

Comparison of the Therapeutic Effects of Salbutamol Nebulize with different Concentrations of Saline on Children with Bronchiolitis

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Abstract

Background

Bronchiolitis, which is the most common infection of the lower respiratory tract among infants, is characterized by acute inflammation, edema, increased mucosal production, and bronchospasm. We aimed to investigate the effects of saline usage with different concentrations and salbutamol on the treatment.

Materials and Methods: This double-blind, randomized clinical trial was performed on 180 pediatric patients with four weeks to 24 months old admitted to Ali-Ibn-Aboutaleb Hospital in Zahedan, Iran, during 2017-18 for possible diagnosis of acute bronchiolitis. Patients were divided into three groups of 60 patients using the permissive block method. The first group received 0.15 mg of Salbutamol Nebulizer and 5 ml of normal saline 0.9%, the second group received saline 3%, and the third group received saline 5% at the same dose as the first group. Clinical status, oxygen saturation, respiratory and heart rate, intercostal retraction, dyspnea, wheezing before treatment and every 20 minutes after treatment up to 3 times, and Clinical Bronchiolitis Severity Score (CBSS) were collected.

Results: In all three groups, there was an increasing trend in oxygen saturation and a decrease in respiratory rate, heart rate, and CBSS. In the first and third groups, there was a significant difference in CBSS after treatment, but in the second group, it was significant only at 20 and 40 minutes after treatment. The mean days of admission for the second group were lower.

Conclusion

It seems that due to its cost-effectiveness, lack of complication and earlier efficacy of 5% hypertonic saline in the treatment of bronchiolitis, hypertonic saline 5% instead of normal saline 0.9% is more effective and more cost-beneficial achieved in bronchiolitis remedy.

Key Words: Bronchiolitis, Children, Salbutamol, Nebulizer.

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1- INTRODUCTION

Bronchiolitis is the most common infection of the lower respiratory tract among infants (1), and is characterized by acute inflammation, edema, increased mucosal production, bronchospasm, affecting airflow in small airways, causing atelectasis, and wheezing. Bronchiolitis affects more than 10% of children (2). Bronchiolitis has a seasonal prevalence with the highest prevalence for those with 3-6 months old (3). Despite current treatments for this disease, there is still considerable mortality and morbidity rate (4). Approximately, 3–8% of infants admitted to this hospital suffering from acute respiratory failure and require mechanical breathing (5). Several meta-analysis studies have shown inefficiencies of therapies such as inhaled bronchodilators, epinephrine, glucocorticoid, and chest physiotherapy (6-9), while these therapies continue to be of great use (10).

Recent studies have shown a positive effect of saline administration on bronchiolitis (11, 12), as well as improved mucociliary function among healthy individuals with bronchiolitis (13-15). Although numerous studies have not considered the use of bronchodilators for the treatment of bronchiolitis, some studies have reported its positive effect, albeit briefly (16, 17). The present study was designed and carried out to investigate different effects of salbutamol in the treatment of bronchiolitis combined with the use of saline at different concentrations, the prevalence of this disease, and various treatments.

2- MATERIALS AND METHODS

2-1. Study Design

We conducted a double-blinded, randomized, controlled trial to compare the efficacy of hypertonic saline (3% and 5%) versus 0.9% (normal) saline for the

treatment of acute viral bronchiolitis. This study was performed on children hospitalized in the pediatric infectious ward of Ali-Ibn-Aboutaleb Hospital in Zahedan, Iran, with four weeks to 24 months old during 2017-18 for possible diagnosis of acute bronchiolitis. The local ethics committee of Zahedan University of Medical Sciences approved the study. On behalf of each child, at least one legal caregiver signed a written informed consent form before the study onset.

2-2. Methods

Patients were divided into three groups (60 patients in each group) of mild (RR <30), intermediate (RR <60) and severe (RR > 60) based on Respiratory Rate (RR) evaluated by the health care provider. Data collectors and outcome assessors did not know the density of each vial. Patients in the intermediate group were divided into three groups using the permissive block method. The first group received 5 ml normal saline 0.9% and 0.15 mg/kg Salbutamol Nebulizer, the second group received 5 ml normal saline 3%, and 0.15 mg/kg Salbutamol Nebulizer and the third group received 5% hypertonic saline 5 ml, and 0.15 mg Salbutamol Nebulizer. Supplementary treatment (e.g. supplementary oxygen and hydration) was administered if needed. Saline was provided to nursing staff with different concentrations in three separate and completely identical dishes, designated by numbers 1, 2 and 3 only. Salbutamol Nebulizer levels were similar for all patients (0.15 mg/kg).

