

Anaesthesia Tutorial of the Week 209

## Intensive care management of pandemic (H1N1) Influenza

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### INTRODUCTION

This article describes the management of critically ill patients with H1N1 2009 Influenza A infection, which caused the 4th worldwide pandemic in 2009 and is currently causing a seasonal epidemic in the UK and a few other countries in the Northern hemisphere.

During the current season, forty-five deaths associated with influenza infection have been reported, the majority due to severe H1N1 2009 virus affecting the young, the pregnant, the obese and those with co-morbidities.

### CLINICAL BACKGROUND

H1N1 viral pneumonitis is caused by a novel variant of influenza A (A (H1N1)) which is similar to seasonal influenza but contains segments of genes from pig, bird and human influenza. It is an enveloped orthomyxovirus.

### EPIDEMIOLOGY

The overall case fatality during the 2009 pandemic was less than 0.5%, ranging from 0.0004 to 1.47%. Approximately 9 to 31% of hospitalised patients were admitted to an ICU, where 14 to 46% of patients died. It affected young people, with 32 to 45% of those hospitalised being under the age of 18 years. People over the age of 60 were relatively spared.

In the UK, from 17th July 2009 to 3 March 2010, there were 25,785 admissions to hospital with H1N1 of whom 9501 were children. Of these, 2326 received critical care (1863 adults and 463 children), with mean critical length of stay of 7.8 days in adults and 6.1 days in children. A total of 496 ECMO (extracorporeal membrane oxygenation) bed days were documented.

Risk factors for development of severe illness with 2009 H1N1 virus infection include:

- Age < 5 years
- Pregnancy
- Chronic congestive heart failure (but not hypertension)
- Chronic lung disease (asthma, COPD, cystic fibrosis)

- Diabetes
- Chronic neuromuscular, seizure or neurocognitive disease
- Immunosuppression
- Morbid obesity (BMI > 40kg.m<sup>-2</sup>)
- Chronic renal or hepatic disease
- Smoking

Pregnant women in the 2nd and 3rd trimester and those that are 2 weeks or less postpartum are most at risk (7 to 10% of hospitalised patients, 6 to 9% of ICU admissions and 6 to 10% of patients who died) despite comprising 1 to 2% of the population.

### CLINICAL FEATURES IN THE CRITICALLY ILL

Most patients have a prodromal illness of pyrexia, myalgia, cough and sometimes gastrointestinal symptoms, lasting between 1 and 9 days prior to admission. The principal presentation leading to ICU admission is diffuse viral pneumonitis associated with severe hypoxaemia. There may also be ARDS, shock and sometimes renal failure. This syndrome accounted for approximately 49 to 72% of ICU admissions for 2009 H1N1 virus infection worldwide. Rapid progression is common, starting on day 4 and 5 after illness onset. Bacterial co-infection may cause multi-lobar consolidation. The lower lung zones are often more affected on CT scan. There may also be multiple areas of ground-glass opacities and small pleural effusions are common.



**Figure 1.** Chest CT showing infiltrates and dense consolidation in a patient with H1N1 pneumonitis

### Summary

This article is adapted from a recent *Anaesthesia Tutorial of the Week* and is largely based on local and published clinical experience gained during the 2009 pandemic of H1N1 influenza. Summary points are:

- Remember to consider H1N1 in the differential of any persistently febrile respiratory illness and isolate or cohort the patient.
- Once level 2 dependency is reached, many patients deteriorate rapidly and early intubation and ventilation is recommended.
- Rescue strategies may be needed, including ECMO if available.
- This condition has a high mortality.

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Of 168 patients admitted to Canadian ICUs in 2009, the majority of whom had the above syndrome, 131 (81%) were mechanically ventilated on the first day of ICU admission, 128 (76.2%) invasively and 55 (32.7%) noninvasively. 47 (85.4%) who initially received noninvasive ventilation ultimately required invasive ventilation.

One third of patients required advanced ventilatory support and rescue therapies for profound hypoxaemic respiratory failure.

Other important features found in patients with severe H1N1 infection include:

- Prolonged exacerbation of asthma and COPD (about 15%) and of other underlying chronic diseases, e.g. congestive cardiac failure.
- Secondary bacterial co-infections were found in 20 to 24% of ICU patients and in 26 to 38% of patients who died during the 2009 pandemic. The most common organisms were *Staphylococcus aureus* (often MRSA), *Streptococcus pneumoniae*, and *Strep pyogenes*.
- Neurological manifestations including confusion, seizures, unconsciousness, acute or post-infectious encephalopathy, quadriparesis and encephalitis.
- Myocarditis, right ventricular dilation and dysfunction.
- Myositis and rhabdomyolysis with raised creatine kinase (CK).
- Croup/bronchiolitis in the paediatric population

### Pathological features

Pathological features at autopsy include diffuse alveolar damage with hyaline membranes and septal oedema, tracheitis, necrotising bronchiolitis, pulmonary vascular congestion, alveolar haemorrhage and pulmonary thromboemboli. Bronchopneumonia with evidence of bacterial co-infection is seen in 26 to 38% of fatal cases.

