Lung protective strategy and prone ventilation resulting in successful outcome in a patient with ARDS due to H1N1

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Summary
Acute respiratory distress syndrome (ARDS) is an acute respiratory condition caused by various pulmonary and extrapulmonary conditions including H1N1 virus infection. ARDS has a high mortality worldwide and in India various studies suggest that mortality in children is as high as 73–75%. Different lung protective ventilation strategies have recently been adopted to reduce mortality. The authors report a successful outcome in a 3.5-year-old child with ARDS secondary to H1N1 infection following use of a very low tidal volume (4–6 ml/kg) along with high positive end-expiratory pressure breathing and prone ventilation. As far as we are aware, this is the first case report of a successful outcome in a child with ARDS secondary to H1N1 in India.

BACKGROUND
Acute respiratory distress syndrome (ARDS) due to pulmonary or extrapulmonary causes has high mortality worldwide and has been the most common cause of death in the current H1N1 pandemic. Use of a lung protective strategy resulted in successful outcome in a child with ARDS due to H1N1 in the high risk group for mortality.

CASE PRESENTATION
A 3.5-year-old child was referred to our hospital for intensive care support. He had a 3-day history of mild fever, cough and cold and a 2-day history of progressive respiratory distress. He also complained of throat pain and had been eating very little for the past 2 days. He was an only child, had been vaccinated appropriately and had normal development. His father had had a cough and cold a week previously and neither the child nor the father had recently travelled long distance.

On arrival, the child appeared very unwell, and was drowsy and centrally cyanosed. He was well nourished and weighed 15 kg. He was saturating 30% in room air and 60% with 15 l/min oxygen. He had severe chest recession with a respiratory rate of 56/min. On auscultation, he had diminished vesicular breath sounds along with bilateral crepitations. He had a good volume pulse at a rate of 146/min and his blood pressure was 98/52 mm Hg. He was immediately intubated with an uncuffed tube with fentanyl and midazolam administration and was ventilated with pressure controlled ventilation with a peak inflation pressure (PIP)/positive end-expiratory pressure (PEEP) of 32/7 and FiO2 of 1.

INVESTIGATIONS
Observation analysis and results
The child was ventilated for 28 days and all blood gases (n=63) were examined. For each test, the PaO2/FiO2 ratio was calculated. These PaO2/FiO2 values were statistically analysed before and after the application of prone ventilation and use of methylprednisolone using the t test. PaO2/FiO2 values were also statistically analysed comparing application of high PEEP1–4 and very high PEEP5–10 using the t test. The child’s PaO2/FiO2 value was 49 during admission, which is indicative of severe hypoxaemia. The mean pH, PaO2 and PCO2 were 7.43±0.10, 77±26 and 51±16, respectively. Mean PaO2/FiO2 was 131±91 (range 627–49). Mean PO2/FiO2 before and after prone ventilation was 122 (n=23) and 135 (n=40), respectively. Although the PO2/FiO2 mean value was higher after prone ventilation was started, the difference was not statistically significant (p>0.5). The mean PO2/FiO2 values with high PEEP1–4 (n=35) and very high PEEP5–10 (≥11) (n=25) were 158±112 and 93±24, respectively. Although clinically we felt that higher PEEP5–10 was beneficial in improving oxygenation, the mean PaO2/FiO2 was lower with higher PEEP. The PaO2/FiO2 results did not improve after starting methylprednisolone and the mean PaO2/FiO2 values before and after starting methylprednisolone were 128±47 (n=21) and 109±53 (n=57), respectively. The deterioration in PaO2/FiO2 after methylprednisolone administration was statistically significant (p=0.02).

