Tracheal Gas Insufflation as an Adjunct to Mechanical Ventilation in Patients with ARDS

Thesis

Submitted in partial fulfillment for the degree of M.D. in Anesthesiology

By

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2004

Acknowledgment

First and foremost thanks to GOD who helped me perform this work. I am greatly honored to express my deepest gratitude to Professor Dr. Ahmed Elbadawy M.Khalil, Professor of Anesthesiology, Cairo University, for his guidance, continuous concern and encouragement, and for his sincere support.

My appreciation and thanks should be expressed to Professor Dr. Yehia Helmy Khater, Professor of Anesthesiology, Cairo University, whose valuable advice and effort have made this work possible.

My sincere thanks to Lecturer Dr. Inas M.Samir, Lecturer of Anesthesiology, Cairo University, for help and support in performing this work.

Last but not least, thanks to my wife, my daughter and to every member of my family for helping me throughout the steps of this work.

Mounir Fayez

ABSTRACT

Lung Protective Ventilatory Strategy (LPVS) implying the use of lower tidal volume and limiting the peak inspiratory pressure during ventilation in patients with ALI and ARDS may reduce injurious lung stretch and release of inflammatory mediator , however the downside of pressure limitation is that the minute ventilation is decreased with subsequent hypercapnia . In addition , the low volumes generated leads to increased tendency to collapse which must be countered by a concurrent lung recruitment strategy .

Key words

Insufflation as an Adjunct to Mechanical Ventilation in Patients with ARDS

Introduction and Aim of Work

Despite recent advances in understanding, the management of acute respiratory distress syndrome (ARDS) remains a challenging clinical problem. Optimization of gas exchange and preventing the iatrogenic propagation of lung injury are cornerstones of its clinical management. A number of novel approaches and adjuncts to mechanical ventilation have been described over the past decade to help achieve these goals, and some have been widely implemented with varying degrees of success.[1,2]

Brochard and colleagues evaluated a lung protective strategy in ARDS that targeted very low plateau airway pressures (=/< 25 cm H2O) and low tidal volumes (<10 mL/kg). They compared this approach with a conventional approach using higher tidal volumes (10-15 mL/kg) with a respiratory rate targeted to maintain eucapnia (PaCO2 38-42 mm Hg), regardless of airway pressures. Mean PaCO2 levels were significantly higher in the study group and mean arterial pH levels were lower. The difference in plateau airway pressures was statistically significant , though it is less clear whether this relatively small difference was clinically important. There were no differences in mortality, duration of mechanical ventilation, incidence of barotrauma, or occurrence of multiple organ failure between the two groups. The authors suggested that the study defined a "safe zone" for mechanical ventilation, avoiding both the risks of ventilator-induced lung injury and the potential problems seen with extreme hypercapnia. The fact that the control group had relatively low plateau airway pressures despite larger tidal volumes suggests that lung compliance may have been less severely deranged in these control patients than in other studies [3].

Introduction and Aim of Work

Tracheal gas insufflation (TGI) as an adjunct to mechanical ventilation delivers fresh gas into the central airways continuously or in a phasic fashion to improve the efficiency of alveolar ventilation or to minimize the ventilatory pressure requirements. Recently, TGI has received increasing attention as an adjunctive tool for lung-protective mechanical-ventilation strategies. Experimental studies in animal and mechanical-lung models have been essential in the quest to understand TGI's mechanisms of action and operational characteristics . Experimental studies in animal models of lung injury have substantiated the potential role of TGI in clinical practice. Currently, the evolution of TGI is entering a phase in which overcoming obstacles to clinical implementation may lead to the development of commercial systems with more widespread TGI application[4].

