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Original Article

Comparison of Efficacy of Nebulisation with Salbutamol versus Adrenaline in Acute Bronchiolitis in Children aged Two Months to Two Years.

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Abstract

Background

Bronchiolitis is an acute, highly communicable lower respiratory tract infection. A variety of agents ranging from nebulised racemic epinephrine, salbutamol and routinely available levo-epinephrine have been tried. The Present study was aimed at comparing the effectiveness of adrenaline and salbutamol in acute bronchiolitis in children aged 2 months to 2 years.

Materials and Methods

The Present study was conducted at Nobel medical College Teaching Hospital over the period of one year from Feb 2018 to Jan 2019. Two different cohorts were identified in which clinically diagnosed cases and were grouped into Group A and Group B to receive the different drugs as per the study protocol. Respiratory Distress Assessment Instrument (RDAI) Scores was used for clinical assessment

Results

The age of the patients ranged from 2 months to 24 months with a median of 8 months. The males constituting about 57.42% of the study population of 155 patients. On comparing the pre-nebulisation variables with 10 and 30 minutes post nebulisation values, it was found that Both adrenaline and salbutamol caused overall significant improvement in RR (p-value <0.00001 in both groups) except in the age group of 19-24 months. Adrenaline was seen to be superior to salbutamol in decreasing the RR (p<0.0001) except for children in the age group of 19-24months. Adrenaline also caused greater rise in heart rate in comparison to salbutamol in all age groups.

Conclusion

This study concludes that Adrenaline was seen to be superior to salbutamol in decreasing the RR and RDAI, although it showed variance with age.

Keywords: *Adrenaline, Bronchiolitis, Salbutamol*

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Introduction

From time immemorial, humanity has been suffering from bronchiolitis, the prevalence of which kept on increasing over the years. Bronchiolitis is an acute respiratory tract infection which is highly communicable and manifests as cough, runny nose, low grade fever, expiratory wheezing, fast breathing and chest retractions [1]. Bronchiolitis usually starts as an upper respiratory infection and is followed by signs of lower respiratory involvement like respiratory distress and evidence of bronchiolar obstruction and narrowing such diffuse wheezing and high-pitched rhonchi [2].

RSV infects ninety percent of children are in the first 2 years of life, and cause lower respiratory tract infection up to 40% of affected children [2-5]. Adenovirus, parainfluenza virus, influenza virus and human metapneumovirus also have been identified as etiological agents for broncioloitis. World Health Organization bulletin, estimated 150 million new cases of bronchiolitis occurring annually of which 11-20 million1 cases were severe enough requiring inpatient treatments [6]. Variations correlating more with hospital or individual preferences than with patient severity have been reflected by various studies conducted in the United States, Canada and the Netherlands [7-9].

There has been controversial use of bronchodilators in bronchiolitis [10]. Various pharmacological agents like parenteral epinephrine, salbutamol and levo-epinephrine to nebulised racemic epinephrine have been used with controversy [11-13]. Injectable epinephrine was used in wheezing infants with good results [14, 15]. Recent clinical guidelines have suggested only supportive treatment measures due to lack of concrete evidence.

Materials and Methods

This is a prospective hospital based comparative study conducted in Nobel Medical College Teaching Hospital and Research Centre located in Khanchanbari, Biratnagar, Nepal from Feb 2018 to Jan 2019. After ethical clearance from the institutional review committee, data was collected from 155 children admitted to the department of pediatrics by means of interview with the parents, clinical examination and laboratory report tracing and entered into a Performa. Sample size was calculated on the basis of similar study conducted in Medical College Teaching Hospital, Kathmandu, Nepal [10]. Taking into account the prevalence of bronchiolitis in previous study, sample size was determined and first 155 children fulfilling the inclusion criteria were included in the study. Children with history of 2 or more respiratory distress in past, family h/o asthma, critically ill children, history of prematurity or mechanical ventilation in past, underlying chronic pulmonary or cardiac disease, bronchomalacia, heart rate(HR) > 200/min, respiratory rate(RR) > 100/min and use of glucocorticoids, sympathomimetic amines or monoamine oxidase inhibitor were excluded from the study.

Diagnosis of acute bronchiolitis was made solely on clinical basis. The procedure was explained to the parents along with risks and benefits. Informed consent (verbal as well as written) was taken from the parents. Heart rate and respiratory rate was recorded and severity of illness was assessed using RDAI (respiratory distress assessment instrument) score [16]. The children were arbitrarily assigned into two groups (A and B). Group A received 0.1 ml/kg of 1 in 10,000 solution of adrenaline. Group B received salbutamol in a dose of 0.15 mg/kg (minimum dose 1 mg). The drug was mixed with normal saline to make a total volume of 3 ml and patient nebulised using oxygen flow of 5-7 L/min thrice at 20 minute intervals. No other drugs like antibiotics, steroids, etc were given during this period. Patient was reassessed 10 minutes and 30 minutes following nebulisation with heart rate, respiratory rate and RDAI scoring.

The comparison of outcomes after intervention was done using paired t-test. Level of significance in our study was < 0.05.The collected data was then coded and entered into Microsoft Excel and transferred to Statistical Package for Social Sciences (SPSS) version 20 for analysis.

