Tamiflu Prophylaxis Tied to Adverse Reactions

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FROM EUROSURVEILLANCE

British schoolchildren and staff given oseltamivir as prophylaxis during the start of the influenza A(H1N1) pandemic reacted poorly to the medication, yet this study's lead author says the findings do not diminish the potential value of the strategy during a pandemic.

"If another pandemic of unknown severity comes along, we will probably do the same," Dr. Mark Strong of the University of Sheffield (England) said in an interview.

"We will act cautiously and use prophylaxis widely in the initial stages if we expect it to be protective. We will only stop doing this when either the strategy no longer has any hope of controlling spread, or if the disease is found to be mild."

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Major Finding: Of the pupils who had taken oseltamivir, 41% reported adverse effects, most often nausea (26%), abdominal pain (20%), and headache (12%); nearly half of the staff who took the drug reported adverse effects.

Data Source: A single-school study of 53 staff and 273 students who were given a questionnaire regarding flulike illness and adverse effects following oseltamivir prophylaxis.

Disclosures: None was reported.

In June 2009, 10 laboratory-confirmed cases of pandemic influenza were identified at a primary school in Sheffield. Representatives of the National Health Service (NHS) in Sheffield offered all the school's students and staff age-appropriate doses of oseltamivir (60 mg for pupils; 75 mg for adults; Tamiflu) twice daily for 5 days prior to closing the school for a week. A total of 53 staff members (91%) and 273 students (92%) accepted.

For their research, Dr. Strong and his colleagues at the university and the NHS distributed a questionnaire 2 weeks after the outbreak to identify the incidence of influenzalike illness and adverse drug effects after the intervention. Response rates were 84% for staff and 62% for pupils.

Of the respondents, 17% of pupils and 17% of staff said they had developed an influenzalike illness, with headache, cough, fever, tiredness, sore throat, and nausea the most common symptoms reported (Euro. Surveill. 2010;15:pii=19565).

Forty-one percent of the 273 pupils who had taken the drug reported adverse effects, most commonly nausea (26%), abdominal pain (20%), and headache (12%); nearly half the 53 adult staff reported adverse effects. Fourteen percent of pupils and 20% of staff reported not completing the course of medication because of adverse effects.

The findings of adverse effects differed slightly from those of two earlier observational studies of oseltamivir prophylaxis in British schoolchildren at the start of the 2009 pandemic (Euro. Surveill. 2009;14:pii=19285; Euro. Surveill. 2009;14:pii=19287). These studies reported adverse effects among more than half of pupils at two different schools.

However, Dr. Strong and his colleagues noted, "the majority of children in the previous studies were of secondary school age, and therefore older than our cohort," which included pupils between the ages of 7 and 12 (mean age 9.5). "It is possible that older children are more likely to either experience, or report experiencing, adverse effects following the use of oseltamivir," they wrote.

Because a number of reported adverse effects overlapped with symptoms of influenza-like illness (for example, nausea), Dr. Strong and colleagues acknowledged in their analysis that it was not possible to determine whether the reported symptoms comprised flulike illness or drug reactions.

A further limitation of their study, they noted, was that it relied heavily on self-reporting by children—the questionnaire included, among other things, a series of smiling or frowning cartoon faces that children could choose from to describe their health state. Moreover, determining the efficacy of the inter-

vention in containing a flu outbreak was not possible in such a study.

The adverse effects, however, were shown to be significant and added weight to the earlier studies, leading investigators to conclude that any prophylaxis attempt had to be balanced against the severity of the targeted disease.

At the time of the intervention, Dr. Strong said, the potential severity of the H1N1 pandemic was unknown, "and though we explained to the children and the families that there could be adverse effects, the uncertainty was such that people were more than happy to take the medication." Had the pandemic proven more severe, Dr. Strong said, the interventions may have seemed more reasonable in hindsight, and "it is all about trading off benefits and harms in the face of uncertainty."

In the case of 2009 H1N1, however, the adverse effects seem to have outweighed the benefits.

"Our findings have two important implications," Dr. Strong and colleagues concluded in their analysis. "Firstly, the benefits of mass treatment in an outbreak setting must clearly be greater than the benefits of targeted treatment. Secondly, any large scale regional or state level system for distribution of antiviral drugs for treatment should ideally include a robust quantification of an individual's probability of infection with influenza virus in order to avoid unnecessary treatment."

In an editorial accompanying Dr. Strong and collegues' findings, epidemiologist Johan Giesecke of the European Centre for Disease Prevention and Control wrote that though the British school studies "add to our knowledge of the spectrum of adverse events when oseltamivir is used for treatment and/or prophylaxis in large groups of children," they also demonstrate "that expected benefits must be weighed carefully against side effects when this drug is considered for outbreak situations."

For future outbreaks, Dr. Giesecke cautioned, it may be best to try to develop "a simple instrument to decide who in the group would be at the highest risk of exposure and infection."

Also, he wrote, "even if antivirals are given to school children in order to diminish spread in society, the studies cited here indicate that this effect is limited—influenza is spreading also outside the school yards." ■