There are two mechanisms by which TGI improves the efficacy of conventional tidal breaths. First, fresh gas that is introduced by the catheter during expiration can dilute the carbon dioxide stored in the series (anatomic) dead-space compartment proximal to its tip. Second, at high catheter flow rates, turbulence generated at the tip of the catheter can enhance gas mixing in regions away from the catheter tip, thereby contributing to carbon dioxide removal. TGI is unlikely to be effective when the alveolar compartment dominates the total physiologic dead space (VD/VT). Nevertheless, the effect of TGI on arterial $PaCO_2$ should be enhanced whenever series dead space contributes to VD/VT significantly or when alveolar ventilation is low [2] . Many investigators have demonstrated that combining TGI with conventional mechanical ventilation and high-frequency jet ventilation augments carbon dioxide elimination. This

approach takes advantage of improved ventilatory efficiency caused by anatomic dead-space washout and the enhanced mixing caused by the catheter turbulence that is generated to permit reduction in tidal volume (VT). Another promising modality is the combination of TGI and external chest vibrations, which enhances intra-airway mixing (peak carbon dioxide transport resistance was displaced from second- to fourth-generation airways) and improves carbon dioxide elimination [4,5,6,7].

TGI can be delivered by a thin catheter placed through the endotracheal tube (terminating within 1 to 2 cm of the main carina) or via a modified endotracheal tube with channels embedded in the walls of the tube . TGI flow can be forward (toward the alveoli) or reversed in direction toward the proximal end of the endotracheal tube . During expiration , TGI reduces dead space by washing carbon dioxide out of the trachea , bronchi , and the endotracheal tube so that with the next breath less carbon dioxide is rebreathed . Continuous forward - flow TGI may also decrease PaCO2 by enhancing distal gas mixing .

The aim of this study is to evaluate the efficacy of tracheal gas insufflation as an adjunct to lung - protective mechanical ventilation , in patients with ARDS . ARDS frequently develops in patients with already established nonpulmonary organ failure . Mortalty in patients with ARDS is increased in patients with nonpulmonary organ dysfunction , especially hepatic dysfunction [9].

During volume-cycled ventilation , continuous TGI augments tidal volume and will increase alveolar distending pressure and the risk for volutrauma in ARDs . The effect can be diminished by using pressure control ventilation , by downward adjusting machine-delivered tidal volume

during volume- cycled ventilation , or by using TGI timed to occur only during expiation (expiration TGI) . Even when using the latter strategy , TGI can impede expiration , resulting in the development of intrinsic positive end- expiratory pressure . Using reverse flow or end-expiratory (rather than pan -expiratory) TGI , or the addition of tracheal gas exsufflation ,may help alleviate this problem . A number of additional safety issues with TGI have been raised including concerns about ensuring adequate humidification , increased risk of airway mucosal injury , and adverse effects on secretion clearance (especially if desiccation occurs) [(10)].

A lung - protective ventilatory strategy with a low tidal volume in conjunction with a plateau pressure limit of 30 cm of H2O attenuated the severity of clinical lung injury and reduced mortality by 22% . It turns out that a lung protective ventilatory strategy has proved to be the most efficacious anti inflammatory treatment ever discovered for acute lung injury (ALI /ARDS) [(10)].

Definitions of ARDS

Since it was first described in 1967, three major definitions have been proposed.

I. Basic definition

In 1967, Ashbaugh and colleagues described the clinical syndrome of "acute respiratory distress syndrome in adults" which is characterized by tachypnea, hypoxemia resistant to supplemental oxygen; diffuse alveolar infiltrates and decreased pulmonary compliance in 12 patients receiving mechanical ventilation. The onset of the syndrome was acute, the majority of patients did not have a history of pulmonary disease and the use of 5-10 cm H2O PEEP was needed to maintain adequate oxygenation. Gross lung specimens resembled hepatic tissue with large airways being free from obstruction. Histological examination revealed hyaline membrane in the alveoli with microscopic atelectasis and intra alveolar hemorrhage. The disease resembles the respiratory distress syndrome in infants.

In a subsequent paper the same investigators refined and elaborated what they coined "the adult respiratory syndrome" in a review of 40 cases. The mechanism of lung injury was either direct (chest trauma, aspiration) or indirect (pancreatitis, sepsis) and despite the heterogeneity of the inciting event, pathophysiological and pathological responses were the same. The use of PEEP was critical in maintaining acceptable oxygen saturation. Recovery from lung injury could be rapid and complete or could progress to interstitial fibrosis and progressive respiratory failure [(11)].

