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Correspondence

Extracorporeal membrane oxygenation (ECMO) as a rescue treatment in acute respiratory distress syndrome caused by AH1N1 virus infection

Sir,

During the period between 2009 and 2010, 105,000 to 400,000 people died all over the world as a result of influenza caused by the novel AH1N1 virus and further 46,000 to 179,000 due to complications following this disease. The young children were particularly susceptible to infection due to the immaturity of the immune system, as well as children immunocompromised due to some primary disease[1,2]. About 10-30 per cent of patients infected with this virus developed symptoms of respiratory failure requiring hospitalization in Intensive Care Units (ICUs). In some cases, the respiratory failure was so severe that the use of extracorporeal membrane oxygenation (ECMO) was necessary[3,4].

In the following years (2012-2014), the virus became active again. Here we report our experience with two children with severe respiratory failure, which developed during the course of a disease caused by the AH1N1 virus, were admitted to the Paediatric ICUs (PICUs) at the two University Hospitals in Poland. ECMO was used as a method of treatment in both.

A five month old male infant (7 kg body weight and 65 cm height) was admitted to the PICU at the Medical University in Poznan on March 2013 due to symptoms of severe respiratory failure caused by pneumonia. Initially, the infant was treated with antibiotics (cefuroxime 2 × 250 mg and amikacin 1 × 120 mg) for seven days at home and then admitted to the district hospital, where ceftriaxone (1 × 700 mg) and fluconazole (1 × 40 mg) were administered without success. As his condition deteriorated, a decision was made to transfer the patient to PICU. A chest X-ray revealed massive bilateral atelectatic and inflammatory lesions within the parenchyma of lungs and presence of pneumothorax. A diagnosis of acute respiratory distress syndrome (ARDS) was made. The child was intubated and put on a ventilator. Drainage of the right pleural cavity was performed. The infusion of catecholamines (norepinephrine and dopamine) was started. Despite the introduction of aggressive mechanical ventilation (peak inspiratory pressure 40 cmH_2O, positive end expiratory pressure +10 cm H_2O, FiO_2 1,0, TV 8 ml/kg), no clinical improvement was observed. After 12 h of ineffective conventional ventilation, the patient was put on ECMO. Because of the suspicion of a possible viral infection, especially with an influenza virus, oseltamivir was administered. In addition, the antibiotic treatment initiated before the transfer to PICU was continued. Tracheal aspirate and pharyngeal swab were collected to confirm the presence of viruses, and a polymerase chain reaction (PCR) test to detect the presence of DNA fragments of bacteria was performed. The results confirmed the presence of the RNA of the AH1N1 virus and the DNA of *Streptococcus pneumoniae*.

Because the primary cause of respiratory insufficiency was pneumonia, a veno-venous ECMO was applied with the use of the paediatric oxygenator QVAROX-ID and the rotational pump BIOPOMPA RotaFlow (Maquet, Sweden). Heparin infusion was given continuously. The rate of heparin infusion was modified according to activated clotting time (ACT) levels. The median level of ACT was kept between 160 and 180 sec. During ECMO procedure, the child was kept on ventilator on synchronized intermittent mandatory ventilation (SIMV) mode. The slow but permanent improvement of oxygenation was observed, which allowed to reduce the oxygen flow on ECMO. On day 11 of ECMO, a haemorrhagic complication, retrovesical haematoma, occurred which was a direct consequence of inserting a catheter into the femoral artery. The surgical intervention was required. For this reason, the patient was taken off ECMO on day 13,

and conventional ventilation was resumed. For the following 21 days, the infant was on ventilator, but the values of parameters were continuously decreased. On day 33, the child was weaned off the ventilator. He was discharged from PICU on day 40 to a pulmonary unit, where he spent another four weeks before being released home.

In February 2014, a nine year old girl (20 kg body weight, 125 cm height) with rare skeletal congenital disorders (epi-metaphyseal dysplasia) was treated due to an infection of upper and then lower respiratory airway, first at home (three days) and then in a district hospital (two days) without any positive effect. Because of the increasing symptoms of respiratory failure, the girl was shifted to the PICU at the University Hospital in Wroclaw. An immediate initiation of aggressive respiratory therapy did not get any success. Arterial blood saturation did not exceed 86 per cent, and oxygen partial pressure in arterial blood was below 65 mmHg. Because the child demonstrated symptoms of a septic shock, the aggressive fluid therapy and the continuous infusions of catecholamines (norepinephrine and dopamine) were started. Within one hour after the admission to the PICU and taking microbiological and viral tests, meropenem and linezolid were administered. All advanced techniques of conventional and non-conventional ventilation, including oscillatory ventilation, were used during the first two days of treatment. None of the ventilation modes resulted in clinical improvement. The oxygenation index remained at the level of 40-50 mmHg. The decision to put the child on ECMO was made with veno-venous technique. Continuous infusion of heparin was used to keep ACT at the level between 160 and 180 sec. During ECMO treatment at the beginning, the girl was ventilated with the oscillator, the conventional ventilation was used. SIMV mode was chosen with parameters representing the lung protective ventilation strategy. On the first day of ECMO, the test result confirmed the presence of AH1N1 influenza virus in the bronchial secretion. Oseltamivir was started. The patient was on ECMO for 16 days. A slow but continuous improvement of the child's general condition was observed. The oxygen saturation increased from 80 to 94 per cent. The administration of the catecholamines was discontinued on day 12. The blood gas analyses as well as the pulmonary compliance showed permanent improvement.

On day 16, the girl was taken off ECMO, and conventional ventilation was started. On the same day, tracheotomy was performed. The tracheotomy tube was removed on day 37. Two days later, the girl was transferred from PICU to the paediatric unit, and after two days, she was discharged.

The analysis of influenza virus (not only AH1N1) fatalities between 2009 and 2011 showed that nearly half (46%) of them were children below five years of age, and among those, 49 per cent belonged to a high-risk group, as classified by the Advisory Committee of Immunization Practices (ACIPs). Moreover, among children who died, only 23 per cent were vaccinated according to the ACIP recommendations[5,6]. Our cases of AH1N1 influenza were also from a high-risk group of infection. None of them was vaccinated against influenza virus. This may explain such a severe course of infection in both patients[7].

The first report on the use of ECMO in the treatment of respiratory failure in patients with AH1N1 virus was published from Australia and New Zealand[3]. As many as 68 patients in these countries *i.e*., 24 per cent of all patients admitted to ICU with diagnosed AH1N1 virus infection had to be put on ECMO. There were three children in this group. Among those put on ECMO, 75 per cent survived[3]. Pham *et al*[8] analyzed a group of 123 patients with AH1N1 infection treated with ECMO in ICUs across France in 2009-2011. The survival rate was higher in young patients and in those with severe hypoxia with the use of ECMO[8]. Among 215 critically ill patients with diagnosed or suspected AH1N1 virus infection admitted to ICUs across Canada, 29.8 per cent were below 18 years of age[9]. Nearly 4.2 per cent of all patients had to be put on ECMO[1,2,9].

The decision to use ECMO in both children in the present study, who developed symptoms of severe respiratory failure as a result of infection, was a crucial factor for their survival. A potential success of this method strongly depends on time factor. The decision should be made not later than on day seven of applying unsuccessful conventional methods of treatment[10]. Further, the two week period of this non-conventional therapy of these two children created an opportunity for their lungs to regenerate, reduced the risk of secondary complications related to aggressive ventilation and finally enabled the children to recover. However, the small number of patients allowed us to draw only limited conclusions. Further study needs to be done on a large number of patients to confirm our findings.

***Conflicts of Interest*:** None.

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