Vaccine Combinations Appear Safe, Effective

BY MITCHEL L. ZOLER

PHILADELPHIA — Administering two or more vaccines simultaneously was safe and immunogenic in results from two separate studies reported at the annual meeting of the Infectious Diseases Society of America.

One study assessed the immune response when healthy girls received concomitant vaccination with a human papillomavirus (HPV) vaccine along with a vaccine for tetanus, diphtheria, and pertussis (Tdap), and a third vaccine with a quadrivalent, conjugated meningococcal formulation (MCV4). The second study tested coadministration of the 2007-2008 seasonal influenza vaccine with an investigational, 13-valent, conjugated pneumococcal vaccine in adults aged 50-59 years.

The results from combined administration of the HPV, Tdap, and meningococcal vaccines are especially relevant to practice because all three are already approved for U.S. use, and the concept of delivering all three simultaneously received endorsement by the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices in 2007 (MMWR 2007;56:1-24). The only piece missing until now was data showing that the concomitant strategy was safe and immunogenic—something the new study now provides, said Cosette M. Wheeler, Ph.D., professor of pathology and obstetrics and gynecology at the University of New Mexico in Albuquerque.

All three vaccines are recommended for administration to adolescent girls, and bundling them together at one time would potentially increase compliance, Dr. Wheeler said in an interview (although the HPV vaccine requires three doses administered over a 6-month period).

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Her study used the Cervarix formulation of HPV vaccine, the Boostrix formulation of Tdap, and the Menactra formulation of meningococcal vaccine. The Cervarix and Boostrix vaccines are marketed by GlaxoSmithKline, which funded the study. Menactra is marketed by Sanofi Pasteur. Dr. Wheeler disclosed that in addition to receiving research support from GlaxoSmithKline, she also received funding for studies from Merck, which markets the HPV vaccine Gardasil, and from Roche Molecular Systems.

The study enrolled 1,283 healthy girls aged 11-18 years at 48 U.S. centers. The researchers randomized the participants to one of six different treatment schemes: HPV vaccine only at months 0, 1, and 6; HPV with Tdap at month 0 followed by HPV only at months 1 and 6; HPV with the meningococcal vaccine at month 0 followed by HPV only at months 1 and 6; all three vaccines at month 0 followed by HPV only at months 1 and 6; Tdap only at month 0 followed by HPV only at months 1, 2, and 7; and MCV4 only at month 0 and then HPV only at months 1, 2, and 7.

The results showed that 1 month after the subjects received any of the concomitant doses, their immune responses all fell within the prespecified criteria for noninferiority, compared with the responses when the vaccines were administered individually. Also, the immune responses to the HPV vaccine 6 months after the final dose, when one dose was given in combination with one or two of the other vaccines, were noninferior to the responses to the HPV vaccine given by itself. The recipients of two or more simultaneous vaccines also had similar incidence rates for solicited local reactions—pain, redness, or swelling, and similar solicited rates of system reactions, including headache, fatigue, and myalgia.

The second study examined concomitant administration of an investigational, 13-valent, conjugated pneumococcal vaccine and the trivalent, seasonal influenza vaccine of 2007-2008 in 1,106 healthy adults aged 50-59 years. The pneumococcal vaccine is similar to a 7-valent vaccine that already has U.S. approval for use in infants and children, Prevnar, with added antigens so that the vaccine protects against strains that commonly cause community-acquired pneumonia, said Dr. Robert W. Frenck Jr., of Cincinnati Children's Hospital Medical Center.

The pneumococcal vaccine was developed by Wyeth (which recently was acquired by Pfizer Inc.), which funded the study. Dr. Frenck had no other disclosures for his study.

One month after vaccination, the immune responses to both vaccines in people who received them simultaneously fell within the prespecified noninferiority limit, compared with the responses in people who received the two vaccines 1 month apart. Simultaneous administration also resulted in similar rates of local and systemic reactions compared with giving the vaccines 1 month apart. ■

To Date, No Safety Signals of Concern With H1N1 Vaccine

BY MIRIAM E. TUCKER

BETHESDA, MD. — Monitoring of influenza A(H1N1) vaccine safety in studies conducted across multiple U.S. government agencies have shown no safety signals of concern so far, nationally or internationally.

