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Application of nebulized 3% hypertonic saline in comparison to conventional therapy for treatment of bronchiolitis and effective on hospital duration of patient.

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Abstract

Objective: To evaluate the using of nebulized 3% hypertonic saline as a treatment to hospitalized infants with bronchiolitis in Karbala providence.
Methods: A total of 161 patients (age mean, 6.29 months) with bronchiolitis were studied. Patients (83) were randomized to receive, repeated doses (4 times/day) of nebulized 3% hypertonic saline and a control group (78) treated with conventional therapy. Staying period at hospital is the principle measuring of the results.
Results: LOS of 3.38 days was determined in patient group, while 4.67 days in the control group with reduction of 27.8% (P=0.001). Treatment with hypertonic saline was sufficiently tolerated with no adverse effects.
Conclusions: application of nebulized 3% hypertonic saline is an effective with low cost for patients hospitalized with moderately severe bronchiolitis.

Keywords: Conventional therapy, Hospital, Bronchiolitis, Etiology.

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Introduction

Bronchiolitis is one of common Lower Respiratory Tract Infection (LRTI) leading to hospital long stay of infants and children at age of two years or less. It indicates to respiratory infection with episode of wheezing in a child at 12-24 months and it mostly caused by viral infection with pneumonia or atrophy [1].

Most bronchiolitis cases in healthy infants and young children are self-limited. Supportive measures is the therapy in most cases to ensure that the patient get enough oxygen level with hydration [2]. Many factors are important to be considered in management of disease such as age of children, infection stage at time of supportive care, disease severity, primary diagnoses, and etiology type and infection site.

At the beginning of the disease course, pharmacotherapy can reverse the obstruction and inflammatory status while alteration of this course may have no benefit in the progress stage of the disease than only obstruction [3-7]. The positive action of pharmacotherapy may be unclear due to the present of predisposing asthma or because of low available information about the early signs and symptoms of bronchiolitis in infants [4,8-10].

Airway edema and mucus plugging can theoretically be reduced by hypertonic saline which also has reduction effect on the persistence pathologic features of acute bronchiolitis [11]. A significant of therapy with nebulized bronchodilator containing of hypertonic saline (3% or 5%) has been indicated by several trials compared with normal saline (0.9%) for hospitalized children with acute bronchiolitis [12-16].

conflicting results is introduced by studies in the ambulatory and emergency departments [17,18]. Saline or saline solution in medicine is usually referred to a sterile liquid of sodium chloride (NaCl) that can be parenterally used [19].

Concentrations of saline solution are ranging from low, normal to high. Higher concentrations of saline are less common applied in medicine, while it is more used in molecular biology. Normal concentration of Saline (NS) is frequently containing 0.90% of NaCl. Physiological saline or isotonic saline is less commonly used due to technically accurate.

The normal saline is commonly used as intravenous solution for patients have a problem to take medicine orally or suffering from dehydration or hypovolemia [19]. The suitable levels of normal saline mainly depends on the patients needs as with persistence diarrhea or with heart failure and its level for adults is typically ranging from 1.5-3 liters per day.

Saline solution is also used for washing of nasal cavity to relieve some common cold symptoms [20]. Such a solution plays a softening and loosing role to clean up the nasal passage for infants and adults. Thus, normal saline can be made at home by dissolving about an amount of half teaspoon of common table salt in a glass of clean tap water.

A sterile tap water should be used for saline solution preparation due to prevent entering of contaminated organism such as *Amoeba naegleria fowlerii* into the nose [20]. Saline solution can be prepared as hypertonic solution at concentration 3% which uses in critical care setting through increased intracranial pressure, or severe hyponatremia [21].

Hypertonic solution also can use as inhalator to help curing of other respiratory problems such as bronchiotitis [22]. It currently suggested using as a first choice for treatment of a cystic fibrosis by the cystic fibrosis foundation.

Treatment by aerosol nebulized hypertonic saline can perform by mechanism depending on disruption the reaction of glycosaminoglycans with IL-8 that reduce inflammation [21]. Hypertonic saline solution has an effect to increase mucociliary clearance of healthy individuals or those with asthma, bronchiectasis, cystic fibrosis, and Sino nasal diseases [22].

