Brief Communication

Prone position and pressure control inverse ratio ventilation in H1N1 patients with severe acute respiratory distress syndrome

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Abstract

Aim: To observe the 28 and 90 days mortality associated with prone position and assist control-pressure control (with inverse ratio) ventilation (ACPC-IRV). **Materials and Methods:** All patients who were admitted to our medical Intensive Care Unit (ICU) who are positive for H1N1 viral infection with severe acute respiratory distress syndrome (ARDS) and requiring invasive mechanical ventilation in prone position were included in our prospective observational study. Six patients who are positive for H1N1 required invasive ventilation in prone position. These patients were planned to ventilate in prone for 16 h and in supine for 8 h daily until P/F ratio >150 with FiO_2 of 0.6 or less and positive end-expiratory pressure <10 cm of H_2O. **Results:** At admission, among these six patients the mean tidal volume generated was about 376.6 ml which was in the range of 6–8 ml/kg predicted body weight. The mean lung injury score was 3.79, mean PaO_2/FiO_2 ratio was 52.66 and mean oxygenation index was 29.83. The mean duration of ventilation was 9.4 days (225.6 h). The ICU length of stay was 11.16 days. There was no mortality at 28 and 90 days. **Conclusion:** Early prone combined with ACPC-IRV in H1N1 patients having severe ARDS can be used as a rescue therapy and it should be confirmed by large observational studies.

Keywords: Influenza A virus, inverse ratio ventilation, pressure control ventilation, prone position, severe acute respiratory distress syndrome

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Introduction

Acute respiratory distress syndrome (ARDS) is a complex syndrome with varied etiology. Influenza viral infection causing severe ARDS is one of the leading causes of increased mortality in the recent years. First case of H1N1 infection was reported by central of disease control in California – April 2009[1] and in India it was reported in Hyderabad – May 2009.[2] Most patients who die due to influenza infection are because of severe hypoxia and multi-organ dysfunction syndrome (MODS).

In 2009 influenza pandemic, there was high mortality in patients with severe ARDS even though patients were ventilated with low tidal volume (volume control) ventilation. Multiple ventilation strategies and rescue therapies have been used to improve oxygenation. Low tidal volume ventilation (volume control) with prone position – PROSEVA trial has shown good outcome

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as compared to low tidal volume ventilation (volume control) with supine position.[3]

In our institution we commonly practice assist control-pressure control with inverse ratio ventilation (ACPC-IRV) for ventilating severe ARDS patients. In our study we combined this ventilation strategy along with prone positioning as a rescue therapy, when the normal supine position and ACPC-IRV failed to improve oxygenation after 12 h of initiation of ventilation.

Materials and Methods

During study period between June 2014 and February 2015, 43 patients were positive for nasopharyngeal or throat swab reverse transcriptase - polymerase chain reaction[4] for H1N1 and only 17 patient's required invasive ventilatory support (ACPC-IRV).

Out of 17 patients, 11 patients showed improvement in terms of oxygenation with regular supine ventilation at the end of 12 h (that is requiring FiO_2 < 0.6 or less, P/F ratio > 150 and positive end-expiratory pressure (PEEP) <10 cm of H_2O) and hence continued the same supine ventilation. Table 1 showing the P/F ratio and Intensive Care Unit (ICU) length of stay between prone and supine ventilated patients.

Six patients didn't show any improvement after 12 h from the commencement of invasive ventilation in supine and hence they were considered for either prone ventilation/extracorporeal membrane oxygenation (ECMO) as salvageable therapy.

Prone ventilation or ECMO therapy consent was initiated between 12 and 36 h of admission to medical ICU for those six patients who didn't improve with normal pressure control with inverse ratio and supine ventilation (1:1 ratio). All six patient attendees agreed for prone ventilation as a salvage therapy and also ethics committee clearance was taken. These patients were planned to prone for 16 h and supine ventilation for 8 h daily till patient is able to maintain a P/F ratio >150 with FiO_2 of 0.6 or less and PEEP <10 cm of H_2O. We followed these six patients who underwent prone ventilation till their hospital stay and followed later up to 90 days.

Results

Table 2 shows the demographic data of these six patients. Among these patients, there were four males and two females. The mean age was 46.16 years. Two patients did not had any co morbidities, where as three patients had only hypertension and remaining one patient had diabetes and hypothyroidism along with hypertension. The mean duration of fever to hospital admission was 6 days.

All these six patients had fever, cough and dyspnoea where as generalized weakness, nausea, vomiting and mean arterial pressure (MAP) <65 mmHg were seen in four patients. Other less common clinical features are headache, bradycardia, pleuritic chest pain and diarrhoea. The mean hemoglobin was 10.93 g/dl and total leucocyte count – 5350 cells/cumm. The serum electrolytes, liver function tests and renal function tests, prothrombin time, International Normalized Ratio and activated partial thromboplastin time were in normal range.

