Role of Inhaled Hypertonic Saline 3% in Treatment of Lung Contusion in Intensive Care Unit

Hend Essam Hasby Ibrahem *[1], Mohamed Elbahnasawy [1], Abdelhady Mohamed Taha [2], Mohamed Ahmed El Heniedy [3], Ahmed Mohamed Saber Hamed [4]

1 Emergency Medicine and Traumatology Department, Tanta University Faculty of Medicine, Tanta, Egypt

2 Cardiothoracic Surgery Department, Tanta University Faculty of Medicine, Tanta, Egypt

3 Vascular Surgery Department, Tanta University Faculty of Medicine, Tanta, Egypt

4 Anesthesia and Intensive Care Unit Department, Tanta University Faculty of Medicine, Tanta, Egypt

Corresponding Author: Hend Essam Hasby Ibrahem

Email: hendhasby25489@gmail.com, mohamed.elbahnaswy@med.tanta.edu.eg, abdelhady.taha@med.tanta.edu.eg, mohamed.elhenadi@med.tanta.edu.eg, ahmed.hamed@med.tanta.edu.eg

Abstract

Background: Lung contusion is an entity involving injury to the alveolar capillaries, without any tear or cut in the lung tissue. lung contusion occurs by rapid deceleration when the moving chest strikes a fixed object and occurs in 25-35% of all blunt chest traumas. The aim of this study is to assess the role of inhaled Hypertonic saline 3% (HTS) in the treatment of lung contusion and to know the effect of HTS in mortality rate and ventilation rate.

Methods: This randomized prospective study was conducted on 80 patients aged from 18y to 65y with lung contusion in ICU admitted to Emergency and Traumatology Department intensive care unit (ICU). Patients were randomly classified using closed envelops and computer-generated random numbers into two groups each group of 40 patients: Group I (Hypertonic saline (3%) this group was treated according to European trauma society plus inhaled HTS 3% three times daily for one week or improvement of patient and discharge from ICU. Group II (Control Group) was treated according to European trauma society plus inhaled water.

Results: Heart rate was statistically insignificantly different between the two studied groups from day 2 to day 7 as ($P > 0.05$). The respiratory rate was significantly lower in group I compared to group II. There was no statistically significant difference of $PaCO_2$, SaO_2 in the two studied groups. There was no statistically significant difference between the two studied groups as ($P > 0.05$) regarding LUS. There was statistically significantly difference of numbers of intubated patients between two groups significantly decrease of numbers at group I when compared to group II ($P < 0.05$). There was statistically significantly difference of duration of ventilation between two groups significantly decrease of duration of ventilation at group I when compared to group II ($P < 0.05$).

Conclusions: Inhaled Hypertonic saline 3% has a role in treatment of lung contusion as it decrease need for intubation and decrease duration of mechanical ventilation.

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Keywords: Hypertonic Saline, Lung Contusion, Intensive Care Unit

DOI Number: 10.48047/NQ.2022.20.16.NQ880550 NeuroQuantology 2022; 20(16):5400:5410

Introduction

Lung contusion is an entity involving injury to the alveolar capillaries, without any tear or cut in the lung tissue. Lung contusion occurs by rapid deceleration when the moving chest strikes a fixed object. Lung contusion occurs in 25-35% of all blunt chest traumas. Lung tissue is crushed when the chest wall bends inward on impact. Other causes are assaults, falls and sports injuries. This results in accumulation of blood and other fluids within the lung tissue. The excess fluid interferes with gas exchange leading to hypoxia. [1]

The pathophysiology of lung contusion includes ventilation/perfusion mismatching, increased intrapulmonary shunting, increased lung water, segmental lung damage, and a loss of compliance. [2]

Clinically, patient's presents with hypoxemia, hypercarbia and tachypnea. Patients are treated with supplemental oxygen and mechanical ventilation whenever indicated. Treatment is primarily supportive. No pharmacologic therapy is effective, treatment is primarily supportive. Intubation and mechanical ventilation are often required to ameliorate the derangements in gas exchange, lung compliance and work of breathing.

