

Effect of treatment with subcutaneous epinephrine versus nebulized salbutamol on O₂ saturation and rate of admission in patients with bronchiolitis

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Abstract

Despite wide spread use of epinephrine β 2-agonists in infants with bronchiolitis since the late 1950s, the efficacy of these drugs remains unproven. The objective of the study is to determine the effective treatment with subcutaneous (s.c) epinephrine versus nebulized salbutamol on O₂ saturation and rate of admission to hospital in patients (age 2 years or less) with bronchiolitis. Single dose of epinephrine (0.01 mg/kg) has been used across various age groups of 2 years or less (maximum dose used was 0.15 mg) and no complications were reported suggesting that the dose is safe; however, the maximum safe dose cannot be interpreted from this study. The response to sc epinephrine in patients younger than 12 months was significantly better than in older patients, suggesting a useful role of s.c epinephrine in bronchiolitis in this age. The s.c epinephrine relieves clinical manifestations of respiratory distress (wheezing, chest retractions, flaring of alar nasi, cyanosis) and improves parameters of respiratory distress (oxygen saturation, respiratory rate) in infants treated for acute bronchiolitis with maximal effectiveness at 30-60 minute. For s.c epinephrine, every patient had his own disposable syringe; while for nebulized salbutamol, all patients share the same nebulizer. So that, s.c epinephrine may decrease the likelihood of transmission of infection between the patients. The s.c epinephrine reduces the admission rate (13%), compared to nebulized salbutamol (24%). The observation that peak action of s.c epinephrine occurs 30-60 minutes after administration suggests the need for caution in repetitive administration during this period.

Key words: Epinephrine, Salbutamol, Bronchiolitis

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Introduction

By age of 2 yr., 50% of children have been infected with bronchiolitis, with severe disease more common among infants aged 1–3 months. Ventilation/perfusion mismatching is by far the commonest cause of hypoxemia in pulmonary disease.

Despite wide spread use of neb. β_2 -agonists in infants with bronchiolitis since the late 1950s, the efficacy of these drugs remains unproven. Less than 20% of a single dose of Sal. is absorbed when administered by nebulization; peak plasma concentrations were reached within 0.5 an hour; the effect usually last approximately 1-2 hours. Statistical improvement in clinical scoring systems seen with the use of beta agonists is not always clinically significant, and desaturations have been reported after Sal. nebulization.

Epi. hydrochloride is being used with increasing frequency in bronchiolitis. S.C administration of it may produce its effects within 10 minutes and maximal effects in about 30 minutes.

Methods

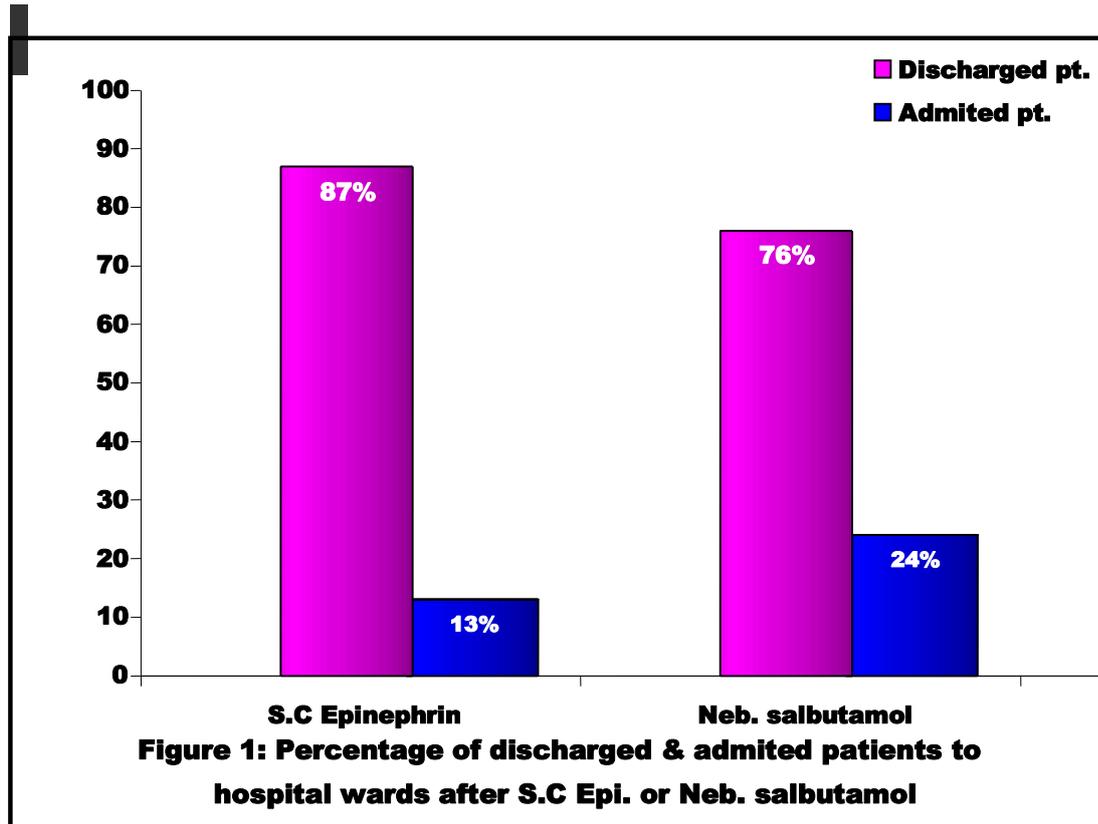
The aim of the study is to determine the effect of treatment with S.C Epi. versus neb. Sal. on O₂ saturation & rate of admission to hospital in patients (age 2 years or less) with bronchiolitis. Two hundred patients less than 2 years of age with a clinical diagnosis of bronchiolitis were enrolled in a prospective, randomized and controlled study to receive either S.C Epi. (n=100) or neb. 0.5% Sal. sulfate (n=100).

