ACIP Expands Maximum Ages for Rotavirus Shots

ARTICLES BY
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ATLANTA — The Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention voted at its summer meeting to expand the maximum ages at which the recently approved infant rotavirus vaccine Rotarix and the established RotaTeq vaccine can be given to simplify and "harmonize" the routine childhood immunization schedule.

The Advisory Committee on Immunization Practices (ACIP) had just voted to add GlaxoSmithKline's infant rotavirus vaccine Rotarix to the schedule.

Rotarix, which was licensed by the Food and Drug Administration in April this year, represents a second oral vaccine option for immunizing infants against rotavirus. Merck's RotaTeq was recommended for routine use in infants by ACIP in Feb. 2006 (MMWR 2006;55[RR-12]1-13).

The two vaccines are equally efficacious, conferring 85%-98% protection against severe rotavirus diarrheal disease and 72%-87% protection against any rotavirus disease. However, they differ in administration schedules: Rotarix is a two-dose series given at 2 and 4 months of age, and RotaTeq is given in three doses at 2, 4, and 6 months. Thus the committee voted to change the maximum ages at which the vaccines can be given to simplify the schedule.

The ACIP did not express a preference for either vaccine, but it did advise the series be completed with the same product whenever possible. If a child switches providers and the product used previously is not available or unknown, the series should be completed with the available product.

Once adopted by the CDC, the new ACIP rotavirus immunization guidelines also are expected to harmonize with those of the American Academy of Family Physicians (AAFP) and the American Academy of Pediatrics (AAP).

Dr. Douglas Campos-Outcalt, the AAFP liaison to ACIP, also expressed support for the recommendation as well as for the availability of a second rotavirus vaccine option: "I think this will make it easier." He noted that surveys by the CDC and AAFP have found that family physicians have been slower than have pediatricians to adopt RotaTeq in the 2 years since it was licensed, in part because of concerns about cost-effectiveness.

"Hopefully, now that there are two vaccines that are equally effective and equally safe, they'll start competing on price and the cost-effectiveness ratio will [improve]," said Dr. Campos-Outcalt of the University of Arizona, Phoenix.

Both liaisons for the AAFP and AAP said the boards of their respective academies will consider approval of the guidelines once the CDC finalizes them, a process that could take a period of several months for both groups.

Dr. Margaret M. Cortese of the CDC's Division of Viral Diseases, outlined the specifics of the document drafted by a working group and which ACIP subsequently approved. The first dose of either vaccine should be administered to infants aged 6-14 weeks and should not be initiated in those aged 15 weeks or greater. This effectively adds 2 weeks to the 2006 recommendation for RotaTeq, which had said dose 1 should be given at age 6-12 weeks.

The interval between doses should be 4 weeks or greater, and all doses should be given by age 32 weeks. Committee members debated whether the language of the final document should say "8 months 0 days" instead of "32 weeks." That decision will be made later by CDC. Either way, this would represent an expansion from the Rotarix clinical trials, which used 24 weeks as the maximum age for dose 2, Dr. Cortese said.

Because the oral applicator of Rotarix contains latex and that of RotaTeq doesn't, any infant with a previous severe anaphylactic reaction to latex should receive Rotateq and not Rotarix. The final language also may include a "precaution" about using Rotarix in children with spina bifida, bladder extrophy, or other conditions that predispose to acquiring latex allergy.

The ACIP also voted to include both vaccines for coverage in the federal Vaccines for Children program, per the new recommendations. ■

Data Suggest RotaTeq May Not Raise The Risk of Intussusception in Infants

ATLANTA — The rotavirus vaccine RotaTeq is not associated with an increased risk of intussusception in infants during either the 1- to 7-day period after vaccination or the 1- to 21-day period, according to data from the U.S. Vaccine Adverse Event Reporting System and the Vaccine Safety Datalink.

However, ongoing monitoring will be needed to fully assess the safety profile of the human-bovine reassortant rotavirus vaccine, researchers said at the June meeting of the Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention. The findings were reported in part in the June issue of Pediatrics (2008;121:1206-12).

