

Role of Hypertonic Saline Nebulization Therapy in Patients with Early Acute Respiratory Distress Syndrome

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ABSTRACT

Acute respiratory syndrome (ARDS) is a life threatening condition with high mortality rates. It is characterized by inflammation of the lung parenchyma leading to impaired gas exchange with concomitant systemic release of inflammatory mediators causing protracted inflammation, increased vascular permeability, increased permeability of alveolar epithelial cells, extravasation of plasma and leucocyte infiltration, and frequently resulting in multiple organ failure. Since inflammation is thought to contribute to the pathogenesis of ARDS, it is rational to explore modulating therapies for this inflammation, provided the adverse effect of such treatment is not excessive. Hypertonic saline nebulizer 3% NaCl is a potent anti-inflammatory agent, and immunomodulator, which exert inhibitory effects in several stages of the inflammatory cascade and would seem to be a logical choice for treatment of ARDS. This study included 60 patients according to sample size admitted to the Department of Critical Care Medicine at the Alexandria Main University Hospital meeting criteria of ARDS according to Berlin's definition. They were categorized into two groups group I (control group) included thirty patients, and group II (study group) included thirty patients who received 4ml of hypertonic saline nebulization once daily for 7 days. All cases were subjected to history taking, clinical examination, assessment of disease severity (APACHEII), laboratory investigations, ABG, and chest X-ray, with measurement of lung mechanics (compliance, airway resistance, peak and plateau pressures, PEEP), hypoxic index, lung injury score (LIS), and SOFA score. Hypoxic index, LIS and SOFA score were significantly improved in hypertonic saline group than control group. Also, intensive care unit (ICU) stay and mechanical ventilation days were reduced in the hypertonic saline group with statistically significant difference. Survival was significantly higher in the hypertonic saline group. Initiation of hypertonic saline nebulization therapy for patients with early ARDS appears to be tolerable and may be beneficial with significant improving in oxygenation with trend to decrease mortality, ICU stay, and mechanical ventilation days and so may be added to protective lung strategy.

Keywords: Acute respiratory distress syndrome (ARDS), hypertonic saline, hypoxic index.

INTRODUCTION

Acute respiratory distress syndrome (ARDS) is a life threatening condition with high mortality rates. The pathophysiological basis of acute respiratory distress syndrome is characterized by excessive and protracted inflammation, increased vascular permeability, increased permeability of alveolar epithelial cells, and extravasation of plasma and leucocyte infiltration. ARDS is often systemic in nature, resulting in hypoxic respiratory failure lead to insufficient oxygen for the body tissues to function, multiorgan dysfunction and death.

Numerous clinical studies have been conducted in patients with ARDS, but great advances in those patients are still lacking and supportive therapies remain

the mainstay in management. Definitive treatment includes the treatment of the underlying cause and a

How to Site This Article:

Tayseer Mohamed Zaytoun, Amr Hassan Dahroug and Hala Mohamed Abdella (2017). Role of Hypertonic Saline Nebulization Therapy in Patients with Early Acute Respiratory Distress Syndrome. *Biolife*. 5(1), pp 74-84.

DOI: 10.5281/zenodo.7360210

Received: 6 January 2017;

Accepted; 27 February 2017;

Available online : 5 March 2017

lung protective ventilation strategy is considered the gold standard treatment. ^(1,2)

Since inflammation is thought to contribute to the pathogenesis of ARDS, it is rational to explore modulating therapies for this inflammation, provided the adverse effect of such treatment is not excessive.

Hypertonic saline 3% NaCl with 513 mEq/L of Na and 513 mEq/L of Cl is a potent anti-inflammatory agent, and immunomodulator, which exerts inhibitory effects in several stages of the inflammatory cascade. Hypertonic saline, at a cellular level, decreases alveolar macrophage activation, PMN recruitment, priming and activation, as well as cell surface adhesion molecule expression, and would seem to be a logical choice for treatment of ARDS. Clinical outcomes in trials on the role of hypertonic saline in ARDS have varied. Clinically, inhaled HTS is used to treat inflammation as in cystic fibrosis. ⁽³⁾ Cystic fibrosis (CF) is the most common life-limiting autosomal recessive genetic disorder in Caucasians. In the clinical setting, Reeves et al ⁽⁴⁾ have also touted the anti-inflammatory effects of nebulized HTS in patients with CF. In their study, aerosolized HTS led to degradation of IL-8 and decreased neutrophil efficiency. Also, total IL-8 levels decreased by 33% in CF patients following treatment with HTS. In CF patients, the data show a reduction in neutrophil chemotaxis as a result of chemokine degradation and disruption of IL-9: glycosaminoglycan complexes, suggesting that the nebulized HTS may be facilitating resolution of inflammation via a similar mechanism post-injury. ⁽⁵⁾ In ARDS, the epithelial sodium channels become overwhelmed, and impaired alveolar fluid clearance leads to pulmonary edema formation. The observation that inhaled HTS alters airway ion permeability may partly explain its recent success in treating bronchiolitis and CF. ^(6,7)

Mandelberg et al ⁽⁸⁾ investigate the effects of nebulized hypertonic saline in treatment of hospitalized infants with viral bronchiolitis on the respiratory epithelium and the mucociliary transport.

Also hypertonic saline used by Taube et al ⁽⁹⁾ in patients with moderate to severe chronic obstructive pulmonary Disease.

