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Original Research Article

Comparative Study on Adrenaline with 3% Hypertonic Solution and 3% Hypertonic Solution by Nebulization in Bronchiolitis in Children

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Conflict of interest: Nil

Abstract

Background: Lower Respiratory Tract Infection (LRTI) is a respiratory disease affect the lung tissue in young children requiring hospitalization for viral or bacterial infections presenting with rapid breathing, chest contractions, and wheezing). Acute bronchiolitis is the cause of half of her LRTIs in children under 2 years of age. Various bronchodilators are used for treatment.

Aim and Objectives: 3% Hypertonic alone versus nebulized epinephrine + 3% Hypertonic in the treatment of LRTI, with particular reference to bronchiolitis with respect to decreased SpO_2, heart rate, respiratory rate, and improvement in Respiratory Distress Assessment Instrument Score (RDAI). to compare. [0-15 max] and patient hospital stays of patients age 1-24 months.

Methods: Children aged 1-24 months with bronchiolitis with LRTI and/or RDAI scores of 0-15 were enrolled was hospitalized. Treatment were given and outcomes were measured.

Results: 115 children enrolled, 57 received adrenaline with 3% Hypertonic 58 received 3% Hypertonic nebulization. Heart rate, respiratory rate, SpO2, dyspnea score, and length of stay improved in both groups. There were no significant differences in these variables between the two groups, except for her SpO2 improvement in the adrenaline and 3% NaCl nebulized group.

Conclusion: In LRTIs including bronchiolitis, Adrenaline with 3% hypertonic solution nebulization is not superior to 3% hypertonic alone in clinical improvement.

Keywords: Bronchiolitis, Adrenaline, 3% Hypertonic, RDAI score, LRTI

Introduction

Lower respiratory tract infection (LRTI). LRTIs are infections below the level of the larynx and can include bronchiolitis, bronchitis, pneumonia, and pleural effusion/empyema. The onset of these symptoms varies with age, the infecting organism, and the site of infection. Acute bronchiolitis is a severe inflammation of the bronchioles caused by a viral infection. In children younger than 2 years of age, bronchiolitis refers to a clinical syndrome characterized by rapid breathing, chest

tightness, and wheezing [1]. It is the leading cause of hospitalization in children under 1 year of age. It usually affects children between the ages of 2 and 6 months [2]. Children usually have a viral infection with a runny nose, cough, low-grade fever, and symptoms of rapid breathing, chest tightness, and wheezing within a day or two. Infants may exhibit hypersensitivity, poor feeding, and vomiting [3]. However, in very young or premature infants, disease symptoms are rare and characteristic of severe pneumonia [4]. Generally, children older than 4 weeks of age have a clinical syndrome of acute bronchiolitis [5]. Risk factors for acute bronchiolitis generally include low bone marrow antibody levels, sex, date of birth, little or no breastfeeding, crowded living conditions, having twins or triplets, and low socioeconomic status, including smoking. [8].

Despite its high prevalence, there is little consensus on the optimal management of acute bronchiolitis. Although drugs such as budesonide and montelukast are useful in children with bronchial asthma [9] treatment for bronchiolitis is primarily supportive. Humidified oxygen is delivered through the nasal cavity or into a headbox. The target number is determined by pulse oximetry. Monitor the child for apnea. Nebulized bronchodilators such as salbutamol and ipratropium are commonly used, but there is no evidence that bronchodilators have a therapeutic role. Breastfeeding or hydration is required [10,11]. Other inhaled bronchodilators may be used: a variety of other therapies, including epinephrine, inhaled and systemic steroids [12,13] aerosolized human DNA, ribavirin, antibiotics, leukotriene receptor antagonists, Heliox, and immunoglobulins [14]. Many of these treatments in infants remain controversial. Therefore, the present study was conducted to compare the efficacy of nebulized epinephrine and 3% NaCl in reducing dyspnea and length of hospital stay in children with LRTI, particularly with regard to bronchiolitis.

Aim & objectives

The main aim of the study to observe the effectiveness of adrenaline with 3% hypertonic solution in comparing with 3% hypertonic solution as nebulized in hospitalized children patients with the respiratory tract infection.

To observe the change in the respiratory rate, heart rate, O_2 saturation, duration of hospital stay and Respiratory Distress Assessment Instrument score in patients.

