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Influenza A (H1N1) vs non-H1N1 ARDS: Analysis of clinical course

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ABSTRACT

Purpose: The purpose of the study is to compare H1N1-induced acute respiratory distress syndrome (ARDS) with ARDS due to other causes of severe community-acquired pneumonia focusing on pulmonary function.
Materials and methods: This is a retrospective data analysis of adult ARDS patients between January 2009 and December 2010 in an ARDS referral center. Patient characteristics, severity of illness scores, modalities, and duration of extracorporeal lung support were evaluated as well as intensive care unit stay and survival. Parameters of mechanical ventilation and pulmonary function were analyzed on day of admission and over the consecutive 10 days using a nonparametric analysis of longitudinal data in a 2-factorial design. In a logistic regression analysis, risk factors for extracorporeal lung support were investigated.
Results: Twenty-one patients with H1N1-ARDS and 41 with non-H1N1-ARDS were identified. Gas exchange was more severely impaired in patients with H1N1-ARDS over course of time. Extracorporeal membrane oxygenation was more frequently needed in H1N1-ARDS. Despite significantly prolonged weaning off extracorporeal lung support and intensive care unit stay in H1N1 patients, the proportion of survivors did not differ significantly. Only Sepsis-Related Organ Failure Assessment score could be identified as an independent predictor of extracorporeal lung support.
Conclusions: Clinical course of H1N1-ARDS is substantially different from non-H1N1-ARDS. Affected patients may require extensive therapy including extracorporeal lung support in ARDS referral centers.

1. Introduction

The novel swine-origin influenza A virus (H1N1) identified in spring 2009 spread rapidly and became a global pandemic [1]. Although most patients diagnosed with H1N1 infection had a mild, self-limiting illness of the upper respiratory tract with symptoms similar to seasonal influenza, up to 20% of hosts developed progressive, severe H1N1 pneumonia requiring admission to an intensive care unit (ICU) [2-4]. In some studies, important risk factors for severe H1N1 infection including younger age distribution, pregnancy, and obesity have been identified [2,5,6].

In Patients with acute respiratory distress syndrome (ARDS) caused by H1N1 pneumonia, refractory hypoxemia, or hypercapnia has been described [7]. In these critically ill patients, ICU admission and mechanical ventilation were necessary in more than 80% of the cases [2,4,8]. Reported mortality rates were up to 58% not only in immunocompromised individuals and patients with underlying comorbid conditions but also in young, otherwise healthy adults [9].

Recommended treatment strategies for H1N1-induced ARDS largely follow ARDS therapy guidelines, which include, for example, low tidal volume (VT) ventilation, adequate positive end-expiratory pressure (PEEP) level, limitation of positive inspiratory pressure, prone positioning, and nitric oxide inhalation. Moreover, administration of extracorporeal membrane oxygenation (ECMO) has been reported as successful rescue therapy [10,11]. With respect to limited resources during pandemics, Grasso et al [12] described an algorithm to avoid ECMO by adjusting PEEP levels to an end inspiratory transpulmonary pressure considered to represent the upper physiological limit. Finally, early use of specific antiviral drugs such as the neuraminidase inhibitor oseltamivir has widely been recommended for patients with H1N1 influenza, as it shortens the disease and carries a survival benefit [13], whereas anti-inflammatory treatment with systemic corticosteroids did not [14].

In our referral center for ARDS treatment with implemented ARDS treatment algorithms including extracorporeal lung support [15], we perceived an increased resource allocation during the H1N1 pandemic.

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Therefore, we investigated a consecutive series of 62 ARDS patients with severe community-acquired pneumonia (sCAP) admitted to our ARDS referral center. The aim of this study was to compare the clinical course of H1N1-induced ARDS in comparison with ARDS due to other infective causes of pneumonia (non-H1N1-ARDS) focusing on pulmonary function. We investigated pulmonary gas exchange and especially detailed ventilatory parameters, risk factors, outcome parameters, and severity of illness over course of time in both patient groups.

We hypothesize that clinical course of H1N1-ARDS is substantially different from non-H1N1-ARDS showing a protracted recovery of pulmonary gas exchange, a more frequent demand of extracorporeal lung support and a prolonged ICU stay.

2. Materials and methods

2.1. Setting

This retrospective study was conducted in the Department of Anesthesiology and Intensive Care Medicine, Charité–Universitätsmedizin Berlin, a referral center for treatment of severe adult respiratory distress syndrome as a part of the German ARDS network (http://www.ardsnetwork.de). During the 2009/2010 H1N1 pandemic, there was a strong cooperation between different Charité centers and the German ARDS network to optimize resource allocation for these patients. The study was approved by local ethics committee.

2.2. Patient eligibility and groups

All patients (>18 years) hospitalized with ARDS according to the American European Consensus Conference definition [16] between January 2009 and December 2010 entered the study.

All patients with sCAP, defined as requiring treatment in an ICU due to an acute infection of lung parenchyma acquired outside a hospital or within 48 hours after admission, underwent an extensive standardized pathogen diagnostic. Among others, this included screening for respiratory viruses from tracheobronchial secretions, bronchoalveolar lavage, and nasopharyngeal swab samples. Soon after the first confirmed H1N1 infections were reported, reverse transcriptase–polymerase chain reaction methods became available for specific testing for H1N1 virus [17] and were included into routine screening at admission.

