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ORIGINAL ARTICLE

Comparison of Nebulized Epinephrine with Intravenous Dexamethasone versus Nebulized Salbutamol in Infants Hospitalized With Acute Bronchiolitis

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ABSTRACT

Objective: To compare mean change in terms of respiratory rate, oxygen saturation and Respiratory Distress Assessment Index (RDAI) score of nebulized epinephrine with intravenous dexamethasone versus nebulized salbutamol in infants hospitalized with acute bronchiolitis.

Study Design: Randomized Controlled Trial

Place and Duration of Study: Pediatric Unit of Khyber Teaching Hospital from 15-10-2016 to 15-042017.

Material and Methods: using non-probability consecutive sampling technique and inclusion criteria 322 patients were included in the study, 166 in group A (nebulized epinephrine with intravenous dexamethasone) and 166 in group B (nebulized salbutamol). SPSS (version 17) was used to enter and analyze the data. A comparison was made in the mean change between the two groups with respect to RDAI, respiratory rate and oxygen saturation at 240 minutes from baseline.

Results: Mean age was 5.30 ± 2.89 in group A and 5.25 ± 3.18 in group B. Male made 68% in group A and 78% in group B. Mean change in RDAI score for group A was 1.86±0.58 and for group B 1.04 ± 0.48 (p-value 0.002). There were no differences in the mean change of oxygen saturation or respiratory rate in both groups (p >0.05).

Conclusion: Combination therapy of epinephrine with dexamethasone had a more significant response in the clinical score only, and RDAI score was found to be more representative of clinical improvement of patients admitted with acute bronchiolitis

Key Words: *Bronchiolitis, Epinephrine, Steroids, Salbutamol, RDAI*

INTRODUCTION

Infant presenting with difficulty in breathing for the first time and is associated with an acute lower respiratory tract infection (LRTI) is defined as bronchiolitis.[1] It is mostly caused by viruses, with respiratory syncytial virus(RSV) making up a lot of the cases.[2] Bronchiolitis is a clinical based diagnosis with typical signs and symptoms. It starts in upper respiratory tract and in a few days, progresses to a lower respiratory infection. It presents as coughing, tachypnea, expiratory

breathing difficulty and increased work of breathing.

Bronchiolitis is a major public health issue with high morbidity and significant costs. *Respiratory Syncitial Virus* makes up 33.8 million episodes of LRTI with 3.4 million children below 5 years of age hospitalized.[3] Generally, bronchiolitis causes 1% to 3% of all infants to be hospitalized,[4,5] and 5% to 6% of admitted infants are managed in the pediatric intensive care unit (PICU)[6,7].

Half of the burden of the world RSV-LRTI is contributed by five countries - India, China, Nigeria, Pakistan, and Indonesia - which makes 43% under-five children.[6]

A study in Multan showed that the months of December, January and February had the highest incidence with lesser cases seen in June, July and August.[7] Another study in two hospitals of Islamabad showed that in admitted children less than 2 years of age, 67% of respiratory viruses were RSV.[8]

Admission to hospital is required if general condition of infant is poor, there is increased work of breathing, decreased oxygen saturation or decrease fluid intake.[9.10]

Symptomatic treatments include nebulized hypertonic saline, bronchodilators, corticosteroids and epinephrine. There still is a lot of controversy regarding both the outpatient and inpatient settings management of bronchiolitis. This variation may be explained by the varying disease severity, difference in care settings and geographical locations.

The rationale of the study was to come with a protocol that would quickly improve the outcomes of patients admitted with acute bronchiolitis in Khyber Teaching Hospital and other similar hospitals which is already over saturated with emergency and diagnostic cases. Currently the protocol in our inpatient is use of nebulized salbutamol alone. Evidence suggested that there is synergistic effect of epinephrine with dexamethasone.[11] Based on available literature, we hypothesized that nebulized epinephrine with intravenous dexamethasone will cause a significant change in the mean respiratory rate, oxygen saturation and RDAI score compared to nebulized salbutamol alone. There was lack of study to see the outcomes in combining two drugs, especially in a hospital like ours.

MATERIAL AND METHODS

The study was conducted in Pediatric Department, Khyber Teaching Hospital from End of October 2016 to April 2017. Total 332 patients with 166 in group A (nebulized epinephrine with intravenous dexamethasone) and 166 in group B (nebulized salbutamol) were selected using non probability consecutive sampling**.**

Patients 6 weeks to 12 months of age including both male and female with 1st time episode of wheezing, cough, runny nose, with only hyperinflation on CXR were included in the study.

Patients with history of similar episode of respiratory distress in the past, prolonged respiratory distress in newborn period, chronic heart disease, chronic lung illness or having received corticosteroids in any form in the preceding 72 hours were excluded from the study.