From the previous studies hypertonic saline can be used in treatment of ARDS through its anti-inflammatory effect partly due to its ability to inhibit neutrophil and macrophage-mediated cytokine production. ^(10,11)

These data further support the role of epithelial damage in the pathogenesis of ARDS. These results suggest that nebulized HTS attenuates ARDS by suppressing epithelial inflammation, supporting further research to its use as a novel strategy to treat ARDS. ⁽¹²⁾

Objective:

To determine the effect of inhaled hypertonic saline on patients with early ARDS as regard hypoxic index ($\text{PaO}_2/\text{FiO}_2$), LIS (Murray score), lung mechanics, mortality, duration of intensive care unit, and mechanical ventilation days.

MATERIALS AND METHODS

This prospective single blinded randomized controlled study was conducted on 60 adult patients according to the sample size of both gender meeting the criteria of ARDS according to Berlin's definition admitted to the department of Critical Care Medicine in the Alexandria Main University Hospital. Full detailed consent was taken from every patient's relatives. Approval for the study was obtained from the ethical committee of Faculty of Medicine.

Both groups are subjected to complete history taking, complete physical examination, arterial blood gas sampling, routine laboratory studies and chest radiography or computed tomography (CT) of the chest.

The patients were randomized by simple randomization technique from 1 to 60 and classified into two groups according to the even and odd numbers:

Group I (Control group) (n=30): odd numbers 1,3,5,7...59.

Group II (Hypertonic saline 3% group, study group) (n=30): even numbers 2, 4, 6, 8, 60.

All patients admitted with ARDS received the main lines of the treatments in the form of treatment of the underlying cause, ventilatory management using protective lung approach. Group II patients (nebulized hypertonic saline group) received hypertonic 3% saline nebulizer for the first seven days in addition.

Inhaled hypertonic saline 3% was supplied in a dose of 4ml once daily for 7 days which administered with a jet nebulizer and the fill volume connected to a compressor with an adequate air flow.

The following measurements were obtained:

1. Arterial blood gas (ABG) before and after inhaled hypertonic saline using (GEM premiere 3500 machine). The main gasometrical variables pH, PO_2 , hypoxic index, and PCO_2 were measured in both samples daily and when there is change in patient condition or change in mode or data of mechanical ventilator.
2. Hypoxic index = Arterial oxygen tension (PO_2) known from ABG/Inspired oxygen fraction (FiO_2) as applied on the ventilator.
3. Lung mechanics estimated every 24 hour and included the following :
 - Peak inspiratory pressure (PIP (cmH_2O): maximum pressure obtained during inspiration.
 - Plateau pressure (Pplt (cmH_2O)): by occluding expiratory tubes at end of inspiration with no air flow (inspiratory hold maneuver).
 - Positive end expiratory pressure [PEEP (cmH_2O)] required.
 - Airway resistance ($\text{cmH}_2\text{O}/\text{L}/\text{S}$): = (PIP-Pplt / inspiratory flow rate).
 - Static compliance (Cst ($\text{ml}/\text{cmH}_2\text{O}$) = (Exhaled tidal volume)/(Plateau pressure - PEEP)
4. APACHE II score [appendix 2] measured on admission.

- 5. SOFA score [appendix 3] measured daily from day 1 to day 7.
- 6. X-ray was done daily and examined for the presence of: lung infiltrates congestion, consolidation, etc.
- 7. Na, CL daily measurement.
- 8. Murray score will be calculated daily (lung injury score) [appendix 1], was estimated daily in the morning based on information obtained from:
 - a) Number of quadrants of infiltrations from chest X-ray.
 - b) Hypoxic index.
 - c) Positive end expiratory pressure (PEEP (cmH₂O)) required on the ventilator to get better oxygenation
 - d) Static compliance
- 9. UOP daily and Cumulative fluid balance (mL) at the end of 7th day.

The following Outcome data were collected

- Days on mechanical ventilator
- Length of stay in ICU
- Complications
- Mortality at 7th, and 28th day

Statistical analysis of the data: ⁽¹³⁾

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. ⁽¹⁴⁾ Qualitative data were described using number and percent. Quantitative data were described using range (minimum and maximum), mean, standard deviation and median. Significance of the obtained results was judged at the 5% level.