Material and Methods

The patients who are hospitalized at age of children 1 months to 2 years with the LRTI with acute bronchiolitis.

Inclusion Criteria:

All cases of bronchiolitis by the Respiratory DISTRESS assessment instrument (RDAI) [14] were scored from 0 to 15 [on a scale of 0 (mild) to 15 (severe)].

All cases of lower respiratory tract infection with a positive chest radiograph and sepsis testing with the Dyspnea Assessment Instrument (RDAI) [12] scored from 0 to 15 on a scale of 0 (mild) to 15 (severe).

Exclusion Criteria

The following children were excluded from the study.

People who have had previous episodes of wheezing.

Children under 1 month old

People with known chronic heart disease.

Immunocompromised people

Patients with heart rate >200/min, respiratory rate >80/min, SpO2 <94% despite oxygen therapy, RDAI score >15, or severe asthenia/paresthesia/convulsions.

Preterm birth with a valid age of less than 4 weeks at the first appointment.

Parental consent was not obtained.

People who have received oral or inhaled corticosteroids in the past 2 weeks.

Received an inhaled medication for an existing illness.

Consent was obtained from the parents of all children.

Diagnosis: Children with lower respiratory tract infection present with high fever, dyspnea, cough, dyspnea symptoms, intercostal muscle contractions, fever, tinnitus, and wheezing. Chest x-ray shows multiple bilateral opacities in lobar pneumonia or bronchopneumonia, pleural effusion, pleural effusion, empyema or hydropneumothorax with tracheal migration and collapse. Sepsis screening including elevated total and differential count, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR).

Heart rate and respiratory rate values for different ages are shown in Table 1. Infants with acute bronchiolitis present with signs of mild-to-moderate hypoxia, and dyspnea, including nasal flaring and use of respiratory muscles. Physical examination revealed wheezing, rales, rhonchi, and prolonged breathing. Other findings were conjunctivitis and severe rhinitis.

Abdominal distension due to lung hyperinflation was also observed in some cases. Diagnosis was primarily clinical and based on the presence of nasal discharge, wheezing cough, fine inspiratory crackles and/or wheezing and chest x-ray.

Monitoring: Clinical status was monitored by pulse oximeter measurement of RDAI score, heart rate, 24- and 72-h respiratory rate, at admission and discharge, and oxygen saturation. The Respiratory Distress Assessment Instrument (RDAI) provides a score from 0 to 17, with higher scores indicating severe respiratory distress. A clinical score of 15 was considered severe disease and was excluded.

Treatment: Supportive care including supplemental oxygen, rehydration, and antipyretics are given as needed. Antibiotics were added for patients with lobar and bronchopneumonia, those with positive septic screens, and those with high fever and positive blood cultures.

In addition, each child in the study was grouped into one of the treatment groups.

Group 1: 3% Hypertonic solution and adrenaline Group nebulized 3% saline and nebulized adrenaline.

Group 2: 3% Hypertonic solution Group: Spray with 3% NaCl.

The criteria for starting additional treatment at any time are:

• RDAI score is 2 points higher than admission score.

RDAI score >15

• SpO_2 <94% despite oxygen therapy

Dose: 2 ml of adrenaline 2 ml of 3% Hypertonic solution per treatment in the first group and 4 ml of 3% Hypertonic solution nebulized per treatment in the second group until clinical improvement or hospital discharge, whichever comes first 8 hourly dose.

Analysis: Outcomes were measured by improvement in oxygen saturation, heart rate, respiratory rate, clinical assessment including dyspnea scores at 24 and 72 hours, and hospital discharge and length of stay.

Statistical Analysis

Analysis was done by Unpaired t-test, one way repeated measures ANOVA were used.

Table 1: Normal value of Heart rate and Respiratory Rate according to age

Age group	Heart Rate (minute)	Respiratory Rate (Minute)
0 day – 3 months	100-180	35-55
3-6 months	90-180	30-45
6-12 months	80-170	25-40
1-2 year	70-140	20-30

Results

A total of 115 patients were involved in study. The mean age of onset in group A was 9.54 weeks, the mean age of bronchiolitis patients was 8.45 months, and the mean age of other LRTI patients was 10.09 months. The mean age of group B was 9.85 months, the mean age of patients with bronchiolitis was 10.50 months, and the mean age of other patients with LRTI was 9.53 months.

