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Original Article

The Efficacy of Nebulized Epinephrine in Children with Acute Asthma: A Randomized Double-blind Trial

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Abstract:

Introduction: Countries like Bangladesh have seen an increase in the prevalence of bronchial asthma. The goal of the study was to compare the efficacy of nebulized salbutamol and nebulized epinephrine in treating children with acute asthma.

Objectives: To assess the clinical improvement of acute bronchial asthma in children following nebulization with salbutamol and epinephrine.

Methodology: This random, double-blind clinical trial was conducted in the paediatric department of the Mymensingh Medical College Hospital. Children of either sex with clinical features of acute exacerbation of asthma, an asthma score >5 to 11, an age range from 6 to 12 years, and the ability to measure peak expiratory flow rate (PEFR) were enrolled in this study. Outcomes were observed by measuring PEFR, respiratory rate, pulse rate, and SaO2 and also by determining asthma scores at 15, 35, 55, and 90 min after nebulization at a regular interval at 0, 20, 40, and 60 min. Differences from the base line and differences between both groups were observed.

Results: A total of 56 patients with acute asthma were enrolled in this study. Among them, 27 children were in the salbutamol group, and 29 patients were in the epinephrine group. Among baseline characteristics, there was no statistically significant difference ($p > 0.05$) between the two groups. Asthma score and respiratory rate decreased more in the salbutamol group with time after nebulization, but no statistically significant differences existed for the follow-up at 15, 35, and 55 minutes. A statistically significant increase in asthma score and respiratory rate was seen at 90 minutes of treatment in the salbutamol group. On the other hand, percent of predicted PEFR and SpO_2 increased with time in both groups, and no statistically significant differences existed except for SpO_2 at 35 min of follow-up in the salbutamol group. The epinephrine-treated group had a higher incidence of side effects as compared with the salbutamol group, but there was no statistically significant difference.

Conclusion: Based on this study, in the treatment of asthmatic children with a mild to moderate exacerbation, both nebulized epinephrine and nebulized salbutamol were effective when given in addition to oral steroids.

Keywords: Nebulized epinephrine, nebulized salbutamol, children, acute asthma

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Introduction:

Asthma is a chronic inflammatory disorder causing hyper-responsiveness of airways to certain stimuli resulting in recurrent variable airflow limitation, at least partly reversible, presenting as wheezing, breathlessness chest tightness and coughing.[1]

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It is common in people of all age group. According to World Health Organization (WHO), Asthma affects an estimated 300 million individuals worldwide. The prevalence of asthma is increasing, especially in children. The World Health Organization (WHO) has estimated that 250,000 asthma fatalities are reported globally each year, along with a loss of 15 million disability-adjusted life-years. Asthma is responsible for about 500,000 hospital admissions each year (34.6% of those patients are 18 years of age or younger).[2] Asthma prevalence in the USA grew from 1980 to 1996 but reached a plateau in 2007 at 9.1% of children (6.7 million).[3] According to the first national asthma prevalence study (NAPS) in Bangladesh about 7 million people (5.2%) suffering from current asthma, more than 90% of whom do not take modern treatment.

There are several clinical practice guidelines that describe the treatment protocol of acute asthma.[4] Most recommend inhaled salbutamol (albuterol) as the mainstay of emergency bronchodilator treatments.[5, 6] Different first-line remedies for severe acute asthma encompass nebulized salbutamol and inhaled corticosteroids.[7] Intravenous magnesium sulfate and parenteral epinephrine are second-line treatments for severe, life-threatening asthma.[8, 9] Finally, when indicated, respiratory support through non-invasive ventilation[10] or endotracheal intubation can be considered. Standard first-line therapies are sufficient for most patients, with only the rare patient requiring intubation.[11]

Nonetheless, there are patients whose presentations are so severe that they fail to respond to standard therapy. For these patients, options are confined. Nebulized epinephrine, which has long been used in emergency rooms to treat upper respiratory infections like croup and lower airway inflammation in bronchiolitis, is one such alternative.[12] However its role in the management of severe acute asthma is unclear.[13] It's mechanisms of action for the reduction of upper airway edema are postulated to include the potent vaso-constrictive effect (α1 effect) as well as decreased mucous production, reduced microvascular leakage (therefore lowering edema), and enhanced mucocilliary clearance. [14]

