Exploring the relative drug of choice between epinephrine and salbutamol in infants suffering with bronchiolitis

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ABSTRACT

Background: Bronchiolitis is a short term viral inflammation of bronchioles in the lower respiratory tract associated with substantial morbidity in young children. There is conflicting evidence regarding the effectiveness of bronchodilators in the management of bronchiolitis.

Objectives: The main objectives of the current study were comparing the effectiveness of nebulized epinephrine and salbutamol in infants suffering with bronchiolitis.

Methodology: This 6 months study was conducted in the Department of Pediatrics, Khyber Teaching Hospital Peshawar, Pakistan between March and August 2011. The study design was randomized controlled trial. A total of 90 children of less than 1 year age were randomly and equally allocated in two groups, each group had 45 patients. Infants in group A were given nebulized salbutamol (0.15 mg/kg) and group B received nebulized epinephrine (0.1 mL/kg) (1:1000). The nebulisation was given in normal saline with an interval of 20 minutes for three times**.** Modified respiratory distress assessment instrument score; a globally recognized scale was used for disease assessment.

Results: The mean mRDAI score before administration of salbutamol and epinephrine was 18.2 $\pm$ 0.5 and 17.8 $\pm$ 2.7 (p = 0.33) respectively which was reduced to 6.1 $\pm$ 1.3 and 7.5 $\pm$ 1.0 after treatment with salbutamol and epinephrine respectively (p = 0.001). The oxygen

saturation in salbutamol and epinephrine groups before treatment 92.6 ± 3.4 and 93.2 ± 5.2 respectively improved to 96.4 ± 1.5 and 97.1 ± 0.8 respectively (p = 0.007). The respiratory rate before administration of salbutamol and epinephrine was 69 ± 7 and 66 ± 6 reduced to 55 ± 4 and 49 ± 4 (p = 0.001). The effect of both drugs caused relative increase in heart rate from 105 BPM ± 4 to 130 BPM ± 5 in salbutamol group while in case of epinephrine it increased from 102 BPM ± 9 to 151 BPM ± 5 (p = 0.001).

Conclusion: Nebulized epinephrine caused a significant decrease in the symptoms of bronchiolitis as compared to the symptoms recorded in infant received nebulized salbutamol.

Keywords: Acute Bronchiolitis, Epinephrine, Salbutamol

INTRODUCTION

Bronchiolitis is an infection of the lower respiratory tract caused by virus. The major symptoms include chest wheezing, shortness of breath and cough. Young children are most commonly infected leading to hospitalization. Bronchiolitis is diagnosed clinically followed by radiographic findings. Most cases of bronchiolitis are caused by the respiratory syncytial virus (RSV) that is also associated with significant morbidity in young children.[1,2] RSV is the pathogen responsible for more than 70% of cases. However, other pathogens which may cause bronchiolitis are parainfluenza virus, adenovirus, and mycoplasma pneumonia.[3] Different clinical symptoms are resulted by inflammation of the bronchioles. Immunoglobulin-E (IgE)-mediated type 1 allergic reactions may be the cause of some clinically severe bronchiolitis. Evidences suggest that Immunoglobulin-A (IgA)-rich colostrum may offer some protection from bronchiolitis.[4, 5]

The predominant symptoms which appear after inflammation are increased mucus secretion, bronchial constriction, alveolar cell death, and mucus debris. Bronchodilators can be used as an adjuvant therapy for bronchiolitis and offer only moderate short-term improvements in clinical characteristics.[6, 7]

In bronchiolitis, as compared to asthma, the desquamation and inflammation of the airway epithelial cells are more extensive. Inhaled adrenergic agonists have been found to be effective in treating both disorders. Also, the delivery of oxygen usually alleviates hypoxemia, which is caused by an imbalance between ventilation and perfusion that lowers blood oxygenation in pulmonary tissues.[8] Bronchodilators and corticosteroids have been found as less effective in the management of bronchiolitis. Research suggests that combination therapy along with oxygen may prove more useful in improving the clinical symptoms of bronchiolitis[9]. Along with drugs, it is necessary maintain proper fluid intake and oxygen supplementation. Many antiviral drugs and vaccines are being studied which may further improve the clinical outcomes in the near future.[10] The current study was designed to evaluate the effectiveness of nebulized epinephrine compared with nebulized salbutamol in the treatment of acute bronchiolitis owing to reduce the morbidity and hospitalization rates due to this common childhood illness.

