

Add Steroids to H1N1-Related ARDS Therapy

BY BRUCE JANCIN

SAN DIEGO — Patients with suspected pandemic influenza A(H1N1)-associated acute respiratory distress syndrome responded favorably overall to an ICU treatment course of high-dose oseltamivir and prolonged low- to moderate-dose corticosteroids in a pilot study.

A marked improvement in lung injury scores was seen in 11 of 13 patients by day 7, and the 15% in-hospital mortality rate was lower than expected in such a critically ill population, Dr. G. Umberto Meduri said at the annual meeting of the American College of Chest Physicians.

On the basis of these findings and the extensive basic science rationale supporting prolonged steroid therapy in acute respiratory distress syndrome, the French Ministry of Health has announced it will fund a randomized controlled trial of this treatment protocol in patients with H1N1 influenza-associated ARDS. However, the results won't be in until after the current seasonal outbreak of 2009 H1N1 flu has ebbed, according to Dr. Meduri of the University of Tennessee, Memphis.

He reported on 13 consecutive patients

who presented to an ICU in a tertiary-care hospital in Buenos Aires with suspected H1N1 influenza and hypoxemic respiratory failure during a 3-week period. Eight were in septic shock. Six had severe ARDS as defined by a $\text{PaO}_2/\text{FiO}_2$ (partial pressure of oxygen in arterial blood to the fraction of inspired oxygen) ratio of 120 or less and a positive end-expiratory pressure of at least 12 cm H_2O ; patients this ill typically have an in-hospital mortality of about 55%, he said.

By day 7 in the ICU, 11 of 13 patients showed significantly improved lung function as defined by at least a 1-point drop on the 4-point Lung Injury Scale, or a score below 2. The degree of improvement was similar among patients with severe ARDS and those with more moderate hypoxemic respiratory failure.

Five patients were extubated by day 7, another 6 by day 14, and 2 later. The mean hospital length of stay was 18.7 days. Four patients developed ventilator-associated pneumonia, and 5 nondiabetic patients required insulin therapy, but there were no cases of GI bleeding or neuromuscular weakness. All 13 survivors were discharged home with no supplemental oxygen requirement.

One patient, an alcoholic with cirrhosis who developed septic shock and severe ARDS, died from progressive multiorgan failure on day 15. The other death was believed to be caused by a pulmonary embolism in a patient with co-



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morbid chronic obstructive pulmonary disease, an outcome that underscores the importance of continuing thrombotic prophylaxis at least until hospital discharge, Dr. Meduri noted.

Upon ICU admission, the treatment protocol entails starting oseltamivir (Tamiflu) via nasogastric tube at 150 mg twice daily for 5 days, followed by 75 mg twice daily for 3-5 days as dictated by the patient's clinical course.

Although Dr. Meduri's protocol originally called for reserving methylpred-

nisolone for patients with severe ARDS and using hydrocortisone at 300 mg/day in the others, he now believes it's simpler to use methylprednisolone in all patients, bearing in mind that those with severe ARDS need higher doses.

Upon ICU admission, patients receive a 60-mg intravenous bolus of methylprednisolone, then a continuous infusion at 60 mg/day for days 1-14, tapering to 30 mg/day on days 15-21, 15 mg/day on days 22-25, and 10 mg/day on days 26-28.

If a patient presents with severe ARDS or worsens to that status at any point, the methylprednisolone dose is 1 mg/kg per day, tapered as detailed in Dr. Meduri's earlier randomized trial involving patients with early severe ARDS unrelated to H1N1 flu (Chest 2007;131:954-63). In the H1N1 flu pilot study, patients remained on steroids for an average of 21 days.

One audience member noted that the 15% hospital mortality in the pilot study was comparable to mortality in patients with extremely severe ARDS using extracorporeal membrane oxygenation (ECMO).

"Most of the ICUs in the world don't have ECMO. Steroids are a good alternative," Dr. Meduri replied. ■

Some Health Care Workers Still Not Immune to Myths About Flu Vaccine

BY BETSY BATES

Fears and misconceptions about influenza vaccination became apparent in a survey of health care workers conducted at a large tertiary children's hospital in the Midwestern United States.