Another name for epinephrine is "powerful bronchodilator" secondary to its β -receptor agonist effect making it a beneficial agent for the remedy of acute asthma exacerbations. In some facilities, epinephrine is still provided parenterally via IV or subcutaneous injection to treat severe asthma emergencies.[9] Epinephrine, however, has well-described adverse effects which may include chest pain, myocardial ischemia, cardiac arrhythmia, severe hypertension and tissue ischemia, particularly when administered intravenously, leading some authors to speculate that the nebulized preparation may be an equipotent but safer method of using epinephrine.[9, 15, 16]

Several studies have all documented increases in pulmonary function and clinical status for nebulized epinephrine but not all were statistically different from salbutamol. Numerous publications have concluded that nebulized epinephrine is equally efficacious and safe as nebulized salbutamol for the treatment of acute severe asthma because side effects were comparable across groups receiving either salbutamol or epinephrine.[17, 18] In a meta-analysis of randomized studies comparing nebulized epinephrine and beta-agonists in the initial treatment of acute asthma, patients who received epinephrine compared to those who received beta-agonists reported a non-significant improvement in pulmonary function.[19] It should be emphasized that no clinical research was found in the literature that explored the impact of nebulized epinephrine in patients who did not get better after receiving first salbutamol treatment. Finally other dose response evidence suggests that while compared with salbutamol, epinephrine is an effective bronchodilator and its effects are less prolonged.[20]

In addition to bronchospasm, airway edema and mucous production are known to be

pathophysiologic factors that cause severe asthma. It's probable that airway edema may predominate in certain patients with severe acute asthma, adding to their respiratory distress. They may better respond to nebulized epinephrine than to nebulized salbutamol or they may respond to nebulized epinephrine regardless of failure to respond to aggressive β2-agonist therapy. Eventually there is evolving proof that genetic variation in the β receptor impacts bronchodilator response to each short and long acting β2-agonist drugs.[21] Bronchial asthma has been showing increasing trend in countries like Bangladesh, which may be amenable to the Hygiene theory focusing on isolation of the children from environmental pollutions making them vulnerable to immunological reaction to many environmental allergen. Because of its persistent nature, childhood asthma consequences in a massive financial burden on households and health system. Considering the financial and technical limitations of health care delivery system of our country especially providing emergency care, safe, available, cost effective treatment guideline for treating common conditions like acute bronchial asthma is needed. More recent work in bronchiolitis has demonstrated the superiority of nebulized epinephrine than nebulized salbutamol. There are limited studies to evaluate the efficacy of nebulized epinephrine in admitted children with acute exacerbation of asthma but the theoretical advantages of epinephrine in reducing airway mucosal edema. The purpose of this study was to compare the efficacy of nebulized epinephrine with nebulized salbutamol among children having acute asthma.

Materials and Methods

This randomized double-blind clinical trial was conducted in Mymensingh Medical College Hospital from October 2016 to May 2017. Children with acute asthma were included, but those with cardiac, renal or hepatic dysfunction, severe asthma, or adverse reactions to inhaled epinephrine were excluded. Materials and instruments include salbutamol respiratory solution containing 5mg of salbutamol per ml, injection adrenaline (1:1000), normal saline, nebulizer with face mask, pulse oximeter, bathroom scale, stadiometer and Peak Flow Meter. Double blinding was conducted by randomly distributing 60 sets of identical vials (each set containing 4 vials) with the same label number in each set. Inhaled drugs were taken from the pharmacist and handed over to the treating physician. Code numbers were preserved by the pharmacist. The study included 70 patients who fulfilled the criteria of acute exacerbation of bronchial asthma. Out of 70, 4 were lack of parental consent, 3 absconded after first nebulization, and 3 developed severe progressive respiratory distress. 56 patients were enrolled in the study, with 27 in the salbutamol group and 29 in the epinephrine group. Data collection formats were filled up, and objective measurement of airway obstruction was recorded with a peak flow meter. Patients were given nebulization with study medications at 0, 20, 40 and 60 min, and oral prednisolone 1mg/kg and supplemental O2 to maintain O2 saturation >92%. Patients were followed up in terms of symptomatic improvement and clinical improvement with improvement of PEFR at 15, 35, 55 and 90 min. Statistical analyses were conducted using SPSS version 21.0 for Windows, using mean values, frequencies, percentages, Chi-square test, Student t-test/unpaired t-test, and P values <0.05 was considered as statistically significant. The research protocol was accepted by the Ethical Committee of Mymensingh Medical College and informed written consent was obtained from each patient's guardian.