RESULTS

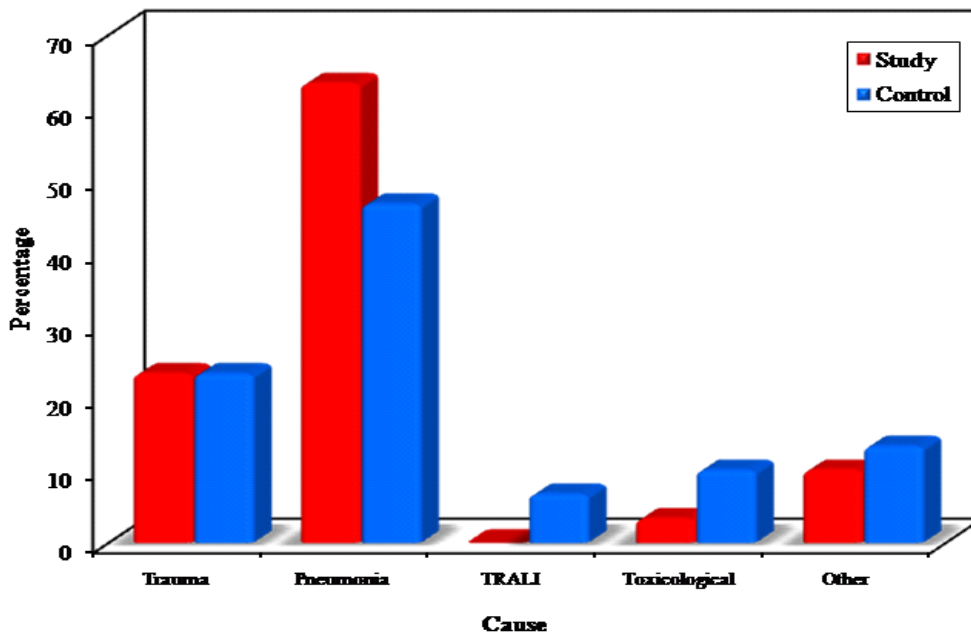
There was no statistically significant difference between the two studied groups regarding age, sex and APACHE II score on admission ([Table-1](#)).

Table-1. Comparison between the two studied groups according to demographic data

	Study (n= 30)		Control (n= 30)		Test of sig.	p
	No	%	No	%		
Sex						
Male	14	46.7	16	53.3	□ □ □ □ □ □	0.606
Female	16	53.3	14	46.7		
Age						
Min. – Max.	20.0 – 69.0		23.0 – 81.0		t= 0.143	0.887
Mean ± SD.	41.30 ± 14.13		41.87 ± 16.44			
Median	38.0		35.50			
APACHE II						
Min. – Max.	5.0 – 22.0		2.0 – 32.0		Z= 1.606	0.108
Mean ± SD.	11.63 ± 4.74		14.03 ± 6.68			
Median	10.50		13.0			

□², p: □² and p values for Chi square test for comparing between the two groups
 t, p: t and p values for Student t-test for comparing between the two groups
 Z, p: Z and p values for Mann Whitney test for comparing between the two groups

Figure-1. Comparison between the two studied groups according to cause of ARDS



Regarding etiology, In group I, pneumonia was the most common cause of ARDS amounting for 46.7 % of the cases (14 patients), followed by, trauma amounting for 23.3 (7 patients) toxicological causes (organophosphorus poisoning) amounting for 10.0 (3 patients), and Transfusion Related Acute lung Injury (TRALI) amounting for 6.7% (2 patients) also, other

In group II, Pneumonia was the commonest cause amounting for 63.3% (19 patients), followed by trauma amounting for 23.3 (7 patients), and Toxicological causes (cyanide poisoning) 3.3%, (1 patients). Other causes amounting for 10.0 % (3 patients) included two burned cases, and one intestinal obstruction case. Others: [Burn, pancreatitis, diabetic ketoacidosis

Table-2. Comparison between the two studied groups according to hypoxic index (HI)

HI	Study		Control
	1 st	2 nd	
1st	(n= 30)	(n= 30)	(n= 30)
Min. – Max.	58.0 – 200.0	65.0 – 237.0	57.0 – 215.0
Mean ± SD.	116.80 ± 29.31	131.37 ± 40.13	106.53 ± 31.62
Median	113.0	119.50	107.50
Significance	p ₁ =0.089, p ₂ =0.002*, p ₃ =0.002*		
2nd	(n= 30)	(n= 30)	(n= 30)
Min. – Max.	61.0 – 237.0	70.0 – 266.0	43.0 – 180.0
Mean ± SD.	136.03 ± 55.19	154.83 ± 61.67	91.88 ± 34.89
Median	127.50	156.0	85.0
Significance	p ₁ =0.001*, p ₂ <0.001*, p ₃ =0.019*, p ₄ =0.114		
3rd	(n= 30)	(n= 30)	(n= 30)
Min. – Max.	62.0 – 351.0	55.0 – 296.0	54.0 – 236.0
Mean ± SD.	131.97 ± 67.97	155.03 ± 61.84	109.98 ± 51.39
Median	109.50	153.50	91.0
Significance	p ₁ =0.160, p ₂ =0.002*, p ₃ <0.001*, p ₄ =0.294		
4th	(n= 30)	(n= 30)	(n= 30)
Min. – Max.	49.0 – 251.0	54.0 – 304.0	37.0 – 202.0
Mean ± SD.	139.50 ± 49.51	175.10 ± 64.70	93.68 ± 45.02
Median	136.0	177.50	80.50
Significance	p ₁ =0.001*, p ₂ <0.001*, p ₃ <0.001*, p ₄ =0.015*		
5th	(n= 28)	(n= 28)	(n= 30)
Min. – Max.	49.0 – 321.0	57.0 – 320.0	40.0 – 226.0
Mean ± SD.	168.43 ± 74.75	185.96 ± 73.17	101.67 ± 51.74
Median	160.0	180.50	84.0
Significance	p ₁ <0.001*, p ₂ <0.001*, p ₃ =0.019*, p ₄ <0.001*		
6th	(n= 28)	(n= 28)	(n= 30)
Min. – Max.	60.0 – 254.0	57.0 – 300.0	42.0 – 210.0
Mean ± SD.	149.54 ± 53.15	187.08 ± 65.56	102.02 ± 52.17
Median	148.0	207.0	77.50
Significance	p ₁ =0.003*, p ₂ <0.001*, p ₃ <0.001*, p ₄ =0.002*		
7th	(n= 26)	(n= 26)	(n= 30)
Min. – Max.	50.0 – 250.0	55.0 – 384.0	40.0 – 204.0
Mean ± SD.	171.88 ± 64.76	225.83 ± 76.09	93.40 ± 54.07
Median	200.0	250.0	72.50
Significance	p ₁ <0.001*, p ₂ <0.001*, p ₃ <0.001*, p ₄ =0.001*		