This study was done in the E.D of Al-Hussain pediatric hospital in Al Diwanya city. Study enrollment occurred in winter season from the first of September 2014 to the first of March 2015.

Results

There is high significant improvement in O₂ saturation at 30 and 60 min., improvement in respiratory rate at 60 and 90 min., heart rate improvement at 60 min. and better improvement in the wheeze, chest retraction, nasal flaring, and reduced rate of admission to hospital in patient who were treated with S.C Epi. than those who were treated with Neb. Sal.

Table (1) show the effects of S.C Epi. and Neb. Sal. on oxygen saturation in patients below 2 years with bronchiolitis.



Time(minute)	Mode of treatment	Oxygen saturation(oximetry)Mean± Std.dev.	P. value
0	Neb. Sal.	90.78±3.8	> 0.05
	S.C Epi.	90.32±3	
30	Neb. Sal.	89.43±5.25	< 0.01
	S.C Epi.	92.21±3.38	
60	Neb. Sal.	90.12±4.27	< 0.05
	S.C Epi.	91.54±4.31	
90	Neb. Sal.	91.11±4.36	> 0.05
	S.C Epi.	92±3.92	

Table 1.

The effects of S.C Epi. and Neb. Sal. on oxygen saturation in patients below 2 years of age with bronchiolitis

Controversy exists surrounding the use of bronchodilators for bronchiolitis, and Epi. hydrochloride is being used with increasing frequency in this group (6, 7).

The results of this study favored the use of S.C Epi. in comparison with Neb. Sal. for treating patients with bronchiolitis regarding the studied variables. For the O₂ saturation, it was highly significant at 30 and significant at 60 min. (table 1); these results are similar to the results of studies done in Turkey (8) and Australia (9, 10). For the respiratory rate it was significant at 60 and highly significant at 90 min. and is similar to the results of an Australian study (11). For the heart rate it was highly significant at 60 min. and is similar to the results of a study in Turkey (7), and Canada (8). To explain the results mentioned above, we should remember the following: α - adrenoceptors are present in the vascular smooth muscles and the stimulation of it result in contraction of bronchial arterioles (4); β_2 - adrenoceptors are present in the bronchial smooth muscles and the stimulation of these receptors result in relaxation of these muscles (4); Infants below 2 years of age (especially below 6 months) had lower β_2 - adrenoceptors density than older children (12, 13); β_1 - adrenoceptors are present in the heart muscle and the stimulation of these receptors increase the heart rate (14- 19); Small dose of Epi. Hydrochloride (0.01 mL/kg of 1:1000) stimulates α - adrenoceptors (3); Large dose of Epi. Hydrochloride (more than 0.01 mL/kg of a 1:1000) stimulates β - adrenoceptors (3); Sal. stimulates β - adrenoceptors (3).

So that, the small doses of Epi. hydrochloride stimulates α -receptors. As a result, the drug may reverse vasodilatation, congestion and edema produced by this mediator. Subsequent improvement in O₂ saturation, respiratory rate, wheeze, chest retraction and flaring of alar nasi will occur. There is no increment in the heart rate when we use a small dose of Epi. because only large dose can stimulate β_1 receptors (3). The improvement in heart rate after 60 min. of S.C Epi. may be attributed to the improvement in the clinical condition of the patient and relief of the distressing factors and not to the direct effect of S.C Epi. Sal. stimulates β_1 adrenoceptors in the heart; therefore, increase the heart rate and also stimulates β_2 adrenoceptors resulting in relaxation of smooth muscles from the trachea to the terminal bronchial tree (20). The adverse effects of Sal. are nasal congestion increase in sputum production, dyspnea, and some vasodilating effect on peripheral vasculature (which decreases diastolic blood pressure), all decrease the O₂ saturation (ventilation/perfusion mismatching) (21). Eighty-seven percent of patients treated with S.C Epi. are discharged well from E.D; compared with seventy-six percent of patients treated with Neb. Sal. One patient (1%) develops central cyanosis after Neb. Sal.