Operational definitions:

Asthma: Asthma is a diverse disease that is typically characterized by chronic airway inflammation. It is also defined by a history of respiratory symptoms such as wheezing, shortness of breath, chest tightness, and coughing that fluctuate in intensity over time, along with varying expiratory airflow limitations.[22]

Acute asthma: Loss of control of any class or variant of asthma having asthma score greater than 5.[22]

Asthma scores for 6-12 years old children:

	Asthma Scoring		
Variable Points	**1 Point**	**2 Point**	**3 Point**
Respiratory rate	≤ 27	28-30	≥ 31
O_2 saturation (%)	> 95 on room air	90–95 on room air	< 90 on room air or with supplemental oxygen
Wheeze	Normal or end-expiratory wheeze	Expiratory wheeze	Inspiratory and expiratory wheeze, diminished breath sounds, or both
Retractions	None or intercostals	Intercostal and substernal	Intercostal, substernal, and supraclavicular
Dyspnea	Speaks in sentences or coos and babbles	Speaks in partial sentences or utters short cries	Speaks in single words or short phrases or grunts

(Kelly et al. 2000)

Dose of epinephrine nebulization:
Epinephrine was administered as 0.03 ml/Kg of 0.1% epinephrine (1mg/ml) to a maximum of 1ml, made up to 4 ml with normal saline.[23]

Dose of salbutamol nebulization:
Salbutamol was administered at 0.15 mg/Kg (0.03 ml/Kg) of 5-mg/ml solution (max.1mL) made up to 4 mL with normal saline.[23]

Results
This experimental study compared the effectiveness of nebulized epinephrine with nebulized salbutamol in managing acute bronchial asthma in 56 children. The mean age difference between the two groups was no longer statistically significant, and the majority of patients were male. The mean age of diagnosis of asthma was 86.0±18.4 months, the average time spent of asthma was 17.0±10.1 months, hospital admissions were 1.4±0.6 times/year, and the mean asthma score was 9.9±1.8 in Salbutamol group. The difference had no statistically significant ($p>0.05$) between two groups (Table I).

Table I: Distribution of the studied patients according to base line clinical characteristics

Baseline characteristics	Salbutamol (n=27)	Epinephrine (n=29)	P value
Mean age (years)	8.5 (±1.7)	8.3 (±1.6)	0.703
Mean weight (Kg)	24.2 (±6.1)	26.2 (±6.8)	0.232
Mean height (cm)	117.8 (±7.8)	117.4 (±8.0)	0.876
Age at diagnosis of asthma (months)	86.0(±18.4)	85.6(±17.0)	0.937
Duration of asthma (months)	17.0(±10.1)	16.4(±8.9)	0.796
Number of attack per year	3.6 (±1.2)	4.03 (±0.87)	0.094
Number of hospital admission/year	1.4(±0.6)	1.6(±0.6)	0.407
Asthma score	9.9(±1.8)	9.7(±1.9)	0.857
SpO_2 (%)	92.8(±2.4)	92.9(±2.4)	0.855
Pulse rate (/min)	111.0(±9.0)	110.6(±9.5)	0.857
Respiratory rate (/min)	34.2(±5.0)	34.7(±5.0)	0.748
Peak expiratory flow rate (L/min)	102.0(±25.0)	106.4(±29.5)	0.550

Values of quantitative variables are expressed as mean (standard deviation).
P value reached from unpaired t-test.