In Figure 2 it is shown that in group A, 32 (56%) of 57 were male and 25 (44%) were female. Among male, 15 (26%) had bronchiolitis and 16 (28%) had other LRTIs. Among women, 10 (17.5%) had bronchiolitis and 16 (28%) had other LRTIs. In group B, 35 (61%) were male and 22 (39%) were female. Among male, 16 (28%) had bronchiolitis and 19 (33%) had other LRTIs. Among female, 10 (17.5%) had bronchiolitis and 12 (21%) had other LRTIs. Overall, 66 (58%) were male and 48 (42%) were female.

Table 2: According to Gender distribution of children

Group	Diagnosis	Gender		Total
		Male	Female	
A	Bronchiolitis	14	11	25
	Other LRTI	17	15	32
	Total	30	27	57
B	Bronchiolitis	15	11	26
	Other LRTI	18	13	31
	Total	34	24	58

There was no significant difference in age, number of male and female patients, number of patients with bronchiolitis and other LRTIs between the two groups. Clinical characteristics were also similar in both groups.

Mean respiratory rate and mean RDAI scores at admission were not statistically significant, while heart rate and mean SpO_2 at admission were statistically significant between both groups. Table 3 shows mean heart rate and mean SpO_2 at admission.

Table 3: Mean Heart Rate and SpO_2 at admission

Group	Diagnosis	Mean HR/min (SD)	Mean RR/min (SD)	Mean SpO_2 (SD)	Mean SpO_2 (SD)
A	Bronchiolitis	118.71(15.98)	119(13.95)	96.71(1.50)	97.02(1.45)
	Other LRTI	120.81(12.30)		97.33(1.30)	
B	Bronchiolitis	116.66(20.13)	128(17.35)	96.41(1.44)	96.45(1.58)
	Other LRTI	129.21(15.31)		96.60(1.70)	
*p	0.007			*p	0.04

At 24 hours, 72 hours and discharge mean heart rate decreased relatively in both groups. 24-hour, 72-hour, and exhaled breath rates were relatively low in both groups.

Mean SpO2 at 24 hours, 72 hours, and discharge increased relatively in both groups. The 24-hour, 72-hour, and discharge RDAI scores were relatively low in both groups.

Table 4 shows mean heart rate, mean respiratory rate, mean SpO2, and RDAI scores at 24 hours, 72 hours, and discharge. The difference between the two groups and between the two groups of patients with bronchiolitis was not clinically significant.

Of the 57 candidates in group A, 31 took antibiotics and 26 did not given antibiotics. In group B, 31 received antibiotics and 26 did not. Antibiotics were given to 5 patients with group A bronchiolitis and 3 patients with group B bronchiolitis. This is illustrated in Table 5.

Table 4: Mean Heart rate, respiratory rate, SpO_2, and RDAI scores at 24 hours, 72 hours, and discharge

	Group	Diagnosis	Mean Heart Rate (SD)	Mean (SD)	Mean RR (SD)	Mean (SD)	Mean SpO_2 (SD)	Mean (SD)	Mean RDAI Score (SD)	Mean (SD)
Ad	A	Bronchiolitis	118.71	119.81	40.80	41.75	96.71	97.02	3.71	4.06
			(15.98)	(13.94)	(9.27)	(9.55)	(1.50)	(1.45)	(1.16)	(1.35)
		other LRTI	120.81		42.70		97.33		4.42	
			(12.30)		(9.90)		(1.35)		(1.41)	
	B	Bronchiolitis	121.73	125.47	41.81	43.52	96.41	96.50	4.00	4.36
			(20.13)	(17.35)	(13.80)	(11.85)	(1.44)	(1.58)	(1.35)	(1.64)
		other LRTI	129.21		45.23		96.60		4.73	
			(15.30)		(10.48)		(1.70)		(1.79)	
24	A	Bronchiolitis	114.02	116.36	36.84	38.44	97.30	97.52	2.89	3.45
			(13.64)	(12.95)	(9.27)	(8.56)	(1.50)	(1.18)	(1.16)	(1.59)
		other LRTI	118.21		40.05		97.74		4.01	
			(12.55)		(9.01)		(1.19)		(1.61)	
	B	Bronchiolitis	115.03	120.52	38.72	41.15	97.11	96.99	3.31	3.99
			(17.11)	(16.36)	(12.55)	(11.28)	(1.24)	(1.39)	(1.19)	(1.93)
		other LRTI	126.01		43.58		96.88		4.68	
			(14.89)		(10.11)		(1.52)		(2.21)	
72	A	Bronchiolitis	108.4	109.90	33.37	34.53	97.92	98.08	1.10	1.30
			(7.27)	(8.66)	(7.16)	(7.55)	(0.86)	(0.76)	(0.64)	(0.98)
		other LRTI	111.44		35.69		98.20		1.50	
			(9.56)		(7.94)		(0.65)		(1.09)	
	B	Bronchiolitis	08.37	111.08	35.72	38.11	97.85	97.83	1.35	1.63
			(9.52)	(10.76)	(11.93)	(11.19)	(0.84)	(0.92)	(0.89)	(1.40)
		other LRTI	113.80		40.50		97.81		1.91	
			(12.58)		(10.51)		(0.97)		(1.66)	
Di	A	Bronchiolitis	101.66	102.66	29.29	29.83	98.66	98.75	0.07	0.20
			(5.68)	(6.45)	(5.68)	(5.35	(0.64)	(0.55)	(0.27)	(0.43)
		other LRTI	103.67		30.37		98.84		0.34	
			(12.30)		(6.94)		(0.44)		(0.49)	
	B	Bronchiolitis	101.74	103.01	29.20	31.51	98.65	98.61	0.12	0.34
			(8.07)	(7.18)	(8.70)	(6.13)	(0.62)	(0.70)	(0.32)	(0.49)
		other LRTI	104.28		33.82		98.57		0.56	

