Improved Oxygenation and Lower Peak Airway Pressure in Severe Adult Respiratory Distress Syndrome*

Treatment with Inverse Ratio Ventilation

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Two patients with the adult respiratory distress syndrome (ARDS) were placed on pressure-controlled inverse-ratio ventilation (IRV) when their condition deteriorated despite optimal treatment with intermittent mandatory ventilation and positive end-expiratory pressure. In the first case, high peak airway pressure was reduced by 50 percent with the institution of IRV. In the second, refractory hypoxemia was eliminated by using an inspiratory-to-expiratory ratio of 4:1. These cases show that IRV may offer certain advantages in the treatment of severe ARDS.

Treatment of the adult respiratory distress syndrome (ARDS) consists of maintaining adequate ventilation and oxygenation while minimizing barotrauma and depression of cardiac function. Despite technical advances in the treatment of ARDS, many patients do not respond adequately to conventional methods of mechanical ventilation, and mortality remains between 40 and 70 percent.

Inverse-ratio ventilation (IRV) is a method of ventilatory support that provides an increased inspiratory time to allow for stabilization of pulmonary units and diffusion of gases. The shortened expiratory phase allows an adequate tidal volume to escape without allowing alveoli to fall below their closing volume.

We present our recent experience using IRV to support two patients with severe ARDS refractory to standard therapy with intermittent mandatory ventilation (IMV) with positive end-expiratory pressure (PEEP).

**Case Reports**

**Case 1**

A 23-year-old previously healthy woman was admitted to our hospital complaining of increased shortness of breath, left-sided chest pain, and cough. Physical examination showed her to be in moderate respiratory distress, with a blood pressure of 94/58 mm Hg, pulse rate of 140 beats per minute, temperature 37.5°C (100°F), and a respiratory rate of 48 breaths per minute. Breath sounds were bronchial in quality at both bases, and her arterial blood gas levels on room air were as follows: pH 7.51; arterial carbon dioxide tension (PaCO₂), 26 mm Hg; and arterial oxygen pressure (PaO₂), 51 mm Hg. The white blood cell count was 1,000/cu mm, with 25 percent neutrophils, 33 percent bands cells, 31 percent lymphocytes, and 10 percent metamyelocytes, and the platelet count was 85,000/cu mm. Sputum for Gram's stain, culture and sensitivity, acid-fast stain, and fungus was not diagnostic. A chest x-ray film showed bibasilar alveolar infiltrates.

After multiple cultures of blood and sputum were obtained, the patient was started on gentamicin, nafcillin, and erythromycin. Despite vigorous pulmonary toilet, the patient's arterial blood gas levels deteriorated. At a fractional concentration of oxygen in the inspired gas (FiO₂) of 0.8 via a nonbreathing mask, her arterial blood gas levels were as follows: pH 7.27; PaCO₂, 45 mm Hg; and PaO₂, 48 mm Hg. The follow-up chest x-ray film showed bilateral diffuse alveolar infiltrates. The patient was intubated and placed on a volume ventilator (Bear II) in the IMV mode. Initial settings were as follows: tidal volume (Vt), 950 ml; respiratory rate, 20 breaths per minute; minute volume (Ve), 15 L; PEEP, 10 to 15 cm H₂O; and FiO₂, 0.55. Peak airway pressures ranged between 60 and 80 cm H₂O, depending on the patient's level of agitation. Static compliance averaged 24 ml/cm H₂O, and the cardiac index was 4.5 L/min/sq m, with a pulmonary arterial pressure of 46/22 mm Hg and pulmonary capillary wedge pressure of 8 mm Hg.

Despite initial improvement with IMV and PEEP, oxygenation further deteriorated (Fig 1), static compliance dropped to 16 ml/cm H₂O, and the decision was made to begin IRV. The patient was paralyzed with pancuronium bromide, anesthetized with diazepam and morphine, and placed on a ventilator (Siemens' Servo 900C) in the pressure-control, time-cycled mode with the following settings: inspiratory pressure, 40 cm H₂O; FiO₂, 0.5; initial inspiratory-to-expiratory ratio (I/E), 2:1; and respiratory rate, 25 breaths per minute. Arterial blood gas levels four hours after instituting this form of therapy were as follows: pH 7.46; PaCO₂, 24 mm Hg; and PaO₂, 89 mm Hg at an FiO₂ of 0.5; compliance remained unchanged. The cardiac index was 4.05 L/min/sq m, with a pulmonary arterial pressure of 42/34 mm Hg and pulmonary capillary wedge pressure of 16 mm Hg.

Over the following 14 days, the patient's chest x-ray film began to show clearing of the alveolar infiltrates, and oxygenation improved. Inspiratory time was gradually decreased from a high of 80 percent (I/E ratio, 4:1) to 50 percent (I/E ratio, 1:1) on day 11, at which time her paralysis and anesthesia were terminated. The FiO₂ was reduced from 0.6 to 0.4 during this same period, and over the following nine days, further reductions in the I/E ratio and FiO₂ were made. On the

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20th day, SIMV and pressure support were initiated, with complete weaning from the respirator occurring on the 25th day, at which time static compliance was 28 ml/cm H$_2$O. The patient was discharged from the hospital one week later, with the following arterial blood gas levels on room air: pH 7.41; PaCO$_2$, 41 mm Hg; PaO$_2$ 63 mm Hg; and saturation, 92 percent. Influenza A titers doubled during her hospitalization.

