

Subarachnoid haemorrhage: the management of neurogenic pulmonary oedema

Clinical problem and domain

I chose this case because I had not encountered neurogenic pulmonary oedema previously and was unfamiliar with its management. I was also surprised from my initial impression of the patient that this case had a good outcome and so was encouraged to research evidence-based management of this condition so that I can manage it optimally in the future.

A 33 year-old female presented to the Emergency Department having been found unresponsive by her partner and “frothing at her mouth”. She was obese, had a history of hypertension, and was 19 weeks postpartum (Caesarean section). She was disorientated and agitated in the Emergency Department with a Glasgow Coma Scale (GCS) of E4M5V3. She was treated with midazolam but required intubation as she was hypoxic with a respiratory rate of 40/min and SpO₂ of 83% on air. Following intubation her SpO₂ remained 82-88% despite an appropriately positioned endotracheal tube and FiO₂ of 1. Differential diagnosis included sub-arachnoid haemorrhage, aspiration pneumonia secondary to seizure, and pulmonary embolus and she was transferred to radiology for CT head and CT pulmonary angiogram (CTPA).

CT head showed extensive subarachnoid haemorrhage extending to basal cisterns and ventricles with early hydrocephalus. CT angiogram revealed a 5mm aneurysm of the right middle cerebral artery. CTPA did not show any evidence of a pulmonary embolism but did reveal extensive airspace shadowing in both lungs. An urgent neurosurgical opinion was sought and she was transferred to ICU for further management.

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Management

On arrival in ICU, her SpO₂ was 78% on FiO₂ of 1.0 via bilevel pressure controlled ventilation 30/5, she had pink frothy sputum from her endotracheal tube, and she was noted to be seizing. She was also hypotensive with an invasive blood pressure of 74/57mmHg giving a mean arterial pressure (MAP) of 63mmHg. She was commenced on phenytoin and neuroprotective measures, including a 30° head-up tilt, taped endotracheal tube, PaO₂ >13kPa, PaCO₂ 4.5-5kPa, MAP >90mmHg, normothermia, and normoglycaemia. A femoral line was inserted to allow inotropic support. Following review by the neurosurgical registrar, she was accepted for transfer to the nearest tertiary neurosurgical centre for coiling of her aneurysm.

She was deemed too unstable for transfer as by this point, her SpO₂ was 60% on FiO₂ of 1.0 (PaO₂ 5.3 kPa). She was discussed with the ICU consultant on-call, who agreed she was too unstable for transfer and suggested increasing her positive end-expiratory pressure (PEEP) and adding in dobutamine in an attempt to increase her MAP. Her family were informed that she was too unwell at that point to be transferred for definitive management, and that she was likely to die or have significant hypoxic brain damage.

She was commenced on airway pressure release ventilation (APRV) and her oxygenation improved PaO₂ 14.7 kPa on FiO₂ 0.95. She was commenced on regular nimodipine. She began to eye open and localise in response to movement. The decision was made to transfer her to the tertiary centre for definitive management. Transfer was uneventful, and she underwent coiling of her aneurysm the next day. She was transferred back to the local neurosurgical high dependency unit 2 days later and suffered an episode of cerebral vasospasm, but went on to make a full recovery.

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Discussion

Hydrostatic pulmonary oedema is pulmonary oedema due to increased pressure in the pulmonary capillaries which develops in the absence of left ventricular failure. Neurogenic pulmonary oedema (NPO) is a common type of hydrostatic pulmonary oedema seen in critical care and usually occurs after a severe neurological event, most commonly subarachnoid haemorrhage (SAH).¹ Reported rates of NPO following SAH vary from 2 - 42.9%, but it is likely that the true incidence is under-reported as it is often poorly recognised.² It has also been reported following spinal cord injury, traumatic brain injury, status epilepticus, intracerebral haemorrhage, subdural haemorrhage, meningitis, embolic stroke, neurological endovascular procedures, and blocked ventriculoperitoneal shunts.^{2,3}