Group A-Adrenaline plus 3% Hypertonic; Group B- 3% hypertonic; HR- heart rate; RR Respiratory rate; SpO_2-Oxygen saturation; RDAI-respiratory distress assessment Instrument; SD- Standard deviation; Adm- Admission; Hrs- Hours; Dis-Discharge; LRTI- lower respiratory infection

One-way repeated-measures ANOVA was used for statistical analysis and the reduction in heart rate, mean respiratory rate, and RDAI scores between the two groups were not statistically significant. While the increase in mean SpO_2 between the two groups was not statistically significant. . was statistically significant. The decrease in heart rate, mean respiratory rate,

mean RDAI score, and increase in mean SpO_2 were not statistically significant in both groups of patients with bronchiolitis. This is illustrated in Tables 6.

To avoid confounding effects of antibiotics, comparisons were made between patients who did not receive antibiotics in the two groups, especially between the bronchiolitis patients in the two groups using one-way repeated measures ANOVA. There was no statistically significant decrease in mean heart rate, respiratory rate, RDAI score, and mean SpO_2 between the two groups. There was no significant difference in the mean length of hospital stay between the two groups and between the bronchiolitis patients in the two groups.

Table 5: Mean Duration of stay and use of Antibiotic

Group	Diagnosis	Mean SD duration of stay (days)	Mean (SD) duration of stay (days)	P value	Antibiotics Given	Antibiotics Not Given
A*	Bronchiolitis**	3.00 (1.13)	4.97 (2.49)	0.2*	5	26
	other LRTI	6.27 (2.65)			26	0
B*	Bronchiolitis**	4.23 (1.94)	5.54 (2.70	0.9**	3	26
	other LRTI	6.86 (2.69)			28	0
Total					61	53
Antibiotics		A+B Bronchiolitis			7	53
		A+B other LRTI			55	0

Table 6: Statistical analysis of parameters

One-way Repeated Measures ANOVA Greenhouse-Geisser		Df	F	P value
Comparison of Group A and B	Mean Heart rate	1.814	1.583	0.210
	Mean Respiratory rate	1.691	1.165	0.308
	Mean SpO_2	1.755	3.373	0.042*
	Mean RDAI score	2.448	0.615	0.573
Comparison of Bronchiolitis in Group A and B	Mean Heart rate	1.53	0.205	0.710
	Mean Respiratory rate	1.304	0.430	0.567
	Mean SpO_2	1.504	0.289	0.289
	Mean RDAI score	2.341	0.452	0.654

Discussion

In present study, groups showed improvement in parameters like heart rate, respiratory rate, SpO_2 and RDAI score. However, the difference between the overall group and bronchiolitis patients was not statistically significant. This may be due to less nebulizer use in both groups, as more frequent use of nebulizer epinephrine resulted in clinically significant improvement. The mean age of onset was 9.54 months for group A and 9.85 months for group B. Peret [5] showed that the incidence of bronchiolitis is higher in children under 1 year of age. Jarty [15] and Chattopadhyay [16] gave similar results.