Patients with history of asthma, smoker, oral bronchodilator, inhaled bronchodilator, and inhaled steroid were more likely to take salbutamol than epinephrine, but the differences were statistically insignificant. Regarding presenting symptoms, this study confirmed that wheeze, breathlessness, chest tightness and cough were present in all the patients in each group. No patient was found exhausted during presentation. 18 (66.6%) patients speak in phrases in Salbutamol group and 23 (79.3%) in Epinephrine group. Feeding difficulty was present in 12(44.4%) in salbutamol group and 13 (44.8%) in Epinephrine group. All of the children had been aware and no longer cyanosed at presentation. Twenty three (85.2%) patients become observed with expiratory wheeze in Salbutamol group and 24(82.8%) in Epinephrine

group. In 25 (92.6%) patients pulse was within 100-160/minute in Salbutamol group and in Epinephrine group it was in 26 (89.7%) patients. Most of the cases PEFR were 40-60% of predicted value, 88.9% in Salbutamol group and 79.3% in Epinephrine group. SpO_2 90-95 percent was found in 21 (77.8%) patients in Salbutamol group and also 21(72.4%) patients in Epinephrine group. Salbutamol and Epinephrine had similar baseline PEFR, percent predicted value, peak expiratory flow rate, percentage change from 0 minute, and percentage of predicted value. After 15 min of treatment, peak flow rate, percentage change from baseline, and percentage of predicted value were insignificant (Table II)

Table II: Mean PEFR status at different times

PEFR (l/min)	Salbutamol (n=27)	Epinephrine (n=29)	P value£
Predicted	196.7 (±45.4)	198.0 (±44.4)	0.917
Baseline (0 minute)	103.1 (±25.4)	104.3 (±28.3)	0.864
Mean % of predicted	52.4 (±4.5)	52.3 (±4.5)	0.975
15 min	114.4 (±28.2)	114.2 (±31.1)	0.980
Mean % change from 0 min	5.6 (±1.8)	4.9 (±1.3)	0.107
Mean % of predicted	58.0 (±3.8)	57.3 (±5.0)	0.533
35 min	130.6 (±32.3)	129.5 (±34.0)	0.904
Mean % change from 0 min	13.7 (±3.9)	12.7 (±2.4)	0.241
Mean % of predicted	66.1 (±3.5)	65.1 (±5.2)	0.384
55 min	141.7 (±35.7)	140.8 (±34.8)	0.917
Mean % change from 0 min	19.3 (±4.6)	18.6 (±3.3)	0.486
Mean % of predicted	71.7 (±3.8)	70.9 (±4.8)	0.512
90 min	148.9 (±36.8)	148.1 (±37.1)	0.935
Mean % change from 0 min	23.0 (±4.0)	22.3 (±3.5)	0.425
Mean % of predicted	75.4 (±3.4)	74.6 (±4.8)	0.461

£ P value reached from unpaired t-test. PEFR=Peak expiratory flow rate

Mean respiratory rate, mean pulse rate and mean SpO_2 at different time interval were found statistically insignificant ($p>0.05$) among salbutamol group and in epinephrine group. But mean asthma score was found statistically significant ($p<0.05$) among two groups. (Table III)

Table III: Comparison of respiratory rate, pulse rate, SpO_2 and asthma score at different period of time

Variables	Salbutamol (n=27)	Epinephrine (n=29)	P value£
Respiratory rate (/min)			
Baseline (0 minute)	34.3 (±5.0)	34.7 (±5.0)	0.748
At 15 min	32.7 (±4.2)	33.2 (±4.2)	0.659
At 35 min	30.0 (±3.9)	31.1 (±4.0)	0.288
At 55 min	27.4 (±3.5)	28.9 (±3.9)	0.132
At 90 min	26.0 (±3.4)	27.8 (±3.7)	0.061
Pulse rate (/ min)			
Baseline (0 minute)	111.0 (±9.0)	110.6 (±9.5)	0.857
At 15 min	105.6 (±11.4)	105.1 (±8.9)	0.847
At 35 min	98.4 (±11.0)	98.8 (±8.8)	0.875
At 55 min	90.7 (±10.5)	92.5 (±8.8)	0.483
At 90 min	86.9 (±8.1)	90.4 (±8.6)	0.126
SpO_2 (%)			
Baseline (0 minute)	92.8 (±2.4)	92.9 (±2.4)	0.855
At 15 min	94.0 (±2.2)	93.7 (±2.4)	0.624
At 35 min	95.0 (±2.1)	94.5 (±2.2)	0.313
At 55 min	96.3 (±1.9)	95.7 (±2.5)	0.278
At 90 min	97.0 (±1.7)	96.3 (±2.4)	0.223
Asthma score			
Baseline (0 minute)	9.8 (±1.8)	9.7 (±1.9)	0.857
At 15 min	8.8 (±2.4)	8.8 (±2.5)	0.973
At 35 min	7.7 (±2.5)	8.5 (±2.7)	0.262
At 55 min	6.6 (±1.8)	7.2 (±2.1)	0.244
At 90 min	6.0 (±1.7)	6.9 (±1.9)	0.057

