

Early Prone Ventilation in Severe Ards: Case Study and Literature Review

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Abstract

Acute Respiratory Distress Syndrome (ARDS) is a severe diffuse lung injury characterized by significantly impaired oxygenation and compliance and invariably results in mechanical ventilation support. While lung protective ventilation strategies remain the main stay of treatment, early prone ventilation plays a crucial role to improve ventilation perfusion mismatch. Prone ventilation with or without Neuromuscular Blocking Agents (NMBAs) are distinctly indicated in severe refractory ARDS to achieve better expansion of the dorsal lung regions with consequent improvement in oxygenation. In addition, it may also lead to reduction in ventilator-induced lung injury for which there is enough evidence present in literature. We report the successful management of an adult mechanically ventilated patient having scrub typhus induced severe refractory ARDS, undergoing early prone ventilation in conjunction with recommended ventilation strategies. Furthermore, recent literature was reviewed to discuss the rationale of prone ventilation in patients with ARDS and the limitations of its use as well as the current place of prone positioning in the management of patients with severe refractory ARDS. In the present era of COVID-19 pandemic, many consensus guidelines endorse early prone ventilation strategies after observing its successful outcomes. Early prone ventilation with NMBAs may be applied as a first-line therapy in patients with severe ARDS.

Keywords: ARDS • Prone Ventilation • COVID-19• Neuromuscular Blocking Agents • COVID-19 • ICU

Abbreviations: ARDS: Acute Respiratory Distress Syndrome • ED: Emergency Department • ET: Essential Thrombocythemia • VILI: Ventilator-Induced Lung Injury • ER: Emergency Room • ICU: Intensive Care Unit

Introduction

Acute Respiratory Distress Syndrome (ARDS) is a clinical syndrome characterized by radiological diffuse bilateral lung infiltration, decreased respiratory compliance and severe hypoxemia. The major goal in ARDS is correction of life threatening hypoxemia and concurrent improvement of respiratory mechanics. Mechanical ventilation is invariably required in this subset of patients with aim of providing optimum oxygenation and at the same time strategies to prevent Ventilator-Induced Lung Injury (VILI). While lung protective strategies remain the main stay of treatment, early prone ventilation plays a crucial role to improve ventilation perfusion mismatch.

Acute Respiratory Distress Syndrome (ARDS) is a clinical syndrome characterized by radiological diffuse bilateral lung infiltration, decreased respiratory compliance and severe hypoxemia. The major goal in ARDS is correction of life threatening hypoxemia and concurrent improvement of respiratory mechanics. However, prone positioning requires advance competence level for attending critical care physicians and nursing staff due to the inherent risk associated with positioning. We report the successful management of an adult mechanically ventilated patient having scrub typhus induced severe refractory ARDS, undergoing early prone ventilation in conjunction with recommended ventilation strategies.

Case Report

An eighteen year old male was admitted to our hospital Emergency Room (ER) after being referred from a private hospital with complaint of fever for seven days and difficulty in breathing associated with cough and sputum production for three days. The patient had no known other co-morbidities. On initial examination, the patient was conscious, oriented but agitated, with bilateral crepitation on auscultation of chest. Initial

hemodynamic measurements were (blood pressure-70 mm Hg/40 mmHg, pulse rate-130 beats/ min., oxygen saturation (SpO_2)-69% on venturi-mask with FiO_2 of 0.6, respiratory rate-56 per minute), indicating for critical care transfer. Patient was subsequently intubated and then shifted to Severe Acute Respiratory Infection (SARI) Intensive Care Unit (ICU) for further management.

In SARI-ICU, patient was initially kept on mechanical ventilatory support: Synchronized Intermittent Mandatory Ventilation-Volume Control (SIMV-VC) mode with initial settings: FiO_2 of 1.0 and positive end-expiratory pressure (PEEP)-8, Tidal Volume (TV)-300 ml and Respiratory Rate (RR)-20/min, Inspiratory/Expiratory time (I/E) ratio-1/2 along with vasopressor (noradrenalin @ 0.025 mcg/kg/min-0.2 mcg/kg/min), with an aim of achieving SPO_2 of at least 94% and Mean Arterial Pressure (MAP) above 70 mm Hg. Subsequently, PEEP was gradually increased to maximum of 12, in accordance with ARDSnet protocol to achieve the desired SPO_2 but with no success [1]. Meanwhile, the patient was tested negative for COVID-19 and hence shifted to non-COVID ICU on the same day for further management.

