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Influenza infection in the intensive care unit: Four years after the 2009 pandemic☆

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ABSTRACT

The role of influenza viruses in severe acute respiratory infection (SARI) in Intensive Care Units (ICU) remains unknown. The post-pandemic influenza A(H1N1)pdm09 period, in particular, has been poorly studied.

Objective: To identify influenza SARI patients in ICU, to assess the usefulness of the symptoms of influenza-like illness (ILI), and to compare the features of pandemic vs. post-pandemic influenza A(H1N1) pdm09 infection.

Methods: A prospective observational study with SARI patients admitted to ICU during the first three post-pandemic seasons. Patient demographics, characteristics and outcomes were recorded. An influenza epidemic period (IEP) was defined as >100 cases/100,000 inhabitants per week.

Results: One hundred sixty-three patients were diagnosed with SARI. ILI was present in 65 (39.9%) patients. Influenza infection was documented in 41 patients, 27 (41.5%) ILI patients, and 14 (14.3%) non-ILI patients, 27 of them during an IEP. Influenza A viruses were mainly responsible. Only five patients had influenza B virus infection, which were non-ILI during an IEP. SARI overall mortality was 22.1%, and 15% in influenza infection patients. Pandemic and post-pandemic influenza infection patients shared similar clinical features.

Conclusions: During influenza epidemic periods, influenza infection screening should be considered in all SARI patients. Influenza SARI was mainly caused by subtype A(H1N1)pdm09 and A(H3N2) in post-pandemic seasons, and no differences were observed in ILI and mortality rate compared with a pandemic season.

Infección por virus influenza en la unidad de cuidados intensivos: Cuatro años después de la pandemia del 2009

Palabras clave:
Virus de la gripe A
A (H1N1) pdm09
Enfermedad tipo gripe
Infección respiratoria aguda grave
Insuficiencia respiratoria aguda

RESUMEN

El papel de los virus influenza en la infección respiratoria aguda grave (IRAG) en Unidades de Cuidados Intensivos (UCI) sigue siendo desconocido. En particular, en el periodo post-pandemia de gripe A (H1N1) pdm09ha sido poco estudiada.

Objetivo: identificar a los pacientes con IRAG por influenza en la UCI, para evaluar la utilidad de los síntomas por influenza (SI) y comparar las características de pandemia vs. post-pandemia de gripe A (H1N1) pdm09.

Métodos: Estudio observacional prospectivo de pacientes con IRAG admitidos en UCI durante las tres primeras temporadas post-pandémica. Se registraron demográficos, características y resultados de los pacientes. Período epidémico de Influenza (PEI) se definió por encima de 100 casos/100.000 habitantes por semana.

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Resultados: Ciento sesenta y tres pacientes fueron diagnosticados con IRAG. SI estaba presente en 65 (39,9%). La infección por influenza se documentó en 41 pacientes, 27 (41,5%) pacientes SI y 14 (14,3%) de los pacientes que no presentaban SI; 27 de ellos durante el PEI. Los virus de influenza A fueron los principales responsables; sólo cinco pacientes presentaron infección por el virus de la influenza B, todos en PEI y sin SI. La mortalidad global fue del 22,1%, y 15% en pacientes con infección por gripe. Pacientes con infecciones de influenza pandémica y post-pandemia comparten características clínicas similares.
Conclusiones: Durante los períodos de epidemia de influenza, la detección de infecciones por influenza deben considerarse en todos los pacientes con IRAG. Influenza IRAG fue causado principalmente por el subtipo A (H1N1) pdm09 y A (H3N2) en las temporadas posteriores a la pandemia y no se observaron diferencias en la presentación de SI ni en la mortalidad en comparación con la pandemia.

Introduction

The world was startled by the unexpected emergence of a novel swine-origin A(H1N1) virus which caused the first influenza pandemic of the 21st century.[1] Influenza A(H1N1)pdm09 virus was the predominant subtype of influenza virus during 2009/10. This virus predominated in the 2010/11 influenza season in Europe but the influenza B virus also circulated widely, being the most prevalent type in countries such as Ireland. In hospitalized cases, the A(H1N1)pdm09 virus was by far the most commonly reported.[2]

During the pandemic period, patients infected by influenza A(H1N1)pdm09 virus were usually young and previously healthy. Obese persons and pregnant women were at increased risk of infection.[1] The main clinical features were respiratory symptoms with signs of pneumonia and in the Intensive Care Unit (ICU) setting, patients were admitted with acute respiratory failure frequently requiring mechanical ventilation. Mortality of patients requiring mechanical ventilation was above 30%.