£ P value reached from unpaired t-test.

In both groups outcomes were measured by measuring the changes from baseline values. Asthma score and respiratory rate decreased with time after nebulization in both groups. More decrease was seen in salbutamol group but the differences were statistically insignificant for the follow up at 15, 35 and 55 min. Statistically significant more decrease of Asthma score (MD, 1.02; 95% CI, 0.139 to1.90) and respiratory rate (MD, 1.40; 95% CI, 0.16 to 2.64) were seen at 90 min of treatment in salbutamol group. On the other hands, percent of PEFR and SpO_2 increased with time in two groups, and the differences were statistically insignificant except SpO_2 at 35 min of follow up in salbutamol group where salbutamol group showed better response for increasing SpO_2 from base line (MD, -0.70; 95% CI, -1.37 to -0.03) (Table IV).

Table IV: Treatment comparison

Outcomes	Time	*Changes from baseline			P value
		Salbutamol group	Epinephrine group	Treatment difference	
		Mean (SD)	Mean (SD)	MD (95% CI)	
Asthma score	15	1.02 (±1.47)	0.93 (1.51)	0.09(-0.69,0.87)	0.863
	35	2.07 (±1.96)	1.21 (1.61)	0.86(-0.08,1.80)	0.075
	55	3.22 (±1.81)	2.52 (1.53)	0.70(-0.18,1.58)	0.119
	90	3.78 (±1.83)	2.76 (1.50)	1.02(0.139,1.90)	0.026
SpO_2 (%)	15	-1.15 (±1.13)	-0.72 (±0.88)	-0.43 (-0.96,0.10)	0.123
	35	-2.22 (±1.42)	-1.52 (±1.09)	-0.70 (-1.37,-0.03)	0.041
	55	-3.52 (±1.65)	-2.76 (±1.41)	-0.76 (-1.57,0.05)	0.068
	90	-4.15 (±1.66)	-3.34 (±1.42)	-0.81 (-1.62,0.002)	0.056
Respiratory rate (breaths/min)	15	1.56 (±1.45)	1.48 (±1.46)	0.08 (-0.68,0.84)	0.852
	35	4.30 (±2.15)	3.59 (±1.72)	0.71(-0.31,1.73)	0.176
	55	6.89 (±2.42)	5.79 (±1.95)	1.10 (-0.06,2.26)	0.067
	90	8.26 (±2.43)	6.86 (±2.28)	1.40 (0.16,2.64)	0.031
PEFR (%)	15	-5.64 (±1.83)	-4.94 (±1.34)	-0.70 (-1.55,0.15)	0.107
	35	-13.74 ± (3.87)	-12.73 (±2.37)	-1.01(-2.71,0.69)	0.241
	55	-19.33 (±4.62)	-18.58 (±3.28)	-0.75 (-2.86,1.36)	0.486
	90	-23.04 (±3.95)	-22.25 (±3.47)	-0.79 (-2.74,1.16)	0.425

Values of quantitative variables are expressed as mean (standard deviation)
SD=Standard deviation; MD=Mean difference, CI=Confidence interval
*Change was defined as the difference between baseline and treatment values.

Epinephrine had a higher incidence of side effects than salbutamol, with 13 (44.8%) having nasal symptoms and 29.6% having tremor (Table V). Hospital stay was more in epinephrine group as compared to the salbutamol group but the difference between these two groups was statistically insignificant.

