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ORIGINAL ARTICLE

Aerosolised hypertonic saline in hospitalized young children with acute bronchiolitis: a randomized controlled clinical trial.

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Abstract:

Objectives: *To determine the effectiveness of aerosolised 3% saline in hospitalised children with acute bronchiolitis.*
Design: *Prospective, randomized, double blinded clinical study.*
Setting: *Referral teaching hospital, from October 2007 to March 2009.*
Patients: *40 children [age less than 2 yrs] were enrolled sequentially and randomized into 2 groups [20 each; Group- A - 3% saline and Group-B – Normal saline].*
Intervention: *4 nebulizations [3% saline or normal saline] were given every day until discharge. Additional inhalations were recorded as add-on nebulisations. Severity was assessed using the clinical severity score daily. Children showing worsening of clinical scores {treatment failure} were dropped from the study.*
Principal outcome measures: *Reduction in clinical severity & the length of hospital stay. Minor outcome measures studied were number of add-on nebulisations required & treatment failure.*
Results: *The reduction in clinical severity scores was 1.8±0.83 in the 3% saline group and 1.7±0.86 in the normal saline group. The length of hospital stay was 2.25±0.89 days in 3% saline group compared to 2.88±1.76 days in the normal saline group. The number of add-on nebulisation was 2.4±4.1 in the normal saline group and 1.7±1.75 in the 3% saline group. These observations were not statistically significant. A significant difference was found in terms of treatment failures between the 2 groups [4 Vs 0] [p=0.03].*
Conclusions: *In hospitalized children with moderate acute bronchiolitis, aerosolized 3% saline is safe and prevented worsening of clinical symptoms but is not superior to normal saline in reducing the clinical severity and the length of hospital stay.*

Keywords: *hypertonic* saline; viral bronchiolitis

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Introduction

Bronchiolitis is one of the most common respiratory tract infections in young children. The treatment of bronchiolitis is mainly supportive in nature. Mild cases are managed at home with antipyretics, hydration and home remedies/cough formulas. Moderate and severe cases need admission and several modalities of treatment including bronchodilators, steroids, antiviral agents have been tried without much success[1, 2].

Certain Western studies have shown that nebulisation with 3% saline along with bronchodilators (adrenaline, terbutaline) was more effective than with normal saline in terms of reduction in the duration of the symptoms and length of hospital stay[3, 4]. The present study was conducted to determine the effectiveness of 3% saline as diluent for salbutamol nebulisation in treating hospitalized children with moderate acute bronchiolitis.

MATERIALS AND METHODS:

Study design and Setting: A prospective randomized double blind clinical trial was conducted in the Department of Pediatrics at the M S Ramaiah teaching hospital during the winter months from October '07 to March '09.

Study Population: Children < 2 years of age, admitted with first episode of lower respiratory tract infection with wheeze and having a moderate respiratory distress with clinical score between 4 and 8, were included in the study. All patients were enrolled within 24 hours of admission .Children with pre-existing cardiac disease, previous wheezing episodes, severe disease [clinical score > 8] requiring mechanical ventilation [saturation < 85% on room air, cyanosis, obtunded consciousness, and/or progressive respiratory failure] were excluded from the study. Written informed consent was obtained and ethical committee approval was obtained from the institution for this study.

Intervention: After enrolment, patients were randomized into two groups using a computer generated random numbers. The eligible patients were recruited sequentially and randomized in a double-blind manner. All patients received humidified oxygen, IV fluids and calculated dose of salbutamol {0.15 mg/kg/dose} for nebulisation either with 3 ml of 3% saline [**Group-A: study group]** or with 3 ml of normal saline [**Group-B: control group]** as diluent. Nebulizations were administered every 6th hourly, until the patient was ready for discharge. Additional nebulisations, as advised by the treating physician were recorded as add-on therapy. Nebulisations were given using a nebulisation chamber, connected to a central source of pressurized oxygen, set to a flow at a rate of 5-6 L/min. Relevant demographic and clinical data were obtained from each patient. A complete blood count and chest X-ray was done on all patients. A clinical severity score as described by Wang et al was assigned to children at enrollment and daily during the study period[5]. Children who showed worsening of clinical scores during the course of the stay were labeled as treatment failure and dropped from the study.

