necrosis of epithelial cells lining small airways, increased mucus production, and bronchospasm. Signs and symptoms are typically rhinitis, tachypnea, wheezing, cough, crackles, use of accessory muscles, and/or nasal flaring.[2] Many viruses cause the same constellation of symptoms and signs. The most common etiology is the respiratory syncytial virus (RSV), with the highest incidence of RSV infection occurring between December and March.[3] Ninety percent of children are infected with RSV in the first 2 years of life, and up to 40% of them will have lower respiratory infection.[4-6] Infection with RSV does not grant permanent or long-term immunity. Reinfections are common and may be experienced throughout life.[7] Other viruses identified as causing bronchiolitis are human metapneumo virus, influenza, adenovirus, and parainfluenza. This variable pattern suggests a lack of consensus among clinicians as to best practices. In addition to morbidity and mortality during the acute illness, infants hospitalized with bronchiolitis are more likely to have respiratory problems as older children, especially recurrent wheezing, compared with those who did not have severe disease.[8-10]

Severe disease is characterized by persistently increased respiratory effort, apnea or the need for intravenous hydration, supplemental oxygen, or mechanical ventilation. It is unclear whether severe viral illness early in life predisposes children to develop recurrent wheezing or if infants who experience severe bronchiolitis have an underlying predisposition to recurrent wheezing.

The treatment of bronchiolitis is mainly supportive in nature. Mild cases are managed at home with antipyretics, hydration and home remedies/cough formulas. Moderate cases may require admission to the hospital and administering humidified oxygen, parenteral fluids to maintain hydration and nebulization with bronchodilators.[11] Nebulization with bronchodilators diluted in normal saline have been used with varying degree of success.[12] Role of steroids in the treatment of bronchiolitis is inconclusive.[13] antiviral agents (ribavirin) are used only special group of children who are at risk of severe disease (chronic lung disease, congenital heart diseases, etc).

There is no role for antibiotics, but are considered whenever secondary bacterial pneumonia is suspected or documented.[14] Recently few western studies have shown that nebulization with adrenaline along with steroid (injectable dexamethasone) was more effective in terms of reduction in the duration of the symptoms and length of hospital stay.[15,16] The new observation appears to be effective and promising. As per our knowledge there is no consensus in treatment of bronchiolitis and no similar clinical studies have been reported from India and hence we have conducted this study in our hospital.

METHODS

A prospective, comparative open label clinical trial was conducted in paediatric department of Jawaharlal Nehru Medical College and Hospital, Ajmer, Rajasthan.

120 clinically diagnosed cases of bronchiolitis were included in the study. Study was conducted for 1 year from May 2015 onwards.

Bronchiolitis was considered as first episode of wheezing along with prodrome of upper respiratory tract infection including rhinorrhea, cough and sometimes low-grade fever, which may progress to dyspnoea in age group of 2 month to 2 years.

Tachypnoea was considered when the child showed respiratory rate.[17]

- 60/min or more for age <2 months
- 50/min or more for age 2-12 months
- 40/min or more for age >12 months

Respiratory distress was considered when the child showed either subcostal, intercostals, suprasternal, supraclavicular retractions or nasal flaring.

All patients were enrolled within 24 hours of admission to the hospital. Patients were examined at the enrolment and every day. Relevant clinical and demographic data was obtained from each case symptoms like (cough, fever, rhinorrhea and respiratory distress) and history of previous wheezing episode, cardiac disease, foreign body aspiration, gestational age, and mode of delivery.

Vital parameters (heart rate, respiratory rate, saturation) were measured and recorded. Patients were examined for presence of cyanosis, pallor, and chest retractions. In systemic examination, emphasis was laid on breath sounds and presence of rhonchi or rhonchi with crepitation.

In every child RDAI score was also calculated on the bases of Lowell et al criteria as tabulated in Table 1.[18]

All cases were classified into 2 groups on the basis of RDAI score

- Mild cases who had score of 4-15
- Severe cases who had score of >15

In every case relevant investigation like CBC, X-ray Chest, ECG, Echocardiography, and ABG was also done as per need to include/exclude from the present study.

All cases were divided in 3 therapeutic groups for the study sequentially as patient admitted in ward.

- Group A: Patients nebulized with adrenaline alone
- Group B: Patients received single dose of intravenous dexamethasone and nebulized adrenaline (in combination)
- Group C: Patients nebulized with 3% hypertonic saline alone

Drug used

Injection adrenaline 1 ml/amp (1:1000 dilutions) available in hospital was used for the study. The dose of adrenaline used was 0.5 ml/kg or maximum 2.5 ml during each nebulization with 3 ml NS dilution.

Injection dexamethasone 8mg/2ml ampoule available in hospital was used. The dose of dexamethasone was 0.15 mg/kg single dose was given via intravenous route. 3% hypertonic saline (i.e. 3 gm sodium chloride per 100 ml bottle) was used in the dose of 4 ml per nebulization irrespective of weight and age.

