Hypertonic 3% Saline in Comparison with 0.9% (Normal) Saline in Treatment of Acute Bronchiolitis

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Abstract

Background
Bronchiolitis is the commonest cause of lower respiratory tract infection in infant. Respiratory syncytial virus is the commonest cause of bronchiolitis. This study aimed to assess the efficacy of nebulized 3% hypertonic saline and salbutamol in the treatment of acute bronchiolitis in comparison with nebulized 0.9% saline and salbutamol.

Materials and Methods
A prospective case second multicenter study was done at two pediatric tertiary centers at the period from 1st of December 2014 to 31 of March 2015. A total of 100 previously well infant and children of age 1-24 months with clinical diagnoses of bronchiolitis who were admitted to the hospital were included. They were divided into two groups, the study group received 4 ml of nebulized hypertonic 3% saline (for 14 days), and second group received 4 ml of nebulized normal 0.9% saline (for 14 days), each co-administer with 0.5 ml salbutamol.

Results
All patients with acute bronchiolitis having similar baseline characteristic, mean age 4.9 ± Standard deviation (SD) months, male gender constitutes 68% of the patients and the majority (67%) of the cases were below 6 months. The mean of clinical severity score at admission was 6.4 for normal saline (NS) group and 6.6 for hypertonic 3% saline (HS) group. The mean length of hospital stay of normal saline group = 4.3 ± Standard deviation (SD) day and for hypertonic saline group was = 4.7 ± Standard deviation (SD) day.

Conclusion
We didn’t find any advantage of hypertonic 3% saline over 0.9% normal saline in terms of length of hospital stay and clinical severity score.

Key Words: Bronchiolitis, Children, Hypertonic, Nebulization, Respiratory rate, Saline.

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1- INTRODUCTION

Acute bronchiolitis is the commonest cause of lower respiratory tract infection in infants resulting in inflammatory obstruction of the small airways (1). During the past three decades, hospitalization rates for infants with bronchiolitis have more than doubled in the United States (2), at a cost of more than $500 million annually (3). By age 2 years 44% children have been infected, with severe disease more common among infants aged 1-3 months, bronchiolitis is seasonal, with peak activity during winter and early spring (1). It is a viral disease caused by, Respiratory Syncytial virus (RSV), Human Parainfluenza virus, Rhinovirus, Human metapneumovirus, Influenza virus, Coronavirus, Human bocavirus, Adenovirus and Mycoplasma pneumonia (4). The small airway diameter in the vulnerable pediatric population makes them susceptible to bronchiolar obstruction from the submucosal oedema, mucous overproduction and cellular debris causing, increase airway resistance, generalized hyperinflation with areas of patchy atelectasis and ventilation-perfusion mismatch. Although, the epithelium recovery starts after 72 hours, the cilia repair takes several weeks. There is emerging data that some patients harbor the virus up to 100 days in their respiratory tract (5).

The peak age of infants hospitalized with RSV bronchiolitis is around 3 months. The illness is usually preceded by exposure to an older contact with upper respiratory tract symptoms within the previous week and the infant first develops a mild upper respiratory tract infection with sneezing and clear rhinorrhea which may be accompanied by reduced feeding and fever of 38.5-39°C (101-102°F). Respiratory distress ensures, wheeze, dyspnea, sometimes paroxysmal cough, and irritability; and the infant is often tachypneic, which interferes with feeding. A child does not usually have other systemic complaints, such as diarrhea or vomiting. Apnea may be more prominent than wheezing early in the course of the disease, particularly with very young infants (6). The physical examination is characterized most prominently by wheezing; the degree of tachypnea does not always correlate with the degree of hypoxemia or hypercarbia. Auscultation may reveal fine crackles, with prolongation of the expiratory phase of breathing; barely audible breath sounds suggest very severe disease with nearly complete bronchiolar obstruction (7).

Bronchiolitis is a clinical diagnosis. The diagnosis may be supported by radiographic or laboratory studies, but these tests are not necessary for diagnosis (8). Routine laboratory tests are not indicated in the infant with bronchiolitis who is comfortable in room air, well hydrated, fed adequately. The white blood cell count is normal or slightly elevated, and the differential cell count may be normal (9).

The disease is self-limiting, typically lasting between (7-10) days (9). Mild bronchiolitis requires explanation and reassurance, but no specific pharmacological or other therapy (10, 11). Bronchodilators and, to a lesser extent, systemic corticosteroids are frequently prescribed in general practice. However, randomized clinical trials of bronchodilators in viral bronchiolitis, whether in the outpatient setting or in hospitalized patients, have shown no clear or sustained benefits (10-12).

Meticulous hand washing is the best method to prevent nosocomial transmission (RSV destroyed by soap and 12 water/alcohol gel). During RSV season, high-risk infants should be separated from all infants with respiratory symptoms (13, 14). Administration of palivizumab (hyper immune RSV specific intravenous immunoglobulin) (15) (15 mg/kg IM once a month), a neutralizing humanized murine
monoclonal antibody against RSV, is recommended for protecting high risk children against serious complications from RSV disease. Immunoprophylaxis reduces the frequency and total days of hospitalization for RSV infections in high-risk infants in about half of cases. Palivizumab is administered monthly from the beginning to the end of the RSV season (usually October-December and March-May, respectively, in temperate Northern hemisphere regions).

