

Characterization of neuraminidase inhibitor – resistant influenza A(H1N1)pdm09 viruses isolated in four seasons during pandemic and post-pandemic periods in Japan

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Influenza and Other Respiratory Viruses

Japan has the highest frequency of neuraminidase (NA) inhibitor use against influenza in the world. Therefore, Japan could be at high risk of the emergence and spread of NA inhibitor-resistant viruses. The aim of this study was to monitor the emergence of NA inhibitor-resistant viruses and the possibility of human-to-human transmission during four influenza seasons in Japan.

To monitor antiviral-resistant A(H1N1)pdm09 viruses, we examined viruses isolated in four seasons from the 2008–2009 season through the 2011–2012 season in Japan by allelic discrimination, NA gene sequencing, and NA inhibitor susceptibility.

We found that 157 (1.3%) of 12 026 A(H1N1)pdm09 isolates possessed an H275Y substitution in the NA protein that confers about 400- and 140-fold decreased susceptibility to oseltamivir and peramivir, respectively, compared with 275H wild-type viruses. The detection rate of resistant viruses increased from 1.0% during the pandemic period to 2.0% during the post-pandemic period. The highest detection rate of the resistant viruses was found in patients who were 0–9 years old. Furthermore, among the cases with resistant viruses, the percentage of no known exposure to antiviral drugs increased from 16% during the pandemic period to 44% during the post-pandemic period, implying that suspected human-to-human transmission of the resistant viruses gradually increased in the post-pandemic period.

A(H1N1)pdm09 viruses resistant to oseltamivir and peramivir were sporadically detected in Japan, but they did not spread throughout the community. No viruses resistant to zanamivir and laninamivir were detected.