Table V: Comparison of Adverse events

Adverse events*	Salbutamol (n=27)	Epinephrine (n=29)	P value
Pallor	04 (14.8)	07 (24.1)	0.380
Nausea	01 (3.7)	04 (13.8)	0.186
Tachycardia	01 (3.7)	04 (13.8)	0.186
Tremor	08 (29.6)	05 (17.2)	0.273
Others[#]	06 (22.2)	13 (44.8)	0.074

Values of qualitative variables are expressed as number (percentage)

*Adverse event happened at any time during the 90 minutes after administering of study drugs.
[#]others adverse events, including excess nasal discharge, cough, sneezing, stinging nostrils, sore throat, and agitation.

Discussion

With the aim of comparing the clinical improvement of children with acute asthma after nebulization with salbutamol and epinephrine, this randomized trial was specifically conducted to ascertain the changes in PEFR, asthma score, respiratory rate, and SpO2 in children before and after nebulization. In this study, a total of 56 patients who had acute asthma were included. Among them, 29 patients received epinephrine, and 27 minors received salbutamol. Age, sex, height, and weight did not differ statistically between the two groups ($p > 0.05$). A similar observation was made, according to earlier studies. [18, 23] In the present study, which was in line with the study by Plint et al.[24], there were no statistically significant differences in the duration of asthma, age at first diagnosis of asthma, baseline mean asthma score, mean peak expiratory flow rate, mean SaO2, mean pulse rate, or mean respiratory rate between the salbutamol and epinephrine groups.

The number of hospital admission was 1 to 2 time/year in both Salbutamol group andEpinephrine group in a study by Plint et al.[24] which was also consistent with the present study. The findings of Langley et al. [25], which were likewise consistent with the current study, showed that there was no difference in oxygen

saturation between the salbutamol group and the epinephrine group. In a study by Haqq et al.[26], which was also compatible with the current study, the baseline pulse rate ranged between 100 and 160 beats per minute, and the PEFR was 40 to 60 percent of the expected value.

Most of the patients in this study had a family history of smoking and asthma in both groups, and there were no statistically significant differences between the two groups ($p > 0.05$), which was in line with a prior study by Plint et al.[24].

All of the patients in both groups of this trial had wheezing, dyspnea, chest tightness, and coughing, which was consistent with earlier research.[26] In the Salbutamol group, 18 (66.6%) and 23 (79.3%) of the patients in Epinephrine group spoke in short, phrased sentences. Only one patient from the experimental group and two from the control group were determined to be worn out during presentation, according to Haqq et al.[26] While being presented, no patient in the current study was determined to be worn out. They also noted that, in the study group, 28 patients spoke in phrases and two in words, compared to 26 patients in the control group who spoke in phrases and four in words, findings that were not dissimilar from those of the current study. [26] In the current trial, which was equivalent to the prior study, feeding trouble was present in 12 (44.4%) of the salbutamol group and 13 (44.8%) of the epinephrine group. [26]

In this study, it was shown that the baseline PEFR (L/min) values for the two groups, both in terms of absolute value and percent anticipated, were very similar. The mean PEFR, mean percent change from 0 minutes (baseline), and mean percent of anticipated value for the Salbutamol group were higher at 15, 35, 55, and 90 minutes after nebulization, but the differences were not statistically significant ($p > 0.05$) between the two groups. After every nebulization at 15, 35, 55, and 90 minutes in each group, the peak expiratory flow (PEF) considerably increased (p 0.05). Peak expiratory flow (PEF) considerably increased in both groups, according to Adoun et al.[17]. Zeggwagh et al.[18] evaluated nebulized salbutamol and nebulized adrenaline in acute severe asthma and found that both groups saw a considerable rise in PEFR, but no statistically significant differences were seen between the two groups. The results of the earlier study are equivalent to those of this one.

The mean pulse rate and respiratory rate in this study decreased following nebulization in both groups, although there was no statistically significant difference between the two groups ($p>0.05$). Plint et al.[24] reported similar results, noting that both groups' respiratory rates and pulse rates decreased after nebulization.