In the ICU, patient was administered continuous infusion of NMBA (atracurium @ 0.3 mg/kg/hr-0.6 mg/kg/hr.) and sedation (Fentanyl (20 mcg/hr-100 mcg/hr.) and propofol (1 mg/kg/hr-3 mg/kg/hr.)) as per the ICU sedation protocol [2]. Patient was kept on Assist Control, Volume Control (AC-VC) mode of ventilation to achieve the desired oxygenation parameters. The PEEP levels were subsequently increased further to the maximum of 16 mm Hg but with little success. The SPO_2 levels reached to the maximum of 70%. Acid Base Gas (ABG) analysis was done (pH-7.10 partial pressure of oxygen (PaO_2)-45 mm Hg, partial pressure of carbon dioxide ($PaCO_2$)-60) and was suggestive of severe respiratory acidosis with hypoxemia. Chest radiograph revealed bilateral mid and lower zone infiltrates (left more than right), consistent with severe ARDS (Figure 1). Methylprednisolone-IV (1kg/day IV), Imipenam-IV (1 gm in 8hours) and Central Venous Pressure (CVP) guided fluids were started as per the sepsis bundle [3-4]. Meanwhile, patient tested positive for scrub typhus hence doxycycline (200 mg/day) was started. Laboratory investigations revealed thrombocytopenia and raised liver transaminases.

On second day of ICU admission, patient was shifted to assist-control, pressure regulated volume control (A/C PRVC) mode of ventilation (initial setting: FiO_2 -1.0 and PEEP 16, TV-300 ml, I/E-1/2, plateau Pressure (Pplat) target of 30 mmHg) with continuous infusion of atracurium (0.3 mg/kg/hr-0.6

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mg/kg/hr.) and sedation, but with no significant improvement in oxygenation parameters. In view of refractory ARDS, prone ventilation management was decided. Patient received prone ventilation for a period of 16 hours, as per the local hospital policy for standard of care. Oxygenation parameters immediately improved and according to the target SpO_2 levels, FiO_2 was gradually decreased. By the end of the second day, FiO_2 and PEEP was decreased to 0.6 and 14 respectively, to achieve the target SpO_2 of $\geq 94\%$. Chest radiograph also showed significant clearing of infiltrates in left mid and lower zones (Figure 1).

On three subsequent days (day 3 to 5) patient again received one cycle (16 hours each) of prone ventilation. His SpO_2 remained above 94% and PO_2 improved further on Day 3 from 80 mmHg to 160 mmHg by the evening of day 5, on FiO_2 of 0.5 and PEEP of 10 mm Hg. Chest radiograph also showed relative clearing of lung infiltrates in bilateral lung zones. Subsequently, patient was kept supine on the same ventilator mode settings. On day 6, atracurium infusion was stopped and FiO_2 and PEEP reduced further to 0.4 mmHg and 6 mm Hg respectively.

On Day 7, patient was off vasopressors and oxygenation parameters remarkably improved on FiO_2 of 0.4 and PEEP of 5 mm Hg. Sedation was stopped and patient was gradually weaned from AC PRVC mode to mere Continuous Positive Airway Pressure (CPAP) mode of ventilation. On day 8, Spontaneous Breath Trials (SBT) were initiated with gradual increase in time period. After observing fair tolerance of SBT, patient was extubated as per hospital extubation criteria. Post extubation, patient was supported with Non-Invasive Ventilation (NIV) and kept on CPAP settings (CPAP of 8 mm Hg, FiO_2 -0.4) for next 12 hours. Chest radiograph also showed improving trends and clearing of infiltrates. Subsequently, patient was weaned from NIV and kept initially on venturi-mask and then on room air with satisfactory oxygenation parameters. On day 14, patient was discharge from ICU to medicine ward and was discharged from hospital subsequently uneventfully.