2-3. Measurements Tools

Patients' clinical status, oxygen saturation, respiratory rate, heart rate, inter-rib retraction, dyspnea, and wheezing were evaluated three times every 20 minutes before and after treatment. Length of hospital stay (LOS) was defined as the number of days from the initial study inhalation until discharge from the

hospital, as recorded in the medical record for each patient.

2-4. Ethical Consideration

This study was approved by the Ethics Committee of Zahedan University of Medical Sciences and was registered with IRCT code 2013050213207N1 at the Iranian Clinical Trial Site.

2-5. Intervention

All the vials containing normal saline and different concentration of hypertonic saline were labelled with three different codes. Medicines were delivered by pressurized oxygen using the oxyhood with the flow meter set at 5 L/min. Supplementary treatments (e.g. supplementary oxygen and hydration) were administered if needed.

2-6. Inclusion and Exclusion Criteria

Inclusion criteria included: under two years old, history of recent viral infection of the upper respiratory tract, leading to wheezing or cracking in the lungs, or clinical diagnosis of bronchiolitis, and clinical severity score of CBSS (Clinical Bronchiolitis Severity Score) was 4-8 at the time of admission. Exclusion criteria included: less than one months or more than two years old, history of recurrent seizures, severe neurological disease, chest compression, immunodeficiency, congenital heart disease, history of preeclampsia (or/and age Pregnancy less than 34 weeks), birth weight less than 2,500 g, oxygen saturation less than 85% at room temperature, CBSS less than four or more than eight, unstable vital signs (heart rate over 200 min, blood pressure above or below two standard deviations, a respiratory rate greater than 70 min), and dissatisfaction with continuing the study.

2-7. Data Analysis

The data of each patient, which include clinical status, oxygen saturation, respiratory rate, heart rate, inter-rib

retraction, dyspnea, and wheezing gathered by authors, were precisely inserted in the prepared questionnaire sheets and then analyzed using the SPSS software version 16.0. Data were analyzed using Mann Whitney U and ANOVA.

3- RESULTS

In this study, 180 infants with moderate severity bronchiolitis who had the necessary criteria were included. Three groups of 60 patients were evaluated. One hundred eight of them (61%) were male, and the mean age was 5.29 ± 3.89 months, ranging from 1-15 months (**Table.1**). In all three groups, there was an increasing trend in oxygen saturation and a decrease in respiratory rate, heart rate, and CBSS at 20, 40, and 60 minutes. In the first and third groups, there was a significant difference in CBSS at both consecutive time points after treatment, but in the second group, it was significant only at 20 and 40 minutes after treatment ($P < 0.001$).

The mean of CBSS in the first, second groups, and the third group were significantly different only at 60 minutes after treatment. There was a significant difference between the first and third groups at all consecutive minutes after treatment in both groups ($P < 0.001$) (**Table.2**). The mean days of hospitalization were 4.63 ± 1.34 , 3.41 ± 1.07 , and 4.61 ± 0.72 days for the first, second, and third groups, respectively. According to One Way ANOVA, there was a significant difference between groups ($P < 0.001$). According to Tukey statistical test, the lowest number of hospitalization days was related to 3% saline, which was significantly different from the other two groups ($P < 0.001$). It is also worth noting that no complication observed by an increase in the concentration of saline. The remedy was sufficient in the third group.

Table-1: The Study groups of patients based on the gender, n=180.

Groups	Number (percentage)		
	Female	Male	All
First Group CBSS	26 (43.3%)	34 (56.7%)	60 (33.3%)
Second Group CBSS	32 (53.3%)	28 (46.7%)	60 (33.3%)
Third Group CBSS	14 (23.4%)	46 (76.6%)	60 (33.3%)
All	72 (%)	108 (%)	180 (100%)

CBSS: Clinical Bronchiolitis Severity Score.

Table-2: Comparison between the first, second, and third groups' at all consecutive minutes after treatment.