TREATMENT
The patient was immediately intubated with an uncuffed tube with fentanyl and midazolam administration and was ventilated with pressure controlled ventilation with a PIP/PEEP of 32/7 and FiO2 of 1. His saturation improved to >90% and the first arterial blood gas analysis showed pH 7.31, PaO2 49, PCO2 51 and base excess (BE) of (−1.3). Chest x-ray was consistent with ARDS (figure 1). The first PaO2/FiO2 ratio of 49 put him in the very high mortality risk category. Oseltamivir was started as the chance of H1N1 being the cause of ARDS was very high and a throat swab was sent for H1N1 analysis. In the next few days his ventilatory requirements were persistently high with high FiO2 while PaO2/FiO2 was persistently below 150. He was ventilated with a moderately high PEEP of 7–10 and...
a PIP between 26 and 32. He developed gastric haemorrhage which was treated with pantoprazole. On day 4 of admission, the throat swab for H1N1 came back positive. In addition to oseltamivir, the patient also received broad-spectrum antibiotics. He was kept under deep sedation and paralysis with fentanyl, midazolam and vecuronium infusions which were continued for the entire period of ventilatory support as it was difficult to keep his saturations up to 89% or 90% whenever sedation was decreased. The ventilatory requirements were closely titrated by regular arterial blood gas estimation. Enteral nutrition was started early on day 5 of admission with 3-hourly nasogastric milk feeds to which sugar and protein supplements were also added a few days later. In the first week there was very little improvement in the ventilatory requirements or the hypoxaemia. The PaO₂/FiO₂ ratio continued to be below 150, only occasionally increasing above 150. There was further deterioration in chest x-ray with increased infiltrates and opacities. To treat hypoxaemia and deteriorating ventilation, the following strategies were applied. The patient was intubated with a cuffed endotracheal tube to prevent air leak. The standard lung protective strategy for ventilation was adopted but with higher PEEP, a lower tidal volume. We aimed at a target tidal volume of 4–6 ml/kg. We also applied prone ventilation on day 9 of admission, keeping the patient prone for 8 h in a 12-h cycle. Our paediatric ventilator had only pressure control mode with three basic modes of synchronised intermittent mandatory ventilation (SIMV), IMV and assist control mode and did not have any volume control mode but showed the pressure–volume curve and both the inspired and expired tidal volumes. Therefore, we progressively increased PEEP to a maximum of 16 with the aim of reducing FiO₂ and maintained a PIP of not more than 34, targeting a tidal volume of 4–6 ml/kg. We had to increase the PIP up to 40 at times to deliver the targeted tidal volume. Methylprednisolone was added on day 10 at a dose of 2 mg/kg/day and was given for a total duration of 2 weeks. In the second week of ventilation, the patient developed high grade fever. The antibiotics were changed according to endotracheal suction and tube tip culture sensitivity results to which he responded over next few days. He subsequently developed surgical emphysema on day 14 of ventilation which was treated conservatively, and pneumothorax on the right side on day 20 of ventilation which was managed by inserting an intercostal chest drain. He had developed hypotension following pneumothorax which was treated with dopamine and resolved in 2 days. Over the following 7 days his ventilatory requirements progressively reduced. He was extubated to face mask oxygen after 28 days of ventilation and was weaned off oxygen in another 15 days. He was discharged home after 50 days in hospital. At the time of discharge, he was completely normal with no neurological or pulmonary complications.

**OUTCOME AND FOLLOW-UP**

The patient was discharged home after 50 days in hospital. At the time of discharge, he was completely normal without any neurological or pulmonary complications. He has remained well and with no neurological sequelae when seen at follow-up.

**DISCUSSION**

According to the Ministry of Health and Family Welfare, Government of India report, as of 28th February 2010, a total of 29,652 cases of H1N1 have been confirmed in...
ARDS, Flori et al found that the initial severity of hypoxaemia has a predictive value for identifying patients at high risk of prolonged mechanical ventilation and death. In fact, an inverse relationship between initial PaO$_2$/FiO$_2$ and risk of prolonged mechanical ventilation and death. In our patient we stopped it after 2 weeks. On statistical analysis also it was found that oxygenation worsened, as indicated by the statistically significant deterioration in the PaO$_2$/FiO$_2$ ratio (p=0.02).

