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CASE REPORT

Pandemic (H1N1) 2009 influenza: experience from the critical care unit

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Summary

This case series details experience of critical care admissions with pandemic (H1N1) 2009 influenza from an intensive care unit in the West Midlands. We present four critically ill patients admitted with severe hypoxia. Two of the patients failed a trial of continuous positive airway pressure and all underwent controlled ventilation within 24 h of admission. Bilevel and high frequency oscillatory ventilation were the most useful modes. Our patients generally had one organ failure and were ventilator dependent for relatively short periods of time. Three of the patients made a full recovery and one required ongoing dialysis. We also discuss service planning and our response to the pandemic. We were well prepared with stocks of personal protective equipment but had to modify plans as the outbreak progressed. Our cases and discussion provide useful information for other intensive care units preparing for the predicted autumn surge of H1N1 cases.

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In April 2009, reports from Mexico of patients infected with a novel influenza A virus began to emerge. The H1N1 virus, of swine flu origin, was causing respiratory illness in affected individuals.

By the end of May, Mexico had reported 4910 confirmed cases and 85 deaths [1]. With evidence of human to human transmission in more than three countries, the World Health Organization (WHO) declared a pandemic [2]. The first British cases were reported at the end of April, with 7447 cases by the beginning of July. Clusters appeared in Scotland, London and the West Midlands. By late July 2009 there had been twenty-nine flu-related deaths in the United Kingdom [3]. In the West Midlands many of the cases have been concentrated in a relatively small area of Birmingham, with the majority of admissions to two of the hospitals. During the peak period between May and July we admitted seven patients with confirmed pandemic (H1N1) 2009 influenza and one with an equivocal result. We believe that this was the highest number of admissions to any unit in England in that period. This case series describes the four admissions that required intubation and ventilation and discusses critical care service planning and the subsequent response to the pandemic.

Case 1

A 44-year-old Afro Reckitt Benckiser Healthcare (UK) Ltd, Slough, Berks; Caribbean male, with no known medical conditions, was admitted to the poisons unit after an unintentional paracetamol overdose. He gave a one-week history of flu-like symptoms and, without intending to harm himself, had taken Lemsip sachets (Reckitt Benckiser Healthcare (UK) Ltd, Slough, Berks; 650 mg paracetamol, 10 mg phenylephrine) in addition to a maximum dose of paracetamol. By day two of his hospital admission he had developed right-sided abdominal pain and became hypoxic necessitating admission to the critical care unit for respiratory support. On admission to the unit, he deteriorated rapidly. After a 3-h trial of continuous positive airway pressure (CPAP), his worsening hypoxia necessitated tracheal intubation. He was stabilised using bilevel pressure ventilation and airway pressure release ventilation (APRV) modes. His chest radiograph showed right-sided consolidation and a pleural effusion and his blood cultures grew staphylococcus. He was lymphopenic on admission. On the basis of his presentation, and a history of flu symptoms in close family members, nasopharyngeal

viral swabs were taken after intubation and confirmed H1N1 infection 72 h later. His pleural effusion was drained and he was treated with piperacillin/tazobactam, clindamycin and a 10-day course of oseltamivir. Once H1N1 had been diagnosed he was transferred to a side room for strict isolation and barrier nursing. In addition to his respiratory problems he developed acute renal failure, hypernatraemia and had transiently raised alanine aminotransferase and international normalised ratio (INR) values. During the initial phase of sedation and ventilation he required vasopressor support. He received continuous veno-venous haemofiltration (CVVH). This was used to reduce the serum sodium concentration and achieve a negative fluid balance in order to optimise his respiratory function. His trachea was successfully extubated after 11 days, but due to ongoing anuria and raised creatinine he was transferred to an acute renal unit. This was the first pandemic (H1N1) 2009 influenza case diagnosed on a critical care unit in England. With the pandemic in its infancy and the virulence of the organism unknown, all contacts of the patient, hospital staff and family members, were offered a prophylactic course of oseltamivir.