Recommendation: Data on optimum dose of S.C Epi. with regard to efficacy and safety is very limited; so that, more studies are needed in this field.

Competing interests

The author declares that there is no conflict of interest.

References

1. Campbell, A.G.M. Respiratory. In: Campbell, A.G. and Mc Intosh, N. (eds). Forfar and Arneil's Textbook of Pediatrics, 6thed, Churchill Livingstone, 2003:778-780.
2. Pickering, L.K. and Snyder, J.D. Respiratory. In: Behrman, R.E. ; Kliegman, R.M. and Jenson, H.B., (eds). Nelson Text book of Pediatrics, 18th ed. Philadelphia, W.B. Saunders Company, 2007; 321:1773-1777.
3. WHO drug information full text, 1999; 1176-1223.
4. Bertram G. Katzung. Organ system effects of sympathomimetic drugs. In: Basic and clinical pharmacology, 9th ed., McGraw-Hill companies, 2004:129-132.
5. Stokes GM, Milner AD, Hodeges IGC, et al. Nebulised therapy in acute severe bronchiolitis in infancy. Arch Dis Child 2006; 58:279-82.
6. MullCC, Scarfone RJ, Ferri LR, et al. Epi. in the E.D treatment of bronchiolitis. Pediatr Res. 2002; 51:100.
7. Abul-Ainine A, Luyt D. Short term effects of Epi. in bronchiolitis [in Turkey]: a randomized controlled trial. Arch Dis Child. 2002; 86:276-279.
8. Ray SM, Singh V. Comparison of S.C Epi. versus neb. Sal. in wheeze associated respiratory tract infection in infants. Indian Pediatr. 2002; 39:12-22
9. Arnold HM. Distribution of adrenoceptors in the body. British Journal of Pharmacology. 2002; 135:1415-1424.
10. Denny FW, Collier AM, Henderson FW, et al. The epidemiology of bronchiolitis. Pediatr 2005; 11:234–236.
11. Christian Schumann. Differences in the survival rate between premenopausal and postmenopausal women with lung cancer: US SEER database. American Journal of BioMedicine 2014;2:315–322.
12. Hall CB, Douglas RG Jr, Geiman JM, et al. Nosocomial respiratory syncytial virus infections. N Engl J Med 1975; 293:1343–1346.
13. Peter Fritz, Anna Murphy, Rowena Clayton, et al. In: Evidence-Based Practice Guideline for the Management of Bronchiolitis in Infants and Children, 2006; 5:20-21.15. Schering Corporation. Proventil (Sal. sulfate) 0.5% solution for inhalation prescribing information (dated 1998 Oct). In: Physicians' desk reference. 53rd ed. Montvale, NJ: Medical Economics Company Inc; 1999; 2872-2873.
14. Smith SR, Ryder C, Kendall MJ et al. Cardiovascular and biochemical responses to neb. Sal. in normal subjects. Br J Clin Pharmacol. 2006; 18:641-644.
15. Barr FE, Patel NR, Newth CJL. The pharmacologic mechanism by which Epi. reduces airway obstruction in respiratory syncytial virus-associated bronchiolitis. J Pediatr. 2000; 16:699–700.
16. Guerguerian AM, Gauthier M, Lebel MH, et al. Ribavirin in ventilated respiratory syncytial virus bronchiolitis. A randomized, placebo-controlled trial. Am J Respir Crit Care Med 1999; 160:829–834.

17. Ahmed MA, Al-Hayali SM, Yousif NG. Radiographic manifestations of inoperable primary bronchogenic carcinoma. *American Journal of BioMedicine* 2018;6(8):507-516.
18. Rodriguez WJ, Gruber WC, Groothuis JR, et al. Respiratory syncytial virus immune globulin treatment of RSV lower respiratory tract infection in previously healthy children. *Pediatrics* 1997; 100:937-942.
19. Kellner JD, Ohlsson A, Gadomski AM, Wang EE. Efficacy of beta agonists in bronchiolitis: a meta-analysis. *Arch Pediatr Adolesc Med.* 1996; 150:1166-1172.
20. Holen Ramani, Lawrence Nofer, Anurag Goepfert, Merton A Bernfield, Ralph M. Sanderson. Syndecan-1 attenuates lung injury following endotoxemia by lessens systemic and pulmonary TNF α /ADAM-17. *American Journal of BioMedicine* 2015;3: 597-618.
21. Shete S, Kim Q, Wu X, Wang X, Dong Q. IL-32 promotes lung cancer cell invasion and metastasis through p38 MAPK signaling pathway: Cancer-associated fibroblast-derived. *American Journal of BioMedicine* 2018;6(10):685-697.