Multiple mechanical ventilation strategies have been tried to determine the optimal method to maximize gas exchange with minimal lung damage in patients with acute lung injury [3]

Computed tomography (CT) is very sensitive for diagnosing pulmonary contusion. This injury is an independent risk factor for development of Acute Respiratory Distress Syndrome (ARDS), pneumonia, long-term respiratory dysfunction, and is associated with 10 to 25% mortality rate [4]

Hypertonic saline (HTS), at a cellular level, decreases alveolar macrophage activation, PMN recruitment, priming and activation, as well as cell surface adhesion molecule expression. Clinically, inhaled HTS is used to treat inflammation in cystic fibrosis (CF) and neonatal bronchiolitis. IL-8, a chemokine expressed by pulmonary epithelial cells and macrophages, is elevated in CF, and inhibited by HTS in vitro. [5]

HTS inhalation has been proposed as a therapy to increase hydration of airway surface liquid in patients with CF.

Elkins et al. reported that patients receiving 3% HTS (4mL via nebulizer bid) had improved lung function and fewer pulmonary exacerbations, compared with patients receiving normal saline (NS) in a similar fashion. HTS was not associated with worsening bacterial infections or inflammation. [6]

Recognizing the central role of the pulmonary epithelium in acute lung injury, nebulization has the advantage of achieving high concentrations of the therapy without producing systemic side effects. [7]

Consequently, we hypothesize that inhaled HTS modulates the pulmonary epithelial inflammatory response following lung contusion and has a role in management of lung contusion.

We aimed to assess the role of inhaled HTS in lung contusion and to know the effect of HTS in mortality rate and ventilation rate.

Subjects and Methods:

This randomized prospective study was conducted on 80 patients aged from 18y to 65y with traumatic lung contusion in ICU admitted to Emergency and Traumatology Department intensive care unit (ICU), Tanta University Hospital, suffering from lung contusion in duration of two years

An informed written consent was obtained from the patient or relatives of the patients. The study was done after approval from the Ethical Committee Tanta University Hospitals with) approval code 33561/12/19(from the start of January 2020 to the end of December 2021

Exclusion criteria were Patients with other lung diseases, hemodynamically unstable patients.

and patients with major trauma (any injury that has the potential to cause prolonged disability or death.

Patients were randomly classified using closed envelops and a computer-generated random numbers into two groups each group of 40 patients: **Group I (Hypertonic saline (3%) Group)** was treated according to European trauma society plus inhaled HTS 3% three times daily for one week or improvement of patient and discharge from ICU. **Group II (Control Group)** was treated according to European trauma society plus inhaled water.

Two groups were treated according to European trauma society: Airway and Breathing: Patients were treated with supplemental oxygen and pulmonary toilet. Patients with hypoxia or difficulty ventilating required airway management and early endotracheal intubation. (Inadequate oxygenation (hypoxia), inadequate ventilation (hypercarbia)). Circulation: Fluid resuscitation with crystalloid aiming to euvolemia and pain control.

All patients were submitted to the following: Detailed history taking including: name, age, mode of trauma. History of lung diseases as Chronic Obstructive Pulmonary Disease (COPD), bronchial asthma, Clinical examination including Blood pressure, respiratory rate, heart rate, and temperature, and local examination, **Routine laboratory investigations** (Complete blood picture, Arterial blood gases, Random blood sugar, Serum electrolytes, Kidney and liver function tests, Radiological Investigations such as (Chest X ray, computed Tomography (CT) chest: patients were assessed by pulmonary contusion score to evaluate state of patients).

Monitoring of patients: 1. A pulse oximetry and cardio-respiratory monitor were used to follow the vital signs of patients including, respiratory rate, heart rate, and blood pressure. 2. Dyspnea was assessed using the Borg scale. The Modified Borg scale (MBS), **3.** Lung ultrasound score (LUS) assessment **[8]** **:** Six lung regions of interest (numbered in the figure), delineated by a parasternal line, anterior axillary line, posterior axillary line, and paravertebral line, are examined on each side [9].

Each lung region is carefully examined in the longitudinal plane, and each intercostal space present in the region is examined in the transversal plane.