The multiple data collection efforts—some preexisting and others a result of the pandemic H1N1 outbreak—represent "strengthened collaboration and communication among government agencies and internationally, with enhanced capacity for timely signal detection, strengthening, and confirmation," Dr. Hector Izurieta told the Food and Drug Administration's Vaccines and Related Biological Products Advisory Committee.

In addition to the FDA, other participating agencies include the Centers for Disease Control and Prevention, the Department of Defense, the Department of Veterans Affairs, the Centers for Medicare and Medicaid Services, and the Indian Health Service, Dr. Izurieta, chief of the FDA's analytic epidemiology branch, said in an interview.

For example, the CDC is currently evaluating 205 reports of serious adverse events following H1N1 vaccine in the Vaccine Adverse Events Reporting System (VAERS). Of those, 70 are among pregnant females. All but 13 were nonserious and none involved maternal death.

Eight deaths following receipt of H1N1 vaccine have been reported to VAERS, including two following live attenuated (intranasal) vaccine and six after inactivated (injected) vaccine. The three that have been evaluated so far had severe underlying conditions. There have been 29 reported cases of anaphylaxis, which is consistent with published estimates following other vaccinations, he said.

Two cases of "possible or probable" Guillain-Barré syndrome have been reported within 1 day of H1N1 vaccine receipt. The short interval "decreases but does not eliminate" the possibility that H1N1 vaccine caused the event. However, to date the rate of reported GBS cases is less than the background rate in the population, Dr. Izurieta said.

Dr. Claudia Vellozzi of the CDC's Immunization Safety Office described the Vaccine Safety Datalink (VSD), an active surveillance program of both the CDC and managed care plans that cover more than 9.5 million people, or 3.1% of the U.S. population, and is used to follow up on safety "signals" obtained from VAERS.

VSD analyses of pregnant women and of 10 GBS cases identified so far have shown no significant associations with either H1N1 or seasonal vaccine, although it's still early, she said.

Dr. Richard Platt of Harvard Pilgrim Health Care and Harvard Medical School, Boston, described a new safety analysis that his institution will conduct in collaboration with health plans covering approximately 25 million people and nine state immunization registries comprising a total population of 14 million; it is called Post-Licensure Rapid Immunization Safety Monitoring. ■

Deformational Plagiocephaly Not Tied to Frequent OM

BY LEANNE SULLIVAN

Children with deformational plagiocephaly do not have significantly higher rates of otitis media, compared with children in the general population, according to a recent study.

Deformational plagiocephaly previously has been reported to be associated with otitis media (OM), but this study did not find a significant association. Children in the study with more severe deformity had a higher rate of ear infection, compared with those with less severe deformity, but this trend also was not significant, wrote Adam Purzycki and his colleagues at the Wake Forest University Medical Center's North Carolina Institute for Cleft and Craniofacial Deformities, in Winston-Salem.

The retrospective study included 1,112 children with deformational plagiocephaly who presented between February 2004 and June 2006. Age at presentation was 3-12 months (mean 5.6 months); 723 were boys and 389 were girls. Of this group, 559 (50.3%) were reported by their parents as having had at least one ear infection, Mr. Purzycki and his coworkers said.

In the patients with deformational plagiocephaly, the incidence of OM was not higher than that reported by the Centers for Disease Control and Prevention for children in general. The severity of deformity showed a nonsignificant correlation with the number of ear infections: Of the 793 patients with the milder plagiocephaly severity levels I-III, 387 (48.8%) had had at least one ear infection. Of the remaining 319 patients with higher severity levels IV-V, 172 (53.9%) had been diagnosed with at least one ear infection. The number of ear infections was determined by self-reports from patients' guardians (J. Craniofac. Surg. 2009;20:1407-11).

A subset of 124 patients were examined by tympanometry to diagnose clinical or subclinical OM or fluid collection resulting from abnormal drainage, which would suggest eustachian tube dysfunction. Of these, 121 had readings indicative of OM. "The significantly high percentage of typanogram readings that pointed to otitis media, whether clinical or subclinical, suggests an overall malfunction of the middle ear drainage function of the eustachian tube in these children," they wrote.

No conflicts of interest or study funding were reported. ■