Researchers in Kansas City, Mo., administered a 44-question survey to 63 physicians, 135 nurses, and 376 allied health care workers at a 317-bed children's hospital where seasonal influenza immunization rates are high, Dr. Mary Anne Jackson said at a press briefing during the annual meeting of the Infectious Diseases Society of America (IDSA).

The survey revealed "significant gaps in knowledge" about influenza transmission, nosocomial spread, and vaccine efficacy and safety among all levels of health care professionals.

The results were "somewhat surprising" for a highly educated, highly immunized group of health care workers who are known to be at high risk of acquiring seasonal influenza and passing it on to vulnerable patients, said Dr. Jackson, chief of infectious diseases at Children's Mercy Hospital in Kansas City.

Physicians were significantly more likely than nurses or other health care workers to know that

they are at high risk of influenza, that the vaccine prevents spread of the disease, and that it is a safe vaccine for adults and children.

Compared with physicians, other health care workers were significantly more likely to erro-



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DR. JACKSON

neously believe that the vaccine can cause influenza.

Further, many allied health care workers and nurses also believed, incorrectly, that an individual must be symptomatic to transmit the influenza virus.

About 75% of physicians advocated policies mandating influenza immunization among health care workers, compared with fewer than half of nurses or allied health care professionals surveyed.

Mandating influenza immunization for health care workers, a highly controversial proposition briefly enacted in New York State in response to the H1N1 influenza pandemic this year, was rescinded by New York Gov. David

A. Paterson on Oct. 22. The governor's office stated that the mandatory vaccination policy for health care workers was dropped due to shortages of vaccine for high-risk populations. Widespread protests, however, were speculated to have played a role in the decision as well.

Based on her study findings and recent public responses to H1N1 vaccine mandates for health care workers, Dr. Jackson concluded that "mandates are going to be difficult."

On the other hand, educational efforts and campaigns aimed at getting health care workers immunized "have failed dismally in most institutions." At Children's Mercy Hospital, a vigorous campaign conducted over several years finally achieved an 85% influenza vaccine rate among employees, compared with an average 40% rate among health care workers across the country.

The rising immunization rate in her institution proved to have a ripple effect, she said. When health care workers were vaccinated against the seasonal influenza virus, their children also were more likely to receive the vaccine.

Dr. Jackson reported no relevant financial disclosures. ■

Reduced Flu Mortality Linked to Statin Use

BY MITCHEL L. ZOLER

PHILADELPHIA — Patients taking a statin at the time they were hospitalized for an influenza infection were significantly less likely to die while in the hospital or immediately after, compared with their counterparts who were not on a statin, in an observational study of 2,800 patients.

The study used data collected during the 2007-2008 flu season by the Emerging Infections Program Hospitalized Influenza Surveillance System. This program collected data on laboratory-confirmed influenza hospitalizations in 10 states, representing 7% of the U.S. population. The study reviewed records for 2,800 patients hospitalized with influenza, of whom 801 used a statin while in the hospital.

During their time in the hospital and the 30 days following hospitalization, the mortality rate was 3.2% among the 1,999 patients who did not take a statin, and 2.1% among statin users. A multivariable model that adjusted for differences between these two

groups found that patients taking a statin had a statistically significant 54% reduced risk for death, reported Meredith Vandermeer, an influenza surveillance epidemiologist with the Oregon Public Health Division in Portland.

"This is the first study to look for a relationship between statin use and death in patients hospitalized with laboratory-confirmed influenza," Ms. Vandermeer said. She speculated that the finding might reflect the anti-inflammatory effect of statins, and suggested that statins are a "possible useful adjunct to antiviral medications and vaccines" for treating influenza infection.

She also cautioned that the study couldn't control for all variables that might have contributed to the effect, and that further study is needed. "We are not saying that patients hospitalized for influenza should be treated with a statin."

This "probably means that if you are on a statin for your cholesterol, there may be some extra benefits," said Dr. Andrew Pavia, a professor at the University of Utah, Salt Lake City. ■