Effect of low tidal volumes vs conventional tidal volumes on outcomes of acute respiratory distress syndrome in critically ill children

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Abstract

Background: Adult data have shown low tidal volume strategy to be beneficial to the outcome of acute respiratory distress syndrome (ARDS).There are little data regarding the effect of different tidal volume strategies on outcomes in children with ARDS. **Aims and Objectives:** The aim of this study was to learn the differences in outcomes from ARDS in children using low vs conventional tidal volumes. **Methods:** All patients with ARDS (aged 1 month to 16 years) admitted to the pediatric intensive care unit from March 98 to June 2004 were studied. Prospective data for low expired tidal volumes (6–8ml/kg) were collected from Jan 2001 to June 2004 (group 1). ARDS patients during March 1998 to December 2000, receiving conventional tidal volumes (10–15 ml/kg) were used as retrospective control (group 2). Etiologies, PRISMIII scores, interventions, and outcomes data were recorded. Standard supportive therapy for ARDS was used in all children using conventional mechanical ventilation. **Results:** A total of 153 (4.67%) patients had ARDS as defined by standard criteria. Groups 1 and 2 had 78 and 65 patients, respectively, with comparable PRISMIII scores. Mortality was 23% (group 1) vs 36.9% (group 2) ($P<0.005$). The mean duration of ventilation and hospitalization in group 1 was significantly lower when compared with group 2 (11 ± 1 *vs* 18 ± 2 days; $P<0.005$) and group 1 (19 ± 2 *vs* 26 ± 3 days; $P<0.005$), respectively. Incidence of pneumothorax was 5% (group 1) as compared with 12% (group 2) ($P<0.01$). Long-term follow-up for incidence of chronic lung disease could not be studied. Common etiologies of ARDS included pneumonia, sepsis, dengue shock syndrome, falciparum malaria, and fulminant hepatic failure. **Conclusions:** Low tidal volume strategy was found to be associated with significantly lower duration of ventilation, hospitalization, incidence of pneumothorax, and mortality when compared with conventional tidal volume strategy in children with ARDS.

Key Words: Acute respiratory distress syndrome, Children, Critically ill, Low tidal volume, Pediatrics, Ventilation

Introduction

Acute respiratory distress syndrome (ARDS) is a clinical syndrome of acute respiratory failure following almost any severe physiologic insult that may or may not have injured lungs primarily. The hallmark of the syndrome is increased permeability of the alveolar capillary membrane, resulting in noncardiogenic pulmonary edema.[1–4] Common precipitating factors include viral or bacterial pneumonia (pulmonary ARDS: ARDSp), shock of any etiology, sepsis, trauma, aspiration pneumonia, near–drowning, and ingestions (extrapulmonary ARDS: ARDS exp).[5] Management includes treatment of primary etiology, mechanical ventilation, and supportive care in

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the intensive care setting. Conventional ventilation is the most readily available modality. Adult data have shown that mechanical ventilation should be delivered with a goal to prevent volutrauma or stretch injury to lungs using low tidal volumes (6–8 ml/kg).[6] In addition, minimal tolerable inspired oxygen with positive end expiratory pressure (PEEP) to achieve PaO_2 of 55–80 mmHg and maximal tolerable arterial pCO_2 of 50–60 mmHg with arterial pH>7.25 (permissive hypercapnia)[7–9] and absence of metabolic (hypoxic) acidosis is aimed for. Pediatric studies all over the world have reported mortality in the wide range of 25–70%.[10–17] To our knowledge, pediatric data regarding comparison of low tidal volume and conventional (10–15 ml/kg) tidal volumes for ARDS are lacking.

The aim of this study was to learn the differences in outcomes from ARDS in critically ill children using low vs conventional tidal volumes using conventional mechanical ventilation.