In our patient, although the effect of very high PEEP and prone ventilation combined did not result in a statistically significant improvement in oxygenation, these two modalities together with a very low tidal volume of 4–6 ml/kg and permissive hypercapnea, in light of low PaO$_2$ having prevented multiorgan failure, resulted in a successful outcome in this child who according to the initial PaO$_2$/FiO$_2$ ratio was at a very high risk for mortality. To the best of our knowledge, this is the first successful outcome of ARDS secondary to H1N1 in the paediatric age group to be reported from India.

In adult patients with ALI/ARDS, the prone position is beneficial in improving oxygenation, the mean PaO$_2$/FiO$_2$ was lower with higher PEEP. This was possible because as soon as oxygenation started to improve the PEEP was lowered and subsequently good PaO$_2$ values were observed even with lower PEEP. The mean pH, PaO$_2$ and PFCO$_2$ values were 7.43±0.10, 77±26 and 51±16, respectively. Mean PaO$_2$/FiO$_2$ was 131±91 (range 627–49). Mean PFCO$_2$ is indicative of permissive hypercapnea, while mean PO$_2$ reflects acceptance of low PO$_2$.

In adult patients with ALI/ARDS, the prone position is known to benefit oxygenation and ventilation. The possible mechanisms involved in improved oxygenation in prone ALI/ARDS patients are: (1) increased lung volumes; (2) redistribution of lung perfusion; and (3) recruitment of dorsal spaces with more homogeneous ventilation and perfusion distribution. However, a randomised controlled trial of prone versus supine ventilation in 102 paediatric patients with ARDS found no difference in ventilator-free days. In our patient, the PaO$_2$/FiO$_2$ ratio was higher after starting prone ventilation, although the difference was not statistically significant (p>0.05) (the mean PaO$_2$/FiO$_2$ ratio was 122 before and 135 after starting prone ventilation).

The effects of low-dose prolonged methylprednisolone infusion (1 mg/kg/day vs placebo for 28 days) on lung function in patients with early severe ARDS were studied in a randomised double-blind placebo controlled trial in the intensive care units (ICUs) of five hospitals and it was found that the duration of mechanical ventilation and ICU length of stay were both reduced.17 In a randomised double-blind placebo controlled trial on 180 patients’ use of methylprednisolone after 7 days of onset of ARDS, it was found that if used within 14 days of onset the oxygenation index improved and the number of ventilator-free and shock-free days reduced. However, when used after 14 days of onset, there was an increase in mortality.18 We started methylprednisolone on the 10th day of ventilation at 2 mg/kg/day according to the protocol of Meduri et al.19 However, as there was no clinically appreciable benefit we stopped it after 2 weeks. On statistical analysis also it was found that oxygenation worsened, as indicated by the statistically significant deterioration in the PaO$_2$/FiO$_2$ ratio (p=0.02).

In our patient, although the effect of very high PEEP and prone ventilation combined did not result in a statistically significant improvement in oxygenation, these two modalities together with a very low tidal volume of 4–6 ml/kg and permissive hypercapnea, in light of low PaO$_2$ having prevented multiorgan failure, resulted in a successful outcome in this child who according to the initial PaO$_2$/FiO$_2$ ratio was at a very high risk for mortality. To the best of our knowledge, this is the first successful outcome of ARDS secondary to H1N1 in the paediatric age group to be reported from India.

**Learning points**

- A tidal volume as low as 4–6 ml/kg is effective in improving oxygenation in acute respiratory distress syndrome (ARDS).
- Prone ventilation improves oxygenation in children with ARDS.
- Lung protective strategies combining very low tidal volumes, prone ventilation, very high PEEP and permissive hypercapnea improved oxygenation and ventilation and resulted in a successful outcome in a child with H1N1 ARDS.

**Competing interests** None.

**Patient consent** Obtained.

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