Discussion

Acute Respiratory Distress Syndrome (ARDS) is a severe diffuse lung injury characterized by significantly impaired oxygenation and compliance and invariably results in mechanical ventilation support [5-6]. In recent

time, significant adaptations have been done in ventilation strategies of ARDS such as low Tidal Volume (TV) ventilation, incremental Positive End-Expiratory Pressure (PEEP) application, administration of neuromuscular blockers and prone ventilation [7].

Traditionally, ARDS patients are divided into mild, moderate and severe categories based on $\text{PaO}_2/\text{FiO}_2$ ratio of 300, 200 and 100 respectively [8]. However, based on ACURASYS and PROSEVA trials, ARDS patients were now classified into two broad categories based on $\text{PaO}_2/\text{FiO}_2$ ratio <150 mmHg and >150 mmHg at PEEP ≥ 5 cm H_2O respectively [9,10]. In ARDS patients with $\text{PaO}_2/\text{FiO}_2$ ratio ≤ 150 mmHg, the mechanical ventilation is generally initiated with lower TV strategies, neuromuscular blockers in refractory cases and early prone ventilation cycles until $\text{PaO}_2/\text{FiO}_2$ ratio improves and is above 150 mmHg [9-10].

Prone ventilation was proposed in treatment of ARDS, to reduce pleural pressure gradients and to restore aeration to dorsal lung segments, leading to improvement in lung ventilation and perfusion mismatch [11]. Two recent meta-analyses have found that prone positioning improves survival irrespective of the level of hypoxemia, provided a lower TV is applied. In recent observational prevalence study (APRONET study) observed that prone ventilation was associated with low rate of complications, a significant increase in oxygenation and a significant decrease in driving pressure [12-13]. Prone ventilation has also been observed to significantly reduced Ventilator Induced Lung Injury (VILI) over the time as global stress and strain imposed by mechanical ventilation is reduced in prone position [14-15].

In this patient, we started early prone ventilation when $\text{PaO}_2/\text{FiO}_2$ ratio was below 150 and continued for 16 hours daily cycles for four consecutive days until $\text{PaO}_2/\text{FiO}_2$ ratio improved and were above 150. However, prone position of a patient on mechanical ventilator is a challenging task and need a competent team in ICU setups. Careful selections of patient's along with adequate preoxygenation, suctioning of endotracheal tube and oral cavity and care of the *in-situ* catheters are the major prerequisites. Trained ancillary staff members are essential requirement for appropriate and safe positioning of patient in prone position. Competence based simulation training and mock demonstration should be encouraged prior to prone ventilation. A checklist of all essential steps for proning should

