Original Article

Iran J Pediatr
Jun 2012; Vol 22 (No 2), Pp: 241-244

Comparison of Epinephrine to Salbutamol in Acute Bronchiolitis

Mohammad-Reza Modaressi*[1,2], MD; Asadola Asadian[3], MD; Jamal Faghihinia[1], MD; Mehrshad Arashpour[1], and Firoozeh Mousavinasab[1], MD, PhD

1. Child Health Promotion Research Center, Isfahan University of Medical Sciences, Isfahan, Iran
2. Pediatric Infectious Diseases Research Center, Tehran University of Medical Sciences, Tehran, Iran
3. Department of Internal Medicine, Isfahan University of Medical Sciences, Isfahan, Iran

Received: *Dec 12, 2010*; Final Revision: *Apr 13, 2011*; Accepted: *Jun 20, 2011*

Abstract

Objective: An appropriate treatment of acute viral bronchiolitis can reduce the symptoms, hospitalization duration and exorbitant costs which is imposed on the families and insurance organizations. This study was conducted to determine the efficacy of epinephrine in comparison with salbutamol in the treatment of the disease.

Methods: Forty infants aged one month to 2 years with acute bronchiolitis in Amin and Al-Zahra hospitals, during 2008, were enrolled in this study. The participants were randomized in two treatment groups to receive epinephrine 0.1 ml/kg or salbutamol 0.15 mg/kg. Three doses of each medication were prescribed at intervals of 20 minutes and continued every 10 minutes after the third dose. The patients in both groups were monitored and rated by RDAI, number of the hospitalized days in the hospital, level of oxygen saturation and vital signs.

Findings: Mean hospitalization duration was 3.3±1.1 and 3±0.9 in the patients receiving salbutamol and epinephrine, respectively (P=0.03). There was a significant difference in assessing RDAI index between the two groups (P=0.03). There were no differences in SPO2, PR, or RR variables in the studied intervals in both groups (P>0.05).

Conclusion: Regarding the effect of epinephrine on reduction of hospitalization duration and the RDAI index in patients with acute bronchiolitis, it seems that using epinephrine instead of salbutamol could be more effective in the management of the disease.

Iranian Journal of Pediatrics, Volume 22 (Number 2), June 2012, Pages: 241-244

Key Words: Bronchiolitis; Epinephrine; Salbutamol; Hospitalization; Upper Respiratory Infections

Introduction

Acute viral bronchiolitis is a common lower respiratory tract disease in infants due to obstruction caused by inflammation of the tiny airways. Almost all the infants up to 2 years old have been infected by this disease. Evidences show that infection with respiratory syncytial virus (RSV) is the cause of 50 to 80 thousand hospitalizations annually in children under one year old in the United States [1]. Bronchiolitis is considered as 60 percent of all the cases of lower respiratory infections in the early childhood and during the first year of life [2] as well as 32 percent

*** Corresponding Author;**
Address: Children's Medical Center; Dr Gharib St, Tehran, Iran
E-mail: modaresi@med.mui.ac.ir

© 2012 by Pediatrics Center of Excellence, Children's Medical Center, Tehran University of Medical Sciences, All rights reserved.

of hospitalized cases due to lower respiratory diseases in this age group [3]. A systemic review from several randomized clinical trials on the effectiveness of beta-agonists suggested that these medications have short-term and less effect on the recovery of this disease [4].

Its treatment by epinephrine was first suggested in 1987 by Wohl and Chernick [5] and since then, many studies and review articles have been published on this treatment method [6-8]. In the study of Bertrand et al (2001) [9], in infants aged 1 to 12 months, mean duration of the hospitalization was 4.1 days in the epinephrine group and 5.2 days in the salbutamol group. Langley et al in 2005[10], in a study on infants aged between 6 weeks to 2 years showed that the efficacy of epinephrine had been better than salbutamol and caused earlier discharge of the children from the hospital in the epinephrine group; also other studies demonstrated that the efficacy of salbutamol and epinephrine was similar [11-13]. In other studies, the researchers announced that epinephrine led to earlier discharge of the patients from the hospital in comparison with salbutamol [14-16].

In a meta-analysis study by Hartling et al [7], the researchers found that in short-term treatment, epinephrine is preferred to salbutamol, but still there were no sufficient evidences available to confirm this theory conclusively. An appropriate treatment of this phenomenon can reduce the symptoms, hospitalization duration and exorbitant costs which is imposed on the families and insurance organizations. Several conducted studies so far failed to prove the preference of epinephrine to salbutamol in treatment of bronchiolitis.

Therefore, this study was conducted to determine the efficacy of epinephrine in comparison with salbutamol on the treatment of the acute viral bronchiolitis.