The worst ultrasound pattern characterizes the region (regional LUS) using the following grading: 0 = normal aeration., 1 = moderate loss of aeration (interstitial syndrome, defined by multiple spaced B lines, or localized pulmonary edema, defined by coalescent B lines in less than 50% of the intercostal space examined in the transversal plane, or subpleural consolidations), 2 = severe loss of aeration (alveolar edema, defined by diffused coalescent B lines occupying the whole intercostal space), 3 = complete loss of lung aeration (lung consolidation defined as a tissue pattern with or without air bronchogram). The LUS is calculated as the sum of the 12 regional scores. AAL = anterior axillary line; PAL = posterior axillary line; PSL = parasternal line; PVL = paravertebral line.

The patient's oxygenation status was monitored by S_pO_2 (Arterial Oxygen Saturation) and P_aO_2 (Partial Pressure of Oxygen) through ABG analysis every 12 hr for 7 days.

Our primary outcome was tracheal intubation and Duration of ventilation, and the secondary outcomes were Mortality and ICU length stay.

Results

In this study, 107patients were assessed for eligibility, 21 patients did not meet the criteria and 6 patients refused to participate in the study. The remaining 80 patients were randomly allocated into two groups (40 patients in each). All patients (80) followed-up and analyzed statistically. **Figure 1**

