

# Study suggests some drug resistance to influenza B medications

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Use of certain common antiviral drugs during a recent influenza B epidemic in Japan showed the development of viruses with partial resistance to the drugs, according to a study in the April 4 issue of JAMA.

Two antiviral drugs, zanamivir and oseltamivir, which are a type of drugs known as neuraminidase inhibitors, have been effective against influenza and are used extensively. There has been documented evidence of the emergence of oseltamivir-resistant type A viruses, but similar information on influenza B viruses has been limited. Influenza B viruses are associated with annual outbreaks of illness and increased death rates worldwide, according to background information in the article.

Shuji Hatakeyama, M.D., Ph.D., of the University of Tokyo, Japan, and colleagues examined the prevalence and transmissibility of influenza B viruses with reduced sensitivity to neuraminidase inhibitors in Japan, where zanamivir and oseltamivir are now used more extensively than anywhere else in the world. In the winter of 2004-2005, an influenza B virus caused a widespread epidemic in Japan, creating an opportunity to assess the effectiveness of neuraminidase inhibitors. The researchers collected influenza B isolates from 74 children before and after oseltamivir therapy and from 348 untreated patients with influenza (including 66 adults). Four hundred twenty-two viruses from untreated patients and 74 samples from patients after oseltamivir therapy were analyzed.

The researchers identified a variant with reduced drug sensitivity in one (1.4 percent) of the 74 children who had received oseltamivir, and seven (1.7 percent) of the 422 influenza B viruses isolated from untreated patients were found to have reduced sensitivity to zanamivir, oseltamivir, or both. Review of the clinical and viral genetic information available on these seven patients indicated that four were likely infected in a community setting, while the remaining three were probably infected through contact with siblings shedding the mutant viruses.

“Continued surveillance for the emergence or spread of neuraminidase inhibitor–resistant influenza viruses is critically important,” the authors write. “Further evaluation of the biological properties of neuraminidase inhibitor–resistant influenza viruses is needed to fully assess their pathogenicity in humans.”

In an accompanying editorial, Anne Moscona, M.D., of Weill Medical College of Cornell University, New York, and Jennifer McKimm-Breschkin, Ph.D., of Molecular and Health Technologies, Parkville, South Victoria, Australia, comment on the findings concerning possible drug resistance to influenza B medications.

“The report by Hatakeyama et al raises more questions than it answers, including questions about viral evolution, biological fitness, and transmissibility. But some facts are strikingly clear. Influenza B mutants with reduced sensitivity to neuraminidase inhibitors are circulating, and these viruses can cause infections with no difference in duration of symptoms, level of viral shedding, or clinical outcome. Contrary to what had been hoped until now, some resistant variants are vigorous pathogens. Whether these viruses arise by spontaneous mutation or through drug selection, or whether they are transmitted within families or acquired from the community, the resistant variants may be here to stay. In light of the recent observation that oseltamivir may be less effective against influenza B than against influenza A, an important

concern is whether suboptimal dosing for these viruses will lead to increased selection of viruses with high-level resistance.”

“Influenza viruses evolve rapidly and nimbly, which compels ongoing investigation of antiviral therapies that use alternative mechanisms of action and target different points in the viral life cycle. The emergence of drug-resistant influenza B should draw attention to the importance of continual monitoring of strains over time and to the need for frequent rethinking of policies for use of antiviral drugs. While the news about resistance is not good and certainly calls into question some of the current assumptions about drug-resistant viruses, an effective response to this news can help contend with the new challenges of influenza.”

Source: JAMA and Archives Journals

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