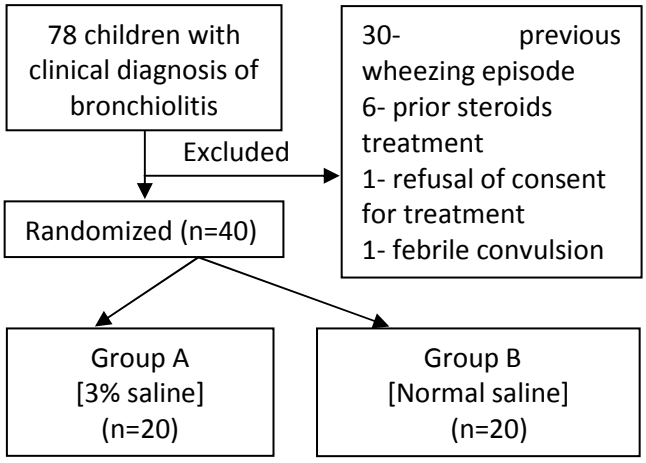
Outcome measures: Major outcome parameters studied were improvement in the respiratory distress {clinical score} and the duration of hospital stay. Other minor outcome measurements were number of add-on nebulisation required and failure rate in each group. The duration of hospital stay, was measured using a method previously validated by the Pediatric Investigators Collaborative Network on Infections in Canada studies of hospitalized children with RSV infection [PICNIC study][6]. Patients were discharged from the study if they were afebrile, maintaining saturation of > 96% in room air without respiratory distress and tolerated oral feeds well.

DATA ANALYSIS

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD and results on categorical measurements are presented in Number (%). Significance was assessed at 5 % level of significance. Student 't' test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (inter group analysis). Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups.

RESULTS

A total of 78 patients were admitted with a clinical diagnosis of bronchiolitis, during the study period. 38 children did not meet the inclusion criteria and were excluded from the study [see flow chart- 1]. 40 children, who met the inclusion criteria were included for the analysis and 20 patients each were randomized in Group A (3% Saline) and Group B (NS).



Flow chart / Fig 1: showing enrollment details

The mean age at hospitalization was 5.93±3.83 months (range 2–12 months) and children less than 6 months constituted 60% of total admissions. Male children were more commonly affected than female children (1.6:1). The mean clinical score at admission was 5.8±1.09, with 5.55±0.88 in the 3% saline group and 6.05±1.23 in the normal saline group. Figure-2 shows the clinical scores of patients during each hospitalized day.

Fig. 2: Clinical severity scores vs. Day of hospitalisation.

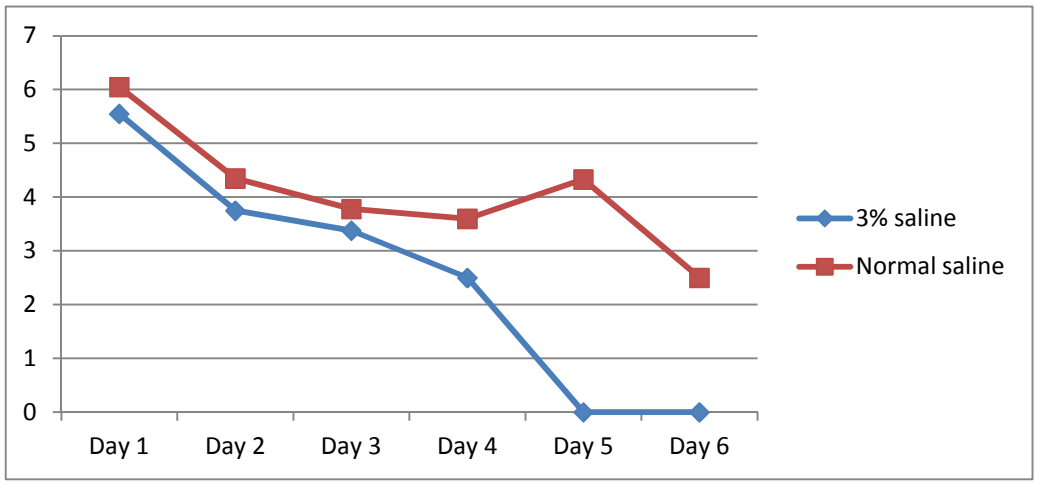


Table 1: Analysis of outcome parameters.