Following SAH, NPO is more common in people more than 30 years old, those with hypertension, posterior circulation aneurysms, a delay to surgery, and a poor clinical grade of SAH.^{1,2,3}

It is usually linked to a sudden increase in intracranial pressure (ICP) and is thought to result from a catecholamine surge secondary to centrally-mediated sympathetic discharge which leads to an increase in systemic and pulmonary vascular resistance (PVR), and an increase in heart rate and contractility.^{1,2,4} The increase in PVR promotes fluid shift into the pulmonary interstitium. The increase in SVR and PVR increase myocardial oxygen demand which can lead to myocardial ischaemia.¹ Sympathetic blockade in animal models has been shown to attenuate this pathological process.⁵ There is also a pressure-induced increase in permeability of the pulmonary vasculature.^{1,4}

NPO is a diagnosis of exclusion, and its management is supportive. Patients typically present with acute dyspnoea, tachypnoea and hypoxia. Pink frothy sputum may be present and there are usually bilateral crackles on examination. Signs of sympathetic nervous system hyperactivity such as tachycardia and hypertension are often present. Chest X-ray typically shows bilateral hyperdense infiltrates.²

The differential diagnosis includes aspiration pneumonitis, community-acquired pneumonia, left ventricular failure, and pulmonary contusions.^{1,2} Of course, the patient may also have another of these pathologies co-existing with NPO. The progression of respiratory failure in NPO is typically rapid, often within 6 hours, although it can occur 12-14 hours after the initial neurological insult.^{1,2} There is usually associated neurological pathology (such as SAH), but in an unconscious patient unable to give a history, this may not be known about.¹

The mainstay of management is treatment of the underlying cause, along with preventing secondary brain injury due to hypoxia and hypotension.^{2,3} Treatment of the underlying cause may require specific treatment such as neurosurgical decompression,

anticonvulsant medication, or osmotic diuretics, depending on the pathology.² Whilst most of these measures will also assist the management of NPO, others (such as inter-hospital transfer) may not.¹ These patients should be managed aggressively, as cardiac dysfunction and NPO are potentially reversible and often have good outcomes. Patients at risk of NPO should be assessed proactively, for example using early echocardiography and cardiac output monitoring.³

Supportive management includes addressing airway, breathing and circulation issues.

Airway

Oxygen should be administered and strong consideration should be given to tracheal intubation. The need for this is determined both by the patient's neurological state and their requirement for mechanical ventilation. Intubation should be performed taking care to avoid increases in ICP whilst maintaining adequate cerebral perfusion.¹

Breathing

Lung-protective ventilation is required to avoid iatrogenic lung injury whilst preventing or treating hypoxaemia. Tidal volumes of 6-7ml/kg should be aimed for, with the use of PEEP to maintain recruitment of alveoli. It is worth noting that high PEEP can reduce venous return and increase ICP and so a sensitive balance must be struck. High frequency oscillatory ventilation and prone positioning have been used successfully in patients with NPO.¹

Patients with raised ICP require a neuroprotective ventilation strategy, aiming for a PaO₂ of greater than 13kPa and PaCO₂ of 4.5-5 kPa.⁶ Lung-protective measures, such as the use of permissive hypercapnia, may conflict with this. Permissive hypercapnia should only be used if ICP monitoring is present. There was a discussion about whether APRV was suitable in our patient, as it would likely lead to an increase in PaCO₂, which could compromise ICP. However, hypoxia also has an adverse outcome on ICP and so, on the balance of risks, the decision was made to address this patient's severe and refractory hypoxia.