eISSN 1303-5150

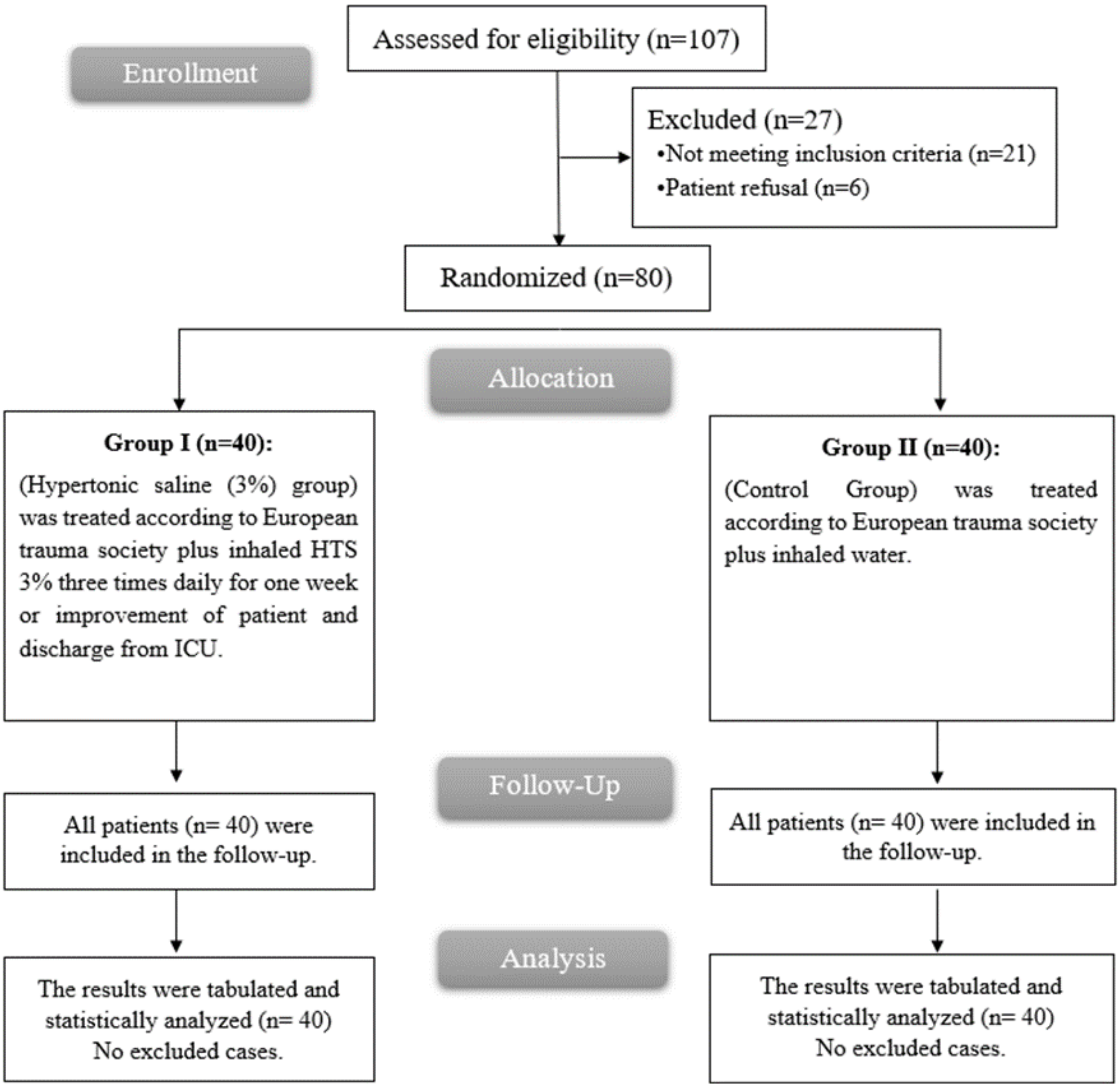

Figure 1: Consort diagram of the studied patients

There was insignificant difference between both groups regarding baseline characteristics. **Table 1**

Table 1: Baseline characteristics of the studied groups

		Group I (n=40)	Group II (n=40)	Sig.	P
Age (in years)		31.2 ± 13.5	32.2 ± 12.0	-0.894	0.374
Gender	**Male**	27 (67.5%)	23 (57.5%	0.853	0.356
	Female	13 (32.5%)	17 (42.5%)		
Smoker		17 (42.5%)	15 (37.5%)	--	--
Medical history	**DM**	5(12.5%)	3(7.5%)	0.565	0.754
	Hypertension	5(12.5%)	5(12.5%)		
Mode of trauma	**Road traffic accidents**	26 (65.0%)	23 (57.5%)	0.999	0.607
	Falling from height	11 (27.5%)	51(37.5%0		
	Runover	3 (7.5%)	2 (5.0%)		
	1	6(15.0%)	5 (12.5%)	2.207	0.531
	2	7 (17.5%)	12 (30.0%)		

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Pulmonary contusion score	**3**	12 (30.0%)	8 (20.0%)		
	4	15 (37.5%)	15 (37.5%)		
Mean Blood pressure		82.4 ± 3.5	82.1± 3.8	0.398	0.692
Temperature		37.3 ±0.5	37.2 ± 0.4	1.499	0.138

Data are presented as mean (SD) or frequency (%)

Heart rate was statistically insignificantly different between the two studied groups from day 2 to day 7 as ($P > 0.05$). **Figure 2a**

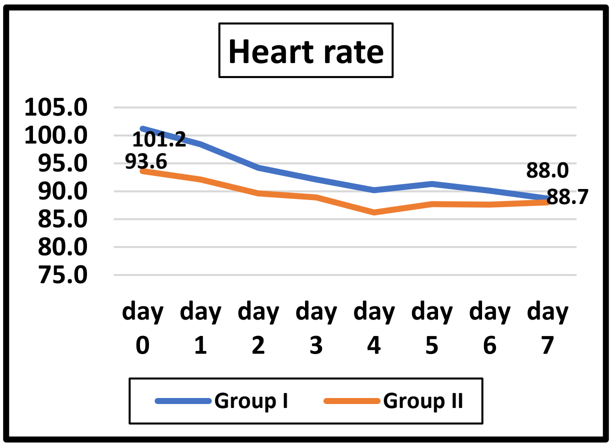
Regarding follow up of the respiratory rate in group I it decreased from 29.7±7.2 at admission, to be 19.7 ± 5.7 in day 7. There was statistically significant difference between the repeated measures analysis as ($P < 0.05$). In group II respiratory rate decreased from 29.0±7.7 at admission, to be 26.4 ± 5.6 in day 7 with no statistically significant difference between the repeated measures analysis as ($P > 0.05$). In comparison between the two studied groups from the day of admission to day 7 there was statistically significant difference of respiratory rate from day 2 to day 7 as ($P < 0.05$). Respiratory rate was significantly lower in group I compared to group II. **Figure 2b**

There was no statistically significant difference of $PaCO_2$ between both groups.

