We present a case of neurogenic pulmonary oedema (NPO) due to subarachnoid haemorrhage that resulted in hypoxia refractory to conventional mechanical ventilation. Prone positioning was employed, resulting in rapid and sustained improvement in oxygenation. We discuss the pathogenesis of NPO and the mechanism of action of prone ventilation. Prone ventilation may be of value in the management of NPO, both in treating life-threatening hypoxia and in optimizing neurological recovery. Further data are required on its effect on intracranial pressure after subarachnoid haemorrhage.

Br J Anaesth 2003; 90: 238–40

Keywords: complications, position, prone; pulmonary oedema, neurogenic; ventilation, mechanical

Accepted for publication: September 18, 2002

Neurogenic pulmonary oedema (NPO) is a rare but life-threatening complication of acute neurological conditions such as subarachnoid haemorrhage (SAH).1 The mortality rate is high and neurological recovery in survivors may be worsened by the resultant hypoxia. Conventional ventilatory management of NPO, involving high mean intrathoracic pressures, may reduce cerebral perfusion and further prejudice neurological outcome.

We present a case of NPO with refractory hypoxia where prone ventilation was used, resulting in marked improvement in oxygenation. The patient went on to make a good functional recovery. A literature search has failed to find previous reports on the use of prone ventilation in NPO.

Case report
A previously well 42-yr-old female collapsed whilst driving her car at low speed. Her Glasgow coma score at the scene was 3. On examination in the accident and emergency department, there were no signs of trauma and she was haemodynamically stable. Her best motor response was withdrawal to pain, with no eye opening or vocalization. Respiration was spontaneous, but her oxygen saturation (assessed by pulse oximetry) was only 92%, despite receiving a high concentration of inspired oxygen. In view of this and given her poor neurological condition, tracheal intubation was performed following induction of anaesthesia using propofol and succinylcholine. Mechanical ventilation was instituted. Copious amounts of frothy sputum were suctioned from the tracheal tube and a chest radiograph showed marked bilateral interstitial shadowing. A computed tomographic scan of the head revealed blood in the basal cisterns and in the third, fourth, and lateral ventricles. The diagnosis of SAH with NPO was made. Aspiration pneumonitis was not thought to be the cause of her respiratory failure.

She was admitted to the intensive care where her management followed established guidelines for the brain-injured patient. Sedation was maintained with infusions of propofol (median dose 4 mg kg\(^{-1}\) h\(^{-1}\)) and alfentanil (7.5 μg kg\(^{-1}\) h\(^{-1}\)). The principle therapeutic goals were to optimize cerebral oxygenation by aiming for a mean arterial pressure of 80–90 mm Hg, and by providing adequate arterial oxygenation and carbon dioxide elimination (\(P_{CO_2}\) ~4 kPa). These goals became extremely difficult to achieve despite administration of oxygen 100%, pressure control ventilation using high inspiratory pressures (up to 40 cm H₂O), a positive end-expiratory pressure (PEEP) of 20 cm H₂O, the use of inverse ratio ventilation, and neuromuscular block using boluses of atracurium. The arterial \(P_{O_2}\) ranged from 5.4 to 8.9 kPa. In addition, progressive hypotension necessitated increasing doses of norepinephrine. Insertion of a pulmonary artery catheter revealed a cardiac output of 2.2 litre min\(^{-1}\) m\(^{-2}\), systemic vascular resistance of 600
dynes s$^{-1}$ cm$^{-5}$, pulmonary artery pressure of 38/31 mm Hg and pulmonary artery wedge pressure (PAWP) of 18 mm Hg, leading to commencement of an epinephrine infusion.

Twelve hours after admission to the intensive care unit, the $P_O_2:F_I_0_2$ ratio was 5.8 kPa (43 mm Hg) and given the inexorable deterioration in oxygenation, a decision was taken to undertake prone ventilation. The result was dramatic with rapid improvement in oxygenation such that after 5 h the $P_O_2:F_I_0_2$ ratio had increased to 36 kPa (274 mm Hg; Fig. 1). Mean arterial pressure was maintained at ~75 mm Hg throughout the period of prone positioning with no change in the requirement for inotropes or vasopressors. Similarly, there was no change in the pulmonary artery pressure. Crude assessment of pulmonary compliance revealed a slight reduction during prone positioning. Prone ventilation was continued for 21 h, until the inspired oxygen concentration was 0.35 with a PEEP of 10 cm H$_2$O. Although there was some deterioration in oxygenation after returning the patient to the supine position, her condition was such that weaning of sedation and ventilation could begin. Three days after admission, the patient was transferred to the regional neurosurgical unit, where cerebral angiography revealed left posterior communicating artery and left anterior choroidal artery aneurysms. These were clipped and although her postoperative recovery was complicated by nosocomial pneumonia, she was discharged home 2 months after the original haemorrhage. Despite a residual mild hemiparesis, she is planning to return to work.

**Discussion**

*Neurogenic pulmonary oedema*

NPO is a potentially life-threatening complication of several acute neurological conditions including SAH, intracerebral haemorrhage, head injury, and seizure. A series of 457 patients with SAH reported a 6% incidence of severe NPO. Increased age and a worse clinical grade of SAH were associated with NPO.

