Fatal Cases of Pandemic (H1N1) 2009 Influenza despite Their Early Antiviral Treatment in Japan

Neuraminidase inhibitors, including oseltamivir and zanamivir, are currently used for treatment of influenza infections. These drugs are also considered to be effective against pandemic (H1N1) 2009 influenza. It is recommended that antiviral drugs should be given especially to patients who are at increased risk of developing complications [1]. In Japan, neuraminidase inhibitors have been widely used, even for seasonal influenza and most cases of pandemic (H1N1) 2009 influenza. We assessed the timing of the antiviral treatment and the patient outcome by comparing fatal cases and severe but non-fatal cases of pandemic (H1N1) 2009 influenza in Japan. During the pandemic, fatal and severe cases were reported to the Ministry of Health, Labour, and Welfare (MHLW). At the same time, the clinical manifestation and clinical course of these cases were posted on the MHLW Web site. A severe case was defined as a patient who required admission to the intensive care unit (ICU) or who required mechanical ventilation. Both fatal and severe cases were confirmed as pandemic (H1N1) 2009 influenza by use of real-time reverse-transcription polymerase chain reaction. We included all 198 fatal cases that were reported from 15 August 2009 (when the first case was reported) through 15 March 2010. We also included 42 severe cases in patients who received antiviral treatment among all 198 fatal cases that were reported from 15 August through 11 October 2009, because the Ministry of Health, Labour, and Welfare stopped reporting severe cases in mid-October.

Of 198 fatal cases, 158 (80%) were reported to have received antiviral treatment; of 56 severe cases, 42 (75%) were reported to have received antiviral treatment. We evaluated the timing of the antiviral treatment after the onset of symptoms between the 2 groups. As a result, the median time from the onset of illness to the initiation of antiviral drugs was 1 day for both groups, with a range of 0–18 days for fatal cases and 0–7 days for severe cases. Furthermore, 104 (66%) of 158 fatal cases and 30 (71%) of 42 severe cases have received antiviral drugs on day 0 or 1 after their onset of symptoms (Figure 1).

Available evidence suggests that early treatment with oseltamivir for patients with pandemic (H1N1) 2009 virus infection may reduce the duration of hospitalization [2] and the risk of progression to severe disease requiring ICU admission or resulting in death [3–5]. In Japan, during the early stage of illness, patients with symptoms of influenza-like illness tend to visit health clinics and start antiviral treatment promptly. We could not see any significant difference between fatal and severe cases in the timing of antiviral treatment after symptom onset. In Japan, where most of the patients had access to early antiviral treatment and hospital care, most of the fatal cases had also received early antiviral treatment. In other countries, those patients who received early antiviral treatment might also have received early hospital care, which can be a potential bias in assessing the impact of antiviral treatment. Although our observational data do not provide direct evidence of the effectiveness of antiviral treatment, our data clearly indicate that some severe cases had fatal outcomes despite their early treatment with antiviral drugs. More data are needed to define the exact impact of early antiviral treatment on outcome of influenza infections, including pandemic (H1N1) 2009 influenza.

Acknowledgments

Potential conflicts of interest. All authors: no conflicts.

Nao Nukiwa, Taro Kamigaki, and Hitoshi Oshitani
Department of Virology, Tohoku University Graduate School of Medicine, Sendai, Japan

References


Reprints or correspondence: Dr Nancy Crum-Cianflone, c/o Clinical Investigation Department (KCA), Naval Medical Center San Diego, 34800 Bob Wilson Dr, Ste 5, San Diego, CA 92134-1005 (nancy.crum@med.navy.mil).

Clinical Infectious Diseases 2010;51(8):990–993
© 2010 by the Infectious Diseases Society of America. All rights reserved. 1058-4838/2010/5108-0025$15.00 DOI: 10.1086/656442

Figure 1. Duration between onset of illness and initiation of antiviral drugs. Both fatal and severe cases were confirmed as pandemic (H1N1) 2009 influenza by use of real-time reverse-transcription polymerase chain reaction. We included 158 fatal cases in patients who received antiviral treatment among all 198 fatal cases that were reported from 15 August 2009 (when the first case was reported) through 15 March 2010. We also included 42 severe cases in patients who received antiviral treatment among all 56 severe cases that were reported from 5 August through 11 October 2009, because the Ministry of Health, Labour, and Welfare stopped reporting severe cases in mid-October.


Reprints or correspondence: Dr Hitoshi Oshitani, Dept of Virology, Tohoku University Graduate School of Medicine, 2-1 Seiryo-cho, Aoba-ku, Sendai, Miyagi 980-8575, Japan (oshitanih@mail.tains.tohoku.ac.jp).

Clinical Infectious Diseases 2010;51(8):993–994
© 2010 by the Infectious Diseases Society of America. All rights reserved. 1058-4838/2010/5108-0026$15.00 DOI: 10.1086/658443