The ventilator setting at the initiation of ventilation has been showed in Table 3. All six patients were intubated and connected to the ACPC-IRV. The mean tidal volume generated was about 376.6 ml which was in the range of 6–8 ml/kg predicted body weight at the beginning.

Table 1: The PaO_2/FiO_2 ratio and Intensive Care Unit length of stay between prone and supine ventilated patients

	Patients who did not improve with initial supine ventilation and later ventilated in prone position	Patients who showed improvement with initial supine ventilation and later continued only in supine position
Number of cases	6/17	11/17
PaO_2/FiO_2 ratio	52.66	112.24
Number of ventilator days	9.4	5.2
ICU length of stay (days)	11.16	7.4

ICU: Intensive Care Unit

Table 2: Demographic profile of 6 prone ventilated patients

Profile	Mean (*n*=6)
Age	46.16
Sex	
Females	2
Males	4
Duration from onset of fever to hospital admission	6 days (mean)

Table 3: Ventilator settings of 6 prone ventilated patients at admission

Profile	Mean (*n*=6)
Mode of ventilation	Assist control/pressure control (inverse ratio ventilation)
Average tidal volume	376.66 ml
Frequency	31 breaths/min
FiO_2	0.96
PEEP	14
Pi	20.66
I: E ratio	1:1-2:1

I: E: Inspiratory: expiratory; Pi: Inspiratory pressure; PEEP: Positive end-expiratory pressure

The Inspiratory: Expiratory (I: E) ratio was initially kept 1:1 and later modified according to the PaO_2 values (maximum was 2:1). The mean inspiratory pressure (Pi) was 20.66 cm H_2O, which was kept to achieve a tidal volume of 6–8 ml/kg predicted body weight and later reduced to about 6 ml/kg predicted body weight. The PEEP of 14 cm H_2O was kept initially and later reduced based on oxygenation parameter (never used more than 14 PEEP). The mean frequency and fraction of inspired oxygen were 31 breaths/min and 0.96 respectively. Figure 1 showing patient being ventilated in prone position.

Table 4 shows the oxygenation parameters at admission. The mean lung injury score (LIS) was 3.79, mean PaO_2/FiO_2 ratio was 52.66 and mean oxygenation index was 29.83. All six patients were proned for 16 h each day. The mean duration from ICU admission to initiation of prone ventilation was 30.66 h. The mean duration of ventilation was 9.4 days (225.6 h). The mean duration of prone and supine ventilation was 66.66 and 159.6 h respectively. The ICU length of stay was 11.16 days. There was no mortality at 28 and 90 days.

The management and complications have been shown in Table 5. Capsule oseltamivir 150 mg twice daily was used for 10 days in view of severe infection. We used tablet prednisolone 40 mg twice daily for 5 days. Patients were sedated and paralyzed using midazolam and atracurium for 2 days and later tapered slowly (average duration of 4.16 days). Vitamin-C (10 days) and omega-3 fatty acids (3 days) were also used in all six patients. Four patients required noradrenalin infusion and one patient vasopressin infusion to maintain MAP > 65 mmHg. Two patients had severe left ventricular dysfunction (myocarditis) and managed with dobutamine infusion.

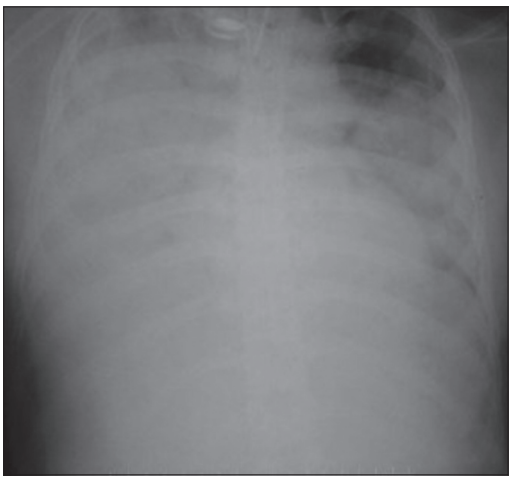

Figure 1: Chest X-ray of our first patient having severe acute respiratory distress syndrome due to H1N1 infection

Orciprenalin was used in two patients for 7 days (10 mg thrice daily) in view of bradycardia. Due to prolonged ventilation required in two patients, they were tracheostomised and later successfully decannulated. With regards to complication, ventilator associated pneumonia was seen in two patients, acute kidney injury in two patients, myocarditis in two patients, critical illness myopathy and atrial fibrillation in one patient each. None of our patients had pneumothorax.