II. Expanded Definition

Over the next two decades the basic definition was thought by many experts to be a hindrance to understanding the syndrome, as the definition was not sufficiently specific. In 1988 Murray and colleagues[12] proposed an expanded definition intended to describe the syndrome in three parts (table.1).

Table 1 Three part expanded definition of ALI/ARDS proposed by Murray and colleagues(12)	
Part One.	Acute or chronic depending on course.
Part Two.	Severity of lung injury depending on LIS.
Part Three.	Cause or associated risk factor.

The first part of the definition addresses the clinical course separating acute from chronic cases; patients with a prolonged course (chronic) were presumably more likely to develop pulmonary fibrosis and to have poor outcome. The second part of the definition, the lung injury score (LIS), quantifies the severity of lung injury from the degree of arterial hypoxemia, the level of PEEP, respiratory system compliance and radiographic abnormalities (table.2). Finally the third part of the definition is the cause or associated medical condition to be mentioned.

Table 2 the lung injury score [12]	
	Score
Chest Radiograph. No consolidation. Consolidation confined to 1 quadrant. Consolidation confined to 2 quadrants. Consolidation confined to 3 quadrants. Consolidation confined to 4 quadrants.	 0 1 2 3 4
Hypoxemia Score. PaO2/FIO2 ≥ 300. PaO2/FIO2 225-299. PaO2/FIO2 175 -224. PaO2/FIO2 100-174. PaO2/FIO2 < 100.	 0 1 2 3 4
PEEP Score (when mechanically ventilated). ≤ 5 cm H2O. 6-8 cm H2O. 9-11cm H2O. 12-14 cm H2O. ≥15 cm H2O.	 0 1 2 3 4
Respiratory system compliance (when available). ≥ 80 ml/cm H2O. 60-79 ml/cm H2O. 40-59 ml/cm H2O. 20-39 ml/cm H2O ≤ 19 ml/cm H2O.	 0 1 2 3 4
The calculation of lung injury score is done by adding the sum of each component then dividing it by the number of components used. No lung injury. Mild to moderate lung injury. Sever lung injury (ARDS).	 0 0.1-2.5 > 2.5

III. American European Consensus Conference definition (AECC)

Many believed that accurate estimates of the incidence and outcomes of ARDS were hindered by the lack of simple uniform definition, especially one that could be used to enroll patients in clinical studies. In 1994 the American-European Consensus Conference on ARDS (AECC) proposed a revised definition for acute lung injury (ALI) and the acute respiratory distress syndrome (ARDS) [13] (table.3).

Table 3 The 1994 AECC definition for ALI/ARDS [13]

Onset	Acute and persistent.
PaO2/FIO2 ≤ 300. PaO2/FIO2 ≤ 200.	ALI. ARDS.
Exclusion criteria.	PAOP > 18 mm Hg, or clinical evidence of left atrial hypertension.
Radiographic criteria.	Bilateral chest infiltrates consistent with pulmonary edema.

They changed “adult” back to “acute respiratory distress syndrome”, recognizing that the syndrome was not limited to adults. The definition requires an acute onset of respiratory failure to exclude chronic lung disease. The severity of lung injury was addressed using the term acute lung injury (ALI PaO2/FIO2 ≤ 300) and acute respiratory distress syndrome (ARDS PaO2/FIO2 ≤ 200) although this was a rough separation of the clinical spectrum of the disease however previous studies had suggested that these cut off values were reasonable and the more liberal oxygenation criteria

might allow clinical trials to capture patients early in the course of the disease[14]. The definition, of ARDS for the first time included exclusion criteria (PAOP > 18 mm Hg or clinical evidence of left atrial hypertension); this allows differentiation between acute lung injury and volume overload patients. Although left atrial hypertension may coexist with lung injury, it is up to the clinician to address whether the changes are primarily due to lung injury or cardiogenic cause. Finally the radiographic data was simplified to the presence of bilateral chest infiltrates consistent with pulmonary edema (i.e. no difference between ALI and ARDS from radiographic criteria).

