New Antibiotic Works In Bronchitis Flare-Up

BY SHERRY BOSCHERT
San Francisco Bureau

SAN FRANCISCO — Clinical signs and symptoms of acute bacterial exacerbation of chronic bronchitis improved in patients treated with 5 days of an experimental ketolide antibiotic, cethromycin, or 7 days of levofloxacin, David A. Eiznhamer, Ph.D., reported.

The phase III, double-blind, multicenter trial randomized 509 outpatients aged 40 years or older to oral therapy with 150 mg of cethromycin per day or 500 mg of levofloxacin per day. Improvements at 14-19 days after enrollment were not significantly different between groups, but the investigators could not rule out the possibility, based on statistical analyses, that cethromycin might be inferior to levofloxacin at those doses, Dr. Eiznhamer said in a poster presentation at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy.

The lead investigator was S. Bukofzer of Abbott Laboratories, which is an investor in Advanced Life Sciences, and all of the investigators came from the two companies.

The 150-mg dose of cethromycin was chosen to minimize adverse events. A new study comparing a 300-mg daily dose of cethromycin with levofloxacin therapy is warranted, said Dr. Eiznhamer of Advanced Life Sciences, the company that is developing cethromycin.

The drug is also being studied in phase III trials for the treatment of community-acquired pneumonia. Advanced Life Sciences plans to submit a new drug application in 2007 with a goal of obtaining Food and Drug Administration approval in 2008, he said in an interview. The conference was sponsored by the American Society for Microbiology.

In an intent-to-treat analysis of 450 patients in the current study, clinical cure was seen in 81% of patients on cethromycin and 84% of those on levofloxacin. Clinical cure was defined as the resolution of at least one clinical symptom (dyspnea, sputum volume, purulence, cough, or fever) and improvement in at least half of the other symptoms.

An intent-to-treat analysis of overall pathogen eradication rates in 231 patients found eradication in 85% of the cethromycin group and 87% of the levofloxacin group.

For *Streptococcus pneumoniae,* however, cethromycin eradicated the organism in 14 (78%) of 18 patients, compared with 23 (92%) of 25 patients given levofloxacin. ■

Four-Hour Antibiotic Rule for CAP May Hamper Care

TORONTO — Adherence to guidelines that recommend early use of antibiotics may lead to inaccurate diagnosis of community-acquired pneumonia and inappropriate use of antibiotics, according to a study presented at the annual meeting of the Infectious Diseases Society of America.

The IDSA guidelines for community-acquired pneumonia (CAP), published in November 2003, recommend the initiation of antibiotics within 4 hours of hospitalization—an indicator that has been linked to incentive compensation of third-party payers to hospitals, said Dr. Manreet K. Kanwar of St. John Hospital and Medical Center in Detroit.

"It's possible that prolonging the antibiotic window to 6 hours may be enough time to better evaluate a patient," Dr. Kanwar suggested.

To determine the effect of this recommendation on CAP diagnosis and associated antibiotic utilization, Dr. Kanwar and colleagues reviewed the charts for 518 patients older than age 21 years both prior to (January through June 2003) and following (January through June 2005) the publication of the guidelines. They collected data on clinical signs and symptoms at presentation, as well as chest x-ray findings, preantibiotic blood cultures, time to antibiotic administration data, Pneumonia Severity Index (PSI) scores, ICU transfer rates, and mortality data.

There were no significant differences between the 199 patients in the preguideline group and the 319 in the postguideline group in age, gender, PSI score, ICU transfer rates, or mortality. In the postguideline group, 66% received antibiotics within 4 hours of triage, compared with 54% of the preguideline patients. The percentage of blood cultures prior to antibiotic administration was higher (70%) in the 2005 group, compared with 47% in the 2003 group. But the final diagnosis of CAP dropped significantly, from about 76% in 2003 to 59% in 2005, and the mean antibiotic utilization per patient increased significantly, Dr. Kanwar reported.

Increases in the misdiagnosis of CAP and inappropriate antibiotic use as a result of compliance with the 4-hour antibiotic rule suggest that many patients received antibiotics for noninfectious processes.

Dr. Kanwar reported having no related financial disclosures.

—Diana MaHoney

THE EFFECTIVE PHYSICIAN

Pertussis Prevention

BY WILLIAM E. GOLDEN, M.D., AND ROBERT H. HOPKINS, M.D.