Methods

All patients diagnosed with ARDS (aged 1 month to 16 years) admitted to the pediatric intensive care unit (PICU) from March 98 to June 2004 were studied as defined by standard criteria (PaO_2/FiO_2 <200).[3] All children were mechanically ventilated with conventional ventilation using pressure-regulated volume control (PRVC) mode on Siemens Servo 300 ventilator. All patients received sedation with midazolam and a nondepolarizing muscle relaxant infusion, as felt necessary. Prospective data for low expired tidal volumes (6—8 ml/kg) were collected from January 2001 to June 2004 (group 1). ARDS patients from March 1998 to December 2000, receiving conventional tidal volumes (10–15 ml/kg), were used as retrospective control (group 2). Demographic data, etiologies, PRISMIII scores, interventions, and outcome data were recorded. Mortality was defined as death in the PICU and survival was defined as survival at discharge from the hospital. Standard supportive therapy for ARDS was used in all patients. Starting January 2001, low tidal volume strategy (6–8 ml expired tidal volume) was practiced in this unit based on the data from ARDS net study.[6]

Because this was a generally accepted strategy, data were prospectively collected to test the practical utility and outcomes, as applied to the pediatric age group. Long-term follow-up for incidence of chronic lung disease could not be studied owing to the long distances of the referral areas and lost follow-ups.

Results

A total of 143/3062 (4.67%, 46/1000 children) patients who had ARDS as defined by standard criteria received conventional mechanical ventilation (Table 1). Groups 1 and 2 had 78 and 65 patients, respectively, with comparable PRISMIII scores; group 1—mean ± SD: 21.3 ± 1.5 and group 2—mean ± SD: 22.1 ± 1.3. Male-to-female ratio was 3 : 1 (107 boys and 36 girls had ARDS). Overall mortality was (41/147) 28.6%: 23% in group 1 vs 36% in group 2 ($P<0.005$). Mean duration of ventilation (11 ± 1 days vs 18 ± 2 days; $P<0.005$) and hospitalization (19±2 days in group 1 vs 26±3 days in group 2; $P<0.005$) was significantly lower in group 1 when compared with group 2. Incidence of pneumothorax was 12% (group 1) as compared with 5% (group 2); $P<0.01$. Common etiologies of ARDS included pneumonia, sepsis, dengue shock syndrome, falciparum malaria, and fulminant hepatic failure (Table 2). Age- and gender-related mortality was similar in two groups.

Discussion

Clinical diagnosis of ARDS is considered if the patient who has had an initiating insult and subsequently develops tachypnea, dyspnea, hypoxemia refractory to increased inspired oxygen concentration (owing to shunting and venous admixture at the level of pulmonary capillaries), diffuse infiltrates on chest X-ray, and decreased pulmonary compliance. These changes have a rapid onset. Congestive heart failure must be ruled out as a cause of pulmonary edema.

Table 1: Severity of illness, interventions, and outcome data

	Group 1 (n=78)	Group 2 (n=65)
PRISMIII scores (mean ± SD)	21.3 ± 1.5	22.1 ± 1.3
PEEP range (cm H_2O)	7–16	7–16
fiO_2 range	0.5–1	0.5–1
Pneumothorax	5% (4/78)	12.3% (8/65)*
Duration of ventilation (days)	11 ± 1	18 ± 2**
Duration of hospitalization (days)	19 ± 2	26 ± 3***
Mortality (%)	23% (18/78)	36.9% (24/65)****

*$P<0.01$.
**$P<0.005$.
***$P<0.005$.
****$P<0.005$.

Table 2: Etiologies of ARDS

Etiology	Group 1 (n=78; %)	Group 2 (n=65; %)
Pneumonia (viral, bacterial, or aspiration)	15 (19.2)	12 (18.4)
Sepsis	28 (35.8)	25 (38.4)
Dengue shock syndrome	10 (12.8)	8 (12.3)
Falciparum malaria	11 (14)	9 (13.8)
Fulminant hepatic failure	5 (6.4)	4 (3.2)
Post-cardiopulmonary bypass	3 (3.8)	2 (3.0)
Near-drowning	3 (3.8)	2 (3.0)
Leukemia	3 (3.8)	3 (4.6)