Case 2

A 37-year-old obese Afro-Caribbean female, with asthma and non-insulin dependent diabetes, presented with a 2-day history of shortness of breath and flu-like symptoms. She was tachycardic, tachypnoeic, pyrexial and hypoxic with ketoacidosis. A chest radiograph showed right-sided atelectasis and she had a raised creatinine kinase and was lymphopenic. She was initially treated on the medical ward as an infective exacerbation of asthma complicated by diabetic ketoacidosis. On day two she deteriorated and was transferred to the critical care unit for tracheal intubation and ventilation. Further inquiries revealed that her son's school had a potential pandemic (H1N1) 2009 outbreak and subsequent swabs confirmed H1N1 infection for which she was given a 10-day course of oseltamivir in addition to co-amoxiclav and clarithromycin. Her lungs were ventilated for 6 days with bilevel and later spontaneous modes. During the initial phase of sedation and ventilation she required vasopressor support. After haemodynamic stabilisation she tolerated a furosemide infusion and responded with a good diuresis and reduced oxygen requirements. Her trachea was extubated and she was discharged to the ward 2 days later and had no further complications.

Case 3

A 32-year-old Asian female, with no known medical conditions, presented to the emergency department with a one-week history of bilateral loin pain and pyrexia. A clinical diagnosis of urinary tract infection was made and she was discharged with co-amoxiclav. The following day she returned feeling more unwell with pyrexia and hypoxia. She had neutrophilia and lymphopenia. Chest radiograph revealed extensive bilateral consolidation with pleural effusions which were not amenable to drainage. Her condition was initially treated as a community acquired pneumonia with clarithromycin in addition to co-amoxiclav. After several hours of treatment the patient became severely hypoxic with a P_aO_2 of 5.62 kPa on 15 $l.min^{-1}$ oxygen by facemask. She was transferred to the critical care unit and received 10 cmH_2O of CPAP with an F_IO_2 of 0.8–1.0. She had no known flu contacts and sepsis with acute lung injury was considered to be the clinical diagnosis. Nevertheless, because of the severe hypoxia she was commenced on a 10-day course of oseltamivir. Nasopharyngeal swabs for influenza were taken. Her creatinine kinase was raised. Progressive respiratory failure necessitated tracheal intubation; however, the patient remained profoundly hypoxic despite using different ventilation modes including bilevel, APRV and inverse ratio ventilation. Intermittent falls in oxygen saturation to 60–70% were managed with manual ventilation using small tidal volumes and airway pressures of less than 25 cmH_2O. This increased the oxygen saturation to around 80%. Interestingly, when this was performed, her lungs felt compliant compared with lungs typically encountered in patients with acute respiratory distress syndrome. A bedside echocardiogram excluded a cardiac anomaly. Clinically, the patient appeared to have a profound ventilation-perfusion mismatch and we suspected that she might have had a pulmonary embolus. In view of her worsening hypoxia and rapid deterioration we decided to administer thrombolysis and commence high frequency oscillatory ventilation (HFOV) with a mean airway pressure of 22 cmH_2O. Her oxygen saturation improved to 98% with an F_IO_2 of 1.0, 3 h later. She required vasopressor support for 24 h whilst heavily sedated. Subsequent nasopharyngeal swabs confirmed H1N1 infection. She remained resistant to changes in her ventilation. A furosemide infusion was commenced on day 3 in order to achieve a negative fluid balance and thereby improve her oxygenation. After 6 days of HFOV she was switched to conventional ventilation and her trachea extubated 4 days later. She made a good recovery and was discharged with no residual neurological sequelae.

Case 4

A 26-year-old Asian female presented with a 3-day history of flu-like symptoms. She was 35 weeks pregnant and her three children and husband were recovering from a flu-like illness. She had no significant past medical history.

