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Influenza A (H1N1) in nephrology patients. The pandemic disease that has put us on guard

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INTRODUCTION. JUSTIFICATION TO ACTION GUIDELINES

The influenza A virus (H1N1) is a new influenza virus resulting from the association of RNA segments of swine, avian and human influenza viruses. Its transmission capacity is high but its virulence is low for people with no associated diseases.

The virus transmits through the air (large-particle droplet > 5µm) and it can survive on inert surfaces for 10 hours. It usually causes a mild influenza-like syndrome, with rapid-onset high fever (usually > 38º C) with shivers, general discomfort, intense asthenia and myalgia, and headache, as well as respiratory tract illness with dry cough. Odynophagia, rhinorrhoea, and nasal congestion are usually less intense than in seasonal influenza. Digestive symptoms may add up, such as nausea, vomiting and diarrhoea. The process requires symptomatic treatment and it may resolve spontaneously. Provided there are no complications, these symptoms usually last from 4 to 7 days.

The incubation period is usually 7 days and its onset should be suspected when fever > 38° C and signs or symptoms of acute respiratory infection appear, non-filiated pneumonia (acute respiratory infection) or when the affected patient has died due to acute respiratory disease of unknown origin. Patients with signs or symptoms of acute respiratory infection meet the criterion for hospital admission.[1-5]

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Action guidelines for influenza A caused by H1N1 virus[5] are justified by the combination of inter-dependant risk factors dependent on the influenza A virus and patients. Among the factors dependent on the virus, it should be highlighted an expected high incidence of influenza A, 30-40% in the general population, high transmission and potentially fatal evolution, in cases of associated co-morbidity. Among the factors dependent on patients, it should be highlighted the inclusion of patients with chronic kidney disease (CKD) in the risk groups and their high rate of hospitalisation.[3-5]

Some groups of experts are studying the hypothesis of a final accumulated incidence of 30%.[6] Up to 2% of the cases are severe. The majority of cases occur in young adults aged between 20-45 years and between 30 and 50% in previously healthy persons; the rest occur in patients with added comorbidity.

Dialysis patients with CKD-5 present a high added comorbidity rate (diabetes mellitus 21%, AHTN 90%, obesity 15%), and a high hospitalisation rate as well. Frequent interaction with health staff during care that requires proximity to patients justifies special attention to isolation and staff protective measures.

In June 2009 WHO increased alert level to phase 6 for global pandemic influenza A (H1N1) due to evidence of its spreading growth in five continents. As of 29 September, 2009, 318,925 people had been infected all over the world, with 3,917 deaths. Hospitalisation rate varies from 7.8% in Chile up to 21.71% in New Zealand. The media may have exaggerated the danger of this pandemic disease in many cases,[7] but it is also true that from the health care area we have to adopt measures to plan an adequate assistance to the affected population in

order to avoid the collapse of primary care and hospital emergency centres.[1-5]

Risk groups to host the H1N1 virus include patients with moderate to acute CKD, patients with chronic heart disease (excluding AHTN), diabetics undergoing treatment, and patients under immunosuppression (kidney transplanted or with kidney condition requiring immunosuppression).

For these reasons and despite the proliferation of documents from health departments at various Spanish Autonomous Regions or even from multinational departments regulating dialysis centres, the SEN considered necessary to clarify and unify criteria, facing the numerous requests received in this sense from various nephrology services and dialysis units in Spain.

For those who may want to consult it, this document is available at **www.senefro.org.**[5] We summarise its main indications as follows:

DEFINITIONS. LABORATORY SAMPLE COLLECTION AND DIAGNOSIS

In its introduction the document takes up the **definitions** of epidemic and pandemic, as well as the definitions of influenza A H1N1 and acuteness degree criteria by which the patients have to be hospitalised.

Special emphasis is set on **sample collection** to confirm diagnosis (naso-pharyngeal exudates, whole blood with or without EDTA).

LABORATORY DIAGNOSIS

At least one of the following tests with positive results is required:

1. New influenza A (H1N1) virus RT-PCR detection, real-time polymerase chain reaction. It is the most affordable test; its result can be ready in less than 24 hours.
2. Increase by four times the titre of neutralising antibodies with respect to the new influenza A virus/H1N1 (this requires two types of saline solution, one from the acute phase of the disease and the other from the convalescent phase, 10 to 14 days subsequently).
3. Virus culture of new influenza A virus (H1N1).

PREVENTION AND INTERVENTION MEASURES. PERITONEAL HAEMODIALYSIS AND DIALYSIS

In relation to the patient on haemodialysis a series of prevention and intervention measures are established. Since the main transmission route is through respiratory secretions, general hygienic measures are specified: hand-washing with soap or alcohol solutions, surgical mask-wearing, surface-cleaning (where the virus can live for hours at room temperature), etc.

Instructions are provided to take advantage of the data obtained by telephone consultation, as well as the criteria for patient referral to emergency wards in cases considered complicated or at risk of becoming severe.

Taking into account the high transmission rate, measures that can be useful for transport of patients are taken, and also recommendations for health staff in close contact with the patients.

A standard is set to adopt prevention measures in haemodialysis units and on how to implement personal protection measures: respiratory isolation (use of mask, gloves, white coat, etc.), cleaning of monitors, dialysis ward, and rooms. Likewise, environmental control measures are established.

Regarding peritoneal dialysis the measures applied will be the same as for haemodialysis, insisting specially in instructing the patient so that they detect themselves possible signs of alarm or severe risk.

PREVENTION MEASURES BY IMMUNISATION

The Health Ministry regulation is already available, and from 16 November there are two vaccines with adjuvant Pandemrics (GSK) and Focetria (Novartis). In the groups considered at risk, such as kidney patient or receiving **inmunosuppression** is recommended for vaccination of seasonal ainfluenza and then, one dose of vaccine virus-specific H1N1.

ANNEXES

The document has 4 annexes associated to it that make reference to: 1) definitions of suspicious case, probability or confirmation of influenza A H1N1; 2) personal protection equipments; 3) signs and symptoms of severity and hospital admission criteria, and 4) specially set aside, an addition with explicit reference to antiviral treatment in patients with impaired renal function.

The board of experts calls special attention to this respect, as Oseltamivir, a neuraminidase inhibitor, is eliminated by the kidneys,[8-10] which is why its doses in patients with reduced glomerular filtration have to be corrected. Precisely for this

reason we believe it is especially important to consult this document to dispel doubts, as there are only two reports in the literature[9,10] with studies in pharmacokinetics of Oseltamivir in the renal patient undergoing peritoneal haemodialysis or dialysis.

We also make a warning in relation to dealing with influenza A H1N1 in the organ donor for transplant and in the solid organ transplantpatient, with the corresponding reference to the document issued by the board of experts of the ONT (Spanish national transplant organisation) of the Ministry of Health, where members representing the S.E.N. were also present.[11]

The experience of all nephrologists and people caring for nephrology patients is highly important for us to deal with an issue that we consider a key aspect.

We have to record our own experience if we want to confirm the facts. We know this may entail an overload to the already overwhelming task of daily endeavour. In spite of this fact, we encourage everyone to record all confirmed cases, by means of a simple file, that is also shown in the document at www.senefro.org and that will easily be filled out online.

Knowledge about the disease, epidemiological data, and definitions may all rapidly change; for this reason the action guidelines will be updated whenever new data makes it worthwhile. The measures may change when the seasonal influenza overlaps pandemic influenza A, next autumn and winter.

As usual, we thank everyone for their generous and essential effort and collaboration.

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