Hypoxia results from an increase in extravascular lung water (EVLW); the extent of this increase correlates directly with the magnitude of the intrapulmonary shunt and the degree of hypoxia. Analysis of haemodynamic data and measurement of pulmonary oedema fluid protein content, both in humans and in animal models, has led to the development of two conflicting theories as to the mechanism of NPO.

Proponents of the hydrostatic mechanism cite the finding of low oedema fluid-to-plasma protein ratio and the frequent presence of left ventricular dysfunction to support the concept that pulmonary venous and hence alveolar capillary hypertension are the cause of NPO. Conversely, some patients have oedema fluid with a high protein level suggesting increased permeability of the alveolar capillary wall. In addition, indices of left ventricular performance (PAWP, central venous pressure and cardiac index) may be normal.

Animal models of NPO using intracisternal injection of veratrine, have revealed that shortly after the cerebral insult, pulmonary blood volume increases with pronounced rises in pulmonary arterial and left atrial pressures. This is thought to be because of the massively increased sympathetic discharge. The magnitude of the pulmonary hypertension correlated in this model with the increase in EVLW. In humans, pulmonary artery pressures of 110/60 mm Hg have been recorded in acute SAH. The pulmonary oedema that results in this situation is clearly hydrostatic in origin, but high pressure can disrupt alveolar capillaries (‘stress failure’), which may subsequently lead to the formation of exudative or high permeability pulmonary oedema. Thus, in different patients with NPO, there may be a hydrostatic mechanism, a high permeability mechanism, or a combination of both mechanisms to explain the increase in EVLW.

Whether knowing the precise cause in individual patients is important, is a matter of conjecture. Our patient had moderate pulmonary hypertension and a low-normal cardiac index, suggesting a degree of left ventricular impairment. However, PAWP was 18 mm Hg at its highest, a borderline figure for the diagnosis of cardiogenic pulmonary oedema. In addition, the introduction of inotropic support did not affect pulmonary artery pressure, PAWP or oxygenation, again suggesting that left ventricular dysfunction was not a major component of the pathophysiology.

As well as being a direct threat to life, the severe hypoxia that results from NPO may worsen the neurological injury. Positive pressure ventilation and the use of high levels of PEEP are frequently required and may worsen cerebral perfusion (and therefore outcome) by reducing cardiac output and by impeding cerebral venous drainage. Any therapy that substantially improves oxygenation and allows a reduction in mean airway pressure and duration of mechanical ventilation may improve survival and neurological recovery.
Prone ventilation

Mechanical ventilation in the prone position improves oxygenation in ~60% of patients with acute lung injury (ALI) or acute respiratory distress syndrome (ARDS). Such patients typically have extensive collapse-consolidation of dorsal lung units when supine. This is partly due to the weight of the overlying heart and high pleural pressures dorsally. When turned prone, there is re-aeration of these opaciﬁed lung units. Although the newly dependent ventral lung experiences a degree of collapse-consolidation, it is much less extensive than that seen dorsally. Regional lung perfusion is not greatly affected by the change in position, with the result that ventilation-perfusion matching and oxygenation are improved. Such improvement in oxygenation allows a reduction in inspired oxygen concentration and mean airway pressure, and as a result may improve outcome of ALI and ARDS.

A recent multicentre study comparing prone and conventional ventilation concluded that although prone ventilation is effective in improving oxygenation, it did not lead to an improvement in survival from ALI and ARDS. It is still generally felt, however, that prone ventilation is an appropriate therapy that may beneﬁt subgroups of patients or improve outcome if used early.

Although prone ventilation is generally safe, the presence of traumatic brain injury (TBI) is a relative contraindication; there is anecdotal evidence that in such patients, with reduced intracranial compliance, prone positioning increases intracranial pressure (Murphy P, personal communication, 2002). There are experimental data that show an increase in intracranial pressure during partial prone positioning in patients with TBI. In patients with poor-grade SAH, a high proportion will have raised intracranial pressure. Although we were not able to measure intracranial pressure in our patient, we were aware of the potential problem and took steps to minimize it. In particular, we avoided impedance of jugular venous drainage by maintaining a neutral head alignment, supporting the face on a viscoelastic (‘jelly’) horseshoe. A 30° head up position was maintained whilst prone. Central venous pressure, a variable potentially correlating with intracranial pressure, did not rise with prone positioning in our patient; the signiﬁcance of this is uncertain.

Maintenance of adequate arterial oxygenation and cerebral perfusion is paramount in SAH. In our patient, oxygenation was adequate and deteriorating despite high levels of PEEP and a fractional inspired oxygen concentration of 1.0. Hence it was felt that prone positioning was appropriate. Whether prone ventilation affected outcome in this case is a matter of conjecture, but the effect on oxygenation was marked. We have been unable to ﬁnd any descriptions in the literature of the use of prone ventilation in NPO. Although NPO may result in ALI and ARDS, the pathophysiology early in its development does not necessarily resemble that of ALI and ARDS. Thus, more data on the response of NPO to prone ventilation would be of interest.

This case illustrates that NPO is survivable and that prone positioning may be of value in its treatment. Concerns about exacerbating intracranial hypertension remain, but this risk must be weighed against the potential beneﬁts of improved oxygenation and reduced mean intrathoracic pressure. More information is required on the effect of prone positioning on intracranial pressure in SAH. Only then may it be concluded whether or not prone ventilation is an appropriate therapy for NPO attributable to SAH or whether it should be undertaken only in conjunction with measurement of intracranial pressure.

References

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