On assessment in the emergency department she was hypoxic, pyrexial and agitated with a significant metabolic acidosis. She was admitted directly to the critical care unit. Admission cardiotocograph (CTG) was normal. Although she was mildly coagulopathic with abnormal liver function and a raised creatinine kinase, HELLP (haemolysis, elevated liver enzymes and low platelets) syndrome was discounted in the absence of hypertensive proteinuria. A chest radiograph revealed bilateral infiltrates and pleural effusions. Nasopharyngeal swabs were taken and subsequently confirmed H1N1 infection. She was started on co-amoxiclav, clarithromycin and a 10-day course of oseltamivir. Over the course of the next few hours her hypoxia worsened and the CTG showed signs of fetal distress. The decision was made to perform an urgent Caesarean section in theatre. Her trachea was intubated on the critical care unit before immediate transfer to the operating theatre. Her care involved close collaboration between critical care, obstetric, neonatology, microbiology and operating theatre staff. Our aims were to optimise patient care and minimise the exposure of hospital staff and contamination of the operating theatre by the H1N1 virus. Contamination was limited by maintaining the integrity of the ventilator circuit between transfers and whilst in theatre. A live female infant was delivered who subsequently tested positive for, and recovered fully from, H1N1 infection. Postoperatively, the patient remained hypoxic with a P_aO_2 of 8 kPa despite ventilation with an F_IO_2 of 1.0. In view of her risk factors, a computed tomography pulmonary angiogram (CTPA) was performed which excluded a pulmonary embolus. Due to her worsening condition with oxygen saturation falling to 70%, she required frequent manual ventilation during which her lung compliance, as experienced with Case 3, felt surprisingly good. In order to optimise her oxygenation, different ventilatory modes were tried including pressure controlled, inverse ratio, APRV, HFOV and bilevel ventilation. The most effective ventilation mode for oxygenation was bilevel with low peak pressures and positive end expiratory pressure (PEEP) levels < 6 cmH_2O. Higher levels of PEEP and ventilatory pressures resulted in rapid oxygen desaturation. Due to extremely resistant hypoxia, a furosemide infusion was commenced. By day 4 her liver function had improved and respiratory support could be reduced. Her trachea was successfully extubated on day 6; she made a good recovery and was discharged to the ward on day 10.

Discussion

Several lessons can be learnt from our experience with pandemic (H1N1) 2009 infected patients on the intensive care unit. The age of our patients was between 26 and 44 years old. Three patients did not have significant underlying health problems. With regards to age, similar epidemiology has been seen in Mexico. It has been reported that 87% of deaths and 71% of severe pneumonia due to H1N1 occurred in the 5–59-year age group. This compares to 17% and 32% respectively in that age group during seasonal influenza outbreaks [4]. The H1N1 viruses were in circulation between 1918 and 1957, which may explain why those over 60 are not being severely affected in the current pandemic [5]. Two of our patients were of Asian origin, and two Afro-Caribbean. This can be attributed to the fact that our hospital serves an ethnically diverse population. It is well documented that Asian immigrants have a higher incidence of vitamin D deficiency, which may increase susceptibility to severe influenza infection [6, 7].

The presenting symptoms of our patients were similar as was their clinical course. All had flu-like symptoms before admission. Other common features included lymphopenia in three patients and raised creatinine kinase in three. This replicates findings in Mexico where 61% had lymphopenia and 62% raised creatinine kinase levels [8]. One patient was pregnant, one had non-insulin dependant diabetes and one had mild asthma. The other two patients were previously fit and well. There have been reports from the USA that critically ill patients with H1N1 did not always have risk factors such as extremes of age, pregnancy, or chronic medical conditions, associated with severe seasonal influenza infection. Fatal disease has occurred in those who were previously healthy [9].

