

## Therapeutic effects of Ventolin versus hypertonic saline 3% for acute bronchiolitis in children

Mohammad-Ali Zamani<sup>1</sup>, Mehran Movahhedi<sup>2</sup>, Seyyed Mohammad-Kazem Nourbakhsh<sup>3</sup>, Forouzan Ganji<sup>4</sup>, Mahmoud Rafieian-Kopaei<sup>5</sup>, Mahmoud Mobasheri<sup>6</sup>, Abolfazl Khoshdel<sup>7</sup>, Shahram Etemadifar<sup>8</sup>, Majid Shirani<sup>9</sup>, Zahra Keivani Hafshejani<sup>\*10</sup>

Received: 16 June 2014

Accepted: 6 January 2015

Published: 6 May 2015

### Abstract

**Background:** Complications of Ventolin as the most common drug used for bronchiolitis are widely known. The present study was conducted to determine the efficacy of hypertonic saline 3%, compared with Ventolin, for treatment of acute bronchiolitis in children.

**Methods:** This double-blinded clinical trial study was conducted in Hajar Hospital, Shahrekord, Iran, from 2011 to 2012. A total of 70 patients under the age of two years with bronchiolitis were divided into two groups of 35 each. Ventolin nebulizer and hypertonic saline 3% nebulizer three times per day were administered in the first (Ventolin) and second (Hypersaline) group, respectively. The length of recovery was compared between the two groups. The data were analyzed by SPSS software (version 22) using chi-square, t-test, paired t-test, and Mann-Whitney.

**Results:** The mean±SD length of recovery was 4.14±0.9 and 3.06±0.6 in the Ventolin and hypersaline groups, respectively. The mean duration of recovery was significantly lower in the hypersaline group ( $p < 0.001$ ).

**Conclusion:** Hypertonic saline 3% nebulizer has more pleasant therapeutic effects on acute bronchiolitis than Ventolin. Therefore, use of hypertonic saline 3% nebulizer is recommended for the treatment of acute bronchiolitis in children under two years old.

**Keywords:** Hypertonic saline solution, Pediatric, Bronchiolitis, Ventolin-albuterol.

**Cite this article as:** Zamani MA, Movahhedi M, Nourbakhsh SMK, Ganji F, Rafieian-Kopaei M, Mobasheri M, Khoshdel A, Etemadifar Sh, Shirani M, Keivani Hafshejani Z. Therapeutic effects of Ventolin versus hypertonic saline 3% for acute bronchiolitis in children. *Med J Islam Repub Iran* 2015 (6 May). Vol. 29:212.

### Introduction

Acute bronchiolitis is the most frequent reason for lower respiratory tract infection and hospitalization due to respiratory disease in infancy. The frequent age of the disease incidence is the first two years of life. About 50000-80000 hospitalizations of the infants under the age of one are attributed to this disease in the USA (1). The

severe form of this disease is much more prevalent in one- to three-month-old infants and responsible for more than 50% of its incidence, causing respiratory syncytial virus, inflammation and small airway obstruction (1). Clinical symptoms of acute bronchiolitis are similar to those of viral pneumonias, with fever, wheezing, and increased respiratory rate as the most im-

<sup>1</sup> Assistant Professor, Department of Pediatrics, Shahrekord University of Medical Sciences, Shahrekord, Iran. zamani@yahoo.com

<sup>2</sup> Department of Pediatrics, Shahrekord University of Medical Sciences, Shahrekord, Iran. alirezannfor@yahoo.com

<sup>3</sup> Assistant Professor, Department of Pediatrics, Tehran University of Medical Sciences, Tehran, Iran. dr.nourbakhsh2010@gmail.com

<sup>4</sup> Assistant Professor, Department of Community Medicine, Shahrekord University of Medical Sciences, Shahrekord, Iran. foruzan2000@yahoo.co.in

<sup>5</sup> Professor, Medical Plants Research Center, Shahrekord University of Medical Sciences, Shahrekord, Iran. rafieian@yahoo.com

<sup>6</sup> Associate Professor, Department of Epidemiology, Shahrekord University of Medical Sciences, Shahrekord, Iran. mobasheri@skums.ac.ir

<sup>7</sup> Associate Professor, Department of Pediatrics, Shahrekord University of Medical Sciences, Shahrekord, Iran. nikakhosh@gmail.com

<sup>8</sup> Assistant Professor, Department of Nursing, Shahrekord University of Medical Sciences, Shahrekord, Iran. shahram\_410@yahoo.com

<sup>9</sup> Assistant Professor, Department of Surgery, Shahrekord University of Medical Sciences, Shahrekord, Iran. shirani.m@skums.ac.ir

<sup>10</sup> (**Corresponding author**) MSc in Nursing, Shahrekord University of Medical Sciences, Shahrekord, Iran. keivaniz@yahoo.com

portant ones (2).