In our survey, 59% were male and 41% female. The results were similar to previous studies by Nagayama [17] and Bozen [18] which showed an increased susceptibility to bronchiolitis in male. Bozen says that the immunosuppressive effects of androgens may be a possible cause, but it is not true that androgens are active or have immunosuppressive effects in childhood. do not think so.

In our study, chills and runny nose were the most common symptoms in (93%), followed by cough in 105 (92%). These observations were similar to those of

Kellner JD *et al* [19] where cough and rapid breathing were prominent symptoms. Although 74% of our subjects had fever, L. Radhi *et al*. 2.7 days. Infants requiring mechanical ventilation were classified as severe, those requiring supplemental oxygen were classified as severe, and those requiring no oxygen and requiring hospital admission for observation were classified as mild. Fever was present in 74% of patients, which was not detected in our study because they had a mild to moderate course of disease based on RDAI score.

Individually significant improvements were observed, but in our study, no statistically significant clinical improvement was observed with nebulized 3% hypertonic compared with nebulized 3% hypertonic alone. This was similar to the results of Bahadili [21] who compared 3% NaCl or hypertonic saline with 0.9% normal saline in 100 infants with acute bronchiolitis.

The mean length of hospital stay was shorter in the group of children treated with 3% hypertonic saline (4.7 ± 1.9 days). A Cochrane review of 7 trials in 581 infants (282 inpatients, 65 outpatients, 234 emergency department patients) with acute bronchiolitis found that 3% saline nebulization reduced hospital stay. Clinical score. nebulization with 0.9% saline [22]. Another Cochrane review concluded that inhaled adrenaline did not improve the length of hospital stay in patients with moderate-to-severe bronchiolitis or the same important clinical outcomes as placebo [23]. This is supported by a large Norwegian randomized controlled trial (RCT) of 404 infants [24]. This finding is consistent with our study. A study by Luo Z [25] found no significant improvement in length of stay in patients receiving nebulized adrenaline compared to placebo. Similar results were observed in a study by Abul-Ainin [26] comparing the short-term effects of nebulized epinephrine and saline placebo in infants with moderate to severe bronchiolitis.

In present study found no adverse events such as tachycardia associated with the use of nebulized adrenaline plus 3% hypertonic. In six of seven trials [22,27] in a Cochrane review, patients received inhaled hypertonic saline combined with bronchodilators, and 3% reported no serious adverse events related to inhaled saline.

Conclusion

Clinical improvement was seen as both groups showed a reduction in dyspnea. Thus, adrenaline with 3% hypertonic nebulization and 3% hypertonic resulted in significant clinical improvement, but there was no significant difference in clinical improvement between the two groups.

Therefore, when used in lower respiratory tract infections, especially bronchiolitis, the efficacy of adrenaline plus 3% Hypertonic is not superior to that of 3% hypertonic nebulization alone. Therefore, nebulization of 3% hypertonic may be the first choice for clinical improvement in bronchiolitis. Nebulization of 3% hypertonic solution may also be used as an adjuvant therapy to improve symptoms in other LRTI patients. No complications or adverse effects were observed during administration of adrenaline plus 3% NaCl or 3% NaCl alone.

References

1. Wohl MEB. Kendig's Disorders of the Respiratory Tract in Children. 7/e. Philadelphia: Saunders; 2006:432-46
2. Henderson FW, Clyde Jr WA, Collier AM *et al*, The etiologic and epidemiologic spectrum of bronchiolitis in pediatric practice. J Pediatr. 1979; 95:35-9.
3. Mallory MD, Shay DK, Garrett J, Bordley WC. Bronchiolitis management preferences and the influence of pulse oximetry and respiratory rate on the decision to admit. Pediatrics. 2003; 111: e45-51.
4. Hall CB, Kopelman AE, Douglas Jr RG *et al*, Neonatal respiratory syncytial virus infection. N Engl J Med. 1979; 300:393-6.