Discussion

Low tidal volume ventilation (ARDS network trial) has shown better outcome in patients having severe ARDS.[5] There is still confusion regarding which rescue mode is best among available treatment. Recently prone position and low tidal volume ventilation has shown better mortality benefit as compared to supine position and low tidal volume ventilation. Combination of pressure control and IRV has been used less frequently for severe ARDS ventilation. In our ICU we commonly practice ACPC-IRV for ventilating a patient with severe ARDS. In our study population we used pressure control mode

Table 4: Oxygenation parameters of 6 prone ventilated patients at admission

Parameters	Mean (*n*=6)
Lung injury score	3.79
PaO_2/FiO_2 ratio	52.66
Oxygenation index	29.83
hours from ICU admission to initiation of prone ventilation (h)	30.66
Mean hours of prone/supine ventilation	66.66/159.6
Number of ventilator days	9.4
ICU length of stay (days)	11.16
28 and 90 days mortality	0

ICU: Intensive Care Unit

Table 5: Management and complications occurred during Intensive Care Unit stay

Profile	*n*=6 (%)
Oseltamivir	150 mg twice daily for 10 days
Prednisolone	40 mg twice daily for 5 days
Atracurium + midazolam	Average 4.16 days in tapering dose
Vitamin-C	500 mg once daily for 10 days
Omega-3 fatty acids	100 ml once daily for 3 days
Noradrenalin	4 patients for average 6 days
Vasopressin	1 patient for 3 days
Orciprenalin	2 patients for 7 days (10 mg thrice daily)
Dobutamine	2 patients for average 4 days
Tracheostomy	2 patients
Complictions	
VAP	2 patients
AKI	2 patients
CIM	1 patient
Pneumo-thorax	0
Myocarditis	2 patients
Atrial fibrilation	1 patient

AKI: Acute kidney injury; VAP: Ventilator associated pneumonia; CIM: Critical illness myopathy

with IRV along with prone positioning [Figure 2] as a rescue therapy in H1N1 patients with severe ARDS who failed the initial ACPC-IRV.

Prone ventilation has been used as one of the rescue therapy in patients having severe hypoxia related to severe ARDS. Recent study by Guérin *et al*.[3] have shown that prone ventilation in severe ARDS has better outcome compared to supine ventilation with significantly decreased in 28 and 90 day mortality.

The prone position has been used in severe ARDS patients since 1974 for improvement in oxygenation. Maximum improvement has been seen in patient having severe hypoxemia. Multiple mechanisms are involved in improvement of systemic oxygenation during prone ventilation such as, reduction of compression of caudal lung by cardiac and abdominal contents, reinflation of more dorsal lung compared to ventral lung, diaphragm shape, changes in hypoxic pulmonary vasoconstriction and differential production of nitric oxide at different parts of the lung. Prone positioning has shown to cause more homogenous lung inflation with reduction in ventilator induced lung injury. Richter *et al*.[6] showed that prone or steep lateral decubitus position can decrease intrapulmonary shunt and improve oxygenation.

Prone-supine study-1[7] used 6 h of prone position daily for 10 days showed no difference in terms of mortality and complication as compared to conventional ventilation. Gattinoni *et al*.[8] showed that during prone ventilation, the reduction in partial pressure of carbon dioxide of 1 mm hg or more showed increase in survival rate. Prone-supine study-2[9] 20 h of prone ventilation per day also showed similar mortality at 28 days as compared to supine group and more complication in prone group. Systemic review[10] showed no reduction in mortality or duration of ventilation but only improvement in oxygenation. Hence this prone position can be used as rescue strategy to improve oxygenation. A review of all meta analyses[11] showed reduced mortality in patients with severe hypoxemia. Recently PROSEVA trial[3] has shown significant reduction in 28 and 90 days mortality when prolonged prone positioning (16 h of prone per day) in severe ARDS patients as compared to conventional ventilation. In our observational study we also used prone positioning for 16 h per day without any mortality at 28 and 90 days. Six patients didn't show any improvement with ACPC-IRV and hence they were considered for either prone ventilation or ECMO as salvageable therapy. Figure 1 showing chest X-ray of our first patient with severe ARDS. These patients were planned to prone for 16 h and supine ventilation for 8 h in total 24 h. Only supine ventilation was maintained when patient is able to maintain P/F ratio >150 with FiO_2 of 0.6 or less and PEEP <10 cm of H_2O.