METHODS

A randomized controlled trials study was conducted in the Department of Pediatrics "A" ward at Khyber Teaching Hospital, Peshawar, Pakistan from March 2011 – August 2011. The ethical approval (No: 133/RD/Cell/KMC) was obtained from the above mentioned hospital. A total of 90 children of less than 1 year age were randomly and equally allocated in two groups, each group had 45 patients. Infants in group A were given nebulized salbutamol (0.15 mg/kg) and group B received nebulized epinephrine (0.1 mL/kg) (1:1000). The nebulisation was given in normal saline with an interval of 20 minutes for three times**.** Modified Respiratory Distress Assessment Instrument Score (mRDAI); a globally recognized scale for was used for disease monitoring along with oxygen saturation and other physical parameters.[11] By using a pulse oximeter, oxygen saturation was determined. mRDAI scale, mentioned below in Table 1, has been previously reported in other RCTs, helps in determining the severity of bronchiolitis based on the patients' clinical symptoms.[2,12] The mRDAI score was re-evaluated after administration of last doses of drugs in their respective groups. Other drugs such as antibiotics or steroids were not administered during treatment period.

Table 1: mRDAI scale with score of different vitals

Wheezing	**0**	**1**	**2**	**3**	**4**	**Score**
Expiratory	None	End	½	3/4	All	4
Inspiratory	None	Partial	All			2
Location	None	2 of 4 lung fields	3 of 4 lung fields			2
Retraction	None					
Supra Clavicular	None	Mild	Moderate	Marked		3
Inter Coastal	None	Mild	Moderate	Marked		3
Sub Coastal	None	Mild	Moderate	Marked		3
Rate of respiration	20-25	26-35	36-45	>45		3

Data analysis

For data analysis Graph Pad prism was used. Unpaired and paired *t*-test was used to find the *p* - value. The *p* – value less than 0.05 was considered as significant.

RESULTS

Patient's demographics

Salbutamol group (Group A)

As mentioned in Table 2, 80% of the patients belong to urban areas. About 82% people resided in crowded areas while remaining 18% had less crowded residential area. With respect to aeration and ventilation, about 60% of were living in well ventilated areas while the remaining ones were located in less ventilated areas.

Epinephrine group (Group B)

As mentioned in Table 2, 85% of the patients were of urban residence and about 77% people resided in crowded area while remaining 22% had less crowded residential area. With respect to aeration and ventilation, about 56% of the patients were living in well ventilated areas while the remaining ones were located in less ventilated areas.

Table 2: Demographics, crowded living, and ventilation status of patients

Living Standards	Types	Group A	Group B
Residence	Rural	9(20%)	7(15.5%)
	Urban	36(80%)	38(84.5%)
Crowded Area	Highly	37(82.2%)	35(77.7%)
	Lowly	8(18.8)	10(22.2%)
Better Ventilation	Good	27(60%)	25(55.56%)
	Poor	18(40%)	20(44.4%)

Signs and symptoms of patients with acute bronchiolitis

The signs and symptoms recorded and observed for patients of both groups were cough, fever, dyspnea, dysphagia (difficulty in swallowing), and rhinitis. Almost all the patients in both groups had cough (100%). Fever was slightly higher in salbutamol group (71%) than epinephrine group (66.6%) while occurrence of dyspnea was slightly higher in epinephrine group than salbutamol group. Dysphagia was equally present in both of the groups (89%) characterized by reluctance to eat even semisolid food.

Table 3: Clinical presentation of patients

Signs & Symptoms	Group A	Group B
Cough	45(100%)	45 (100%)
Fever	32(71%)	30(66.6%)
Dyspnea	38(84.5%)	40(89%)
Dysphagia	40(89%)	40(89%)
Runny Nose	45(100%)	45(100%)

mRDAI scores and pulse oximetry of patients

The results of mRDAI and pulse oximetry are shown in Table 4. After administration of nebulized salbutamol, there was drastic and positive progress in the condition of patients indicated by lowering of respiration rate (from 69 to 55), lowering of mRDAI scores (from 18.2 to 6.1), and increase in oxygen saturation (from 92.6 to 96.4). Increase in heart rate was also observed.