Subjects and Methods

This study was done on 40 children >2 years old during winter 2008 to spring 2008 in Isfahan, Iran. The target population included 1 month to 2 year old infants admitted to Amin and Al-Zahra hospitals and diagnosed as acute bronchiolitis by the ICU or ward physicians.

Children with history of two or more respiratory distresses, wheezing, family history of asthma, those who suffered from chronic pulmonary heart disease, suspected heart disease, bronchomalacia, previous use of bronchodilator and glucocorticoids, those treated with monoamino oxydase inhibitors (MAOI), tachycardia >180/min, and respiratory rate >100/min,[4,10-16] were not included in the study. Studied population was selected by nonrandomized simple sampling method and the children were placed in one of the two groups by the random allocation software. The first group was given one dose of 0.1 ml/kg l-epinephrine in a concentration of 1.10000 and the other group received salbutamol 0.15 mg/kg at a minimum volume of 1 mg mixed with normal saline. Each volume was 3 cc, which was nebulized using oxygen flow 8 liters per minute. Three doses of each medication at intervals of 20 minutes were prescribed; 10 minutes after the third dose, the patient was rated again by Respiratory Distress Assessment Instrument (RDAI), the most commonly used tool for severity assessment. During this medication, no other medications like antibiotics and steroids were prescribed for them. In infants with fever, solely fluid therapy was used. Thereafter, the patient was monitored and re-rated by RDAI. We repeated this procedure with RDAI daily. The level of oxygen saturation was measured on admission and daily after each prescription through pulse oximetry (SPO2). Vital signs were recorded completely at admission and daily, pulse rate (PR) and respiratory rate (RR) after each prescription and after the last prescription for 3 hours.

The other studied variable was the number of the days in the hospital. This variable was measured in all cases that were given medication for bronchiolitis, patients who received oxygen because of bronchiolitis or underwent intravenous fluid therapy. This was a triple-blind study, i.e. the patient, physician and statistical analyst were unaware of the treatment.

The data were analyzed using Software SPSS 16 and $P<0.05$ was considered as significant.

Table1: Mean (standard deviation) of RDAI in the studied groups

	RDAI	
	Salbutamol	Epinephrine
0 min	14.3 ± 1.8	12.8 ± 2.4
10 min	12.6 ± 1.4	10.6 ± 2.1
180 min	10 ± 1.5	8.2 ± 2.2
1st day	7.3 ± 2	4.5 ± 1.5
2nd day	4.3 ± 2.6	3.1 ± 2.2
3rd day	3 ± 2	1.8 ± 2.4
4th day	1.3 ± 1.3	0
5th day	0	0
***P* value** (Between groups)	0.02	

RDAI: Respiratory distress assessment instrument

Findings

In this study 40 patients, consisting of 20 (50%) males and 20 (50%) females, were studied. The mean age of the patients was 387±207.5 days (range 52-710 days). Mean age of the patients in salbutamol group was 409.6±207.6 days and in epinephrine group 364±210.4 days (*P*=0.5). Mean and standard deviation of the patients' weight was 9449.4±2767.3 (range 4300 to 13650) gr. Mean and standard deviation of the patients' weight was 9871.2±2595.8 in patients receiving salbutamol and 9027.5±2933.7 in epinephrine group (*P*=0.3). Regarding the association of used medication type and hospital stay, the mean and standard deviation of the patients' hospitalization duration was 3.3±1.1; this was 3.7±1.1 with median of 4 (minimum 2 and maximum 4) in the patients receiving salbutamol and 3±0.9 with median of 3 (minimum 2 and maximum 4) in epinephrine patients (*P*=0.03). The mean and SD values of the obtained RDAI from ANOVA in repeated observations in the studied intervals in both groups are given in Table1 (*P*=0.02).

Discussion

The present study aimed to determine the effectiveness of nebulized epinephrine versus nebulized salbutamol in the treatment and successful discharge of acute bronchiolitis. The outcome of this study showed that there was a significant difference between hospitalization duration of the patients receiving epinephrine compared to those receiving salbutamol. In addition, there was a significant difference in assessing RDAI index between the two groups of patients.

To agree with the results of the present study, previous reports have found that the efficacy of epinephrine had been better than salbutamol and resulted in short-term clinical improvement and earlier discharge of the children from the hospital [9,10,14-16]. Also a meta-analysis study carried out by Hartling and colleagues (2003)[7], established that short-term treatment with epinephrine is preferred to salbutamol, but still there were no sufficient evidences available to verify this theory conclusively. In contrast, in some studies the researchers demonstrated that the effectiveness of salbutamol and epinephrine was similar[11-13], which is not in accordance with the present study. Walsh et al (2008) also showed that in children up to the 18th month of life, emergency department treatment of bronchiolitis with nebulized racemic albuterol led to more successful discharges than nebulized epinephrine[17].