Nebulization was done at 0, 30, 60 minutes interval and then 4 hourly till improvement of symptoms.

The major outcome parameters studied to find out the efficacy of treatment were improvement in respiratory distress (clinical score) and the duration of hospital stay.

Each day the child was assessed for fever, tachypnoea, respiratory distress, SpO_2, oxygen requirement, feeding, RDAI score and they were given treatment till improvement. Nebulization was stopped when RDAI score reaches 4 and then duration in improvement was calculated from the day of admission.

The Statistical software namely SPSS and some statistical methods were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

Table 1: Respiratory distress assessment instrument (RDAI).

Symptom	Score					Maximum Score
	0	1	2	3	4	
*Adapted from Lowell et al.[18]						
Wheeze/Crackles						
During expiration	None	End only	½ Phase	¾ Phase	Throughout	4
During inspiration	None	Partial	Throughout	-	-	2
Lung fields involved	None	<2 of 4	>3 of 4	-	-	2
Retractions						
Supraclavicular	None	Mild	Moderate	Marked	-	3
Intercostal	None	Mild	Moderate	Marked	-	3
Subcostal	None	Mild	Moderate	Marked	-	3
Total						17

RESULTS

In present study 74 (61.66%) out of 120 patients of bronchiolitis belonged to age group of 2-6 months. Males were more affected than females with ratio of 2.15:1. Cough and fast breathing were most common presenting symptoms in all patients at admission. Most of patients (83.3%) had hyperinflated lung field in X-ray finding. In present study, we found that children with preterm birth delivery had severe disease. The mean RDAI score was found to be reduced highest in adrenaline plus dexamethasone group that is 2.37±0.80 within 24 hours of registration of patients whereas mean RDAI score was reduced only 1.675±0.85 in adrenaline group and 1.325±0.94 in 3% hypertonic saline group. This difference was found statistically significant. (p=0.0001).

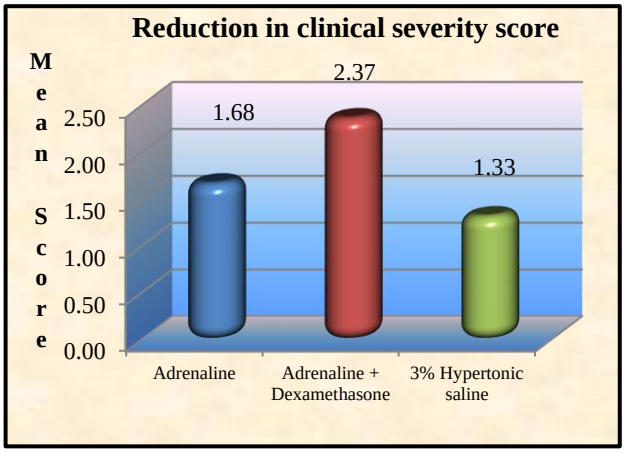

Figure 1: Reduction in clinical severity score.

The mean duration of hospital stay was calculated as the time taken for the hospitalised patients to meet the discharge criteria.

It was slightly higher in the both adrenaline group (5.22±1.81 days) and 3% hypertonic saline group (4.85±1.44) when compared to adrenaline plus dexamethasone group (3.85±1.40 days). No. of children in the adrenaline plus dexamethasone group stayed lesser time as compared to rest of the two groups. The mean difference between the two groups A and B is 1.37±0.412 days whereas mean difference between two groups B and C is 1.00±0.36 days. In present study, we found a 26.24% reduction in the length of hospital stay in group B compared to Group A and 20.61% reduction in length of hospital stay in group B compared to group C. The difference was statistically significant. (p-0.0001). Difference between Group A and Group C was statistically not significant. (p-0.310).

Total 6 patients have shown tachycardia after giving adrenaline nebulization. Tachycardia was mostly due to systemic effect of adrenaline after absorption through pulmonary capillaries.

Table 2: Reduction in clinical severity score.

Reduction in clinical severity score	Adrenaline	Adrenaline + dexamethasone	3% hypertonic saline	Total mean
Mean ± SD (Reduction)	1.6750±0.85	2.37±0.80	1.3250±0.94	1.7917±0.96
p-value		0.0001		

Table 3: Length of hospital stay in days.