After approval from hospital ethical and research board, the patients included in the study were directly admitted from the A&E Department or OPD with the diagnosis of bronchiolitis. The purpose, risks and benefits of the study were explained to all included patients, and informed written consent was obtained from all included patients. Participants, selected by non-probability consecutive sampling, were randomly assigned by lottery method to one of the two study treatments: group A, nebulized 1:1000 dilution epinephrine (0.5 ml/kg subject to a maximum of 2.5 ml with 3 ml saline) plus intravenous dexamethasone, or group B, with nebulized salbutamol (0.15 mg/kg with 2 ml saline). It was administered through a Gt012-100 Nebulizer with Mask driven by 100% oxygen at a rate of 6 liters per minute for five minutes (apart from routine oxygen and intravenous fluids) at 0,30,60 minutes. The parenteral treatment consisted of 1.0 mg of dexamethasone per kilogram of body weight (maximum dose, 10 mg). Rest of management was according to standard protocol. All the infants were assessed in the beginning (baseline) and at 240 minutes for Respiratory Distress Assessment Instrument score (RDAI), respiratory rate (RR), and oxygen saturation. Adverse events during

hospitalization were monitored and reported within 24 hours.

Data was recorded on a predetermined proforma. Mean ±SD was calculated for quantitative variables which were RDAI score, respiratory rate and oxygen saturation. Frequency and percentage was used to calculate qualitative variable which was gender. SPSS (version 17) was used to enter and analyze the data. A comparison was made in the mean change between the two groups with respect to RDAI, respiratory rate and oxygen saturation at 240 minutes from baseline.

Outcomes (RDAI, respiratory rate and oxygen saturation) in both the groups were compared by using independent t-test. p value <0.05 was considered as significant.

RESULTS

In this study mean age of the patients in group A was 5.30 ± 2.89 while in group B, mean age was 5.25 ± 3.18 (table 1).

TABLE 1: Age distribution (n-332)

AGE (Months)	Group A (%)	Group B (%)
2-7	129 (78.0)	126 (76.0)
7-12	37 (22.0)	40 (24.o)
Total	**166 (100.0)**	**166 (100.0)**
Mean Age	5.30 ± 2.89	5.25 ± 3.18

Gender distribution among 166 patients in group A was analyzed as 113 (68%) male and 53 (32%) female. While group B, 103 (78%) out of 166 were males and 63 (22%) females (fig 1).

At arrival the mean respiratory rate in group A was 73 ± 5.5 and in group B 75 ± 5.8. The mean oxygen saturation at arrival in group A was analyzed as 91.73 ± 1.84 and in group B 91.61 ± 1.64. While the RDAI score was 11.45 ± 1.78 in group A and 11.74 ± 1.71 in group B (table 2).

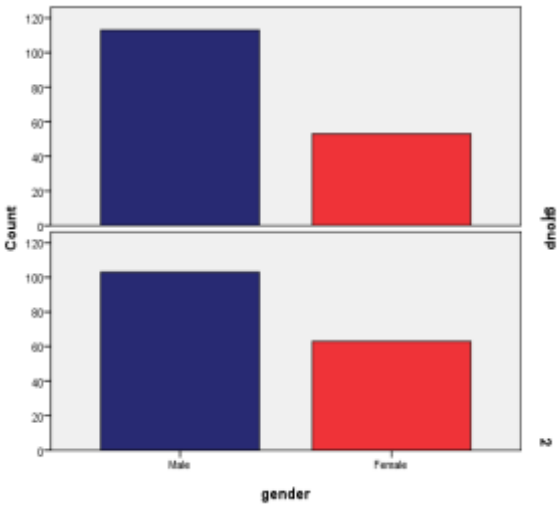

Fig 1: Gender distribution

TABLE 2: Baseline characteristics at arrival

Baseline characteristics	Group A	Group B	p-Value
Age	05.30 ± 2.89	5.25 ± 3.18	0.15
Respiratory rate	73.00 ± 5.5	75.00 ± 5.8	0.70
Oxygen saturation	91.73 ± 1.84	91.61 ± 1.64	0.32
RDAI score	11.45 ± 1.78	11.74 ± 1.71	0.25

Independent t-test was applied *Significant if p value is < 0.05

Analysis was done of the outcomes at 240 minutes. The respiratory rate in group A was 65 ± 6.3 and in group B was 68 ± 6.3. The oxygen saturation in group A was 93.58 ± 1.95 and in group B 91.61 ± 1.64. While the RDAI score was 9.59 ± 1.72 in group A and 10.73 ± 1.66 in group B (table 3).