p₁: p value for Mann Whitney test for comparing between control and 1st reading study group
 p₂: p value for Mann Whitney test for comparing between control and 2nd reading study group
 p₃: p value for Wilcoxon signed ranks test for comparing between 1st and 2nd reading in the study group
 p₄: p value for Wilcoxon signed ranks test for comparing between 1st day and each other periods in study group
 *: Statistically significant at p ≤ 0.05

causes were burn, pancreatitis, diabetic ketoacidosis (DKA) and chronic myeloid leukemia (CML) amounting for 13.3 % (4 patients each).

(DKA) and chronic myeloid leukemia (CML)]. Collectively, direct (pulmonary) injuries to the lung were responsible for 70% of cases (21 patients) with ARDS in group I, and 86.7% of cases (26 patients) in

group II. On the other hand, indirect (extra pulmonary) causes were responsible for 30.0 % of cases (9 patients) in group I, and 13.3% of cases (4 cases) in group II. There was no statistically significant difference between the two groups as regarding etiology of ARDS either individually or collectively (P=0.340, P=0.117 respectively) (Figure-1).

Regarding ABG, hypertonic saline has non-significant effect on pH, HCO₃, PaCO₂ at different time intervals during study period.

Hypoxic index (PaO₂: FiO₂ ratio) improved significantly throughout the seven days of the current study in the study group in comparison to the control group. There was significant increase of hypoxic index in

Figure-2. Comparison between the two studied groups according to hypoxic index

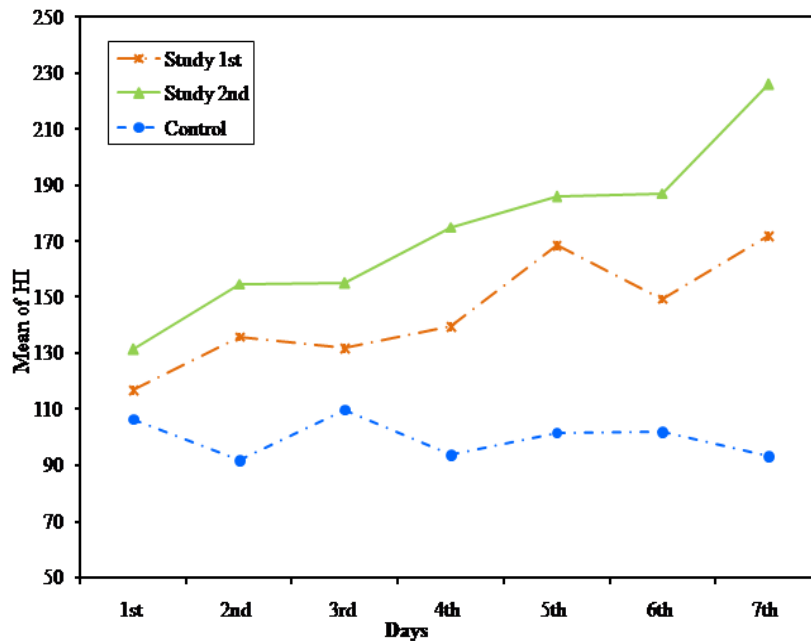
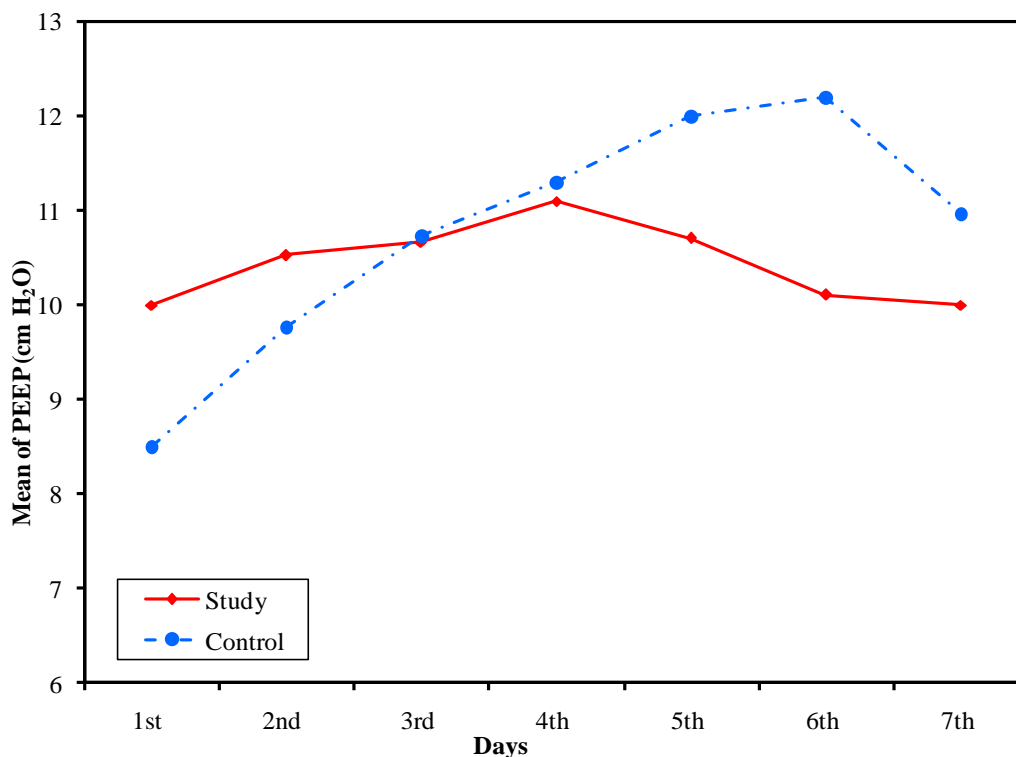