Candidates for immunoprophylaxis include children who have lung disease or were born very prematurely. Children < 2 years of age with chronic lung disease requiring supplemental oxygen or other medical therapy currently or within the 6 months before the RSV season should receive prophylaxis for the 1st 2 RSV seasons if they have severe lung disease, and only for the 1st RSV season for less severe lung disease.

Children <2 years of age with hemodynamically significant congenital heart disease (heart failure, cyanosis, pulmonary hypertension), are also candidates for this therapy. Infants should receive seasonal RSV prophylaxis up to 12 months of age if they were born at < 28 weeks of gestation, and up to 6 months of age if they were born at 29-31 weeks of gestation. Infants born between 31 and 34 weeks of gestation should receive prophylaxis only if they have other risk factors. Adverse events with palivizumab are uncommon.

An enhanced-affinity version of the antibody is in late-stage development as a second-generation drug (16). There is no licensed vaccine against RSV. The challenge for development of live agents has been to produce attenuated virus candidates have been engineered in the laboratory from cold-passaged strains of RSV, according to a basic strategy that yielded the live poliovirus and influenza virus vaccine strains (17).

2- MATERIALS AND METHODS

2-1. Study design and setting

This is a prospective comparison study was done at the pediatric wards of the Al-Imamein Al-Kadhimein Medical city and the Child Central Teaching Hospital, in Baghdad city, Iraq, at the period from the 1st of December 2014 to 31 of March 2015. A total of 100 previously well infants and children of age ranging from 1 month to 24 months with a clinical diagnosis of acute bronchiolitis were included in the study.

2-2. Participants

We divided patients into 2 groups. The first group (50 patients) received nebulized solution containing 3% hypertonic saline 4 ml and 0.5 ml salbutamol every 6 hours (for 14 days) in addition to the usual treatment of bronchiolitis (oxygen, hydration and suction on need); while the second group (50 patients) received nebulized normal saline 0.9% 4 ml and 0.5 ml salbutamol every 6 hours (for 14 days) in addition to other lines of treatment of bronchiolitis.

Patients with the following conditions were excluded from the study: any patient with history of previous wheezing, patient with congenital heart disease, patient with chronic respiratory disease, critically ill patient, and patient who received steroid. Other patients were excluded from the study, if two courses of nebulization were not delivered or if there was clinical deterioration.

2-3. Data Collection
For each patient in both groups, the following data was recorded: age, gender, residence, type of feeding, family history of atopy, parental smoking then full examination was done and each patient was examined to record and follow the following signs: chest retraction, wheeze, respiratory rate, oxygen saturation within half hour after nebulization.

2-4. The Clinical Parameters

The respiratory rate, oxygen saturation, level of consciousness and the clinical severity score (CSS) as described by Wang et al. (18) were checked on admission and followed up daily (Table.1).

2-5. Statistical Analysis

Statistical analysis was done using SPSS version 20 software programs, Chi square and independent t-test sample were used and a P-value < 0.05 was considered significant.

Table-1: Checklist of Wang et al. for clinical severity score (CSS) assessment

<table>
<thead>
<tr>
<th>Variables</th>
<th>Scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory rate, breaths/min</td>
<td>0</td>
</tr>
<tr>
<td>&lt; 30</td>
<td>31-45</td>
</tr>
<tr>
<td>Wheezing</td>
<td>None</td>
</tr>
<tr>
<td>Retraction</td>
<td>None</td>
</tr>
<tr>
<td>General condition</td>
<td>Normal</td>
</tr>
</tbody>
</table>

3-RESULTS

The distribution of cases according to age and gender of the patients; 67(67%) patients were less than 6 months, 25(25%) patients between 6-12 months age and the remaining 8(8%) patients were more than 12 months, the male sex constitutes 68% of the cases and the female constitutes 32% of the cases as shown in Table.2.

The distribution of cases according to the risk factors; in group-1, 26% of the patients had family history of atopy, 48% of the patients had history of parental smoking, 52% of the patients were exclusively on breast feeding and 6% of the patients were premature. In group-2, 16% had family history of atopy, 64% had history of parental smoking, 44% of the patients were exclusively on breast feeding and 8% of the patients were premature P-value were not significant for all, as shown in Table.3. The baseline characteristics of both groups; in group-1: the mean and standard deviation (SD) for age was 5.1 (± 1.6), the male/female ratio was 2.5:1, the mean and SD for Respiratory rate (RR) was 55 (± 63), the mean and SD for oxygen saturation (SPO2) was 93.4 (± 2.9), and the mean and SD for CSS was 6.4 (± 1.8). In group-2, the mean and SD for age was 4.8 (± 1.9), male/female ratio was 1.7:1, the mean and SD for RR was 58 (± 92), the mean and SD for SPO2 was 94 ± 1.3, and the mean and SD for CSS was 6.6 (± 1.5). P-value were not statistically significant regarding baseline characteristics, as in Table.4.