It has currently been trialed in acute bronchiolitis patients [23]. A sputum and cough can be induced by hypertonic saline inhalation, which can help to split the sputum from the bronchi and improve the obstruction of airway [23,24]. Thus, theoretical benefits provided by this mechanism may increase the treatment rate of acute bronchiolitis by applying hypertonic saline as nebulizer solution.

Nebulizer saline aerosol was synthesized by Fisoneb@ ultrasonic nebulizer (Canadian Medical Products Ltd. Markham, Ontario, Canada) and the saline concentration was increased later to 3, 4, and 5% used as mouthpiece for 7 min with no need to valve or nose clips [25]. To evaluate using of 3% nebulized hypertonic saline for treating moderate or severe infants with bronchiolitis, and it's efficacy in decreasing duration of hospitalization.

Methods

Patients

The study was conducted in Karbala teaching hospital for children over 15 months from 1st of November 2016 to 30th January 2018. Children admitted for treatment of moderate and severe bronchiolitis up to age 18 months were participated in this study. Disease was diagnosed based on the history of viral infection of upper respiratory parts, and other symptoms such as detection of wheezing or crackles in chest, saturation level of oxygen to less than 94% and detection of significant distress in respiratory as measured by a Respiratory Distress Assessment Instrument (RDAI) at score of more than 4 [26].

Patients included in the study were divided in to two groups, a study group was treated with 4 ml of 3% HS nebulizer few hours after admission, then every 6 hours, and the control group was treated by the conventional treatment ordered by the attending physician. Inhaled therapies were used by stable condition infant through a tight-fitting facemask, or head box, due to its more suitability to use by them. Clinical response was determined by using RDAI scores (Table 1) and $Sa0_2$ level in the beginning of the study and then three times a day. Length of infant stay at the hospital was determined.

Patients with the following findings are excluded from the study:

- History of last episode of wheezing.
- Patient with chronic cardiopulmonary disease or immunodeficiency.
- Critically ill patient at presentation.
- Patient referred to intensive care unit.

Ethics approved

The study was approved by informed oral consent obtained from care giver of each patient before enrollment.

Statistical analysis

Data were analyzed by Excel of Window Microsoft and by the software SPSS version 12.0.1 (SPSS Inc, China) (Table 1).

Chemical parameter	Score 0	Score 1	Score 2	Score 3
Respiratory rate (per minute)	None	40-60	60-70	>70
Use of accessory muscles	None	1 accessory muscle used	2 accessory muscle used	>3 accessory muscles used
Color/Cyanosis	Pink in room air/no cyanosis	Cyanosed when crying	Pink with oxygen or cyanosed in room air	Cyanosed with oxygen or cardio-respiratory arrest
Ausculatory findings	Normal	Decreased air entry, no Rhonchi heard	Decreased air entry, Rhonchi heard	Silent chest

Table 1. Modified Respiratory Distress Assessment Instrument (RDAI).

Results

About 161 infants (mean age, 6.3 months; range, 17 days to 18 months) with bronchiolitis were enrolled in this study from our center from 1st of November 2011 to 30th of January 2013. Two patients have been excluded from the study because they were deteriorated and referred to RCU, both of them were from the control group. The study showed that the admitted patients from 0-6 months are more than other age groups and it's about 56% from total patients *vs.* about 44% from the other two age groups as shown in Figure 1.

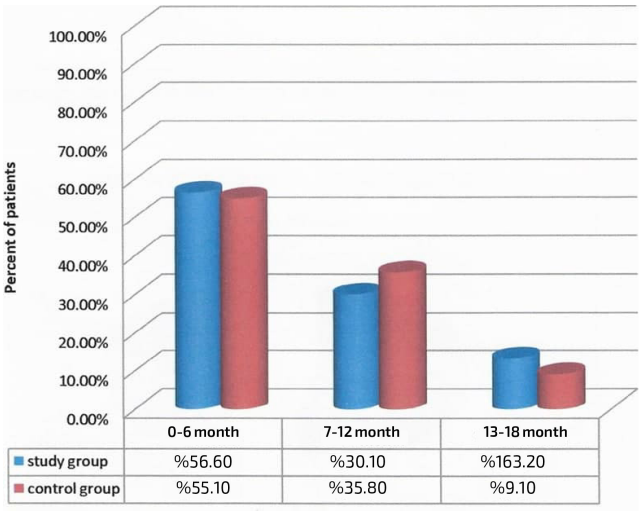

Figure 1. Show age distribution in study and control group.