Research is needed to find the appropriate treatment for this disease. The treatment is often supportive therapy, including fluid therapy, anti-fever drugs, and oxygen (3). Some investigations have been recently conducted on the therapies like bronchodilators including salbutamol and epinephrine as nebulized (2,4). In infants particularly under age of six months, edema and inflammation in bronchioles could lead to respiratory distress because of small diameter of airways (1).

There is no consensus on use of bronchodilators and/or beta-agonists (5,6). Most works have indicated that bronchodilators have no role in treating these patients (7). Today, inhaled salbutamol (Ventolin) is used for treating bronchiolitis patients in Iran's hospitals while several studies have indicated that this drug does not work (8-12). In many studies, the positive effect of hypertonic saline has been observed on recovering bronchiolitis symptoms (9,10). Also, some studies comparing different concentrations of hypertonic saline have obtained similar results. For example, comparative study of hypertonic saline 3% and 7% indicated a greater therapeutic effect of hypertonic saline 3% than that of hypertonic saline 7% in treating bronchiolitis symptoms and decreasing duration of treatment (13,14). Hypertonic saline 3% was also found as better and more efficient than normal saline and hypersaline 3% nebulizer (15,16).

In addition, a research conducted to compare hypertonic saline 3% with the drugs used for bronchiolitis like Ventolin indicated that hypertonic saline 3% and Ventolin had a greater therapeutic effect than Ventolin and normal saline on treating bronchiolitis symptoms (17). In some studies, Ventolin and hypertonic saline 3% had similar therapeutic effect on symptoms developed by mild to moderate viral bronchiolitis and were free of complications, as well (18). Regarding the widely known complications of Ventolin as the most common drug used for bronchiolitis and that no study has been

yet conducted to compare the efficacy of Ventolin and hypertonic saline 3% on bronchiolitis in Iran, the present study was conducted to determine the efficacy of hypertonic saline 3% on treatment of acute bronchiolitis, in comparison with Ventolin.

### Methods

This research is a double-blinded clinical trial study conducted in 2011-2012 on 70 referring patients with acute viral bronchiolitis. Registration code of IRCT 2012110510222N2 was issued by Iranian Registry of Clinical Trials for this study. The samples of study were examined for severity of simulated disease prior to enrollment and the patients with acute status and causing a predetermined error in the study were excluded from the investigation. Inclusion criteria were patients with mild to moderate respiratory status, the first wheezing, and obtaining a score of lower than nine in Respiratory Distress Assessment Inventory (RDAI), the most common clinical scoring tool for acute bronchiolitis developed based on wheezing and intercostal retraction (19). All patients were frequently visited and examined by a pediatrician in Hajar Hospital, Shahrekord, Iran till completion of their hospitalization. After the informed consent was obtained from the patients' guardians, the patients were assigned into two groups of case and control. Group one underwent treatment with Ventolin nebulizer and group two with hypertonic saline 3% nebulizer. The prescribed dose of Ventolin was 0.1 mg/kg and the required concentration was obtained by distilled water. To obtain hypertonic saline 3% solution, 3 ml sodium chloride 5% was mixed with a 5-cc vial of distilled water. The two medicinal combinations were administered to the patients of the two groups every four hours by a nebulizer instrument. The inhaled medicine accompanied with oxygen was nebulized to the patients by a face mask. Other therapies including oxygen and fluid therapy were used for all patients. Clinical symptoms of the patients and the length of recovery since hospitali-

zation initiation were calculated for each patient and registered in a special checklist based on the defined RDAI criterion and day. The data were analyzed by SPSS software (version 22) using chi-square, t-test, paired t-test, and Mann-Whitney.

### Results

In this study, 70 patients were randomly assigned to two groups of 35 each. Group one underwent treatment with Ventolin nebulizer (Ventolin group) and group two with hypertonic saline 3% nebulizer (Hypersaline group). The mean±SD age of the patients was 14.1±5.6 months in the Ventolin group and 12.6±5.6 months in the hypersaline group.