Analysis was done for the mean change in clinical parameters from baseline to 240 minutes. In group A the mean change in respiratory rate was 9 ± 3.0, while in group B it was 7 ± 2.7. The mean change in oxygen saturation in group A was 1.99 ± 1.95 and 0.83 ± 0.51 in group B. While the mean change in RDAI score in group A was 1.86 ± 0.58 and 1.04 ±0.48 in group B. The mean difference was statistically significant only for the RDAI score (table 4).

TABLE 3: Assessment at 240 minutes

Assessment at 240 minutes	Group A	Group B	p-Value*
Respiratory rate	65.00±6.30	68.00±6.3	0.476
Oxygen saturation	93.58±1.95	91.61±1.64	0.053
RDAI score	9.59±1.72	10.73±1.66	0.863

Independent t-test was applied

TABLE 4: Mean change of outcomes

Mean change	Group A	Group B	p-Value
Respiratory rate	9.00±3.0	7.00±2.7	0.157
Oxygen saturation	1.99±1.95	0.83±0.51	0.133
RDAI score	1.86±0.58	1.04±0.48	0.002*

Independent t-test was applied
*Significant if p value is < 0.05

No adverse reaction was documented during the study.

DISCUSSION

The result supported the hypothesis regarding the RDAI score but it was rejected regarding respiratory rate and oxygen saturation.

The baseline characteristic of our study showed the average age to be 5 months, similar to the mean age in the related studies conducted[11,12] (table 2). An Indian study showed the mean age to be 2 months.[13] While one conducted in a Pakistani hospital showed the average to be 9 months, and another study had average age of 8 months.[14,15]

The female to male ratio in this study was 2:3, (fig 1) similar to a study carried out in Ontario, while studies conducted in Saudi Arabia was 2:3 for group A but 1:1 for group B.[11,12] The one in Pakistan also had a 1:3.2 female to male ratio.[16]

The Ontario study had an average respiratory rate of 48/min while in my study, as well one conducted in India, the average respiratory rate was double on arrival.[12,13] Assessment at 240 minutes the respiratory rate decreased to 65/min for group A and 68/min for group B in my study (tables 2 and 3). In our study there was no statistical significant difference in the mean change in respiratory rate at 240 minutes from baseline between the two groups (p value of 0.157). Similar to the research in Saudi Arabia indicated no statistical difference over time between the two study groups (p-value 0.15).[11] The Canadian research when adjusted at 60 minutes from baseline for epinephrine and dexamethasone group showed no significant difference.[12]

In our work, as well as the one carried out in India, the average oxygen saturation on arrival was 91%, as opposed to the threshold values of 97% (Canada), and 96% (Saudi Arabia).[11-13] At the 240 minute mark, oxygen saturation improved to 93.58% and 92.38% for group A and B respectively in our study. The difference between the two groups was nearly significant at 240 minute, but no difference was seen in the mean change. There was no change observed across both the groups in Saudi Arabia study (p-value 0.15).[11] Similarly there was no significant change in the epinephrine and salbutamol group of Canadian study after 60 minutes (p-value 0.59).[12]

The mean RDAI at arrival was 11.45 and 11.74 for group A and B respectively. Over the time span of 0-240 minutes the score decreased for both groups, with a mean 9.49 observed in A and a mean of 10.73 in B. Statistical significance was observed regarding the mean RDAI score difference between the two groups (1.86 and 1.04 in group A and B respectively with p-value of 0.002). The study conducted in Saudia Arabia had RDAI score of 7.6 and 8.6 for group A and B respectively on arrival that decreased to 4.5 and 5 at 240 minute assessment.[11] Though the score improved individually from the baseline, it was not significant in their study (p-value 0.82). Research by an Indian study, showed no significant differences between the primary outcome variables of the 2 groups within the first 120 min and at 24 hours but significant differences on the 5th day for RDAI score was observed.[17]

The systematic review studies done in 2006 by Cochrane showed a possible benefit with epinephrine use in bronchiolitis managements of outpatients.[18] It was noted in a number of research works that there was lower admission rate over 7 days in the children who were administered dexamethasone combined with nebulized epinephrine compared to the placebo given (17.1% Vs. 26.4 %).[19]

The improvement in the clinical scoring system was seen in my study with the use of combination therapy of epinephrine with dexamethasone.

CONCLUSION

Combination therapy of epinephrine with dexamethasone had a more significant response in the clinical score only, and RDAI score was found to be more representative of clinical improvement of patients admitted with acute bronchiolitis

There were no differences in oxygen saturation or respiratory rate outcomes in the studied intervals in both groups (p>0.05).

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Conflict of interest: There was no conflict of interest among the contributors during the study.

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