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LEARNING OBJECTIVES

After studying the literature presented in this issue, participants should be able to:

- Recognize the impact of antiviral therapy on mortality and outcomes of influenza requiring hospitalization
- Address the importance of reporting early influenza symptoms in patients with conditions associated with high-risk complications

TARGET AUDIENCE

This educational activity is designed for pediatricians, primary care physicians, pediatric and family nurse practitioners, neonatologists, infectious disease specialists, allergists, pulmonologists, immunologists, and other healthcare professionals involved in the care and management of pediatric respiratory patients.

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Impact of Antiviral Therapy on Outcomes of Influenza Requiring Hospitalization in Ontario, Canada

Editor's Note: This article highlights the value of treating hospitalized high-risk adults with an effective antiviral. Although the study was not conducted with a pediatric at-risk population, the potential benefits of treating high-risk children with an influenza-related hospitalization can be inferred.

Influenza is a common cause of morbidity and mortality among older adults. Neuraminidase inhibitors have been shown to reduce the severity and duration of symptoms, as well as the risk of complications associated with influenza type A and type B infections. However, studies demonstrating these antiviral effects often involved relatively young, healthy adult outpatients treated within 48 hours after the onset of symptoms. To assess whether neuraminidase inhibitors may benefit patients with severe and/or complicated influenza, McGeer and colleagues conducted a prospective cohort study to examine the antiviral effect of a neuraminidase inhibitor, oseltamivir, on influenza-associated mortality, and outcomes of influenza requiring hospitalization in south central Ontario, Canada.

Patients, who were diagnosed with laboratory-confirmed influenza and were admitted to hospitals that participated in the Toronto Invasive Bacterial Diseases Network during the 2004-2005 and 2005-2006 influenza seasons (January 1, 2005 through May 31, 2006) were recruited for the study. Their demographic and medical data were collected by patient and

physician interview and chart review. The main outcome of this study was death within 15 days after symptom onset.

A total of 541 eligible patients were identified. The median rate of disease was 1.0 case per 1,000 hospital admissions during the 2004-2005 season and 0.44 cases per 1,000 admissions during the 2005-2006 season. Detailed clinical data were available for 512 of 541 eligible patients. There were 185 children (<15 years of age), none of whom died and none of whom were treated with antiviral drugs. Thus, children were excluded from further analysis. The median age of the 327 adults was 77 years (range, 15-99 years), 166 (51%) were men, 245 (75%) had a chronic

underlying illness, and 216 (71%) had been vaccinated against influenza. Of these adult patients, 184 (59%) presented to the emergency department within 48 hours after symptom onset, and most (278 patients [89%]) presented within 96 hours after the onset of symptoms. Moreover, 52 (16%) patients required intensive care unit admission, and 27 (8.3%) patients died within 15 days after symptom onset. Twenty-three deaths were judged to

The authors showed that oseltamivir therapy was active against influenza and associated with a significant reduction in mortality within 15 days after symptom onset.

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Disclosures:

* Dr Piedra is professor of pediatrics and molecular virology and microbiology at Baylor College of Medicine, Houston, Texas. He has indicated that he receives grant/research support from MedImmune, Inc., Sanofi Pasteur and Novartis Pharmaceuticals; is a speaker for MedImmune, Inc.; and is an ad hoc consultant for Hoffman-La Roche, Inc., MedImmune, Inc., Novartis Pharmaceuticals, Sanofi Pasteur and Merck & Co., Inc.

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Impact of Antiviral Therapy (Continued)

be attributable to influenza. Coded discharge diagnoses included influenza in only 187 (57%) of the patients.

At hospital admission, most patients (290 patients [89%]) were treated with antibacterial agents, and 106 (32%) patients were also prescribed antiviral drugs. Except for 3 patients receiving amantadine, all 103 patients were prescribed oseltamivir 75 mg twice daily for 5 days or an equivalent dose after adjustment for renal failure. The authors showed that oseltamivir therapy was active against influenza and associated with a significant reduction in mortality within 15 days after symptom onset (odds ratio [OR], 0.21; 95% confidence interval (CI), 0.06-0.80). Significant reduction in mortality was also observed when the analysis was restricted to

adults ≥ 65 years old (OR, 0.24; 95% CI, 0.06-0.92). Oseltamivir therapy had no apparent impact on length of hospital stay in survivors.

These observations suggested that influenza remains a significant burden of illness in this highly vaccinated population in Ontario, Canada. Treatment with oseltamivir was associated with significant reduction in mortality in adult patients hospitalized with influenza even though antiviral therapy was initiated in many patients after 48 hours of symptom onset.