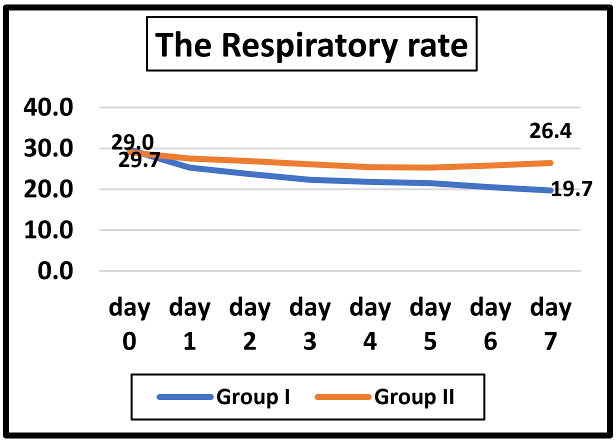
There was statistically significant difference of PaO_2 in the two studied groups in the following days (at admission, 3b,5a,6a,7a,7b). Regarding follow up of PaO_2 changes in group I (cases) it increased from the day of admission to day 7 from 76.7 ± 13.0 at admission to be 103.2 ± 17.4 in day 7b**,** there was statistically significant increase of repeated measures analysis. However, in group II (control) it increased from 82.3±11.3 at admission to be 92.5 ± 12.1 in day 7b but there was no statistically significant difference between the repeated measures analysis as ($P > 0.05$). **Figure 2c**

There was no statistically significant difference of SaO_2 in the two studied groups, Regarding follow up of the SaO2 in the arterial blood (SaO_2) changes in group I (cases) it increased from the day of admission to day 7 from 90.7±3.8 at admission to be 97.1±3.7 in day 7b, there was statistically significant increase of repeated measures analysis as ($P < 0.05$) However in group II (control) it increased from 91.30±3.82 at admission to be 94.00±4.65 in day 7b but it was statistically insignificant as ($P > 0.05$). **Figure 2d**

eISSN 1303-5150



Figure(a) Heart rate between the studied groups



Figure(b): Respiratory rate between the studied groups

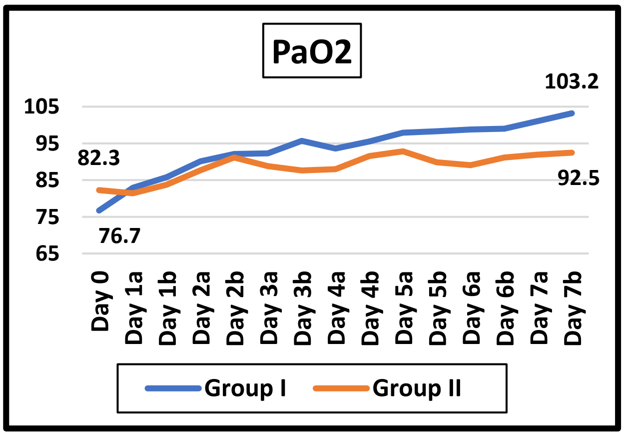


Figure (c):PaO2 between the studied groups

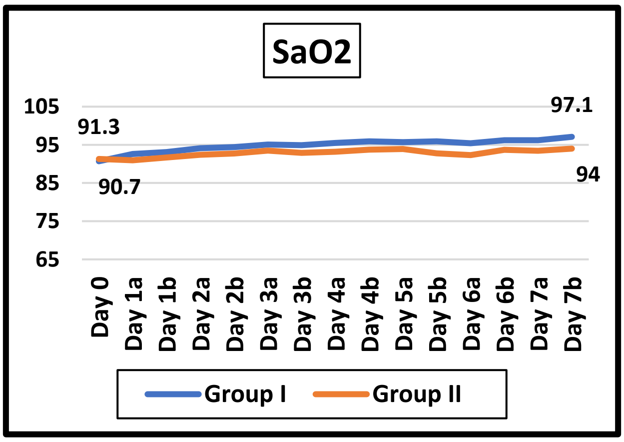


Figure (d):PaCO2 between the studied groups

Figure 2: Heart rate , respiratory rate and oxygen saturation between the studied groups