In our study there is slight male predominance, in the study group male to female ratio was 1.2:1, *vs.* 1.1 1 in the control group as shown in Figures 2 and 3 respectively.

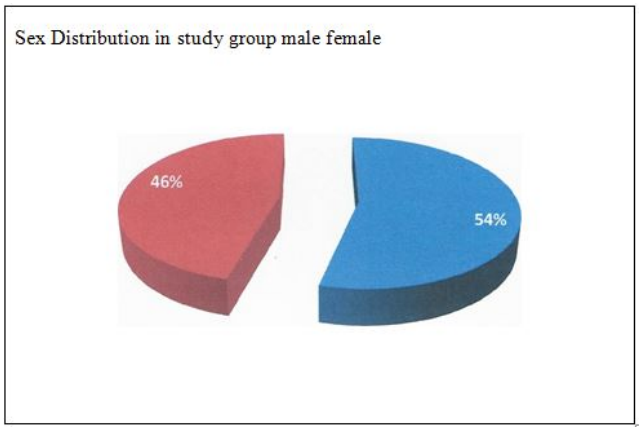

Figure 2. Show sex distribution in study group.

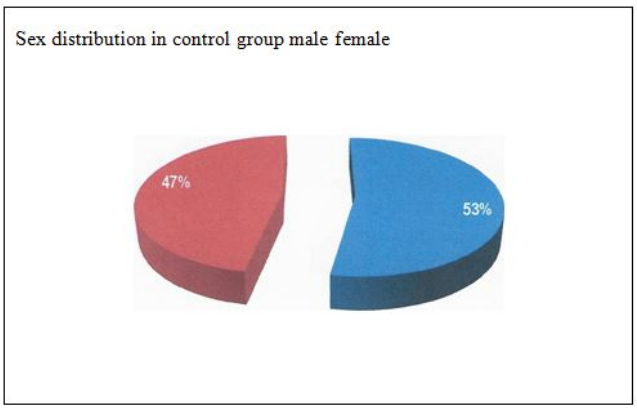

Figure 3. Show sex distribution in control group.

Regarding the address, the patients from the urban areas were more than rural areas for both study and control group as shown in Figures 4 and 5.

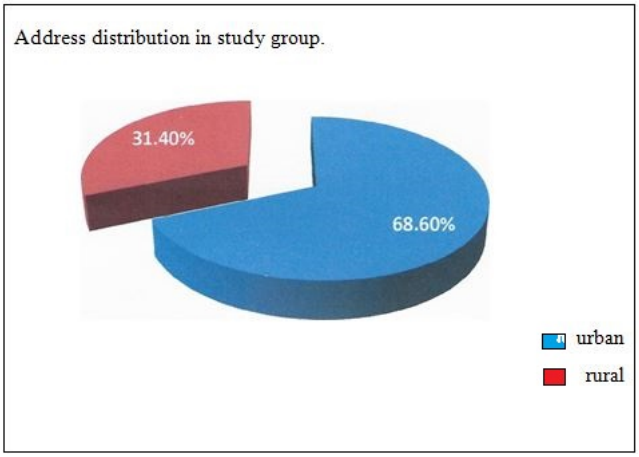

Figure 4. Show address distribution in study group.

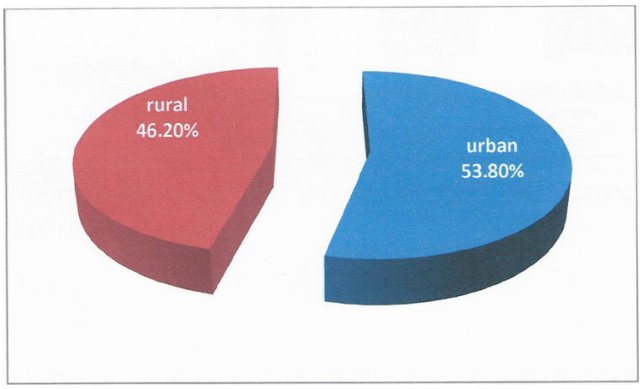

Figure 5. Show address distribution in control group.

Feeding pattern during 1st six months for all patients is shown in Figure 6, and the percentage of breast feeding is more than bottle and mixed feeding.