Results

A total of 155 patients of age between 2 months to 24 months arriving in the outpatient or emergency department and diagnosed a case of acute bronchiolitis during a period of one year were included in the study. The age of the patients ranged from 2 months to 24 months with a median age of 8 months. Majority of study subjects were in age of 2 months to 12 months and there was no sex differentiation as far as age of the patients was concerned.

All of these patients were randomly allocated to one of the two study groups (Group A and Group B). Seventy eight patients were included in Group A (in which they were nebulised with adrenaline) and 77 patients constituted the Group B (in which the patients were nebulised with salbutamol).

Table 1: Age and Sex Distribution

AGE	MALE	FEMALE	TOTAL
(months)	n (%)	n (%)	n (%)
2-6	33 (56.90)	25 (43.10)	58 (37.42)
7-12	31 (58.49)	23 (43.39)	54 (34.20)
13-18	15 (57.70)	11 (42.30)	26 (16.77)
19-24	10 (58.82)	7 (41.17)	17 (10.96)
Total N (%)	89 (57.42)	66 (42.58)	155 (100.0)

In Group A, median age of patient was 8 months. While in Group B, the median age of patient was 7 months. Both the groups were thus, found to be comparable. In adrenaline group, the mean respiratory rate prior to nebulisation was 68.06 ± 8.97 while in salbutamol group pre-nebulisation respiratory rate was found to be 66.66 ± 8.62. The mean value of heart rate in Group A at the time of presentation was 124.63 ± 6.71 per minute. In the Group B, mean value of heart rate was 123.8 ± 6.86 per minute. Both the groups were found to be comparable with respect to pre-nebulisation heart rate. The mean value of RDAI score in all 78 patients of adrenaline group was 10.81 ± 2.54 while in 77 patients of salbutamol group was found to be 10.53 ± 2.64.

Table 2: Pre-nebulisation Respiratory Distress Assessment Instrument (RDAI) Score

AGE (MONTHS)	RDAI SCORE			
	GROUP A (MEAN±S.D)	GROUP B (MEAN±S.D)	DIFFERENCE OF MEAN±S.D	p value
2-6	11.87 ± 2.99	11.71 ± 3.00	0.16 ± 0.79	>0.05
7-12	10.67 ± 1.60	10.0 ± 1.81	0.67 ± 0.47	>0.05
13-18	9.09 ± 1.81	9.33 ± 2.09	0.24 ± 0.76	>0.05
19-24	9.57 ± 2.93	10.3 ± 3.05	0.73 ± 1.46	>0.05
TOTAL	**10.81 ± 2.54**	**10.53 ± 2.64**	**0.28 ± 0.42**	**>0.05**

Mean value of respiratory rate in adrenaline group patients after 10 minute post-nebulisation was found to be 57.65 ± 8.48 per minute. The mean respiratory rate at 10 minute after nebulisation was 59.87 ± 8.63 in salbutamol group. The mean value of heart rate in Group A 10 minutes after nebulisation was 136.83 ± 6.64 per minute. In the salbutamol group, mean of heart rate was 130.57 ± 7.32 per minute. The mean value of RDAI score in all 78 patients of adrenaline group at 10 minute after nebulisation was 5.83 ± 1.95 while in 77 patients of salbutamol group was found to be 7.39 ± 2.61.

Table 3: Post-nebulisation Respiratory Distress Assessment Instrument (RDAI) Score at 10 minutes

AGE (MONTHS)	RDAI SCORE AT 10 MINUTES	
	GROUP A (MEAN ± S.D)	GROUP B (MEAN ± S.D)
2-6	6.67 ± 2.10	9.07 ± 2.66
7-12	5.56 ± 1.52	6.96 ± 1.78
13-18	4.72 ± 1.68	5.40 ± 1.8
19-24	5.14 ± 2.26	6.7 ± 2.58

Both adrenaline and salbutamol caused overall significant improvement in RR. This difference was also found to be significant when evaluated in different age groups except in the age group of 19-24 months and overall significant increase in heart rate occurred in both groups after 10 minutes of nebulisation in both the groups. A significant difference in decrease in RDAI score was observed 10 minutes after nebulisation in both the groups.

The mean value of Respiratory rate in adrenaline group patients after 30 minute post- nebulisation was found to be 57.33 ± 8.44 per minute. The mean respiratory rate at 30 minute after nebulisation was 60.02 ± 8.91 in salbutamol group. The total mean value of heart rate in adrenaline group (78 patients) 30 minutes after nebulisation was 140.73 ± 6.83 per minute. In the salbutamol group of 77 patients, mean of heart rate was 132 ± 7.99 per minute. The mean value of RDAI score in all 78 patients of adrenaline group at 30 minute after nebulisation was 5.83 ± 1.95 while in 77 patients of salbutamol group was found to be 7.39 ± 2.61. This mean value at 30 minute was identical to that at 10 minute of nebulisation in both adrenaline and salbutamol group.

