Letter

Severe influenza A (H1N1)v in patients without any known risk factor

Carles Alonso-Tarrés, Cristina Cortes-Lletget, Sara Pintado and Assumpta Ricart

Microbiology-Consorci de Laboratoris Intercomarcal, Hospital General de l'Hospitalet, Avda. Josep Molins, 29-41, L'Hospitalet de Llobregat, Barcelona 08906, Spain

Corresponding author: Carles Alonso-Tarrés, carlesmicro@gmail.com

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See related research by Rello *et al*., http://ccforum.com/content/13/5/R148

A proportion of pandemic flu cases requires critical care. Several risk factors are associated with progressive illness. The World Health Organization recommends prompt antiviral treatment when risk factors are present [1]. Nevertheless, in Rello and colleagues' work, 15 out of 32 critical pandemic flu patients did not have any risk factor [2].

In our hospital, 25 pandemic flu cases have been diagnosed by RT-PCR thus far. Three of these cases required critical care. Noteworthy, those patients had been visited in emergency services 2 to 3 days before. The clinical picture did not prompt the physician to prescribe any antiviral, and oseltamivir treatment was delayed 5 days or more. In contrast, in the group of patients who did not require critical care (22 patients), only three patients had a prior emergency visit (Fisher's exact test $P = 0.009$) and 18 patients received antiviral treatment in the first 48 hours of symptoms (Fisher's exact test $P = 0.009$).

In Rello and colleagues' study, the median number of days from illness onset to initiation of antiviral treatment was 4 days. Patients with risk factors were probably treated immediately, however, and patients without any risk factors were probably treated later. Some evidence suggests that early antiviral treatment is associated with a good prognosis [3]. Rello and colleagues may provide the mean of treatment delay days in patients without any risk factor and any putative differences with the rest of patients. Early antiviral treatment with active antiviral drugs may prevent severe cases in patients without any risk factor. The authors may also inform about any other difference in this group of patients.

Authors' response

Jordi Rello and Alejandro Rodríguez, for the H1N1 SEMICYUC Working Group

We appreciate the interest from Dr Alonso-Tarrés and colleagues in our article and their insightful observations regarding management of severe influenza A (H1N1)v. We agree that several points about antiviral treatment should be clarified.

Recent observational studies suggested that antiviral treatment started within 4 days after illness onset may reduce mortality among adult patients hospitalized with influenza [4] and may enhance viral load decrease and viral clearance [5]. In our study, no significant delay in the first dose of antiviral was observed in patients with comorbidities (6.5 ± 5.0, median 6 days) versus those without comorbidities (4.5 ± 3.8, median 4 days) [2]. No differences were observed regarding the severity of illness (Acute Physiology and Chronic Health Evaluation II score, 12.9 ± 7.9 vs. 14.5 ± 5.9; $P = 0.50$), organ dysfunction (Sequential Organ Failure Assessment score, 6.9 ± 4.2 vs. 6.2 ± 2.0; $P = 0.54$) or mortality (26.7% vs. 23.5%; $P = 0.98$) between groups.

In a recent multicenter observational study [6], however, receipt of antiviral drugs in <48 hours was the only variable associated with positive outcome. In our study, eight (25%) patients received antiviral therapy within 48 hours after onset of symptoms, and one patient died (12.5%) [2]. Delayed initiation of antiviral therapy (>48 hours) was associated with high risk of death (odds ratio = 2.90, 95% confidence interval = 0.30 to 28.0) and a mortality of 29.7%.

PCR = polymerase chain reaction; RT = reverse transcriptase.

Whereas randomized controlled trials are warranted to prove clinical benefit of early antiviral therapy, current observations suggest that a delay in antiviral therapy may contribute to increase the viral load, to delay shedding and to complications. Prompt diagnosis and early antiviral prescription should therefore be considered in patients with influenza-like illness for 2009 pandemic influenza.

Competing interests

The authors declare that they have no competing interests.

References

1. **WHO Guidelines for Pharmacological Management of Pandemic (H1N1) 2009 Influenza and other Influenza Viruses** [http://www.who.int/csr/resources/publications/swineflu/h1n1_use_antivirals_20090820/en/index.html]
2. Rello J, Rodríguez A, Ibañez P, Socias L, Cebrian J, Marques A, Guerrero J, Ruiz-Santana S, Marquez E, Del Nogal-Saez F, Alvarez-Lerma F, Martínez S, Ferrer M, Avellanas M, Granada R, Maraví-Poma E, Albert P, Sierra R, Vidaur L, Ortiz P, Prieto Del Portillo I, Galván B, León-Gil C; the H1N1 SEMICYUC Working Group: **Intensive care adults patients with severe respiratory failure caused by influenza A (H1N1)v in Spain.** *Crit Care* 2009, **13:**R148.
3. Jamieson DJ, Honein MA, Rasmussen SA, Williams JL, Swerdlow DL, Biggerstaff MS, Lindstrom S, Louie JK, Christ CM, Bohm SR, Fonseca VP, Ritger KA, Kuhles DJ, Eggers P, Bruce H, Davidson HA, Lutterloh E, Harris ML, Burke C, Cocoros N, Finelli L, MacFarlane KF, Shu B, Olsen SJ, Chavez G, Harriman K, Winter K, Aragon D, Comstock N, Cosgrove S, *et al.*: **H1N1 2009 influenza virus infection during pregnancy in the USA.** *Lancet* 2009, **374:**429-430.
4. Aoki FY, Macleod MD, Paggiaro P, Carewicz O, El Sawy A, Wat C, Griffiths M, Waalberg E,Ward P; IMPACT Study Group: **Early administration of oral oseltamivir increases the benefits of influenza treatment.** *J Antimicrob Chemother* 2003, **51:**123-129.
5. Lee N, Chan PKS, Hui DSC, Rainer TH, Wong E, Choi KW, Lui GCY, Wong BCK, Wong RYK, Lam WY, Chu IMT, Lai RWM, Cockram CS, Sung JJY: **Viral loads and duration of viral shedding in adults patients hospitalized with influenza.** *J Infect Dis* 2009, **200:**492-500.
6. Jain S, Kamimoto L, Bramley AM, Schmitz AM, Benoit SR, Louie J, Sugerman DE, Druckenmiller JK, Ritger KA, Chugh R, Jasuja S, Deutscher M, Chen S, Walker JD, Duchin JS, Lett S, Soliva S, Wells EV, Swerdlow D, Uyeki TM, Fiore AE, Olsen SJ, Fry AM, Bridges CB, Finelli L; for the 2009 Pandemic Influenza A (H1N1) Virus Hospitalizations Investigator Team: **Hospitalized patients with 2009 H1N1 influenza in the United States, April–June 2009.** *N Engl J Med* 2009, **361:**1935-1944.