Regarding follow up of the MBS changes in group I (cases) it decreased from the day of admission to day 7 from 5.2 ±2.0 at admission to be 2.4±1.6 in day 7**,** there was statistically significant decrease of repeated measures analysis as ($P < 0.05$). In group II (control) it decreased from 6.1±2.2 at admission to be 4.0±2.2 in day 7 it was statistically significant as ($P <0.05$). Figure 3a

The mean of the lung ultrasound score in group I (cases) was 13.9±8.6 at admission, then decreased to be 11.0±6.0 in day 7**.** The mean of the lung ultrasound score in group II (control) was 15.1±10.5 at admission, then decreased to be 13.0±8.3 in day 7. There was no statistically significant difference between the two studied groups as ($P > 0.05$). Figure 3b

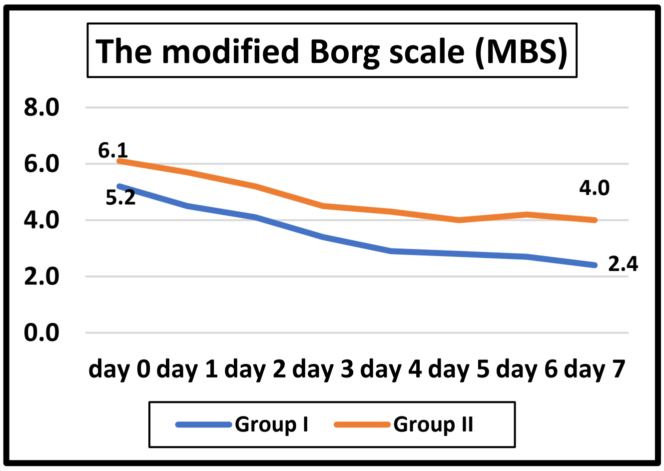


Figure (a)The MBS follow up among the two studied groups

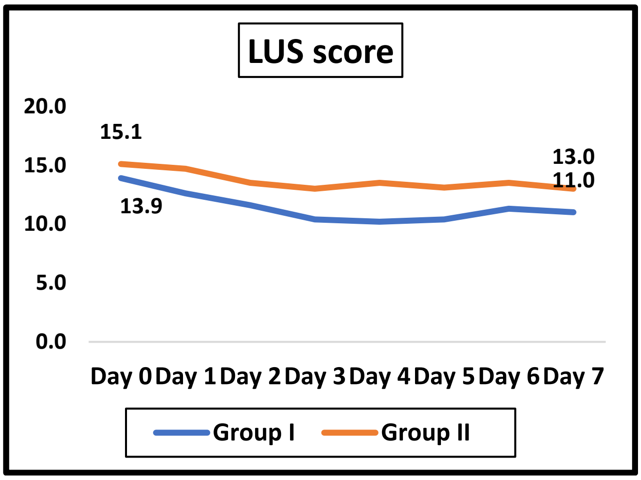


Figure (b):The LUS score comparison between the two studied groups

Figure 3: MBS and LUS score between studied groups

7 patients (17.5%) were intubated and mechanically ventilated in group I (cases). with mean value of duration of ventilation 4.24±0.38. But at group II 15 patients (37.5%) were intubated and mechanically ventilated with mean value of duration of ventilation 6.53±0.40.

There was statistically significantly difference of numbers of intubated patients between two groups significantly decrease of numbers at group I when compared to group II **(P < 0.05).** There was statistically significantly difference of duration of ventilation between two groups significantly decrease of duration of ventilation at group I when compared to group II **(P < 0.05). Table 2**

Mean of duration of ICU stay was 8.47±4.38 and 10.20 ±4.59 at group I (cases) and group II (control) respectively. In this study 4 cases of **mortality** were recorded in group I and 13 cases of mortality were recorded in group II. There was statistically significant different between both groups **(P < 0.05). Table 3**

Table 2: Primary outcomes between the studied groups

		Group I (n=40)	Group II (n=40)	χ^2	P
Intubation	Intubated	7 (17.5%)	15(37.5%)	4.013	0.045*
	Not intubated	33 (82.5%)	25 (62.5%)		
Duration of ventilation (in days)		4.24 ± 0.38	6.53 ± 0.40	-6.250	0.001*

Data are presented as mean (SD) or frequency (%)

Table 3: Outcome comparison between the two studied groups.