Background

Pertussis is an acute cough illness that remains endemic in the United States despite routine childhood immunization since the 1940s. In June 2005, a vaccine containing acellular pertussis antigens, tetanus toxoid, and reduced diphtheria toxoid (Tdap) was licensed for use in persons aged 11-64 years. The Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices has recently published recommendations for the use of Tdap in adults.

Conclusions

Pertussis, an acute bacterial respiratory infection spread by coughing or sneezing, has an incubation period of 7-10 days. The classic illness begins with 1-2 weeks of coryza, intermittent cough, and less commonly, high fever (the catarrhal phase). This is followed by 4-6 weeks of spasmodic cough with posttussive emesis and inspiratory whoop (paroxysmal phase). Finally, the convalescent phase of gradual improvement occurs over a period of 4-6 weeks.

Patients with pertussis are most contagious during the catarrhal and early paroxysmal phases but may remain infectious for more than 6 weeks. Antibiotic therapy begun after the onset of cough does not affect the course of the illness but is recommended to reduce disease transmission.

Since the 1980s, the number of reported cases of pertussis has increased, particularly in adolescents and adults. Pertussis is the least well controlled of the reportable vaccine-preventable diseases in this country.

Adults with pertussis often have protracted cough and may have secondary complications; however, the illness is most severe in infants under 12 months old. Adult caregivers are a likely source of infection in many infant cases. Vaccination is the most effective strategy to prevent the morbidity of pertussis and reduce its spread.

Diagnostic testing for pertussis is less than ideal: Culture is 100% specific, but the fastidious nature of the bacterium makes the sensitivity quite variable. Polymerase chain reaction testing is used in many facilities, but protocols are not standardized. Serology and direct fluorescent antibody techniques are available but are not recommended by the CDC.

Nosocomial outbreaks of pertussis have been documented in inpatient, outpatient, and residential care settings. Health care workers can be infected with pertussis and potentially spread this illness to their patients.

Implementation

Tdap vaccine should be given to almost all adults under age 65 years. It may be used in place of one dose of tetanus-diphtheria toxoids (Td) vaccine at the time a routine booster dose is due or may be administered in place of Td for wound prophylaxis. Safety has been demonstrated for vaccine intervals as short as 2 years from the last Td immunization.

Adults with a history of prior pertussis illness should receive Tdap according to the above recommendations. The duration of immunity after native illness is unknown but may begin to wane within 7 years. There is no increased vaccination risk for those with prior pertussis illness.

In the United States, only the Sanofi Pasteur Tdap vaccine Adacel has been licensed for use in persons 19 years of age and older. Adolescents may be vaccinated with Adacel or the GlaxoSmithKline Tdap vaccine Boostrix, which is not approved for those over 18 years.

Tdap vaccines have not been studied in adults 65 years and older and are not licensed for this age group.

Vaccination of adults under 65 years of age who have or anticipate contact with infants is recommended. Ideally, the vaccine should be given at least 2 weeks prior to infant contact to allow the antibody response to develop. Infants should be vaccinated on time for pertussis with the appropriate routine childhood vaccines.

Tdap vaccine should be given to women of childbearing age prior to pregnancy. It may be given immediately post partum in new mothers not previously vaccinated, including those who are breast-feeding. Because of lack of data on use during pregnancy, the manufacturer has set up a registry of women vaccinated during pregnancy; information on these patients should be reported to Sanofi Pasteur (800-822-2463).

Tdap vaccination is recommended for health care providers (who have not previously received Tdap) as soon as possible; those providing direct patient care to infants under 12 months of age are the highest priority, followed by all others providing direct patient care.

Investigation and control of pertussis after unprotected exposure in health care settings is labor and time intensive. Cost-benefit analyses have supported the offset of vaccine cost by reduced investigation and control of outbreaks.

Tdap may be given at the same time as other vaccines as long as each is administered at a different injection site with a separate syringe.

Health care facilities and all adults should maintain updated records of immunization status.

Reference

Kretsinger, Katrina, et al. Preventing tetanus, diphtheria, and pertussis among adults: Use of tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine. MMWR 2006;55(RR-17):1-37.

DR. GOLDEN *(right) is professor of medicine and public health and* DR. HOPKINS *is program director for the internal medicine/pediatrics combined residency program at the University of Arkansas, Little Rock. Write to Dr. Golden and Dr. Hopkins at our editorial offices or imnews@elsevier.com.*