The mean±SD length of recovery was 4.14±0.9 days in the Ventolin group and 3.06±0.6 in the hypersaline group. The mean length of recovery was significantly lower in the hypersaline group ( $p<0.001$ ). The mean±SD RDAI criterion on the days two, three, four, and five was respectively 5.68±1.3, 4.85±1.6, 3.62±1.6, and 1.42±0.8 in the Ventolin group and 4.25±1.5, 3.2±1.5, 2.54±1.6, and 0.9±0.54 in the hypersaline group; the mean RDAI criterion was significantly lower in the hypersaline 3% group ( $p<0.001$ ).

### Discussion

The general purpose of conducting this study was to compare the efficacy of hypertonic saline 3% with that of Ventolin on treating acute bronchiolitis in the children under two years. In this study, two groups (35 patients in each group) of infants hospitalized for bronchiolitis in Hajar Hospital, Shahrekord, Iran were investigated. According to the results of this study, the mean length of recovery was 4.14±0.4 days in the Ventolin group and 3.0±0.6 in the hypersaline group. The patients under hypersaline treatment recovered more rapidly, which is clinically and economically important as 50000-80000 hospitalizations of under one-year-old infants has led to expending about 300 million dollars per year in the USA (1). Other studies reported the

therapeutic effect of hypertonic saline 3% on acute bronchiolitis in children.

In Kuzik et al study, use of hypertonic saline 3% nebulizer had more pleasant outcomes than the normal saline nebulizer (15). Also, Anil et al who used some medicinal combinations (Ventolin nebulizer with normal saline, epinephrine with normal saline and hypertonic saline 3%, and normal saline alone) for treating acute bronchiolitis in the children found no significant difference among the groups; the effect of hypertonic saline 3% was similar to that of other medicinal combinations (9). In Zhang et al study, hypertonic saline 3% was more effective than normal saline (16). Mandelberg et al compared hypertonic saline 3% nebulizer, epinephrine, and normal saline and found hypertonic saline 3% as therapeutically more effective on bronchiolitis symptoms (13). In Ater et al study to compare Ventolin nebulizer and normal saline with Ventolin and hypertonic saline 5%, hypertonic saline 5% had a better therapeutic effect in the children with bronchiolitis than normal saline (20).

In addition, the decreased length of hospitalization after hypertonic saline 3% was observed in some studies (10,13,17,20).

The results of this study indicated that the mean RDAI criterion on the day of hospitalization and prior to treatment initiation had no significant difference between the two groups. The RDAI criterion indicating the disease severity had no significant difference between the two groups of study. In addition, the mean RDAI criterion was significantly lower in the hypertonic saline 3% group, indicating that use of hypertonic saline 3% nebulizer was obviously more efficient than Ventolin after hospitalization (the day one), i.e. from the day two to the last day of hospitalization. The greatest efficacy was noted on the day two after hypertonic saline 3%, irrespective of the last day of hospitalization. In Sarrell et al study, there was no significant difference prior to study between the two groups, but an obviously better effect was noted by the use of hypertonic saline 3% nebulizer between the

day two and the last day of hospitalization. However, the highest effect was observed in the day two. The effect of hypertonic saline 3% was obviously better than that of normal saline on the day one in Sadbhavna et al study, but no difference was observed between the two groups on the day two (17,21).

The length of hospitalization in our study was 2-6 days, similar to other studies (13,15,16). Although the mechanism of hypertonic saline 3% was not examined in the present work, hypertonic saline 3% was demonstrated to increase mucus clearing in Dasgupta et al study (22). Also, Tomooka et al examined the effects of hypertonic saline on recovery of respiratory symptoms. These effects included improvement of mucous cilia's function, decrease in mucous edema and inflammatory mediators, mechanical clearing of secretions, and improvement of mucus function (23). On the other hand, no complication was observed by the use of hypertonic saline 3% nebulizer throughout the study in the studied patients, which is consistent with other studies (9,13,18).

### Conclusion

Regarding the obtained results in this study and comparing them with those of other studies, we found hypertonic saline 3% nebulizer as having more pleasant therapeutic effects than Ventolin on treating acute bronchiolitis in the children under two years. Moreover, use of hypertonic saline 3% leads to no remarkable drug-related complications in the children; the reason is that it is free of medicinal compounds. In addition, the treatment costs would decline considerably and hence use of hypertonic saline 3% nebulizer is recommended for treatment of acute bronchiolitis in children under the age of two.

### Acknowledgements

We gratefully thank Research and Technology Deputy of Shahrekord University of Medical Sciences.

### Conflict of interest

The authors report no conflict of interest.