In this study, the mean SpO2 increased in both groups following nebulization, although there was no statistically significant difference between the two groups ($p>0.05$).Similar results were previously noted by Plint et al.[24], who noted a rise in SpO2 following nebulization in both groups, but more so in the salbutamol group, which is also similar to the current study.

In this study, the mean asthma score decreased in two groups after nebulization. Asthma score was higher in Epinephrine group but the differences were statistically insignificant ($p<0.05$) between two groups. This indicates that acute Asthma was more improved in Salbutamol group. Plint et al.[24] observed greater pulmonary index score in epinephrine group after nebulization which also indicate that the improvement of acute asthma was more after nebulization with salbutamol. This was consistent with the present study.

In both groups outcomes were measures by measuring the changes from baseline values. Asthma score and respiratory rate decreased with time after nebulization in both groups. More decrease was seen in salbutamol group but the differences were statistically not significant for the follow up at 15, 35 and 55 min. Statistically significant more decrease of Asthma score (MD, 1.02; 95% CI, 0.139 to1.90) and respiratory rate (MD, 1.40; 95% CI, 0.16 to 2.64) were seen at 90 min of treatment in salbutamol group. Aside from SpO2 at 35 min of follow-up in the salbutamol group, where the salbutamol group showed better response for increasing SpO2 from baseline (MD, -0.70; 95% CI, -1.37 to -0.03), percent of predicted PEFR and SpO2 increased with time in both groups,

and the differences were not statistically significant. Plint et al.[24] reported similar findings and found that the salbutamol group significantly reduced respiratory rate and pulse rate. However, there was no statistically significant difference between the two groups, even though the salbutamol group showed a greater increase in SpO2 from baseline.

Regarding side effects including pallor, nausea, tachycardia, tremor, and others (excess nasal discharge, cough, sneezing, stinging nostrils, sore throat, and agitation), there was no discernible difference between treatment groups in this study. However, compared to the salbutamol group, the group treated with epinephrine experienced more side effects. Particularly, 6 (22.2%) participants in the salbutamol group and 13 (44.8%) patients in the epinephrine group both experienced nasal symptoms. Tremor occurred more frequently in the salbutamol group (29.6%) than in the epinephrine group (17.2%). When compared to the salbutamol group (3.7%), tachycardia was more prevalent in the epinephrine group (13.8%). Similar adverse effects were also noted by Plint et al. [24]. As for side effects such as pallor, nausea, tachycardia, and feeling tremor, there was no discernible difference between treatment groups in this area either. In contrast to the salbutamol group, the epinephrine-treated group much more frequently had various adverse symptoms (such as excessive or brownish nasal discharge, cough, sneezing, stinging nostrils, sore throat, and agitation) (p 0.001). Nasal symptoms were present in 21 patients treated with epinephrine versus 10 patients treated with salbutamol. One serious side effect, which Langley et al. [25] determined was unrelated to the study drug and happened in a kid taking salbutamol, was a fever higher than 39°C (rectal). Additionally, they discovered that children receiving epinephrine experienced pallor and tremors more frequently than those receiving salbutamol. In their study, pallor was identified in 19.40% (6/31) of the epinephrine group and 6.50% (2/31) of the salbutamol group. Tremor was found in 19.40% (6/31) of the epinephrine group and 9.70% (3/31) of the salbutamol group. Vomiting happened in 19.4% (6/31) of the epinephrine recipients and in 25.8% (8/31) of the salbutamol recipients. However, compared to the current study, these differences were not statistically significant.

Conclusion

Based on the study, it could be concluded that in the management of children with asthma having a mild to moderate exacerbation, both nebulized epinephrine and nebulized salbutamol are effective when given in addition to oral steroids. Moreover, the improvement of acute asthma was greater after nebulization with salbutamol, and side effects were greater after nebulization with epinephrine, although no statistical difference existed.

Conflict of interest: Regarding this study, there were no competing interests.

Limitation of the study

The present study has some limitations, including a limited sample size and a short study duration at one particular hospital in Mymensingh.

Recommendation

To employ nebulized epinephrine in children with acute asthma, additional studies might be conducted at other hospitals in Bangladesh with a large sample size and over an extended period.

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