Laboratory findings at presentation in patients with severe disease typically include normal or low-normal leukocyte counts with lymphopaenia, thrombocytopenia, elevated serum aminotransferases, CK, creatine and LDH.

### Diagnosis

Clinicians should maintain a high degree of suspicion in patients with undiagnosed respiratory or pyrexial illness. The best method of confirmation is detection of viral RNA by real-time reverse transcriptase-polymerase chain reaction (RT-PCR), performed on samples taken from nasopharyngeal aspirates or swabs. Endotracheal and bronchoscopic aspirates have higher yield in patients with lower respiratory tract illness.

## CLINICAL MANAGEMENT

### Drug therapy

If there is pneumonia or evidence of clinical progression then oseltamivir 150mg bd for 10 days without interruptions is recommended. Doses of up to 450mg bd have been used successfully in healthy adults. Intravenous zanamivir (Relenza) is the preferred option for hospitalised patients with suspected or documented oseltamivir-resistant 2009 H1N1 virus infection or who are unable to absorb by the enteral route.

High dose steroids have no role in ARDS but prophylactic heparin should be prescribed.

### Ventilatory management

*The role of non-invasive ventilation (NIV) and continuous positive airway pressure (CPAP)*

Prompt intubation is indicated in many patients who are deteriorating rapidly by the time they get to ICU. There may be a role for NIV in a subset of patients whose progression is slower, or in whom it is agreed that invasive therapies are inappropriate.

### Invasive ventilation

Based on current evidence patients with H1N1 should be managed with lung protective ventilation as per the ARDS network protocol (below).

#### Protective lung ventilation strategy

- Aim for  $\text{SaO}_2 > 88\%$ , with  $\text{pH} > 7.2$ . Optimise PEEP.

- Tidal volume  $< 6\text{ml.kg}^{-1}$   
(Use ideal body weight:

Males  $50 + [0.91 \times (\text{height} - 152.4)]\text{cm}$

Females  $45 + [0.91 \times (\text{height} - 152.4)]\text{cm}$

- Plateau pressure  $< 30\text{cmH}_2\text{O}$

Permissive hypercapnia is employed to avoid higher pressures. If targeted ventilatory goals are not met then rescue therapy should be employed. This constitutes prone ventilation, increasing PEEP, recruitment manoeuvres, inverse ratio up to 4:1 and blood transfusion to improve haematocrit ( $>40\%$ ).

### PEEP

High levels of PEEP (16 to  $30\text{cmH}_2\text{O}$ ) have been used with variable response in terms of oxygenation. During weaning PEEP should be cautiously weaned to less than  $20\text{cmH}_2\text{O}$  before weaning  $\text{FIO}_2$  significantly.

### Prone positioning

Proposed mechanisms of action for proning include: alveolar recruitment, improvement in V/Q matching by improved ventilation to the dorsal lung regions, elimination of the heart's compressive effects on the lung and better drainage of respiratory secretions.

Although up to 70% of patients with ARDS show improved oxygenation, no mortality benefit has been shown. Risks include endotracheal tube obstruction, loss of central vein access during the manoeuvre and risk of pressure sores.

### Recruitment manoeuvres (RM)

These aim to open collapsed lung units and increase functional residual capacity by increasing transpulmonary pressure. RM may be usefully employed on patients on high PEEP who desaturate rapidly on disconnection from the ventilator.

There are several techniques and the patient may be prone or supine.

#### Example of a recruitment manoeuvre

- Ensure haemodynamic stability and Set FiO<sub>2</sub> to 1.0 for 15 minutes.
- Set the ventilator rate to zero and apply 30cmH<sub>2</sub>O PEEP for 40 seconds. Return to normal ventilation with PEEP of at least 15cmH<sub>2</sub>O to prevent de-recruitment.
- If unresponsive repeat with 35cmH<sub>2</sub>O for 40 seconds after 15 minutes
- If still unresponsive repeat with 40cmH<sub>2</sub>O for 40 seconds after 15 minutes.

Other techniques have been used as rescue therapies, but are generally not available in resource-poor settings. These are outlined in the table below.