Confirmed cases of H1N1 virus were enrolled in the study group of H1N1 patients (H1N1-ARDS). Patients with sCAP without a detection of H1N1 virus were considered as non-H1N1-ARDS. Subgroup analysis comprised patients with and without extracorporeal lung support (ECMO and pumpless extracorporeal lung assist [pECLA]) in both of the respective groups. Patients with viral pneumonia other than H1N1 (ie, cytomegalo virus or influenza A/B) or with pulmonary infections occurring later than 2 days after hospitalization (regardless of which hospital: our center and others) fulfilled criteria for hospital-acquired pneumonia and were, therefore, excluded from our study.

2.3. Patient characteristics and collection of data

We collected demographic (sex, age, height, and weight) and anamnestic (presence of predefined comorbidities) data upon ICU admission. Patient data management system COPRA (COPRA System GmbH, Sasbachwalden, Germany) was used to collect clinical data, scorings (Simplified Acute Physiology Score II [SAPS II] and Sepsis-Related Organ Failure Assessment [SOFA]), and ventilatory parameters (plateau pressure [millibars], PEEP [millibars], respiratory rate [per minute], VT [milliliters], fraction of inspired oxygen [F_{IO_2}] [%], Pa_{O_2}/F_{IO_2} ratio, dynamic pulmonary compliance [milliliters per millibar], calculated as Vt/[plateau airway pressure {Pplat} − PEEP]) and duration of mechanical ventilation (minutes) within our ARDS center. Delta P (millibars) was calculated as Pplat − PEEP.

We assessed commencement (day after admission), modalities (ECMO, pECLA, type of cannulation, oxygenator gas flow [liters per minute]), and duration of extracorporeal lung support (days). Extracorporeal blood flow was measured continuously (liters per minute). Pa_{O_2} (millimeters of mercury), Pa_{CO_2} (millimeters of mercury), pH, and lactate (milligrams per deciliter) were evaluated at ICU admission and several times daily thereafter. To ensure the best possible comparability of oxygenation, it was standard of care to take at least 1 arterial blood sample at a F_{IO_2} of 1.0 per day, which we chose for this study. In case this standardized measurement was not available, the arterial blood gas analyses providing the worst Pa_{O_2}/F_{IO_2} ratio was chosen for analysis.

Oxygenation index (OI) was calculated as (mean airway pressure [Pmean] × F_{IO_2} × 100)/Pa_{O_2}); lung injury score (Murray) was calculated as described elsewhere [18]. All clinical and functional data were collected and evaluated at ICU admission and over course of time for the first consecutive 10 days. We recorded data on length of ICU stay and survival. Microbiological data were collected from the succeeding 48 hours after hospital admission.

2.4. Intensive care unit admission, diagnostic protocol, and treatment

Acute respiratory distress syndrome patients were transferred from referring hospitals to our center by an experienced retrieval team of our department. Patients enrolled in the study were treated according to local ICU standard operating procedures (SOPs), implementing severe sepsis bundles, goal-oriented depth of sedation, and fluid balance [19]. Acute respiratory distress syndrome treatment followed local SOPs describing differential indications and duration of advanced therapeutic interventions following specified response criteria as published previously [15].

2.5. Ventilator settings and management of extracorporeal lung support

In patients with and without extracorporeal lung support, low VT ventilation with 6(-8) mL/kg of predicted body weight (PBW) and plateau pressures less than 30 cm H_2O was pursued whenever possible, following recommendations based on the results of the ARDSNet trial [20]. Positive end-expiratory pressure was titrated according to the high PEEP table of the ALVEOLI study [21]. As soon as feasible, we integrated spontaneous breathing to pressure-controlled ventilation modes. Fraction of inspired oxygen was set for a Pa_{O_2} of greater than 60 mm Hg or oxygen saturation greater than 90%. Extracorporeal membrane oxygenation was implemented as salvage therapy for severely hypoxemic patients. Veno-venous ECMO was the modality of choice for severe hypoxemic failure in both H1N1-ARDS and non-H1N1-ARDS patients. Fast-entry criteria comprised Pa_{O_2}/F_{IO_2} less than 50 mm Hg or oxygen saturation less than 90% for more than 2 hours. If conservative treatment options were exhausted, ECMO was commenced if Pa_{O_2}/F_{IO_2} remained less than 80 mm Hg. Arterio-venous pECLA was considered in patients with profound hypercapnia (Pa_{CO_2} >80 mm Hg with respiratory acidosis of pH <7.2) and sufficient oxygenation (Pa_{O_2}/F_{IO_2} >80 mm Hg).

Extracorporeal membrane oxygenation blood flow was adjusted for the oxygenation target stated above but kept to a maximum suction pressure of −60 mm Hg via the drainage cannulae. The F_{IO_2} over the ECMO membrane was set to 1.0, whereas F_{IO_2} on the respirator was lowered to less than 0.4 if oxygen levels allowed for reduction. When respiratory function improved (F_{IO_2} <0.4 and Pa_{O_2} >80 mm Hg), pressure levels on the ventilator were reduced on a daily basis until ECMO could be weaned off by reducing blood flow, gas flow, and F_{IO_2} over the membrane.

2.6. Statistics

Discrete variables are given as counts or percentage; continuous variables, as medians with 25th to 75th percentiles. For demographics