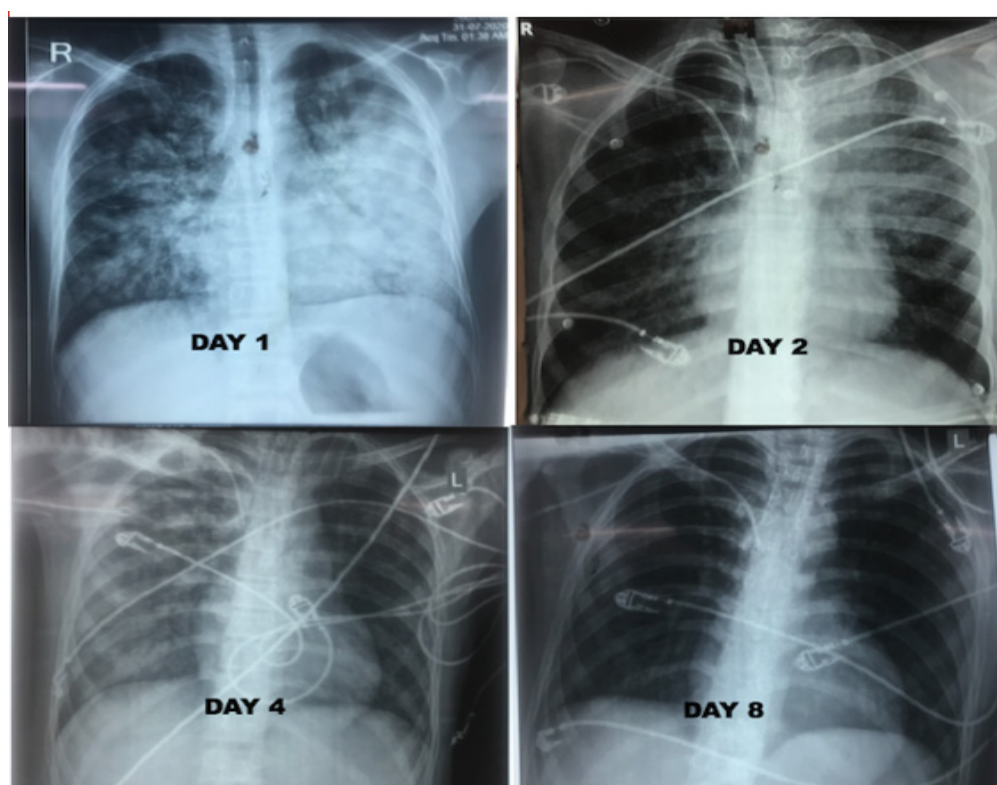


Figure 1. Chest radiograph also showed significant clearing of infiltrates in left mid and lower zones.

be made and sign off while positioning. All pressure points such as face, shoulders, knee and anterior pelvis should be supported and repositioned at frequent intervals. A protocol based conduct of proning will certainly prevent complications and critical incidents in this subset of patients.

In PROSEVA trial, prone ventilation was administered on an average of 16 hours/day until sustained oxygenation improvement was achieved, defined as $\text{PaO}_2/\text{FiO}_2 > 150$ mm Hg with PEEP < 10 cm H₂O and $\text{FiO}_2 < 0.6$, for at least 4 hours in subsequent supine position. Although optimal duration of proning is still unclear, objective variables such as $\text{PaO}_2/\text{FiO}_2$ ratio, static and dynamic compliance, resistance and airway pressures (peak and plateau) are crucial for overall improvement. The authors feel that further research may be required to find out more optimal objective criteria for initiation and termination of prone ventilation.

In severe ARDS patients Neuromuscular Blocker Agents (NMBAs) have been used as a rearmost measure to diminish ventilator dyssynchrony, administered mainly as infusion with deep sedation. Recent studies have asserted the favorable effects of NMBAs with overall increase in survival in aforesaid subset of patients and hence recent consensus guidelines recommend NMBAs as an adjunct in refractory severe ARDS [16]. However, there are still concerns about ICU acquired neuromuscular weakness and other risks such as diaphragm paralysis, atelectasis and anaphylaxis related to NMBA. Slutsky et al. In a systematic review observed a positive effect of NMBA on oxygenation after 48 hours of administration in patients with reduced $\text{PaO}_2/\text{FiO}_2$ ratio. They infer that it may be due to decrease in ventilator-induced lung injury and subsequent barotrauma after NMBAs administration. NMBA also may have an anti-inflammatory effect, causing reduction in oxygen consumption by active muscle groups. Similar findings were also observed by a recent meta-analysis [17]. However, NMBA does not lead to reduction in the mortality risk, ventilator-free days, duration of mechanical ventilation for severe ARDS patients.

In the mentioned patient, we administered NMBAs in early course of ICU ventilator management especially in conjunction with prone ventilation with excellent results. Many modifications in prone ventilations such as prolong proning cycles; early awake proning and post extubation proning have also been described [18]. Nevertheless, ICU physicians should be aware of contraindications and should only provide proning after weighing the benefit to risk ratio in patients with severe ARDS. In the present era of COVID-19 pandemic, many consensus guidelines endorse early prone ventilation strategies after observing its successful outcomes [19].

Conclusion

Prone ventilation along with advance ventilation strategies certainly remains the central axis of survival outcome in severe ARDS patients. Early prone ventilation should be initiated as an integral component of comprehensive management strategies formulated in refractory ARDS patients. Critical care physicians should ensure that adequate skill and competence is attained by all caregivers including nursing and other ancillary staff while positioning the aforementioned subset of patients along with all precautions required during the period of prone ventilation.

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