ARDS net study[6] was a prospective, randomized, multicenter trial of 240 patients with two groups using 12 *vs* 6 ml/kg tidal volume, PEEP of 5–18 cm H_2O, and FiO_2 of 0.3–1 showed 25% reduction in mortality in the 6 ml/kg group. In another study, use of higher positive-end expiratory pressure with lower tidal volumes (open-lung approach)[8,9] has been used with improved results. In our study low tidal volume strategy was found to be associated with significantly lower duration of ventilation, hospitalization, pneumothorax, and mortality when compared with conventional tidal volume strategy in children with ARDS using comparable levels of FiO_2 and PEEP (PEEP ranged from 7 to 16 cm H_2O and FiO_2 ranged from 0.5–1). The incidence of chronic lung disease and oxygen dependence seem to be related to the duration of ventilation as well as volutrauma/stretch injury to lungs.

In our study population, owing to long distances, being a referral center, follow-up data for incidence of chronic lung disease could not be studied.

ARDS *per se* carries a mortality ranging from 25 to 75%.[10–17] Lodha *et al.* reported a mortality of 75% on a retrospective chart review on pediatric patients with ARDS from an Indian PICU in New Delhi.[15] At the authors' institution severe ARDSs with associated multiorgan failure had 49% mortality, directly related to the number of organ systems involved.[17,18] More recently, mortality as low as 30% has been reported from adult data.[16] This is attributed to the better understanding of conventional ventilation and supportive measures. In our study, overall mortality in all patients with ARDS was 28.6%, but the conventional tidal volume group had 36% mortality.

Pelosi *et al.*[5] reported possible differences in underlying pathology, respiratory mechanics, and response to PEEP in pulmonary and extrapulmonary ARDS. Direct insult (ARDS p) leads to injury of alveolar epithelium. This causes alveolar filling by edema, fibrin, collagen, and neutrophilic aggregates—described as pulmonary consolidation. In indirect insult (ARDS exp) the first target of damage is the vascular endothelial cell, with an increase in vascular permeability. Cytokine levels are also significantly different between ARDS p and ARDS exp. In our study this particular aspect was not studied in detail; however, 19% of patients had ARDS p and majority were ARDS exp.

In the above-mentioned study, the presence of nonpulmonary organ dysfunction (hepatic, renal, hematological, or gastrointestinal) and the presence of central-nervous-system dysfunction were identified as risk factors for increased mortality. The present authors and others[18–23] have reported a higher mortality directly related to the number of organs involved in Multiple Organ dysfunction Syndrome (MODS).

Flori *et al.*[12] published a paper in which highest mortality occurred in patients with near drowning (54%), associated cardiac disease (39%), and sepsis (31%). Lower mortality was found in patients with pneumonia (4%), aspiration (12%), and other associated diseases (27%). There was no relationship among mortality, age, gender, or past medical history. Mortality in this study was twice as high (26%) in patients presenting with ARDS with PiO_2/FiO_2 ratio of less than 200 as compared with acute lung injury (ALI) with PiO_2/FiO_2 ratio of less than 300. We used PaO_2/FiO_2 ratio less than or equal to 200 for defining ARDS and did not analyze the mortality separately for patients with ALI. At our institution, high-frequency ventilation,[24] nitric oxide,[25,26] and extracorporeal membrane oxygenation (ECMO)[27] have not been tried for ARDS patients as yet. However, corticosteroids[28–30] have been used during fibroproliferative phase. Recently, prone positioning is being used in severely hypoxemic patients not responding to low-volume conventional ventilation in supine position.

Conclusion

This study supports the use of low tidal volume strategy in critically ill pediatric patients with ARDS. Low-volume strategy may result in significant reduction in the duration of ventilation, hospitalization, pneumothorax,

and mortality in critically ill children with ARDS. Further multicenter studies are needed to document the differences between pulmonary and extrapulmonary ARDS and their outcomes in critically ill children with ARDS.

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