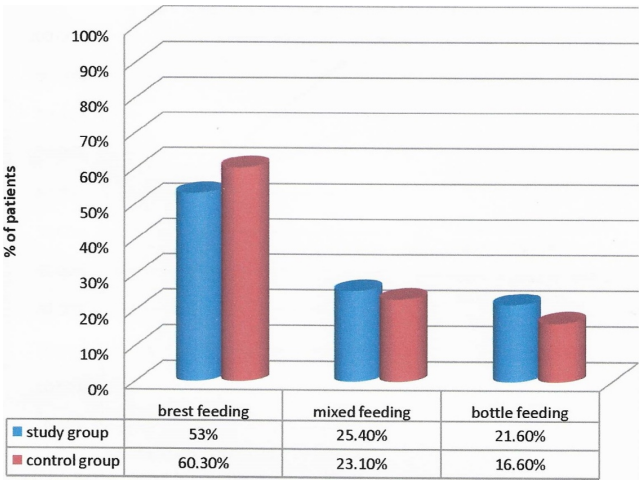

Figure 6. Show feeding pattern during 1st 6 months of life in different age groups.

Improvement in 02 saturation is more rapid in study group than control group within the 1st two days of treatment as shown in Figure 7.

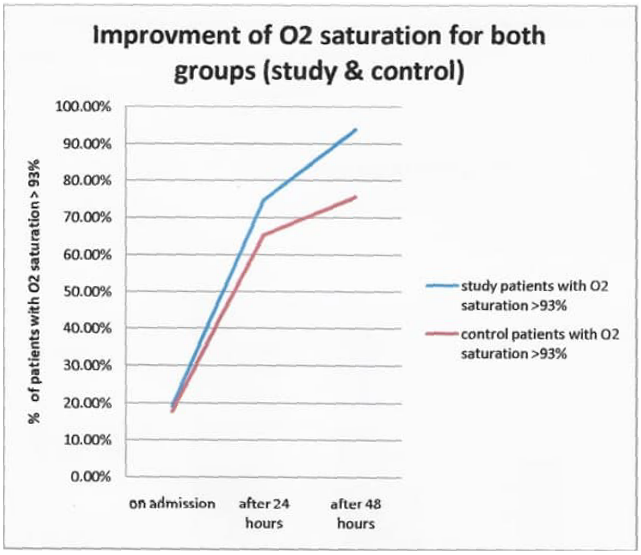

Figure 7. Show percentage of saturation up to 48 hours of treatment in both and study groups.

Patients who stay in the hospital less than 3 days in study group were 44 patients *vs.* 36 patients in control group, and patients who stay in the hospital from 3-6 days was 39 patients in study group *vs.* 22 patients in control group.No patient stay more than 6 days in the study group *vs.* 20 patients stayed more than 6 days (7-11 days) in control group as shown in Figure 8 and Table 2.

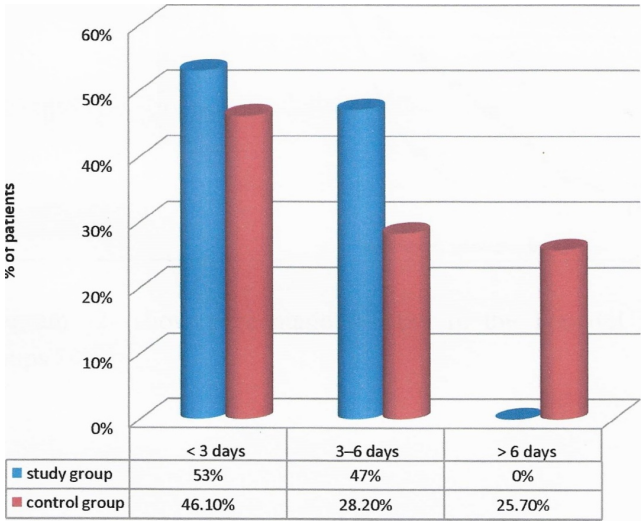

Figure 8. Show percentage of duration of hospitalization in study and control group.