Figure-3. Comparison between the two studied groups according to PEEP



the 2nd reading after hypertonic saline in all days in comparison to 1st reading before hypertonic saline. Also there was statistically significant increase in the hypoxic index from day 4 to day 7 in comparison to day 1 in the study group at the 1st reading (Table-2 and Figure-2).

As regard PEEP, there was decrease (improving) of PEEP in the study group in comparison to the control group that was statistically significant in 6th day (Figure-3).

Regarding serum Na and serum Cl- there were no significant changes after hypertonic saline nebulizer in the study group during study period.

As regard the lung mechanics (PIP, Plateau pressure, static compliance, airway resistance), no significant difference was found between the two groups at different periods of the study.

Lung injury score (LIS) (Murray score) was assessed daily in the current study, there was decrease (improving) in the mean of Murray score in the study

Figure-4. Comparison between the two studied groups according to Murray score

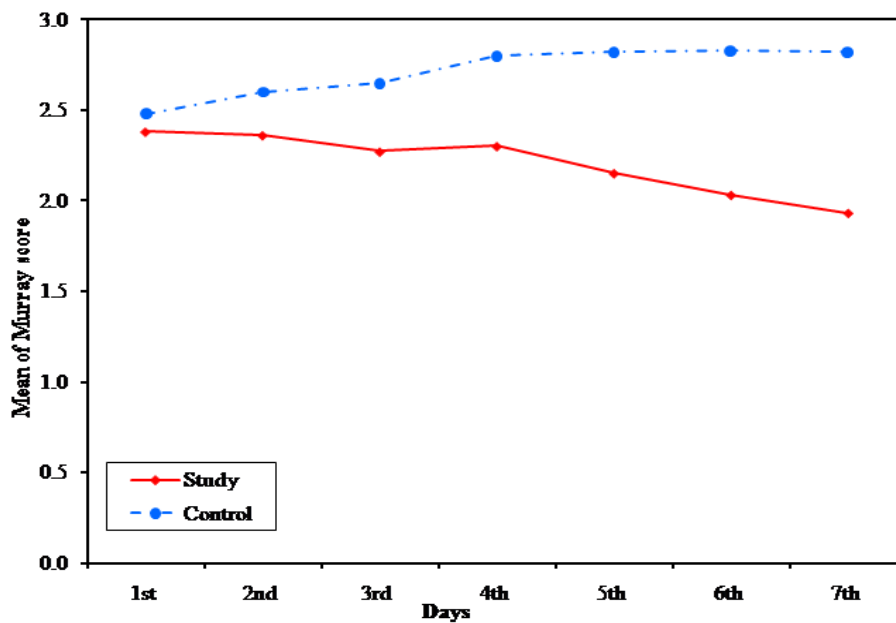
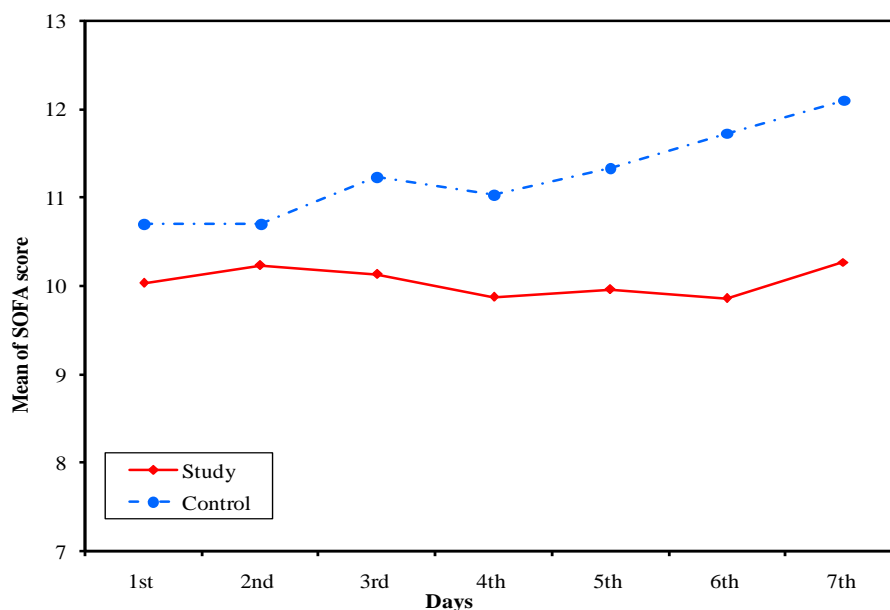