#### High frequency oscillatory ventilation (HFOV)

- HFOV ventilates the lung with low tidal volumes (lower than anatomical dead space) and avoids volutrauma and barotrauma.
- No proven mortality benefit over conventional lung protective ventilation but useful for rescue therapy for unresponsive patients.
- Complications include retained secretions, mucus plugging, air trapping and airway damage attributable to high gas velocities.

#### Airway pressure release ventilation (APRV)

- Described as continuous positive airway pressure (CPAP) with regular, brief, intermittent releases in airway pressure. Unlike CPAP it facilitates both oxygenation and removal of CO<sub>2</sub>.
- Spontaneous breathing is possible.
- No proven mortality benefit over conventional methods.
- Use limited in patients with COPD and asthma due to gas trapping.

#### Cardiovascular management

It is vital to assess how well each patient responds to intravenous fluid administration. However inappropriate fluid administration may worsen ventricular function and oxygenation. Where available, echocardiography and/or invasive cardiovascular monitoring such as oesophageal Doppler, LiDCO or PICCO are useful.

#### Extracorporeal membrane oxygenation (ECMO)

This is a specialised resource but where available referral for ECMO should be considered in the first week of ventilation for refractory hypoxaemia. In several countries there has been some expansion of ECMO capacity outside of the main centres.

#### Extracorporeal carbon dioxide removal

Where available, devices such as the *Novalung*<sup>TM</sup> may be necessary to treat significant acidosis due to hypercarbia, especially in the setting of concurrent increased intracranial pressure.

#### Renal management

Achievement of negative fluid balance guided by calculation of the patient's *dry weight* by either diuretics or continuous ultrafiltration improves oxygenation. Renal replacement therapy is required in 10 to 50% of cases and may be chosen electively as the mode of fluid balance, even if renal failure is not present.

Patient's dry weight can be estimated as:

ICU admission weight – weight (= volume) of any resuscitation fluid given up to that point.

#### Nutrition management

The use of high calorie feeds to avoid fluid overload is suggested.

#### Sedation and neurological management

Many patients with H1N1 appear to need high doses of sedation due to a combination of irritable airways and encephalopathy/encephalitis. CNS imaging and lumbar puncture have a role in the exclusion other causes of fever and delirium.

#### INFECTION CONTROL

Healthcare staff should be vaccinated if offered.

Patients with suspected H1N1 should be isolated or cohorted depending on the number of cases on the unit. Isolation should take place for up to 7 days after illness onset or until 24hrs after resolution of fever and respiratory symptoms (whichever is longer) and for the severely immunocompromised this should be for the duration of the illness.

Use of personal protective equipment for care of patients with H1N1 infection is highly recommended to reduce staff infection to prevent transmission within the hospital.

Aerosol generating procedures such as suctioning, chest physiotherapy, intubation, tracheostomy care, bronchoscopy and CPR should be performed in closed single-patient areas with minimal staff present. Operators should wear single use protective gloves, gowns, eye protection and FFP3 masks or 3M respirator masks.

Entry into a cohorted area with no contact with patients requires use of hand hygiene and a surgical mask as a minimum. Close contact with a patient requires a plastic apron and gloves to be worn.

Staff do not need to keep changing masks each time they move away from the cohorted areas, however they do need to remove gloves and clean as per standard infection control precautions.

More detail on infection control is available in the UK DoH document 'Pandemic influenza: Guidance for infection control in critical care', 2008.

#### Respiratory care issues

- Disposable patient respiratory equipment must be used whenever possible.
- Closed systems should be used whenever possible, e.g. suction
- All respiratory equipment used on patients, including transport ventilator circuits and manual resuscitation aids, should include a high-efficiency bacteria/viral breathing system filter (BS EN 13328-1)
- The ventilator circuit should not be broken unless absolutely necessary.
- For planned circuit breaks, appropriate PPE & FFP3 respirators should be worn.

#### SUMMARY

Further advice is available concerning resource and contingency planning for further pandemics of H1N1 influenza from the link below. In the event of a further surge in cases, the implications for triage and limitation of therapy are huge, particularly in countries with limited resources.

It is vital to consider H1N1 in the differential diagnosis of any persistently febrile respiratory illness and to promptly isolate or cohort the patient. Those patients who deteriorate to a level where HDU admission is needed are likely to deteriorate rapidly and early intubation and ventilation is recommended. Ventilatory rescue strategies may be needed and have been briefly described. In many countries these will not be available, and in those that they are, their use will be limited to supra-regional centres. Even with these rescue therapies, this condition has a high mortality

#### **REFERENCES and FURTHER READING**

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