**Case 2**

A 33-year-old man was admitted to our hospital with abdominal pain and obtundation. He had a previous history of alcoholism and pancreatitis, for which he had been hospitalized numerous times. Physical examination was significant for a systolic blood pressure of 90 mm Hg (in a MAST suit) with a pulse of 110 beats per minute, respiratory rate of 36 breaths per minute, and temperature of 31.6°C (89°F). Bronchial breath sounds were heard over the entire left lung, with coarse inspiratory crackles at the right base; diffuse tenderness was noted on abdominal examination.

Laboratory data included the following: white blood cell count, 28,000/cu mm, with 71 percent neutrophils, 10 percent band cells, and 6 percent lymphocytes; sodium, 125 mmol/L; potassium, 6.1 mmol/L; chloride, 82 mmol/L; bicarbonate, 33 mmol/L; blood urea nitrogen, 89 mg/100 ml; creatinine, 6.8 mg/100 ml; glucose, 2,000 mg/100 ml; and amylase, 504 mg/100 ml. At an FIO$_2$ of 1.0 via T-tube, the patient's blood gas levels were as follows: pH 7.00; PaCO$_2$, 28 mm Hg; and PaO$_2$, 69 mm Hg. The chest x-ray film showed complete opacification of the left lung, with a right lower lobar alveolar infiltrate.

The patient was treated for aspiration pneumonia and pancreatitis. After numerous cultures of blood and sputum were obtained, he was started on penicillin, gentamicin, and clindamycin, and was given appropriate fluid replacement. He was initially placed on a ventilator (Bennett MA-1) in the IMV mode at a respiratory rate of 12 breaths per minute, FIO$_2$, of 1.0, VT of 700 ml, and PEEP of 5 cm H$_2$O. Static compliance was 28 ml/cm H$_2$O, pulmonary arterial pressure was 25/17 mm Hg, and pulmonary capillary wedge pressure was 4 mm Hg. Within 24 hours the patient's compliance dropped to 18 ml/cm H$_2$O, pulmonary arterial pressure increased to 42/34 mm Hg, and pulmonary capillary wedge pressure rose to 15 mm Hg. The PaO$_2$ fell from 70 to 40 mm Hg (despite an FIO$_2$ of 1.0 with increasing PEEP and peak airway pressures), and follow-up chest x-ray films showed diffuse alveolar infiltrates bilaterally.

The refractory hypoxemia and poor compliance on conventional therapy led us to begin IRV at an initial ratio of 2:1 for the first four hours until euvolemia was attained, with rapid advancement to 4:1 for the following 48 hours (Fig 2). During this same period the patient's metabolic abnormalities were corrected, the chest x-ray film began to clear, and FIO$_2$ was decreased from 1.0 to 0.4, with a concomitant doubling of PaO$_2$ from 40 to 80 mm Hg. Paralysis and anesthesia were discontinued on the fifth day, when the I/E ratio was 1:1, compliance was 40 ml/cm H$_2$O, pulmonary arterial pressure was 34/24 mm Hg, and pulmonary capillary wedge pressure was 14 mm Hg. The patient was successfully extubated on the ninth day of hospitalization.

**DISCUSSION**

In humans, as with animal models of ARDS, IRV has
been shown to improve oxygenation while allowing both lower peak airway pressure and PEEP to be applied.14 Our cases of severe ARDS highlight two aspects of the disease which seem to benefit most by using this alternative form of ventilatory support.

Prompted by concern over the significant peak airway pressure being generated (80 cm H2O), patient 1 was placed on IRV in an effort to minimize the inevitable barotrauma associated with higher levels of peak airway pressure and PEEP.15 Once on IRV, she experienced a 50 percent drop in peak airway pressure, 66 percent reduction in PEEP, and 22 percent reduction in VE. Despite these lower pressures, the PaO2 improved significantly.

Maintaining adequate oxygenation is frequently a problem in patients with ARDS, and it proved to be the major difficulty in managing case 2. The patient’s PaO2 fell shortly after he entered the hospital and showed no response to increasing FIO2, PEEP, and peak airway pressure; however, after beginning IRV, the peak airway pressure PAP decreased 20 percent, PEEP decreased 33 percent, and again a significant improvement in PaO2 was observed.

The improved oxygenation at lower peak airway pressure observed in these cases supports observations noted in the animal and human literature14 and confirms what has been known in neonatal ventilation for some time.28 Why oxygenation improves during IRV is uncertain. The role of mean airway pressure has been debated;29 however, our data support the more recent study by Bowe et al28 suggesting that it is not the major determinant of oxygenation. Although paralysis with anesthesia (as applied to both of our patients) may reduce oxygen consumption, improve chest wall compliance, and result in better oxygenation, it is unlikely to explain the significant increases we observed. This is supported by case 1 (Fig 1), when on the ninth day a premature switch back to IMV (really a trial of volume-controlled normal-ratio ventilation) resulted in a drop of 30 mm Hg in PaO2 despite the same FIO2 and continued paralysis.

We suggest that because of an early and sustained insufflation, IRV results in progressive alveolar recruitment with stabilization of surfactant-deficient regions. In addition to improved oxygenation, an overall improvement in ventilation would be an expected corollary and indeed was observed, as evidenced by the drop in PaCO2 which both patients experienced after placement on IRV at the same or lower VE.

Inverse-ratio ventilation offers an alternative method of ventilatory support to be considered when managing patients with severe ARDS. Our cases demonstrate that IRV leads to improved oxygenation with decreased peak airway pressure and stress the need for further studies to more clearly understand this method of ventilation, as well as the indications for its use.

REFERENCES