5. Parrott Rh, Kim Hw, Arrobio Jo *et al*, Epidemiology of respiratory syncytial virus infection in Washington, DC: II. Infection and disease with respect to age, immunologic status, race and sex. Am J Epidemiol. 1973; 98:289-300.
6. Glezen WP, Paredes A, Allison JE *et al*, Risk of respiratory syncytial virus infection for infants from low-income families in relationship to age, sex, ethnic group, and maternal antibody level. Jpediatr. 1981; 98:708-15.
7. Spencer N, Logan S, Scholey S, Gentle S. Deprivation and bronchiolitis. Archdis child. 1996; 74:50-52.
8. Jansson L, Nilsson P, Olsson M. Socioeconomic environmental factors and hospitalization for acute bronchiolitis during infancy. Acta Paediatr. 2002; 91:335-8.
9. Rudolph CD, Rudolph AM, Hostetter MK, Lister G, Siegel NJ. Pediatrics. 21/e2003:716-721.
10. Zorc JJ, Hall CB. Bronchiolitis: recent evidence on diagnosis and management. Pediatrics. 2010; 125:342-9.
11. Scottish Intercollegiate Guidelines Network. Bronchiolitis in children: a national clinical guideline. Scottish Intercollegiate Guidelines Network; 2006.
12. Shah MB, Gohil J, Khapekar. S, *et al*. Montelukast's budesonide as a first line preventive therapy in mild persistent asthma in 2-18 y. Indian J Pediatr2014;81:655-9.
13. Gohil JR, Sheladiya AM, Adithya NB, Bhojak RD. Adrenaline and dexamethasone, vs adrenaline and fluticasone, vs adrenaline alone in bronchiolitis: a randomized controlled trial. Asian J Pediatr Res.2020;3(1):20-8.
14. Carvalho WBD, Johnston C, Fonseca MCM. Bronchiolitis in Roger's Textbook of Intensive Care. 4/ed. Philadelphia: Wolters Kluwer Lippincott Williams & Wilkins. 2008: 716-721.
15. Jartti T, Lehtinen P, Vuorinen T, Ruuskanen O. Bronchiolitis: age and previous wheezing episodes linked to viral etiology and atopic characteristics. Pediatr infect dis J. 2009; 28:311-7.
16. Chattopadhya D, Chatterjee R, Anand VK *et al*, Lower respiratory tract infection in hospitalized children due to respiratory syncytial (RS) virus during a suspected epidemic period of RS virus in Delhi. J Trop Pediatr. 1992; 38:68-73.
17. Nagayama Y, Tsubaki T, Nakayama S *et al*, Gender analysis in acute bronchiolitis due to respiratory syncytial virus. Pediatr Allergy Immunol. 2006; 17:29-36
18. Boezen HM, Jansen DF, Postma DS. Sex and gender differences in lung development and their clinical significance. Clin Chest Med. 2004; 25:237-45.
19. Kellner JD, Ohlsson A, Gadomski AM, Wang EE. Efficacy of bronchodilator therapy in bronchiolitis: a meta-analysis. Arch Pediatr Adolesc Med. 1996; 150:1166-72.
20. El-Radhi AS, Barry W, Patel S. Association of fever and severe clinical course in bronchiolitis. Arch Dis Child. 1999; 81:231-4.
21. Al-bahadily AK, Al-Omrani AA, Atiya AA. Hypertonic 3% saline compared to 0.9%(normal)saline in treatment of acute bronchiolitis. IntJPediatr. 2017; 5(1):4209-16.
22. Zhang L, Mendoza-Sassi RA, Wainwright C, Klassen TP. Nebulised hypertonic saline solution for acute bronchiolitis in infants. Cochrane Database Syst Rev. 2017; (12):CD006458.
23. Hartling L, Bialy LM, Vandermeer *et al*. Epinephrine for bronchiolitis. Cochrane Database Syst Rev. 2011; 15:CD003123.
24. Oymar K, Skjerven HO, Mikalsen IB. Acute bronchiolitis in infants, a review. Scand J Trauma ResuscEmerg Med. 2014; 22:23.

25. Luo Z, Liu E, Luo J *et al*, Nebulised hypertonic saline/salbutamol solution treatment in hospitalized children with mild to moderate bronchiolitis. Pediatr Int. 2010; 52:199-202.
26. Abul-Ainine A, Luyt D. Short term effects of adrenaline in bronchiolitis: a randomised controlled trial. Arch Dis Child. 2002; 86:276-9.
27. Lawley LP, Siegfried E, Todd JL. Propranolol treatment for hemangioma of infancy: risks and recommendations. Pediatr Dermatol. 2009; 26:610-4.