	Group I (n=40)		Group II (n=40)		χ^2	P
Improved	36	90.0%	26	66.7%	**6.366**	**0.012***
Died	4	10.0%	13	33.3%		
Duration ICU (days)	8.47±4.38		10.20 ± 4.59		1.718	0.090

Data are presented as mean (SD) or frequency (%)

Discussion

Pulmonary contusion is a common finding after blunt chest trauma. It occurs in 25-35% of all cases. Alveolar capillaries are injured due to the trauma, which results in accumulation of blood and other fluids within lung tissue. The fluids interfere with gas exchange, leading to hypoxemia. The consequences of pulmonary contusion include ventilation/perfusion mismatching, increased AV shunts and loss of compliance of lung parenchyma.

This injury is an independent risk factor for development of Acute ARDS, pneumonia, long-term respiratory dysfunction, and is associated with 10 to 25% mortality rate. [10, 11]

These physiological consequences are manifested within hours from injury and usually resolve within 7 days. Computed tomography (CT) is a sensitive and main diagnostic tool. Clinical symptoms include hypoxemia and hypercapnia, manifested predominantly during 72 hours from injury. Patients are usually treated conservatively. [12]

HTS inhalation has been proposed as a therapy to increase hydration of airway surface liquid in patients with CF, it was not associated with worsening bacterial infections or inflammation. [13, 14]

In this study we aimed to know the role of Inhaled HTS in modulating the pulmonary epithelial inflammatory response following lung contusion and its role in management of lung contusion.

The study was conducted on 80 patients divided equally into two groups. Group I (cases group) and group II (control group). First group was treated with supplemental oxygen plus inhaled HTS 3times daily for one week or improvement of patient. Second group was treated with supplemental oxygen plus inhaled placebo.

Because till now there is no proved benefit of the usage of inhaled HTS 3% as a successful treatment of lung contusion, trials have been done to reveale its role in modulating the pulmonary epithelial inflammatory response following lung contusion and its role in management of lung contusion.

Our results showed that inhaled HTS was effective in treatment of lung contusion as the following:

The mean of respiratory rate changes in group I (cases) was 29.7±7.2 at admission and decreased to be 19.7±5.7 at day 7. The mean of respiratory rate changes in group II (control) was 29.0±7.7 at admission and decreased to be 26.4±5.6 at day 7.

In comparison between the two studied groups from the day of admission to day 7 there was statistically significant difference of respiratory rate from day 2 to day 7 as ($P < 0.05$).

The mean of the Partial pressure of oxygen in the arterial blood (PaO2) in group I (cases) was 76.7 ± 13.0 at admission, then increased to be 101.1 ± 16.8 in day 7.

The mean of the Partial pressure of oxygen in the arterial blood (PaO2) in group II (control) was

82.3±11.3 at admission, then increased to be 91.9 ± 10.4 in day 7.

There was statistically significant difference of PaO2 in the two studied groups.

According to outcome: A-Primary outcome: 14 patients (35%) were intubated and mechanically ventilated in group I (cases). with mean value of duration of ventilation 8.48±4.38. But at group II 15 patients (37.5%) were intubated and mechanically ventilated with mean value of duration of ventilation 12.53±5.40. There was statistically significantly difference of duration of ventilation between two groups significantly decrease of duration of ventilation at group I when compared to group II (P < 0.05).

B-secondary outcome: In this study 4 cases of mortality were recorded in group I and 13 cases of mortality were recorded in group II. There was statistically significant different between both groups (P < 0.05).