Table 4: Post-nebulisation Respiratory Distress Assessment Instrument (RDAI) Score at 30 minutes

AGE (MONTHS)	RDAI SCORE AT 30 MINUTES	
	GROUP A (MEAN ± S.D)	GROUP B (MEAN ± S.D)
2-6	6.67 ± 2.10	9.07 ± 2.66
7-12	5.56 ± 1.52	6.96 ± 1.78
13-18	4.72 ± 1.68	5.40 ± 1.8
19-24	5.14 ± 2.26	6.7 ± 2.58

Both adrenaline and salbutamol caused overall significant improvement in RR. This difference was also found to be significant when evaluated in different age groups except in the age group of 19-24 months. HR showed significant increase in both groups (p value of <0.0001 in both). This increase in HR was found to be significant in all age group. RDAI was seen to decrease significantly in both the groups. This difference was significant in all age groups.

On comparison of efficacy of adrenaline and salbutamol in respect to change in parameters, Adrenaline was seen to be superior to salbutamol in decreasing the RR except in children between the ages of 19-24 months at both 10 and 30 minutes post nebulisation. The change in HR was found to be more in adrenaline group in comparison to salbutamol in both post nebulisation. Adrenaline nebulisation was found to be superior to salbutamol nebulisation in decreasing RDAI in all children in both 10 and 30 minutes post nebulisation except those in the age group of 19-24 months.

Table 5: Comparison of efficacy of adrenaline and salbutamol nebulisation between pre-

AGE (months)	RDAI SCORE (pre-nebulisation v/s 10 minutes after nebulisation) MEAN OF DIFFERENCE ± S.D		
	GROUP A	GROUP B	p value
2-6	5.2 ± 0.67	2.64 ± 0.76	<0.00001
7-12	5.11 ± 0.44	3.04 ± 0.51	<0.00001
13-18	5.11 ± 0.44	3.93 ± 0.71	<0.00001
19-24	4.43 ± 1.39	3.61 ± 1.26	>0.05
Total	4.98 ± 0.36	3.14 ± 0.42	>0.05

Discussion

Bronchiolitis is an important cause of lower respiratory tract infection. Despite widespread use of bronchodilators, no concrete evidence has been achieved on the type, duration and dosage of the drugs for treatment. Various randomized placebo-controlled studies have been conducted to investigate the effectiveness of bronchodilator use, but no definite results have been obtained regarding their effects on heart rate, respiratory rate and clinical score improvement.

The age of the patients ranged from 2 months to 24 months with a mean of 9.23 ± 5.72 months. The significant factor in our study was that most of the patients belonged to 2 months to 6 months of age (58; 37.41%). Study from Nepal Medical College Teaching Hospital (NMCTH) also showed that 52.0% children below 2 years of age had acute lower respiratory tract infections, of which 31.6% had acute bronchiolitis [10]. They also concluded that acute bronchiolitis was observed in patients younger than 2 years of age only. American academy of pediatrics found that more than one third of children develop bronchiolitis during the 1st 2 years of life [16]. Glezen et al. also concluded that 2/3rd of hospitalized children with RSV associated bronchiolitis less than 1 year of age [17]. However, the mean age of patients in study by Langley *et al*. was 6.4 months which was lower than the mean age of enrolment in our study [18].

Our study included 89 males and 66 females, the male constituting about 57.42% of the study population of 155 patients. Weber et al. and Iwane et al. also documented that for unknown reason bronchiolitis occurs as much as 1.25 times more frequently in males than in females [7, 16]. Study from Nepal Medical College Teaching Hospital showed that the incidence of lower respiratory tract infection, including bronchiolitis, involved 58.9% of male. Both the studies showed male predilection [10].

Glenn Flores and Ralph I. Horwitz, in 1995 suggested in their meta-analysis that ß2-agonist therapy did not have a clinically significant impact on physiologic measures [19]. Another contradictory study by Patel et al. suggested that there were no significant group differences in primary outcome, by intent-to-treat analysis, nor in the secondary analysis using survival curve methods [20]. A Abul-Ainine and D Luyt in his interven-

tion review published in Cochrane Library 2004, comparing epinephrine and placebo (n=5) for inpatients, found that there was one significant outcome favoring epinephrine [21]. Our study is also favored by Langley et al. who found that epinephrine resulted in significant improvement in wheezing and the total RDAI score on day 2 and over the entire stay ($p<0.05$) [18].

Conclusion

Among the patients with bronchiolitis, in the age group from 2 months to 2 years who were studied, there was male preponderance. Pre-nebulisation HR, RR and RDAI were recorded and both groups were found to be comparable. On comparing the pre-nebulisation variables with 10 and 30 minutes post nebulisation value, it was found that both adrenaline and salbutamol caused overall significant improvement in RR except in the age group of 19-24 months. Adrenaline was seen to be superior to salbutamol in decreasing the RR except for children in the age group of 19-24months. The change in heart rate was found to be more in adrenaline group in comparison to salbutamol. RDAI was seen to decrease significantly in both groups but adrenaline was found to be superior to salbutamol in decreasing RDAI in all children except those in the age group of 19-24months.

Conflict of Interest

We declare no conflict of interest.

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