Neuraminidase Inhibitors Blunt Flu Complications

VITALS

Major Finding: In the four trials totaling 475 high-risk patients, the rate of flu-related pneumonia, bronchitis, sinusitis, pharyngitis, and other complications was 8% in neuraminidase inhibitor–treated patients, compared with 25% with placebo.

Data Source: A meta-analysis of 11 placebo-controlled randomized trials of oseltamivir or zanamivir.

Disclosures: The meta-analysis was supported by the nonprofit Alfa Institute of Biomedical Sciences. Dr. Falagas reported having no financial conflicts.

BY BRUCE JANCIN

FROM THE ANNUAL EUROPEAN CONGRESS OF CLINICAL MICROBIOLOGY AND INFECTIOUS DISEASES

VIENNA — It's well established that timely prescription of the neuraminidase inhibitors can reduce the duration of seasonal influenza symptoms.

Now there's good evidence that the drugs are effective in reducing influenza-related complications, too, according to Dr. Matthew Falagas.

A meta-analysis of 11 placebo-controlled randomized trials—10 of them double blind—demonstrated that treatment with oseltamivir (Tamiflu) or zanamivir (Relenza) reduced the overall rate of flu-related complications by 26% in otherwise healthy patients with confirmed seasonal influenza, he reported at the meeting.

The magnitude of benefit was substantially greater in high-risk patients than in those who were previously healthy.

In the four trials totaling 475 high-risk patients, the rate of flu-related pneumonia, bronchitis, sinusitis, pharyngitis, and other complications was 8% in neuraminidase inhibitor–treated patients compared with 25% with placebo—for a 63% relative risk reduction, said Dr. Falagas, director of the Alfa Institute of Biomedical Sciences, Athens.

In the six trials totaling nearly 2,000 subjects in which administration of antibiotics was an end point, treatment with a neuraminidase inhibitor conferred a 23% reduction in the use of antibiotic therapy, Dr. Falagas continued.

The overall reduction in flu-related complications in the group receiving antivirals was driven by a highly significant 50% decrease in the rate of acute otitis media.

Indeed, the number of patients who needed to be treated (NNT) with a neuraminidase inhibitor to prevent one additional case of acute otitis media was 18.

There were consistent albeit weaker trends for lower rates of pneumonia, sinusitis, and the other flu-related complications in neuraminidase inhibitor–treated patients, none of which achieved significance.

For example, the incidence of pneumonia in the placebo group was just 2%, and it was estimated that roughly 330 patients would need to be treated with a neuraminidase inhibitor to prevent one additional case of pneumonia.

Only four trials included mortality as a study end point. There were no deaths.

The magnitude of benefit was substantially greater in high-risk patients.

DR. FALAGAS

The 11-trial meta-analysis involved 5,315 randomized patients.

Three of the trials were done in children; the rest were done in adults and adolescents.

The magnitude of risk reduction with neuraminidase inhibitor therapy was similar in children and adults, and with oseltamivir compared with zanamivir.

Whether these meta-analysis results apply to 2009 H1N1 influenza–related complications as well is anybody's guess, in Dr. Falagas's view, because there are as yet no good randomized controlled trials of neuraminidase inhibitors in patients infected with H1N1 flu.

He deemed the safety profile of the drugs to be acceptable.

There were no significant differences between the neuraminidase inhibitors and placebo in the rates or severity of any adverse events.

Although the rate of nausea/vomiting was 13% in the neuraminidase inhibitor–treated patients compared with 6.4% with placebo, this trend fell shy of statistical significance.

There was a 30% reduction in diarrhea with the neuraminidase inhibitors, but again this failed to reach significance.

Of note, none of the trials recorded neuropsychiatric adverse events.

One audience member observed that in February the World Health Organization recommended that the neuraminidase inhibitors generally be reserved for high-risk patients in the setting of H1N1 flu.

Does this new meta-analysis argue for using the drugs in otherwise healthy patients as well? he asked.

Not really, Dr. Falagas replied.

The observed overall significant reduction in flu-related complications occurred as a result of the sharp drop in acute otitis media, which "is not a killer disease," he said.

There was no significant reduction in the far more serious complication of pneumonia and no apparent treatment impact upon mortality.

It's thus quite reasonable in Dr. Falagas's view to save these fairly costly drugs for high-risk patients, thereby minimizing problems with the development of antiviral resistance.

"Our data are not in disagreement with the WHO recommendation that neuraminidase inhibitors are best for high-risk patients," the physician stressed. ■

Flu Vaccine May Reduce Risk of Acute Asthma Episodes

VITALS

Major Finding: The odds ratio of having acute asthma episodes for the vaccinated group was 0.78, when the instrumental variables method was used.

Data Source: A retrospective cohort of 138,935 children and adults with persistent asthma drawn from the MarketScan Commercial Claims and Encounters database, 22% of whom received the seasonal flu vaccine.

Disclosures: Dr. Saha said the findings do not represent the official position of the CDC. He reported no conflicts of interest.

BY ROXANNA GUILFORD-BLAKE

FROM THE NATIONAL IMMUNIZATION CONFERENCE

ATLANTA — Individuals with persistent asthma who received the seasonal influenza vaccination appeared to have fewer episodes of acute asthma than did those who were not vaccinated, according to Shubhayu Saha, Ph.D., of the Centers for Disease Control and Prevention's National Center for Environmental Health.

The findings corroborate current guidelines that recommend the vaccine for patients with persistent asthma, Dr. Saha said in a poster presentation at the conference sponsored by the CDC.

A retrospective cohort of children and adults who met the HEDIS (Healthcare Effectiveness Data and Information Set) definition of persistent asthma was drawn from the MarketScan Commercial Claims and Encounters database, Dr. Saha commented.

Those with chronic obstructive pulmonary disease, cystic fibrosis, and emphysema were excluded from the study.

Of 138,935 individuals in the cohort, 22% received the vaccine in the 2006-2007 flu season (August 2006 to March 2007).

Bivariate comparisons indicated that acute asthma episodes requiring an emergency department visit and/or hospitalization during the follow-up period were more frequent in those who received the vaccine (4.9%) than in those who did not (4.0%), Dr Saha and his investigators reported.

The findings of this study corroborate current findings that recommend the seasonal influenza vaccine for patients with persistent asthma, both children and adults.

However, those in the treatment group also were younger, had higher Charlson comorbidity scores, used more controller medications, and had more acute asthma episodes in the past.

To control for potential confounding where asthma patients with poorer prognoses also were more likely to get the influenza vaccine, the investigators used instrumental variable and propensity score matching methods to obtain unbiased estimates of the effect of vaccine on acute asthma episodes, Dr. Saha explained.

Each approach yielded similar and statistically significant results—results that were contrary to those of the bivariate comparisons.

Controlling for age, sex, region, health plan, comorbidity, and past asthma exacerbation, the instrumental variables method indicated the odds ratio of having acute asthma episodes for the vaccinated group was 0.78.

When the propensity score matching methods were used with four different matching algorithms, the vaccinated group consistently had an odds ratio of 0.7 for experiencing acute asthma episodes, the investigators reported.

"Estimates from both instrumental variable regression and propensity score matching show [the] significant protective effect of the influenza vaccination in reducing acute asthma episodes among individuals with persistent asthma in a population with employer-based health insurance," Dr. Saha said.

The researchers involved in this study acknowledged several limitations.

The data did not include factors such as ethnicity and income.

Moreover, the claims data did not capture vaccines received outside of the health plan—for instance, at a retail clinic or school.

Because the research was limited to an employer-based population, the findings cannot be readily generalized to other populations, Dr. Saha and his associates said. ■