### References

1. Goodman D. Inflammatory Disorder of the Small. In: Nelson Textbook of Pediatrics. Behrman RE, Kliegman RM, Jenson HB, eds. 17th ed. Philadelphia, WB Saunders 2003;1415-7.
2. Wright AL, Taussig LM, Ray CG, Harrison HR, Holberg CJ. The Tucson Children's Respiratory Study. II. Lower respiratory tract illness in the first year of life. *Am J Epidemiol* 1989;129:1232-46.
3. Lowell DI, Lister G, Von koss H, MCCarthy P. Wheezing in infants: the response to epinephrine. *Pediatrics* 1987;79:939-45.
4. Kellner D, Ohlsson A, Gadomski AM, Wang EE. Bronchodilators for bronchiolitis. *Cochrane Database Syst Rev* 2000. CD001266.
5. Sethi GR, Nagarg E. Evidence based treatment of bronchiolitis. *Indian J Pediatr* 2004;71: 733-7.
6. Scarfone RJ. Controversies in the treatment of bronchiolitis. *Curr Opin Pediatr* 2005;17:62-6.
7. Schindler M. Do bronchodilators have an effect on bronchiolitis? *Crit Care* 2002;6: 111-2.
8. Dawson-Caswell M, Muncie HL JR. Respiratory syncytial virus infection in children. *Am Fam Physician* 2011; 83: 141-6.
9. Anil AB, Anil M, Saglam AB, Cetin N, Bal A, Aksu N. High volume normal saline alone is as effective as nebulized salbutamol-normal saline, epinephrine-normal saline, and 3% saline in mild bronchiolitis. *Pediatr Pulmonol* 2010; 45: 41-7.
10. Tal G, Cesar K, Oron A, Houri S, Ballin A, Mandelber GA. Hypertonic saline/epinephrine treatment in hospitalized infants with viral bronchiolitis reduces hospitalization stay: 2 years experience. *Isr Med Assoc J* 2006; 8:169-73.
11. Coffins E. Bronchiolitis: in-patient focus. *Pediatr Clin North Am* 2005;52: 1047-57.
12. Bertrand P, Aranibar H, Castro E, Sanchez I. Efficacy of nebulized epinephrine versus salbutamol in hospitalized infants with bronchiolitis. *Pediatr Pulmonol* 2001;31, 284-8.
13. Mandelberg A, Tal G, Witzling M, Someck E, Houri S, Balin A, Priel IE. Nebulized 3% hypertonic saline solution treatment in hospitalized infants with viral bronchiolitis. *Chest* 2003;123: 481-7.
14. Jacobs JD, Foster M, Wan J, Pershad J. 7% Hypertonic saline in acute bronchiolitis: a randomized controlled trial. *Pediatrics* 2014;133:8-13.
15. Kuzik BA, AL-qadhi SA, Kent S, Flavin MP, Hopman W, Hotte S, et al. Nebulized hypertonic saline in the treatment of viral bronchiolitis in infants. *J Pediatr* 2007; 151:266-70.
16. Zhang L, Mendoza-Sassi RA, Wainwright C, Klassen TP. Nebulized hypertonic saline solution for acute bronchiolitis in infants. *Cochrane Database Syst Rev* 2008. CD006458.
17. Sarrell EM, Tal G, Witzling M, Someck E,

Houri S, Cohen HA, et al. Nebulized 3% hypertonic saline solution treatment in ambulatory children with viral bronchiolitis decreases symptoms. *Chest* 2002; 122:2015-20.

18. Luo Z, Liu E, Luo J, Li S, Zeng F, Yang X, et al. Nebulized hypertonic saline/salbutamol solution treatment in hospitalized children with mild to moderate bronchiolitis. *Pediatr Int* 2010;52: 199-202.

19. Mull CC, Scarfone RJ, Ferri LR, Carlin T, Salvaggio C, Bechtel KA, 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.

20. Ater D, Shai H, Bar BE, Fireman N, Tasher D, Dalal I, et al. Hypertonic saline and acute wheezing

in preschool children. *Pediatrics* 2012; 129: e1397-403.

21. Sadbhavna P, Neeraj D, Deepak T. Utility of hypertonic saline in the management of acute bronchiolitis in infants: a randomized controlled study. *Int J Clin Pediatr* 2013; 2:24-9

22. Dasgupta B, Tomkiewicz RP, Boyd WA, Brown NE, King M. Effects of combined treatment with rhDNase and airflow oscillations on spinnability of cystic fibrosis sputum in vitro. *Pediatr Pulmonol* 1995;20: 78-82.

23. Tomooka LT, Murphy C, Davidson TM. Clinical study and literature review of nasal irrigation. *Laryngoscope* 2000;110:1189-93.