Groups	0 to 20 minute changes			20 to 40 minute changes			40 to 60 minute changes		
	Mean	SD	P-value	Mean	SD	P-value	Mean	SD	P-value
First Group CBSS	-0.33	0.60	<0.001	-0.50	0.59	<0.001	-0.63	0.66	<0.001
Second Group CBSS	0.03	11.18	0.982	-1.00	0.92	<0.001	-1.98	11.57	0.19
Third Group CBSS	-0.70	0.84	<0.001	-0.73	0.75	<0.001	-0.68	0.85	<0.001

CBSS: Clinical Bronchiolitis Severity Score. The first group received 5 ml normal saline 0.9% and 0.15 mg/kg salbutamol nebulizer, The second group received 5 ml normal saline 3% and 0.15 mg/kg salbutamol nebulizer, The third group received 5% hypertonic saline 5 ml and 0.15 mg salbutamol nebulize.

4- DISCUSSION

In this double-blind, randomized clinical trial, the therapeutic effects of combination Salbutamol Nebulizer with different concentrations of saline (0.9% normal saline, 3% hypertonic saline and 5% hypertonic saline) were studied among 180 infants with bronchiolitis. The mean age of the participants was 5.29 ± 3.89 months, which was consistent with the mean age of bronchiolitis. In this study, the mean hospitalization days for the first group were 4.63 ± 1.34 , 3.41 ± 1.07 , and 4.61 ± 0.72 days for the first, second, and third groups, respectively. The lowest number of hospitalization days was related to 3% saline, which was significantly different from the other two groups. The remedy was sufficient in the third group, but it was sufficient in the second group at the end of the hospitalization. It seems that the use of 5% saline could reduce the elongation of hospitalization and could be intended as a sufficient therapy instead of 3% and 0.9% saline. Moreover, the 5% saline is more accessible compared to

others and is much beneficial for families and hygiene systems. The complication was not observed in any group, and it figured that this therapy could be substituted for other treatments for uncomplicated patients. In a prospective, double-blinded, randomized clinical trial study, Köse et al. compared the efficacy of salbutamol/hypertonic saline 7% and 3% to 0.9% saline/salbutamol in the treatment of acute bronchiolitis. Their evaluated outcomes were LOS and CSS. Their findings indicated that hypertonic saline 7% and 3% could not reduce the LOS and improve the CSS of infants with acute bronchiolitis (22). Another study conducted in the Netherlands by Teunissen et al. compared the effect of hypertonic saline 3% and 6% with normal saline in hospitalized children with acute bronchiolitis. They demonstrated that though saline 3% and 6% are safe, they had not any advantages compared to normal saline regarding LOS, duration of supplemental oxygen use or tube feeding (23). Our study demonstrated that

nebulization with hypertonic saline, 5% could significantly reduce LOS and had more advantages. According to a study by Wainwright C et al., it was reported that 80% of cases occur in the first year of life and peak at 2-6 months old (18). In a study (2011), which was conducted on 120 infants with bronchiolitis in Turkey by Ilke et al., the mean scores of CBSS scores after treatment were significantly lower in all groups after treatment compared to pre-treatment ($P = 0.001$). However, there was no significant difference between the groups, and it was found that the combination of 3% hypertonic saline and salbutamol had no therapeutic advantages in improving CBSS criteria compared to the control group (normal saline and salbutamol) (19).

While in our study there was a significant difference between groups two and three, one and two at 60 minutes after treatment and between groups one and three from the beginning of treatment, this may be due to differences in sample size and working method (CBSS assessment interval). In the study conducted by Jayashree (2013), it was found that hypertonic saline reduced the length of hospital stay in patients compared to the normal saline recipient group (24.1%, equivalent to 1.16 days' decrease). In this study, consistent with our study, there was a decrease in the need for hospitalization (20). In the study conducted by Zhi-Yong Wang et al. (2019), indicating a beneficial effect of 3% HalfSalin nebulizing on decreasing readmission rates compared to NormalSalin nebulizing ($RR=0.93$; 95% $CI=0.70, 1.23$) (21). In the present study, it was found that the use of 5% hypertonic saline compared to normal saline and hypertonic saline 3% from the very first minutes after treatment was effective in reducing CBSS. However, hypertonic saline 3% at 60 minutes after treatment was as effective as 5% hypertonic saline in

reducing CBSS and required time to improve hypertonic saline 3% efficacy.

4-1. Study Limitations

The only limitation of this study was the discontinuing of remedy by patients, which fortunately no one decided to.

5- CONCLUSION

It seems that due to its cost-effectiveness, no complication and earlier efficacy of 5% hypertonic saline in the treatment of bronchiolitis, it is recommended to use 5% hypertonic saline instead of normal saline 0.9% in the treatment of bronchiolitis.

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7- CONFLICT OF INTEREST: None.

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