Pentacel Vaccine Safety, Efficacy Data Mounting

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SAN FRANCISCO — Two phase II clinical studies of a combination vaccine suggest that it is safe and immunogenic, investigators reported in poster presentations at the annual meeting of the Infectious Diseases Society of America.

An open study of 3,022 healthy infants found comparable immunogenicity and safety results among four lots of the Pentacel vaccine, which is used to immunize against diphtheria, tetanus, pertussis, polio, and *Haemophilus influenzae* type b (Hib), reported Kathryn M. Edwards, M.D.

Seroresponse and seroprotection rates were immunogenic with vaccine from all four lots despite coadministration with pneumococcal conjugate (Prevnar) vaccine. In some previous reports, Prevnar vaccine was associated with interference with coadministered pertussis or Hib vaccines, said Dr. Edwards, professor of pediatrics at Vanderbilt University, Nashville, Tenn. She has received funding from Sanofi and from Aventis-Sofitel, part of the Sanofi-Aventis Group, which makes the vaccine. Her associates in the study were employed by Sanofi Pasteur Inc.

Sanofi-Aventis has applied to the Food and Drug Administration for licensing to market Pentacel in the United States. If approved, the four-dose series of Pentacel could reduce the number of recommended childhood vaccine injections by two. Pentacel is licensed for pediatric use in nine countries.

In the current study, the largest single study of Pentacel vaccine in the United States, healthy infants at 23 clinical centers received concomitant Pentacel and Prevnar vaccines at 2, 4, and 6 months of age. They previously had received hepatitis B vaccine, with second and third doses of that vaccine given at 2 and 6 months of age.

Systemic reactions within 3 days of Pentacel vaccination included fever in 11%-20% of infants, fussiness in 60%-71%, and crying in 35%-45%. Two of three serious adverse events that were temporally associated with vaccination were considered to be possibly related to the vaccine.

One 2-month-old developed a hypotonic hyporesponsive episode (HHE) that began 2 hours after the first dose and lasted 8 hours. The infant recovered without treatment, had no sequelae, and received no further doses. This is the first episode of HHE reported in more than 16,000 doses of Pentacel administered so far, Dr. Edwards noted. Another 2-month-old had about eight afebrile seizure episodes 3 days after the first dose, each lasting less than 1 minute. The child was hospitalized for a day and was discharged after normal brain imaging and EEG results. Exam results 2 weeks later were normal. A febrile seizure in a third child with acute otitis media was considered unrelated to the vaccine.

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A separate study presented at the meeting extended previous results from a randomized, controlled, multicenter study that found comparable safety and immunogenicity among three doses of Pentacel vaccine; individual administration of vaccines for polio and Hib; and a combination vaccine for diphtheria, tetanus, and acellular pertussis (DTaP).

The current data looked at a fourth dose of Pentacel vaccine in 430 infants or separate administration of the Hib and DTaP vaccines in 419 infants at 15 months of age. The protocol criteria were met by 371 in the Pentacel group and 349 in the control group. The vaccines were coadministered with three doses of Prevnar vaccine and two doses of hepatitis B vaccine in the first part of the study.

Immune responses to each antigen remained comparable between the Pentacel vaccine group and the control group after the 15-month doses in the second part of the study, reported Fernando Noriega, M.D., of Sanofi Pasteur, Swiftwater, Penn., and his associates.

There were no serious adverse events related to the vaccine and no reports of HHE. The investigators found no clinically relevant differences between the safety profiles of the Pentacel vaccine and the DTaP vaccine, Dr. Noriega said. ■

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