Figure-5. Comparison between the two studied groups according to SOFA score



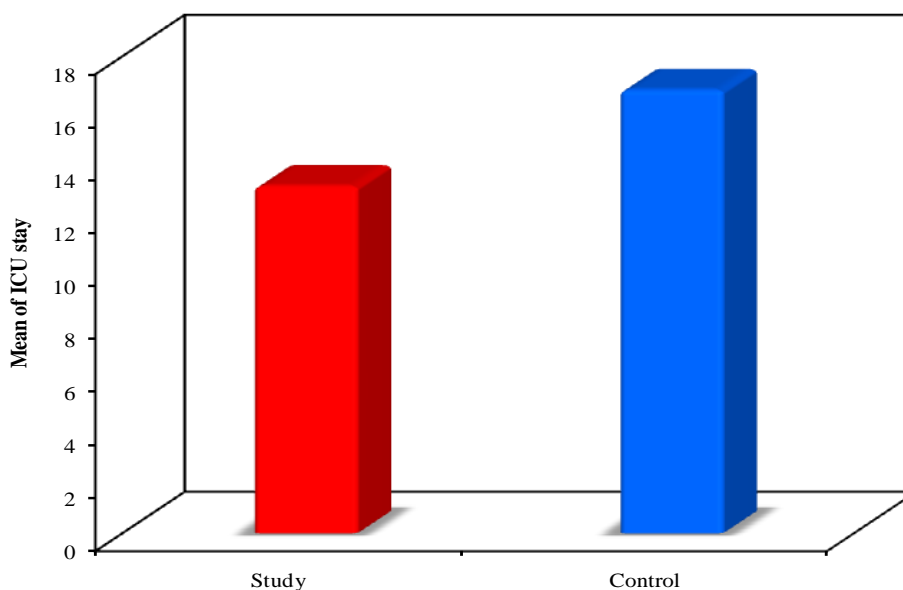
group in comparison to the control group that was Regarding prognosis, 7th day mortality, all patients

Table-3. Comparison between the two studied groups according to outcome

	Study (n= 30)		Control (n= 30)		Test of sig.	p
	No	%	No	%		
7 day mortality						
Survival	30	100.0	30	100.0	□	-
Non Survival	0	0.0	0	0.0		
28 day mortality						
Survival	22	73.3	9	30.0	□□□ 11.279*	0.001*
Non Survival	8	26.7	21	70.0		
Mechanical ventilation days						
Min. – Max.	7.0 – 14.0		7.0 – 16.0		t= 3.733*	<0.001*
Mean ± SD.	9.60 ± 2.40		11.83 ± 2.23			
Median	9.50		12.0			
ICU stay						
Min. – Max.	8.0 – 20.0		10.0 – 30.0		t= 4.020*	<0.001*
Mean ± SD.	13.10 ± 2.73		16.73 ± 4.13			
Median	13.0		15.50			

□², p □ □ □² and p values for Chi square test for comparing between the two groups
 MC: Monte Carlo for Chi square test
 t, p: t and p values for Student t-test for comparing between the two groups
 *: Statistically significant at p ≤ 0.05

Figure-6. Comparison between the two studied groups according to ICU stay



significant from day 3 till day 7 (Figure-4).
 SOFA score was assessed daily in the current study, on admission in hypertonic saline group ranged from 7.0 to 14.0 while in control group ranged from 7.0 to 15.0, there was decrease (improving) in the mean of SOFA score in the study group in comparison to the control group that was significant in day 6 (Figure-5).
 Regarding ICU stay and days (Table-3, Figure-6, 7) of mechanical ventilation, there was significant decrease in the study group in comparison to the control.

were still surviving in both group ,but 28th day mortality, the survival was more common among the hypertonic saline group in comparison to the control group with statistically significant difference between the two groups (p=0.001) (Figure-8).
 Regarding complications, there was significant difference between the two groups related to VAP which was more common in the control group (P = 0.014).

DISCUSSION

body tissues to function, multiorgan dysfunction and

Figure-7. Comparison between the two studied groups according to Mechanical ventilation days