Critical care admission was triggered by severe hypoxia. The overwhelming problem was oxygenation. Two patients failed a trial of CPAP and all patients required invasive ventilation within 24 h of admission to the critical care unit. Bilevel was the preliminary mode of invasive ventilation for all patients. Two of our patients, cases 3 and 4, were extremely difficult to oxygenate despite using different ventilatory modes. On manual ventilation, their lung compliance was good considering the degree of hypoxia. Ventilation in the bilevel mode with an inspired pressure of up to 26 cmH_2O and an I:E ratio of 1:2 resulted in tidal volumes of 10–12 $ml.kg^{-1}$. However this was not effective in maintaining oxygenation. The addition of PEEP > 6–7 cmH_2O compounded the above. Neither inverse ratio ventilation nor APRV resulted in any improvement. Ventilating in bilevel mode with lower tidal volumes around 4–5 $ml.kg^{-1}$ and PEEP levels < 6 cmH_2O did improve oxygenation. One of the more severe cases benefited from HFOV using an initial mean airway pressure of 22 cmH_2O. This resulted in an improvement of oxygen saturation from 65% to 98% after around 3 h. The patient in case 4 was tried on HFOV but this failed to improve oxygenation. In these cases of

extreme hypoxia, the prone position was considered but not required. As all patients were haemodynamically stable, furosemide diuresis, to achieve negative fluid balance, was commenced after initial resuscitation. Negative fluid balance was achieved in one patient by CVVH. Our interpretation is that the patients behaved as though they had a significant ventilation/perfusion mismatch. Thus, it may have been helpful to have had measurement of pulmonary artery pressures.

There is limited information regarding critically ill patients with pandemic (H1N1) 2009 infection, but a case series from Michigan suggested bilevel and HFOV to be the most effective modes of ventilation [8]. Their patients required ventilation for similar times to ours, between 6 and 11 days. All except one of our patients had single organ failure (respiratory), with vasopressors being required to counteract the hypotensive effect of sedation rather than to treat septic shock. All except the first patient received oseltamivir within 24 h of admission to the critical care unit.

Once H1N1 infection had been recognised within the hospital, trust policy required anyone admitted with pyrexia and respiratory illness to be swabbed for H1N1 and started on oseltamivir immediately. Early treatment with antivirals is optimal to reduce illness in seasonal influenza infection [10]. In the Michigan case series the average time to antiviral treatment from the onset of symptoms was 8 days. There was also a higher rate of multiple organ dysfunction syndrome with nine out of 10 patients requiring vasopressors for septic shock and six out of 10 requiring renal replacement therapy [8]. Our patients became very unwell quickly, and were profoundly hypoxic, but responded to invasive ventilation. They required ventilation for relatively short periods of time and generally required single organ support.

Although our case series consists of a small number of patients, our experience may be helpful for clinicians in the UK as information surrounding pandemic (H1N1) 2009 is scant. Young patients and those without pre-existing medical conditions are developing severe disease. Further analysis of the ethnicity of critically ill patients may be required to determine whether severe infection is more common in immigrant populations.

Knowledge of the groups most likely to become seriously ill has public health implications. If a vaccination against H1N1 is to be limited or staggered, priority populations will be different to those targeted by the seasonal flu immunisation campaigns. The Department of Health (DoH) has published pandemic flu guidelines for the event of demand outstripping supply for critical care beds [11]. In this situation, decisions regarding admission to critical care and provision of ongoing support should be made according to clinical judgement assisted by a severity scoring system such as SOFA (Sequential Organ Failure Assessment) [12]. Our patients experienced a period of deterioration following commencement of invasive ventilation. If these patients had been formally assessed according to DoH guidelines, and in the event of excessive demand for critical care beds, they would have fulfilled the criteria for palliative care.