Length of hospital stay (days)	Adrenaline (n=40)	Adrenaline+ dexamethasone (n=40)	3% hypertonic saline (n=40)	Total (n=120)
1-2 days	2	7	1	10
3-4 days	12	25	19	56
>4 days	26	8	20	54
Mean± SD (days)	5.22±1.8	3.85±1.40	4.85±1.44	4.64±1.65
p-value	0.0001			
Mean difference (days)	The mean difference between group A and group C is 0.375±0.376 days which is statistically not significant (p=0.310)			
	Between group B and group A: 1.37±0.412 days and between group B and group C: 1.00±0.36 days			
Percentage reduction	Group B shows 26.24% reduction as compared to group A and 20.61% reduction in hospitalisation duration as Compared to group C			

DISCUSSION

Bronchiolitis is a disease of the younger age group. It usually affects children less than 2 years of age, with children less than 6 months being affected with more severe disease.[19]

During the study period, starting from May 2015 to May 2016 total of 8650 patients were admitted in paediatric ward at JLN Hospital Ajmer Rajasthan (India). Out of that 1830 patient have diagnosed as respiratory disease. Total 120 patients were admitted with a clinical diagnosis of bronchiolitis included for the study on first come first admission basis, randomized into three groups. All 120 enrolled patients were discharged when they fulfil discharge criteria. As per study all of our children were hospitalized within the first year of life with the mean age at hospitalization being 7.0042±5.54 months (range 2-24 months) and children less than six months constituted 61.66 % of all admission. This was more in comparison with the population based retrospective study done by Fjaerli et al, to find out the incidence and risk factors for RSV disease.[20] The median age of presentation in their study was 6 months and children <6 months constituted about 45% of the study population.

Bronchiolitis usually affects boys more than girls.19 In our study, we also found a male predominance accounting for 68.3% of all admissions. The M: F ratio of our study population was 2.15:1. This observation minor increase incidence in male in our study compared to the studies done by Jone TJ et al involving south Indian children, with the M: F ratio being 1.6:1. Fjaerli et al also demonstrated a male predominance in Norway.[20-21]

Wheezing is the predominant finding in bronchiolitis. In our study wheezing, cough and fast breathing were present in all the children (100%). Common cold (running nose) and upper respiratory symptoms were in 93.3% and fever in 84.1% of children. This was in comparison with studies done by Kabra SK et al and Kumar N et al.[22,23] In their studies, cough (98% and 100%), fever (75% and 67.7%) and fast breathing (90% and 100%) were the predominant symptoms. Tachypnoea signs of viral illness like nasal catarrh and on auscultation rhonchi and scattered rales are the predominant findings.

In bronchiolitis, chest radiography reveals hyper inflated lungs.[19] In our study we found that most of the radiological features were consistent with bronchiolitis 83.3% and in 16.6% the radiographs were normal. Our observations were consistent with the findings of Schuh et al, who in acute bronchiolitis and found that Chest X-ray was routinely done for most of the babies (72%) and the findings were consistent with bronchiolitis in most of the cases (90%).[24]

The confounding factors for severe disease were includes male sex, prematurity, malnutrition and overcrowding. Simoes EAF critically reviewed literature examining risk factors for development of severe respiratory syncytial virus lower respiratory tract infection (RSV LRI), and found that male sex, young age, birth in the first half of the RSV season, day care attendance, and crowding/siblings are independent risk factors for the development of severe RSV bronchiolitis in American children.[25]

The principle outcome measure studied in current study was the reduction in clinical severity which was measured in terms or difference between the clinical scores on day 1 and day 2. As per study the mean reduction in clinical severity was 1.67±0.85 in adrenaline group, 2.37±0.80 in adrenaline plus dexamethasone group and 1.32±0.94 in 3 % hypertonic saline group. Adrenaline plus dexamethasone shows 23.7% reduction, adrenaline group shows 16.7% reduction and 3% hypertonic saline group shows 13.2 % reduction in clinical score between day 1 and 2. This difference was statistically significant (p= <0.0001). This was similar to Kyuncu et al results reviewing nebulized adrenaline plus dexamethasone for acute bronchiolitis in infants.[26] They found that there was significant reduction in the clinical severity scores with the adrenaline nebulization and dexamethasone as compared to nebulized adrenaline alone (p value=0.01). This study concludes that a single dose of dexamethasone added to nebulized L-epinephrine treatments, resulted in a better clinical outcome measure than treatment with bronchodilators alone, on the fifth day after treatment of mild to moderate bronchiolitis.[26]

In present study, the length of hospital stay was calculated by the duration required to meet discharge criteria. The mean duration of hospital stay was 4.64±1.65 days in our study population. In the adrenaline plus dexamethasone group the length of hospital stay was slightly lesser when compared to plain adrenaline and 3% hypertonic saline group. The difference was statistically significant. By using adrenaline dexamethasone combination, we found that there was a reduction in hospital stays by 1.37±0.412 days (26.2%) compared to adrenaline group and 1.00±0.36 days (20.61%) reduction as compare to 3 % hypertonic saline. This difference was statistically significant. Difference between group A and group C was statistically not (p=0.310) significant. This observation was similar to the findings from Bentur et al, found the dexamethasone and nebulized adrenaline combination has a mean reduction of 2.6±0.2 days (26%) compared to only adrenaline nebulization group.[27]

CONCLUSION

In conclusion, findings of our study suggest that combination of nebulized adrenaline and dexamethasone is better in terms of reducing clinical severity, length of hospital stay in hospitalized children with moderate severity of acute bronchiolitis in comparison to adrenaline alone and 3% hypertonic saline alone.

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