	3% saline (Group A) (n=20)	Normal saline (Group B) (n=20)	p- value
Reduction in Clinical severity score	1.80±0.83	1.70±0.87	**0.712**
Length of hospital stay in days	2.25±0.89	2.88±1.76	**0.165**
Mean difference in LOS (days)	0.63±0.87		
Percentage reduction in LOS	**24%**		

P<0.05 – statistically significant. LOS – length of hospital stay.

The principle outcome parameters studied were reduction in clinical severity and the length of hospital stay. The mean reduction in clinical severity scores was 1.75±0.84 with 3% saline group, being slightly better [1.8±0.83] than the normal saline [1.7±0.86] in reducing the severity of the disease. The mean duration of hospital stay was 2.56±1.41 days. It was 2.25±0.89 days in the 3% Saline group and 2.88±1.76 days in the normal saline group. The mean difference in length of stay was 0.63±0.87 days and there was a 24% reduction in the length of hospital stay in 3% saline group compared to the normal saline group. The number of add-on nebulisations was also higher in the normal saline group [2.4±4.1 Vs 1.7±1.75] when compared to the 3% saline group. But all the above observations were not statistically significant. There were 4 treatment failures in the normal saline group and none in the 3% saline group, which was a statistically significant [p= 0.03] finding in our study.

DISCUSSION

The management of bronchiolitis, especially the moderate to severe disease, is a widely debated issue in the recent times. An infectious disease of viral etiology, which manifests with wheezing, akin to reactive airway disease, but does not respond to bronchodilator therapy or steroids in the same fashion, had evoked huge interest on this disease and extensive research has been done to find out what works and what does not work in its management. The only proven and well accepted therapeutic measure is the administration of humidified oxygen. The opinion has been divided with contrasting results with respect to bronchodilator therapy. Recently 3% saline nebulisations has been tried in the treatment of moderate to severe bronchiolitis and found to be promising. Sarrell et al[4], in their study on ambulatory patients with bronchiolitis, found 3% saline to be effective in reducing the symptoms and severity of the disease, when co-adminstered with a

bronchodilators. Later Mandelberg et al[3], conducted a study on 52 children hospitalized with moderate to severe disease and found that 3% saline nebulisations reduced the severity as well as the length of hospital stay in these children. Subsequently studies by Tal et al[7] and Kuzik et al[8] showed similar results. A Cochrane review[9] of the above mentioned studies, recently published states that the nebulisations with 3% saline is effective in reducing the length of hospital stay and the severity of the disease in hospitalized children with moderate to severe acute bronchiolitis.

In the present study, the principle outcome measure was the reduction in clinical severity, which was measured in terms of difference between the clinical scores on day 1 and day 2. There was 32% reduction in the clinical severity with 3% saline compared to 28% with normal saline. However this difference was not statistically significant [p=0.712]. In terms of the mean duration of hospital stay, we did not find any statistically significant difference {0.63±0.87 days [24%], with 3% saline group having fewer days of hospitalization} between the 2 groups. Similarly, fewer add-on nebulisations were required in 3% saline group which was not statistically significant. However, there were 4 treatment failures from the normal saline group and none in the 3% saline group and this observation was statistically significant [p=0.03]. The lack of statistical significance in the present study, inspite of the observations similar to the previous published studies can be attributed to the relatively small sample size, younger age of the study population and relatively low clinical scores.

Bronchiolitis, an infectious disease with seasonal prevalence where environmental and demographic factors also play a vital role in disease causation, requires regional guidelines for its management. Extrapolation of results from western studies may not be apt for our conditions. In view of the results from Cochrane metaanalysis and lack of statistical significance from the present study, further studies are required to find out whether 3% saline to prevents/reduces the worsening of symptoms, as observed in our study.

CONCLUSION

The findings of the present study suggests that 3% saline is not superior to normal saline in terms of reducing clinical severity, length of hospital stay and number of additional nebulizations in hospitalized children with moderate severity of acute bronchiolitis. However 3% saline nebulization was found to be safe, prevented worsening of disease process and had less treatment failures.

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