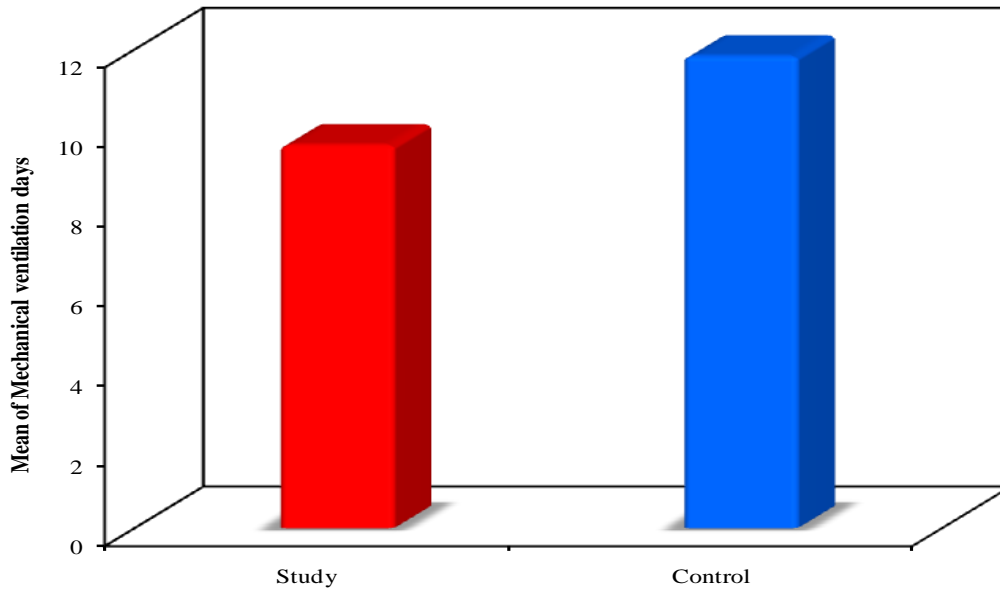
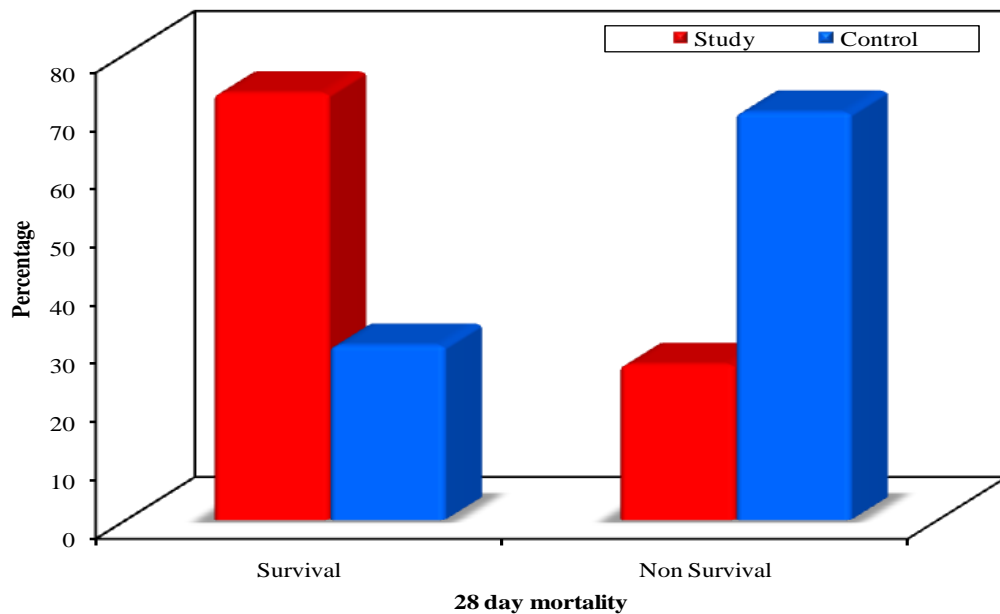


Figure-8. Comparison between the two studied groups according to ICU stay



Acute respiratory distress syndrome (ARDS) is a life threatening condition with high mortality rates. The pathophysiological basis of acute respiratory distress syndrome is characterized by excessive and protracted inflammation, increased vascular permeability, increased permeability of alveolar epithelial cells, and extravasation of plasma and leucocyte infiltration. ARDS is often systemic in nature, resulting in hypoxic respiratory failure that lead to insufficient oxygen for the

death. ^(15, 16)

Treatment strategies, with the exception of low tidal volume protective lung strategy, have had little impact on outcomes. Since inflammation is thought to contribute to the pathogenesis of ARDS, it is rational to explore modulating therapies for this inflammation, provided the adverse effect of such treatment is not excessive.

Most pharmacological approaches are at experimental stage. Some therapies may be more effective in early ARDS and some others may only be

useful in its prevention. In general, pharmacological options have little or no effect once the disease progresses to the fibrotic phase. Inhaled medications for improving oxygenation are for example nitric oxide, surfactant replacement, β -agonists, prostaglandin E1, heparin, and corticosteroids. Study done by Dahroug et al is considered one of the first trials that demonstrate the effect of nebulized corticosteroids in patients with ARDS. It showed that administration nebulized budesonide (Pulmicort nebulizer) at early phase of ARDS produced improvement in oxygenation.⁽¹⁷⁾

Hypertonic saline 3% NaCl with 513 mEq/L of Na and 513 mEq/L of Cl is a potent anti-inflammatory agent, and immunomodulator, which exerts inhibitory effects in several stages of the inflammatory cascade and would seem to be a logical choice for treatment of ARDS.

In the clinical setting, Reeves et al⁽⁴⁾ have touted the anti-inflammatory effects of nebulized hypertonic saline (HTS) in patients with cystic fibrosis (CF). Hypertonic saline induces an osmotic flow of water into the mucus layer, rehydrating secretions and thereby improving mucus rheology.

Tomooka et al⁽¹⁸⁾ suggested four mechanisms for the favorable effect of hypertonic saline solution in a study of patients suffering from sinonasal diseases: (1) decreasing mucosal edema, (2) decreasing inflammatory mediators' concentration, (3) mechanically clearing inspissated mucus, and (4) improvement in overall mucociliary function and transport. From the previous studies hypertonic saline can be used in treatment of ARDS through its anti-inflammatory effect partly due to its ability to inhibit neutrophil and macrophage-mediated cytokine production. So, we conducted our study to use HTS as a novel treatment for ARDS.