To our knowledge, the present study is the first study in Iran that revealed the efficacy of nebulized epinephrine compared to nebulized salbutamol in the management of acute bronchiolitis. It is possible that the improvement has been related to the α-effect of the medication[16]. As a limitation and problem of the current study we could state the low sample size which was caused by the time and budget limitations. This might be a reason for discrepancies between our study with some other studies. Considering that the studied researches in this regard could not confirm the preference of using epinephrine instead of salbutamol, further

studies are needed with a larger sample size and more comprehensive level considering other relevant variables. A large number of multi-centered trials therefore are recommended to observe the efficacy of epinephrine compared to salbutamol and to capture clinically significant outcomes in patients with bronchiolitis.

Conclusion

The obtained results of the present study in consistence with a number of other investigations, showed that using epinephrine instead of salbutamol, in 1 month to 2 year old infants with acute bronchiolitis, might be an effective step in improving the disease regarding its effect on the reduction of the hospitalization duration and the RDAI index.

Acknowledgment

The authors acknowledge the assistance of the following: Mr Akbari for help with statistical analysis.

Conflict of Interest: The authors declare that they have no competing interests.

References

1. Goodman D. Bronchiolitis. In: Behrman. RE, Kliegman. RM, Jenson HB. Text Book of Pediatrics. 17th ed. Philadelphia: Saunders. 2004; Pp: 1415-7.
2. Wright AL, Taussig LM, Ray CG, et al. The Tucson Children's Respiratory Study II. Lower respiratory tract illness in the first year of life. *Am J Epidemiol* 1989;129(6):1232-46.
3. McConnochie KM, Roghmann KJ, Liptak GS. Hospitalization for lower respiratory tract illness in infants: variation in rates among counties in New York State and areas within Monroe County. *J Pediatr* 1995;126(2):220–9.
4. Kellner JD, Ohlsson A, Gadomski AM, et al. Bronchodilators for bronchiolitis. *Cochrane Database Syst Rev* 2000:CD001266.
5. Wohl ME, Chernick V. State of the art: bronchiolitis. *Am Rev Respir Dis* 1978;118(4): 759-81.
6. Hartling L, Wiebe N, Russell K, et al. A meta-analysis of randomized controlled trials evaluating the efficacy of epinephrine for the treatment of acute viral bronchiolitis. *Arch Pediatr Adolesc Med* 2003;157(10):957-64.
7. Hartling L, Wiebe N, Russell K, et al. Epinephrine for bronchiolitis. *Cochrane Database Syst Rev* 2004;(1):CD003123.
8. King VJ, Viswanathan M, Bordley WC, et al. Pharmacologic treatment of bronchiolitis in infants and children: a systematic review. *Arch Pediatr Adolesc Med* 2004;158(2):127-37.
9. Bertrand P, Aranibar H, Castro E, et al. Efficacy of nebulized epinephrine versus salbutamol in hospitalized infants with bronchiolitis. *Pediatr Pulmonol* 2001;31(4):284-8.
10. Langley JM, Smith MB, LeBlanc JC, et al. Racemic epinephrine compared to salbutamol in hospitalized young children with bronchiolitis, a randomized controlled clinical trial. *BMC Pediatr* 2005;5:7.
11. Ralston S, Hartenberger C, Anaya T, et al. Randomized, placebo-controlled trial of albuterol and epinephrine at equipotent Beta-2 agonist doses in acute bronchiolitis. *Pediatr Pulmonol* 2005;40(4):292-9.
12. Patel H, Platt RW, Pekeles GS, et al. A randomized, controlled trial of the effectiveness of nebulized therapy with epinephrine compared with albuterol and saline in infants hospitalized for acute viral bronchiolitis. *J Pediatr* 2002;141(6): 818-24.
13. Beck R, Elias N, Shoval S, et al. Computerized acoustic assessment of treatment efficacy of nebulized epinephrine and albuterol in RSV bronchiolitis. *BMC Pediatr* 2007; 7:22.
14. Sanchez I, De Koster J, Powell RE, et al. Effect of racemic epinephrine and salbutamol on clinical score and pulmonary mechanics in infants with bronchiolitis. *J Pediatr* 1993; 122(1):145-51.
15. Mull CC, Scarfone RJ, Ferri LR, et al. A randomized trial of nebulized epinephrine *vs* albuterol in the emergency department treatment of bronchiolitis. *Arch Pediatr Adolesc Med* 2004; 158(2):113-8.
16. Ray SM, Singh V. Comparison of nebulized adrenaline versus salbutamol in wheeze associated respiratory tract infection in infants. *Indian Pediatr* 2002;39(1):12-22.
17. Walsh P, Caldwell J, McQuillan K, et al. Comparison of Nebulized Epinephrine to Albuterol in Bronchiolitis. *Acad Emerg Med* 2008; 15(4):305-13