After administration of nebulized epinephrine improvement is observed in the symptoms as indicated by lowering of respiration rate (from 66.8 to 49.7), lowering of mRDAI scores (from 17.8 to 7.5), and increase in oxygen saturation (from 93.2 to 97.1). Increase in heart rate was also observed.

Increase in heart rate by epinephrine was greater as compared to the nebulized salbutamol. Also, lowering of respiration rate was greater in epinephrine-administered patients. On the other hand, reduction in mRDAI scores was comparatively greater in salbutamol group when compared with epinephrine group.

Table 4: Comparison of response to therapy with nebulized salbutamol versus epinephrine

	Before Therapy			**After Therapy**		
Parameter Measured	**Group A Mean (SD)**	**Group B Mean (SD)**	***p* - value**	**Group A**	**Group B**	***p* - value**
Respiratory Rate (Breaths Per Min)	69 ± 7.2	66 ± 6.1	$p = 0.09$	55 ± 4.5	49 ± 4.9	$p = 0.001$
Heart Rate (Beats Per Min)	105 ± 4.8	102 ± 9.9	$p = 0.16$	130 ± 5.3	151 ± 5.9	$p = 0.001$
m-RDAI	18.2 ± 0.5	17.8 ± 2.7	$p = 0.33$	6.1 ± 1.3	7.5 ± 1.0	$p = 0.001$
Oxygen Saturation (%)	92.6 ± 3.4	93.2 ± 5.2	$p = 0.51$	96.4 ± 1.5	97.1 ± 0.8	$p = 0.007$

DISCUSSION

In young children viral bronchiolitis is a common disease. At present, the treatment of bronchiolitis consists of supportive therapy only. Early life viral bronchiolitis increases the risk of pediatric asthma development.[13] Urbanization seems to play an important role in disease prevalence.[14] In our study majority of infants suffering with bronchiolitis were from urban areas. mRDAI scores in our study were reduced in both of the cases. Nevertheless, a more reduction in mRDAI scores was observed in salbutamol-administered-patients than that of epinephrine administered-patients. However, another study conducted by Ainiune A.A. et al, revealed no difference between epinephrine and saline nebulization in terms of

mRDAI score reduction.[15] Pulse oximetry has been considered as one of the best technique to assess respiratory distress in children.[16] For oxygen saturation, pulse oximetry showed comparable results in both groups.

Our study demonstrates that nebulized epinephrine is more effective than nebulized salbutamol in reducing the respiratory rate. Similar results were found in another study, which showed a considerable improvement with the use of nebulized salbutamol and epinephrine therapy. The effectiveness of nebulized epinephrine was also found to be significantly higher than that of salbutamol.[11]

Our findings are consistent and in accordance with the findings as in other studies which determined that infants with bronchiolitis being treated with nebulized epinephrine/epinephrine in a hospital setting have more rapid relief from symptoms and earlier discharge than those treated with salbutamol.[8]

One proposed reason for superior effect of epinephrine may be because of it being the naturally occurring ligand of beta receptors. In contrast to epinephrine, salbutamol is a synthetic drug and hence not a natural ligand of beta receptors.[17]

Epinephrine has action on heart, increases heart rate and consequently respiration rate which can further facilitate gaseous exchange in bronchiolitis. Another positive effect of epinephrine owing to its action on alpha receptors in nasal blood vessels is their vasoconstriction reliving nasal congestion. Alpha mediated action may decrease mucous secretions and hence congestion. Salbutamol possesses no effect on alpha receptors.[18]

CONCLUSION

This study revealed that nebulized salbutamol and epinephrine both are almost equally effective in acute bronchiolitis. However, nebulized epinephrine showed more effects than salbutamol due to its actions on various receptor sites. Oxygen saturation is a positive outcome of bronchodilating effects of both of the drugs. Nevertheless, multicenter and controlled randomized studies are required to confirm and elaborate further the results in different settings on a large sample size.

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Disclosure of interest

The authors report no conflict of interest.

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