The mean and SD changes in parameters (RR, SPO2, CSS) in both groups after 24 hours of treatment in group-1, the mean and SD for RR were decreased by 4.3 (± 1.3), the mean and SD for SPO2 was increased by 2.1 (± 0.9) and the mean and SD of CSS was decreased by 0.2 (± 0.16). In group-2: the mean and SD for RR was...
decreased by 4.9 (± 2.2), the mean and SD of SPO2 was increased by 2.9 (± 0.82) and the mean and SD of CSS was decreased by 0.3 (± 0.2). P-value were not statistically significant regarding all parameters, as in Table.5.

The mean and SD changes in parameters (RR, SPO2, CSS) in both groups, in group-1: the mean and SD for RR was decreased by 8.6 (± 2.3), the mean and SD of SPO2 was increased by 3.2 (± 0.7) and the mean and SD of CSS was decrease by 0.6 (± 0.34). In group-2: The mean and SD of RR was decreased by 7.8 (± 1.9), the mean and SD of SPO2 was decreased by 3.8 (± 0.95) and the mean and SD of CSS was decreased by 0.5 (± 0.32). P-value was not statistically significant regarding all parameters, as shown in Table.6.

The length of hospital stay; in group-1: the mean and SD was 4.3 (± 1.6) day. In group-2: The mean and SD was 4.7 (± 1.9) day. P-value were not statistically significant between two groups, as in Table.7. The Median clinical severity scores were monitored daily since admission till discharge and didn’t show statistical significant differences between two groups.
4- DISCUSSION

This study showed that most of the cases of acute bronchiolitis were under the age of 6 month (67%), which agrees with Dr. Sharma, who found 79% of the patients were below 6 months. The study showed that risk factors contributing to severe or complicated bronchiolitis and baseline characteristics were similar in both groups of patients and they were of no statistical significance, the mean age was 4.9 months which is similar to Dr. Sharma and Dr. Kuzik (19, 20).

The male/female ratio was 2.1:1 while in Dr. Sharma (19) study was 2.6:1 and Dr. Kuzik (20) study was 1.4:1. In this study there was small difference between group-1 and group-2 of patients regarding the mean of changes in clinical parameter (RR and SPO2) after one day and two days of treatment which was not significant statistically. The same is seen if we compare the change in CSS in both groups after 1 day and 2 days of treatment (P-value was not significant). These results are similar to the result of Dr. Sharma et al. (19), but they disagree with [Mandelberg 2002 (21), Zhang (16), Kuzik 2007 (20)]. These studies have reported better improvement in clinical severity score with HS, but the magnitude of improvement differed on different treatment days varying from 15.7% on day 1 to 29.4% on day 3 which was statistically significant. In this study, the mean length of hospital stay was 4.5 (± 1.7), the mean of group-1 was 4.3(± 1.6) and the mean for group-2 was 4.7 (± 1.9) with insignificant p-value. This result agree with the result of Dr. Sharma et al. (19), who concluded, nebulized 3% HS is not superior to 0.9% saline regarding the duration of hospitalization of patients with acute bronchiolitis.

On the other side, 3 studies [Mandelberg 2003 (21), Tal 2006 (22), Kuzik (20)], all are inpatients trials demonstrated benefit of nebulized 3% saline in reducing the duration of hospitalization and the pooled results showed that infants treated with nebulized 3% saline had statistically significant shorter mean length of hospital stay compared to these treated with nebulized 0.9% saline with MD of -0.94(95%) (1-1.48 to -0.4, P=0.006) and this represent a 25.9% reduction from mean length of hospital stay in the 0.9% saline group. The mean length of hospital stay in Kuzik et al. (20) in control group was 3.5 (± 2.9) days and the mean for HS group was 2.6 (± 1.9) days. A reduction in the mean of length of hospital stay of one day was previously proposed as being clinically significant (23).

4-1. Limitations of the study
In this study the data collection, it was reflect percentage of our province and not-all cities in our country. The children including in our study composed about all cases attend to hospital. We need more information and studies for covering such subjects.

5- CONCLUSION

Most of cases of acute bronchiolitis present below 6 month of age (67%). The study didn't find any advantage of hypertonic 3% saline over normal 0.9% saline in terms of length of hospital stay and clinical severity score. The mean changes in RR, SPO2 after treatment were not significant between both groups (Normal saline vs. Hypertonic 3% saline).

5-1. RECOMMENDATIONS

Hypertonic saline decreases airway edema, improves mucus rheologic properties and mucociliary clearance and thus decreases airway obstruction. But our study was not shown significant beneficial effect. We recommend further large-scale trial to prove its clinical benefits before recommending its routine use in patients with acute bronchiolitis.

6- CONFLICT OF INTEREST: None.

7-ACKNOWLEDGMENTS

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