Early data from the European Centre for Disease Prevention and Control (ECDC) revealed that in France, Ireland, Spain and the United Kingdom the 2011/12 influenza season was dominated by influenza A(H3N2) virus with scarce circulation of influenza A(H1N1)pdm09 virus and influenza B virus. Since week 40/2011, 43,233 influenza viruses from sentinel and non-sentinel sources were typed: 39,296 (91%) tested positive for influenza A and 3937(9%) for influenza B. Of the influenza A viruses, 21,526 were subtyped: 20,656 (96%) as A(H3N2) and 870 (4%) as A(H1N1)pdm09. In comparison to the 2010/11 season, the proportion of subtype A(H3) among hospitalized cases increased and was associated with a greater predilection for extreme age groups.[3,4] During 2012/13 season the proportion of subtype A(H1) was similar to subtype A(H3) and there was also a tendency towards balance between influenza A and B with the largest proportion of cases in the 45–64 year-old group.[5]

Unfortunately, hospital surveillance for severe acute respiratory infections (SARI) was a weak link in the European strategy of surveillance in a pandemic.[6] Furthermore, very few data are available in the literature on risk factors and clinical presentation of post-pandemic influenza virus infection in SARI.

The main objectives of the present study were to identify patients with influenza virus SARI admitted in ICU during a post-pandemic period and to assess usefulness of influenza-like illness (ILI) in its diagnosis. Secondary objectives were to compare the clinical features of confirmed cases of influenza infection during pandemic A(H1N1)pdm09 vs. post-pandemic period.

Materials and methods

This prospective observational study was designed to assess SARI patients admitted to the ICU of a large tertiary care hospital in Barcelona, Spain, in a post-pandemic influenza period. Data were collected during the 2011/12, 2012/13 and 2013/14 seasons (every season from week 48 to week 18 the following year). In Catalonia, the influenza epidemic period (EIP) was defined as more than 100 cases/100,000 inhabitants per week and established as week 52/2011 to 10/2012, week 3/2013 to 9/2013 and week 2/2014 to 7/2014.

Patients with severe chronic illness in whom respiratory failure was an expected terminal event were not included. Data were reported by attending physicians reviewing medical charts, radiology and laboratory records within the first 24 h of ICU admission.

The study was approved by the institutional review board of Hospital Universitari Vall d'Hebron, Barcelona, Spain. Patients' identification remained anonymous and the ethics committee waived the requirement for informed consent due to the observational nature of the study (Ref. PR(AG)283/2011).

The ICU admission criteria and therapeutic decisions for all patients, including determination of the need for intubation and type of antibiotic and antiviral therapy administered, were applied by the attending physician according to standard clinical practice in the unit.

A SARI case was defined as sudden onset of fever (>38 °C), cough or sore throat in the absence of any other diagnosis and shortness of breath or difficulty in breathing.[7] Nosocomial SARI was defined as patients who fulfilled requirements for SARI and nosocomial infection.[8] ILI was determined when a patient presented two or more of the following: fever, cough, myalgia, headache, sore throat, sudden onset of symptoms or malaise, based on criteria suggested by a standardized definition for European institutions.[7]

Respiratory specimens from upper and lower respiratory tract were collected at admission from all enrolled patients. Total nucleic acids were extracted using NucliSense easyMAG (bioMérieux, Marcy lÉtoile, France) according to the manufacturer's instructions. Influenza viruses and other respiratory viruses was detected. The detection of influenza viruses and other respiratory viruses were performed either by immunofluorescence (D^3 *Ultra 8*™ DFA Respiratory Virus Screening & Identification Kit, Diagnostic HYBRIDS, USA), by real-time multiplex RT-PCR (Anyplex II RV16 Detection Kit, Seegene, Korea) or by influenza-specific (GeneXpert Flu, Cepheid, USA) assays. In addition, a specific one-step multiplex real-time RT-PCR was performed for influenza subtyping (H1pdm09 and H3) on FLUAV-positive samples.[9]

The following information was recorded: demographic data, comorbidities, time of symptoms onset and of hospital admission, microbiological and radiographic findings at ICU admission. Intubation and mechanical ventilation requirements, laboratory findings at ICU admission and medical complications during ICU stay were also recorded. Comorbidities were defined as the pathological antecedents of each patient. Chronic obstructive pulmonary disease (COPD) was defined as a disease state characterized by the presence of airflow limitation due to chronic bronchitis or emphysema.[10] The airflow obstruction could be accompanied by airway hyper-reactivity and could be partially reversible. Immunocompromised state was defined as primary immunodeficiency or