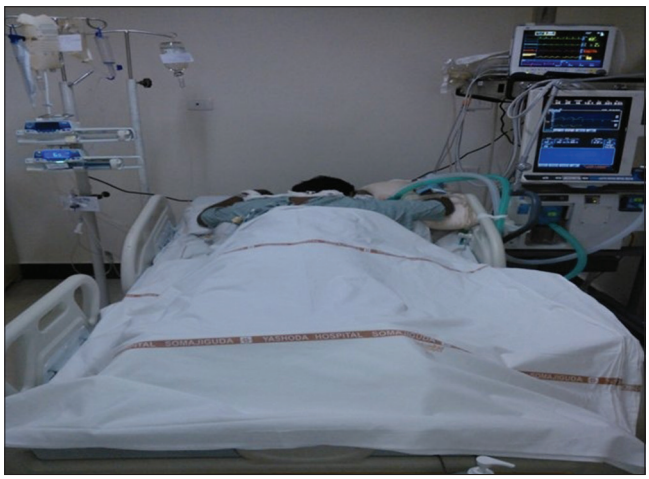

Figure 2: Patient being ventilated in prone position

In our study group the mean age was 46.16 years (males-4 and females-2). Hypertension was seen among 4 of 6 patients included in the study. Most common clinical features are fever, cough and dyspnoea followed by generalized weakness, nausea, vomiting, MAP <65 mmHg, headache, bradycardia, pleuritic chest pain and diarrhoea. The mean duration of fever to hospital admission was 6 days.

The ventilator setting has been showed in Table 3. The mean tidal volume generated was about 376.6 ml which was in the range of 6–8 ml/kg predicted body weight. The I: E ratio was initially kept 1:1 and to a maximum of 2:1. The mean Pi was 20.66 cm H_2O. The maximum PEEP of 14 cm H_2O was kept initially and later reduced based on oxygenation parameter. The mean frequency and fraction of inspired oxygen were 31 breaths/min and 0.96 respectively.

The severity of ARDS and duration of ventilation is shown in Table 4. The mean LIS was 3.79, PaO_2/FiO_2 ratio: 52.66 and mean oxygenation index: 29.83. The mean duration from ICU admission to initiation of prone ventilation was 30.66 h. The mean duration of ventilation was 9.4 days (225.6 h). The mean duration of prone and supine ventilation was 66.66 and 159.6 h respectively.

All six patients were treated with capsule oseltamivir 150 mg twice daily for 10 days since our patients had severe infection with MODS, we used the double dose as recommended by WHO. Tablet prednisolone 40 mg

twice daily for 5 days was used. The role of steroids in management of H1N1 related ARDS is controversial. Few studies[12,13] suggest that early and low dose corticosteroids are inefficient and may be even harmful where as others[14,15] have shown the improvement in LIS and hemodynamic stability. Broad spectrum antibiotics (deescalated later after bronchoalveolar lavage fluid culture and sensitivity) along with Vitamin-C (10 days) and omega-3 fatty acids (3 days) were also used during management of these patients. All patients were sedated and paralysed using midazolam and atracurium for 2 days and later tapered slowly (average duration of 4.16 days). Four patients required noradrenalin infusion and one patient vasopressin infusion to maintain MAP > 65 mmHg. Two patients had severe left ventricular dysfunction (myocarditis) and managed with dobutamine infusion. Orciprenalin was used in two patients for 7 days (10 mg thrice daily) in view of bradycardia.

The ICU mortality of H1N1 patients with severe ARDS is about 10–38% and increases up to 58% in patients requiring invasive mechanical ventilation.[16] Sahoo *et al*.[17] in their study shown that out of seven patients, five patients had MODS. The commonest organ involved was renal. In our study acute kidney injury was seen in two patients but recovered without any need of dialysis. Ventilator associated pneumonia was seen in two patients (acenetobacter was found in both patients), myocarditis in two patients, critical illness myopathy and atrial fibrillation in one patient each. None of our patients had pneumothorax (probably due to maintenance of lower tidal volume and lesser PEEP). Figure 3 showing chest X-ray of the same patient at the end of prone ventilation on 6th day.

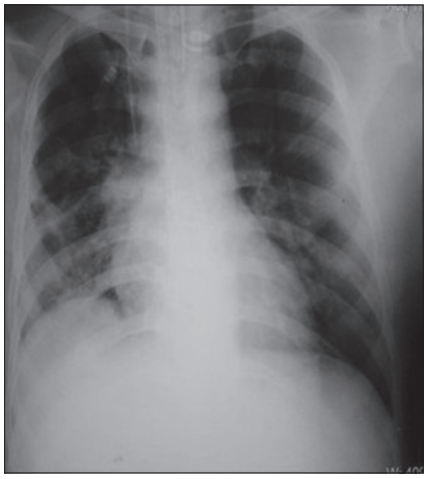

Figure 3: Chest X-ray of the same patient at the end of prone ventilation on 6th day

The ICU length of stay depends upon severity of infection, preexisting comorbidities, BMI > 30, co-infection and MODS.[18] The mean ICU length of stay in our patients was 11.16 days. There was no mortality at 28 and 90 days.

Conclusion

Early prone combined with ACPC-IRV in H1N1 patients having severe ARDS can be used as a rescue therapy for better outcome and it should be confirmed by large observational studies.

Acknowledgements

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Conflicts of interest

There are no conflicts of interest.

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