In our study, both groups were matched regarding age, sex, and APACHEII score on admission. Pneumonia was the most common cause of ARDS in both groups. Similarly, pneumonia was the most common cause of ARDS in study done by dahroug et al that studied the effect of nebulized corticosteroids in patients with ARDS.⁽¹⁷⁾

Hypoxic index (PaO₂: FiO₂ ratio) improved significantly throughout the seven days of the current study in the study group in comparison to the control group. There was significant increase of hypoxic index in the 2nd reading after hypertonic saline in all days in comparison to 1st reading before hypertonic saline. Also there was statistically significant increase in the hypoxic index from day 4 to day 7 in comparison to day 1 in the study group at the 1st reading. This finding is consistent with the results obtained by Inci et al.⁽¹⁹⁾ in rats after HCl instillation. The PaO₂ values, however, were only significantly different among the injury and control groups at the T30 time point and returned to baseline values at subsequent time points. Although the PaO₂/FiO₂ ratio gradually increased throughout the study, these values remained lower in the treated groups compared with the non-injured groups. Although the PaO₂ value and PaO₂/FiO₂ ratio gradually increased over the observation period, a similar

response was not observed in pulmonary compliance, which remained lower for the duration of the study. Vascular occlusion and hypoxic vasoconstriction may shift blood from non-aerated to aerated lung areas, thus contributing to oxygenation improvement.

As regard PEEP, there was decrease (improving) of PEEP in the study group in comparison to the control group that was statistically significant in 6th day.

As regard SOFA score was assessed daily in the current study, on admission in hypertonic saline group ranged from 7.0 to 14.0 while in control group ranged from 7.0 to 15.0, there was decrease (improving) in the mean of SOFA score in the study group in comparison to the control group that was significant in day 6.

Lung injury score (LIS) (Murray score) was assessed daily in the current study, there was decrease (improving) in the mean of Murray score in the study group in comparison to the control group that was significant from day 3 till day 7.

In agreement with our study, Kellett et al⁽²⁰⁾ in a long-term prospective trial. These authors studied effectiveness of hypertonic saline nebulization on long-term infection rate, quality of life and lung function in patients with stable bronchiectasis. Also Riedler and colleagues⁽²¹⁾ investigate the effects of nebulised HS in CF to reduce the frequency of pulmonary exacerbations and also has small effect on improvement in quality of life in adults.

Regarding prognosis, 7th day mortality, all patients were still surviving in both group, but 28th day mortality, the survival was more common among the hypertonic saline group in comparison to the control group with statistically significant difference between the two groups (p=0.001).

Regarding complications, there was significant difference between the two groups related to VAP which was more common in the control group (P = 0.014).

This was in agreement with Murray et al⁽²²⁾ whose in vitro research has shown that hypertonic saline reduces biofilm formation by *Pseudomonas aeruginosa* and the production of associated virulence factors. Also, hypertonic saline appears to increase the levels of two thiols that are protective against oxidative injury – glutathione and thiocyanate in the airway surface liquid and explained that VAP was less among hypertonic saline group.⁽²³⁾

Regarding ICU stay and days of mechanical ventilation, there was significant decrease in the study group in comparison to the control.

Mandelberg et al⁽⁸⁾ investigated the effects of nebulised HTS in treatment in hospitalized infants with viral bronchiolitis saline solution on the respiratory epithelium and the mucociliary transport. Moreover, in their study, the in-hospital stay was reduced by 25%, from 4 days in the 0.9% saline solution group (group 1) to 3 days in the 3% saline solution group (group 2).

Finally, although these good results of using HTS in early ARDS, I think we should wait for the results of the RCT that investigate safety of inhaled hypertonic saline in patients with acute lung injury who had been intubated and mechanically ventilated for <72 hours and meet

international consensus criteria for ARDS but their results are in progress.⁽²⁴⁾

To date, only low-tidal volume ventilation using lung protective approach has demonstrated a clear benefit in improving survival of patients with ARDS.

It is also becoming increasingly clear that a combination of interventions is more likely to succeed than just one intervention applied in isolation. Finally, ARDS is usually associated with multi-organ dysfunction and any improvement in lung function only will not translate into successful outcome unless other organ functions also improve.

CONCLUSION

From the current study, we can conclude that:

- Inhaled hypertonic saline 3% NaCl administered by nebulization through breathing circuit of mechanical ventilation in patients with early ARDS could improve oxygenation and may therefore added to protective lung strategy.
- Inhaled hypertonic saline 3% NaCl in early ARDS is associated with improvement in SOFA score, and LIS score.
- Inhaled hypertonic saline 3% NaCl in early ARDS is associated with shorter duration of mechanical ventilation and shorter ICU stay, and improved survival.
- Inhaled hypertonic saline 3% NaCl in early ARDS is associated with fewer complications with significant reduction in Ventilator associated pneumonia (VAP), and without electrolyte disturbance in the hypertonic saline group.

Limitations of the study:

- The relatively smaller number of the cases may affect the results of the study.
- Included heterogeneous cohort of pulmonary and extra pulmonary causes of ARDS.
- We didn't classify cases according to the degree of ARDS (mild, moderate, severe), and this may affect the results.

Conflict of Interests

Authors declare that there is no conflict of interests regarding the publication of this paper.

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