McGeer A, Green KA, Plevneshi A, et al. Antiviral therapy and outcomes of influenza requiring hospitalization in Ontario, Canada. *Clin Infect Dis*. 2007;45:1568-1575.

COMMENTARY

H. CODY MEISSNER, MD, Chief, Division of Pediatric Infectious Disease, Tufts-New England Medical Center, Boston, Massachusetts.

During non-pandemic years, influenza in the United States causes an average of >35,000 excess deaths and >200,000 hospitalizations, resulting in greater morbidity and mortality than that caused by all other vaccine-preventable diseases combined. Annual vaccination is the most important strategy for disease prevention. Antiviral medications (zanamivir, oseltamivir) demonstrate activity against both influenza A and B viruses and are licensed for both treatment and prophylaxis. Both medications have been shown to reduce the duration of symptoms in patients by about 1 day relative to placebo recipients when therapy is initiated within 48 hours of onset of symptoms—particularly when disease is caused by type A influenza. Most studies evaluating influenza antiviral efficacy have been conducted among otherwise healthy pediatric and adult outpatients. Data supporting the effectiveness of antiviral therapy for treatment of persons at increased risk for serious complications are limited; therefore, the study by McGeer et al suggesting that a reduced mortality rate among hospitalized older adults, including those with comorbidities, is reassuring.

Patient Knowledge and Attitudes About Antiviral Medication and Vaccination for Influenza

Editor's Note: This article addresses the adult's knowledge of antivirals against influenza. It is important that adults and parents be informed about available agents for treating influenza in order to consider them as a potential treatment for their children, as well as to understand the optimal benefits of timely treatment with antiviral therapy.

It has been shown that influenza affects 5% to 20% of the population each year, and influenza-associated illness is responsible for nearly 51,000 deaths and 226,000 hospitalizations annually in the United States. While vaccination remains a vital method for influenza control and prevention, the neuraminidase inhibitors oseltamivir and zanamivir have been shown to reduce influenza requiring hospitalization, influenza-related bacterial complications, and the duration of illness.

Appropriate use of antiviral medications is pivotal for effective management of acute influenza, and requires education of both physicians and their patients. Guidelines for using these drugs have been provided by the Centers for Disease Control and Prevention; however,

antiviral medications for influenza treatment and prevention remain underutilized. The objectives of this study were to assess patient knowledge and attitudes about antiviral medication and vaccination for influenza.

Gaglia and colleagues conducted a cross-sectional survey of adult patients in an internal medicine clinic from April through June 2006. Of 400 patients who were offered the survey, 280 patients (70%) responded and completed the survey. Thirty-eight percent of respondents had at least 1 disease associated with a high risk of influenza-related complications. Only 55% of the respondents received influenza vaccination for the most recent influenza season.

Overall knowledge regarding antiviral medication was poor in these patients. Eight antiviral

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Patient Knowledge and Attitudes (Continued)

knowledge questions were asked, and the mean percentage of correct answers was 40%. One patient (<1%) answered all questions correctly, while 47 (18%) answered all questions incorrectly. Two hundred five patients (84%) were willing to pay something, but only 90 respondents (37%) were willing to pay >\$20 for antiviral medication. For antiviral treatment to be effective, patients must present promptly to their physician. However, only 37 patients (13%) reported calling their physician within 48 hours after the onset of influenza-like symptoms.

Moreover, patients with conditions associated with a high risk of complications from influenza were not more knowledgeable about antiviral medication than other patients, nor were they more likely to report calling their physician within 48 hours after the onset of symptoms or to report receipt of influenza vacci-

nation for the previous influenza season.

Gaglia et al concluded from their survey that patients are poorly informed about antiviral medication and its benefits. Patient knowledge deficits and the relatively high cost of the medication are among the potential barriers to effective treatment with antiviral drugs. Patients need to be better informed of the potential benefit of antiviral therapy and the need to present early for treatment. More efforts should be focused on patients who are at high risk for influenza and its complications. Furthermore, development of education programs on antiviral medication and vaccination for physicians and patients is recommended.

Patient knowledge deficits and the relatively high cost of the medication are among the potential barriers to effective treatment with antiviral drugs.

Gaglia MA Jr, Cook RL, Kraemer KL, et al. Patient knowledge and attitudes about antiviral medication and vaccination for influenza in an internal medicine clinic. *Clin Infect Dis*. 2007;45:1182-1188.

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