Our study was the first one to prove the effectiveness of HTS 3 % inhalation in treatment of lung contusion in human beings , trials have been done on animals as shown in M. Wohlauer et al (Nebulized HTS attenuates acute lung injury following trauma and hemorrhagic shock) which has been done on rats and conclusion of study was Inhaled HTS attenuates post shock acute lung injury by exerting an anti-inflammatory effect on the pulmonary epithelium, suggesting a new clinical strategy to treat ALI/ARDS. [15]

Markus Koch et al (Inhalation therapy with HTS (3%) – A treatment option for airway disease in children). [16]

Results of the study were: Patients in the age groups 0-1(43%), 1-3(24%), 3-5(18%), 5-10(29%), >10 (11%) with acute bronchitis (36%), chronic bronchitis (20%), bronchiolitis (19%) and asthma (11%) benefitted in terms of secretolysis, cough, course of the disease and days off childcare/school. The reduced need for additional mucolytics, the acceptance and tolerability, as well as the very low rate of side effects with the 3% HS treatment were rated as very good.

Jeffrey Baron et al (HTS for the Treatment of Bronchiolitis in Infants and Young Children: A Critical Review of the Literature). **[17]** The results of this study showed that hospital admission rates were significantly reduced for patients who received 3% HTS.

Luo et al concluded that frequent inhalation of HTS is not only safe but also significantly reduces length of hospital stay. In addition, the authors concluded that HTS relieves signs and symptoms faster than does NS in patients with moderate to severe bronchiolitis. [18]

This is the first study that avoided the use of bronchodilators as a confounding variable and still demonstrated improvements in the HTS group. The limitations of this study include the fact that multiple outcomes were sought without power analysis. 5408

Elkins et al. reported that patients receiving 7% HTS (4 mL via nebulizer bid) had improved lung function and fewer pulmonary exacerbations, compared with patients receiving NS in a similar fashion. HTS was not associated with worsening bacterial infections or inflammation.[19]

Opposite to our results, Sharma and his colleagues., (2013) found no difference in mean length of hospital stay in 0.9% saline (63.93 ± 22.43 hours) & 3% HTS (63.51 ± 21.27) groups (P=0.878). Pandit et al., (2013) also found that, the mean ±SD length of stay in hospital in HTS and normal saline group was 3.92 ±1.72 days and 4.08 ±1.90 days respectively. There was no significant difference noted between two groups (P = 0.67). **[20]**

In 2014, Florin et al conducted a prospective, randomized clinical trial that evaluated the use of nebulized 3% HTS vs NS for bronchiolitis in the

ED. At 1 hour after study medication administration, the HTS group had significantly less improvement in the median RACS compared with the NS group .The main difference between groups was a greater reduction in RRs in the NS group. [21]

There were no significant differences in secondary outcomes. The authors assessed patients 2 hours after study medication administration if they remained in the ED. The authors concluded that use of HTS, after standard treatment, in the ED showed less improvement than did use of NS. Based on these results, they recommended against a single dose of 3% HTS in the acute care setting, based on essentially one vital sign, RR, as a component of the RDAI score (The respiratory distress assessment instrument) score. Although not statistically different, the subjects with a high baseline severity score had improvements in both the HTS and NS groups. Additionally, differences in baseline characteristics between groups, use of a single dose of HTS, short assessment times (1 hour for most patients), and the use of an active control may have affected the outcomes of this study.

Conclusions:

This study recommends role of inhaled HTS 3% in treatment of lung contusion. This study suggests that for the outcome of ICU length of stay, pneumonia, duration of ventilation and mortality rate inhaled HTS is superior to inhaled water in patients with lung contusion.

Acknowledgments: there is none to be declared

Disclosure statement

The author (s) did not disclose any potential conflicts of interest.

Data availability

The data arrangements used and evaluated in this present study were available from the corresponding author upon reasonable request.

Abbreviations list

HTS	Hypertonic saline
ICU	intensive care unit
ARDS	Acute Respiratory Distress Syndrome
CF	cystic fibrosis
NS	normal saline
COPD	Chronic Obstructive Pulmonary Disease
CT	computed Tomography
MBS	Modified Borg scale
LUS	Lung ultrasound score
AAL	anterior axillary line
PAL	posterior axillary line
PSL	parasternal line
PVL	paravertebral line

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eISSN 1303-5150