Circulation

There are no specific evidence-based recommendations about the haemodynamic management of NPO. Although the pulmonary circulation may be overloaded due to catecholamine-induced vasoconstriction, the systemic circulation is often relatively hypovolaemic so volume resuscitation may be more effective than diuretics at restoring the circulating volume.^{1,3} It is important to assess patients' volume status and use IV fluids judiciously. Hypotension can be exacerbated by drugs used to treat vasospasm following SAH. Indeed, diuretics may be contraindicated and may precipitate harmful cerebral vasospasm.¹

With regard to drug therapies, the exact choice depends on the patient. General advice is to maintain adequate tissue oxygenation, aiming for a cardiac index (CI) greater than 2.5 L/min/m² as well as avoiding tachycardia and maintaining SVR less than 1000 dyne/s/cm⁵.¹ Pulmonary artery catheterisation may be useful in this situation.

Dobutamine, a beta-adrenergic agonist, has been used to offset the increase in SVR seen in NPO. Deehan and Grant undertook a retrospective review of all patients with NPO admitted to their unit over a 45-month period. They were noted to have low CI and left ventricular stroke work index (LVSWI), suggesting severe left ventricular dysfunction.

Pulmonary artery wedge pressure (PAWP), mean pulmonary artery pressure (MPAP) and systemic and pulmonary vascular resistance indices (SVRI and PVRI) were typically increased in their population, however their MAP was normal, suggesting that widespread vasoconstriction was not the predominant cause.⁴ Twelve of their 20 patients received dobutamine and the authors examined the effects of this on their haemodynamic parameters. They found that dobutamine significantly increased CI and LVSWI and reduced PAWP and SVRI, as well as significantly improving oxygenation, as measured by PaO₂: FiO₂ ratio. It is worth noting that 5 of the patients who received dobutamine had also received other vasoactive agents, so the effects cannot be attributed solely to dobutamine.

Alpha-adrenergic antagonists have been shown to prevent NPO and quicken its recovery in animal studies.^{2,3} Phentolamine competitively blocks alpha adrenoceptors and antagonises circulating catecholamines to reduce blood pressure.⁵ There are human case reports showing it to be effective, however no human trials investigating its safety or efficacy in the management of NPO. Davison *et al* reported a case of NPO following intracranial haemorrhage secondary to a ruptured arteriovenous malformation (AVM). The patient was transferred to ICU post-operatively following resection of the AVM and developed NPO on day 3. Their patient had a PaO₂ of 9kPa and PaCO₂ of 10 kPa on FiO₂ 70%, an elevated pulmonary artery pressure (50/30mmHg) and cardiac index (5.4 L/min/m²), and hypertension requiring multiple antihypertensive agents. Intravenous phentolamine was commenced on day 11 and led to a reported improvement in oxygen requirements, gas exchange and radiographic appearances. When their hospital supply of phentolamine ran out the patient deteriorated, but then once again improved when the phentolamine was restarted. Other antihypertensive medications were stopped over the subsequent 24 hours and phentolamine was weaned off on day 13.⁵ Interestingly, they measured serum and urinary catecholamine levels and were able to show a surge in catecholamine levels associated with haemodynamic instability and respiratory failure, followed by catecholamines resolving to normal with treatment with phentolamine and resolution of symptoms. Phentolamine can be used in hypertensive patients, but it may provoke hypotension, leading to a reduction in cerebral perfusion pressure which is likely to be detrimental.

Most cases of NPO resolve within 24 to 48 hours with treatment, however with unresolved brain injury and raised ICP, it may persist.²

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Lessons learnt

I am now aware of the prevalence and presenting features of neurogenic pulmonary oedema, and have learned that its management is aimed at treating the underlying pathophysiology. I have discovered that cardiovascular dysfunction associated with neurogenic pulmonary oedema should be managed aggressively, as the likelihood of cardiovascular and neurological recovery is high. The evidence for the use of alpha-blockers in NPO comes mainly from animal studies and case reports, and although their routine use cannot be recommended, a trial of alpha-blockers may be considered in suitable patients in whom the blood pressure permits. I am now much better prepared to recognise and manage NPO the next time I encounter it in clinical practice.

114 words

Total 1964 words

References

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