IV. Comparison between definitions

The basic definition can be considered as clinical description of the disease rather than a definition, and it has the merit of being the first to describe such syndrome. The main idea behind the expanded and the AECC definitions is to specify a criteria for patient enrolment in clinical investigations, however both of them are believed to have both advantages and disadvantages (table.4). The expanded definition describes well the clinical spectrum, separating acute from chronic courses, also identifies the cause and clinical severity through LIS. However lung injury score is not predictive of outcome and does not include exclusion criteria so patients with volume overload can be included. The AECC definition has the advantage of being simple and easy to use; however this simplicity carries many drawbacks. For example they categorize patients only by oxygenation criteria even without considering PEEP which has great impact on oxygenation criteria, however this issue was a point of great argument, but for sake of simplicity they agreed on not mentioning PEEP level [15], also the

chest X-ray criteria does not separate between ALI and ARDS and also the cause of ARDS not to be mentioned is also a major draw back.

Table 4 comparison between various definitions of ARDS

Reference	Year	Criteria	Advantages	Disadvantages
Petty and Ashbaugh[11]	1971	No criteria	First description and describes Clinical manifestations well.	No specific criteria to identify patients.
Murray et al[12]	1988	3 part definition. LIS.	Identify clinical spectrum. Identifies etiology.	LIS not predictive of outcome. Does not include exclusion criteria
Bernard et al[13]	1994	Acute onset. ALI or ARDS. Bilateral chest infiltrates. PAOP < 18 mm Hg.	Simple and easy to use. Recognizes clinical spectrum	Does not specify the cause. Radiographic data are not specific.

The AECC criteria is currently the adopted definition because, it is simple and easy to use, does not depend on sophisticated parameters or investigations and allows standardization of patients enrolled in clinical trials. Moreover, the benefit of adopting a single definition appeared in the results of ARDS network study, which was the first large, multicenter human study to show a benefit from any intervention in ALI/ARDS. In 1998, the consensus group revised the definition, although no major changes were made, yet they recommended that the epidemiological data of each patient enrolled in clinical studies to be mentioned [16].

Etiology and Risk Factors

To date, more than 60 causes of ARDS have been identified. Additional causes continue to emerge as adverse pulmonary reactions to new therapies are discovered. Although the list is long, epidemiological studies have shown that ARDS are associated with a few common causes or predisposing conditions (table 5) [17-20].

Table 5 Summary of predisposing factors for ARDS[17-20]
Sepsis.
Aspiration.
Pneumonia
Trauma and Burns.
Massive blood transfusion.
Following relief of upper airway obstruction.
Lung and bone marrow transplant
Drugs. (Aspirin, opioids, radiological contrast media)
Leukoagglutinin reactions.
Others. (Drowning, cardiopulmonary by pass

1. Sepsis:

Sepsis is the most common cause of ARDS. [18-22] It should be considered first in any patient who develops otherwise unexplained ARDS in association with a new fever, hypotension, or a clinical predisposition to serious infection. The risk of developing ARDS may be especially high

among septic patients with a history of alcoholism, possibly because alcoholism results in decreased concentrations of glutathione in the epithelial lining fluid and thus predisposes to oxidative injury [23,24].

2. Aspiration of gastric contents:

Approximately one third of hospitalized patients who experience a clinically recognized episode of gastric aspiration subsequently develop the syndrome[18.20.25]. In the original description of massive gastric aspiration, it was suggested that a pH less than 2.5 was necessary to cause severe lung injury[26]. More recent animal studies have shown that aspiration of non-acidic stomach contents can also cause widespread damage to the lungs, suggesting that gastric enzymes and small food particles also contribute to the lung injury[27].

3. Infectious pneumonia:

Pneumonia is probably the most common cause of ARDS developing outside of the hospital [28]. Common pathogens include Streptococcus pneumoniae,[29] Legionella pneumophila, Pneumocystis carinii, Staphylococcus aureus, enteric gram negative organisms, and a variety of respiratory viruses [30,31]. Nosocomial pneumonias can progress to ARDS as well: Staphylococcus aureus, Pseudomonas aeruginosa, and other enteric gram-negative bacteria are the most commonly implicated pathogens.

4. Severe trauma and surface burns:

Several mechanisms can contribute to the ARDS seen with trauma or burns [32].

- Bilateral lung contusion is an important factor after blunt injury to the chest [33].