Characteristics	3% saline (study group) 0=83	Conventional treatment (control group) 0=78	P value
Age, months, mean	6.37	6.21	0.2
Male/female, n	45/38	41/37	
Address urban/rural			
Feeding pattern, breast feeding/others	44/39	47/31	
Body weight-Kg, mean	7.49	7.54	0.187
Baseline severity score	6.48	6.28	
Baseline O_2 saturation, %			
O_2 saturation, %, 24 hour after admission	95.04	93.34	0.019
O_2 saturation, %, 48 hour after admission	95.97	94.87	0.013
Chest X-ray, n (%)	57 (68.6%)	53 (67.94%)	
Normal	20 (24.09%)	23 (29.48%)	
Pneumonia		2 (2.56%)	
Collapse			

Table 2. Baseline characteristics of enrolled children.

Discussion

In the present study most of patients were age less than one year, especially between 0-6 months n=47(56.6%) for study group and n=43(55.1%) for the control group), as shown in Figure 1 and this is possibly because of smaller airway in this age group. So, the mean age of our patients was 6.29 months (6.37 for the study group and 6.21 for the control group) as shown in Table 2. This is in line with Kuzik et al. [23]. A slight male predominance with a percentage of male: female (1.2: 1 in study group, and 1.1: 1 in control group) as shown in Figures 2 and 3, this is in line with Kuzik et al. In the other hand this percentage was less than that in Nadhim et al. [26].

The patients that we studied came from different areas in our city urban more than rural and there percentage shown in Figures 4 and 5 Feeding pattern at the 1st six months of life for both groups were 56.65% exclusive breast feeding as shown in Figure 6 and this percentage agree with Nadhim et al. that show 54% exclusive breast feeding [25]. Improvement in O_2

saturation in study group is much better than control group after 24 hours and 48 hours of treatment as shown in Table 2 and in Figure 7 this will enable the physician to discharge the patient earlier, with decreasing LOS. In our study SaO_2 is taken after enrollment to start with and 3 times daily thereafter. It is an important indicator of response to treatment and improvement of the general condition, so the scoring system (RDAI) decreased. Kuzik et al. and Al Ansary et al. depend on the improvement in SaO2 [23,25].

Some studies reported that the average length of hospitalization is 3-4 days in healthy infants older than six months who require hospitalization [27]. Improvement in the respiratory status was typically observed over 2-5 days, while wheezing was persisted in some infants for a week or more. The course may be longer in young infants and those with co-morbid conditions such as chronic lung disease. These children usually severely affected and may require ventilation help [28]. Duration of hospitalization is found to be less in study group than control group and this shown in Figure 7, patients that stay in the hospital less than 3 days were 44 patients (53%) in study group *vs.* 36 patients (46.1%) in control group, while patients stay for 3-6 days were 39 patients (47%) in study group *vs.* 22 patients (28.2%) in control group, finally 22 patients (25.7%) stay in hospital more than 6 days in control group only.

Patients in the control group had a mean of LOS about 4.67 days, *vs.* 3.38 days in the study group with a reduction in LOS of 1.3 days (a reduction percent of 27.8% ; P=0.001). The number of patients of each group that daily remaining in hospital was shown in the Figure 7. This study proved that inhaled 3% hypertonic saline is an effective treatment for patients hospitalized with moderate-severe bronchiolitis. Repeated inhalations (mean 4%) of nebulized HS can reduce the LOS to approximately 1.3 day in study group compared with control group. This is a clinically relevant benefit with the potential for widespread impact on the treatment of bronchiolitis. This study is in line with Kuzik et al. [23].

The routine uses of 3% hypertonic saline for the treatment of hospitalized infants who have bronchiolitis have also a significant economic benefit. The LOS reduction is not only reduce time of infants returning to home, but will also reduce hospital costs. There is exceed $580 million per year as an estimated hospital costs for bronchiolitis in the US and that may include the common using of NS bronchodilators nebulizer. Thus, the substitution of NS with such price of 3% HS, with low LOS, has the potential to reduce more than $150 million annually in the US healthcare system [23]. However, no data obtained about the hospital cost in Iraq.

Conclusion

Inhaled 3% HS is effective therapy to infants admitted to the hospital with moderately severe bronchiolitis and also it is an inexpensive. More studies are needed to determine the typical dosing and to identify any more benefits from co-administered bronchodilator. Study with a greater sample size in different centers is important to perform for determining the effective and safety of hypertonic saline for the treatment of infants with many severity levels of bronchiolitis. Also, more researches are needed to identify if the hypertonic saline is efficiency to use with or without other bronchodilator therapies and also to determine the typical delivery interval, concentration, and delivery device (e.g, ultrasonic and jet nebulizer).

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