Our critical care service began preparation for a pandemic in 2006. By 2007 we had a detailed plan in place. Members of the critical care senior team were an integral part of the trust emergency planning and were instrumental in developing a stockpile of disposables and personal protective equipment. Our plan, like many other hospitals, was designed to cope with a full-blown pandemic that would originate in the Far East and take 2–4 weeks to get to the UK. We had prepared for 'Flu Armageddon' with mass casualties. Once three of our four side rooms had been filled with H1N1 cases, we were to decant the non-H1N1 patients to a satellite critical care unit within the hospital, allowing the existing unit to be devoted to H1N1 patients. However, we were unprepared for both the speed at which the virus reached the UK and for a situation whereby few patients required hospital admissions and fewer still required critical care admission. Of all the adult patients admitted with H1N1, 15% were admitted to the critical care unit. This amounted to no more than five patients at any one time. We had to revise our surge plan a number of times to cope with a threat that varied in its nature and intensity as the weeks progressed.

One half of the unit was sealed and the H1N1 patients restricted to an 'H1N1 positive area'. Those patients awaiting H1N1 confirmation were cared for in side rooms to prevent nosocomial influenza infection. No visitors were allowed into the 'H1N1 positive area'. Staff wore theatre gowns and FFP3 masks whilst in this area and undertook standard decontamination when moving to the 'non-H1N1 area' and leaving the critical care unit. Initially, HFOV was avoided due to infection control concerns; however, once oscillator circuits with antiviral filters became available this was revised.

In the first month alone, 4000 disposable FFP3 masks were used. One thousand staff members, in order of likely exposure, were fit-tested for their masks. That is, they underwent a series of tests to ensure that no air leakage occurred around the mask during active use. It quickly became evident that roughly 50% of staff developed significant leaks. This, again, had been anticipated and a stock of 100 re-usable respirator-type FFP3 masks was available. These produced an adequate seal in roughly 95% of staff members though they did occasionally cause skin irritation when worn for prolonged periods.

As the rest of the hospital continued to work normally, we had to cope with an increased workload complicated by the infection control measures we put in place to

protect both staff and patients. Whilst critical care staff were initially concerned, they were reassured by the personal protective equipment provided and measures taken to reduce the chance of viral transmission. Nevertheless, many other departments did not have masks fit-tested, including services essential to the critical care unit such as radiology. This caused some concern amongst those staff members and led to small delays in patient care until adequate fit-testing had been undertaken.

In the wider hospital, there were problems ensuring that other medical personnel were adequately fit-tested. This restricted their capability to care for H1N1 patients and caused some conflict with paragraph 10 of *Good Medical Practice* [13]. During the national containment phase, contact tracing was carried out by the Health Protection Agency (HPA) and all contacts were prescribed a prophylactic course of oseltamivir, obtained via their general practitioner. When it became clear that the virus was no longer being contained in the local community, the hospital moved into the mitigation phase, ahead of the rest of the country. At this point the protocol for prophylaxis changed, causing a degree of confusion and upset amongst some relatives.

Of great importance in this rapidly developing scenario were regular telephone conferences, arranged by the WHO and HPA, between units around the world experiencing pandemic (H1N1) 2009 infections. This allowed rapid and efficient transfer of clinical and logistic information and helped enormously in ongoing contingency planning. The importance of information sharing has been highlighted in a recent paper by Ercole et al. [14], who showed that attempting to predict critical care bed occupancy during the pandemic is difficult. Expected numbers are subject to wide variations depending on hospital admissions. They suggest sentinel reporting and real time modelling to aid decision making as the pandemic unfolds. Our unit has produced clinical notes to aid other colleagues within our critical care network and has developed a self-assessment tool specifically aimed at assisting local ICUs to develop their pandemic contingency plans. As we prepare for a surge in patients over the next few months, a number of areas of the 'pandemic plan' continue to be developed. Triage systems should be reviewed. In order to facilitate critical care provision in satellite units around the hospital, equipment such as monitoring platforms, syringe pumps and ventilators should be standardised. All hospital staff must be fit-tested for FFP3 and educated on decontamination procedures. Shift rotas should allow for a predicted 40% staff absence rate. Most importantly, there needs to be efficient and open sharing of information between units caring for these patients to improve overall knowledge of this long anticipated and evolving event.

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