The safety of the vaccine has been under scrutiny because a previous rotavirus vaccine, RotaShield, was associated with intussusception. It was pulled from the market in 1999 after reports from the U.S. Vaccine Adverse Event Reporting System (VAERS) found it had a 37-fold elevated risk for intussusception in the 3-7 days after the first dose.

Dr. Penina Haber of the Immunization Safety Office at the CDC presented the VAERS data for RotaTeq, including sensitivity analysis to compensate for incomplete reporting to the passive system and to estimate the number of doses administered.

Between RotaTeq's licensure on Feb. 1, 2006, through March 31, 2008, VAERS received 2,600 reports of adverse events associated with the vaccine, of which 26% were serious. The most frequently reported events were diarrhea and vomiting, and 44% of all events involved the first of the three vaccine doses. During that time period, Merck & Co. distributed a total of 14,274,551 doses of RotaTeq.

The reports included 267 confirmed cases of intussusception, of which 91 were reported 1-21 days after receipt of the vaccine and 48 of those 91 (53%) were reported within 1-7 days. There was one death 16 days after receipt of dose two, said Dr. Haber.

In sensitivity analyses, it was estimated that if VAERS reporting were 100% complete and 100% of the vaccine had been administered, the observed rates of intussusception after any dose were lower than expected for both the 1- to 21-day period post vaccination (92 vs. 242) and the 1- to 7-day period (49 vs. 81). But if reporting and administration were at 50%, it seemed there would be a statistically significant association between administration and intussusception for the 1- to 7-day period, with relative risks of 2.25 after any dose and 4.14 after dose one.

However, VAERS is not designed to test hypotheses, said Dr. Haber. That is done by Vaccine Safety Datalink (VSD), a system designed to test hypotheses generated by VAERS by linking vaccination data from several HMOs to patients' medical outcomes.

Dr. James Baggs, also with the CDC's Immunization Safety Office, presented the VSD data. The system's Rapid Cycle Analysis method is an alternative to postlicensure vaccine safety study methods that typically take years to complete, and can identify prespecified vaccine adverse events in "near real time."

In seven of eight VSD sites, children who received any dose of RotaTeq from age 4 weeks to 48 weeks were identified and compared with those aged 4-52 weeks enrolled in VSD during 1991-2004. Of 205,179 doses administered, 5 observed intussusception cases were identified from the computerized data, compared with 6.65 that would have been expected from the age-adjusted 1991-2004 background rate. After the 77,162 first doses, there were 2 intussusception reports, compared with an expected rate of 1.39. That relative risk, of 1.44, did not reach the specified threshold required to generate a safety signal.

None of the five cases occurred within 1-7 days of vaccine receipt, and subsequent medical record validation results showed that two of the five cases met the case criteria for intussusception, with neither occurring following dose one. Taken together, data from VAERS, VSD, and the prelicensure trial suggest the risk for intussusception after a first dose of RotaTeq is not greater than one to two per 50,000 first doses administered, Dr. Baggs said.

The researchers are also starting a Rapid Cycle Analysis of GlaxoSmithKline's Rotarix. ■

Mary Ellen Schneider, New York Bureau, contributed to this report.

Rotavirus Season Is Later, Less Severe Than Past 15

ATLANTA — Rotavirus activity in the ongoing 2007-2008 season in the United States seems to have been delayed in onset by 2-4 months and to have diminished in magnitude by more than 50%, compared with the previous 15 seasons, coinciding with increasing rotavirus vaccine coverage.

The good news, from an interim analysis of data from the National Respiratory and Enteric Virus Surveillance System (NREVSS), was reported at a meeting of the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices by Cathy Panozzo of the epidemiology branch of the CDC's Division of Viral Diseases. The findings were reported on the same day in an early release of the CDC's Morbidity and Mortality Weekly Report (2008;57:697-700).

Before the 2007-2008 season, rotavirus disease followed a winter-spring pattern, with a median start in mid-November, median peak in mid-March, and median end in mid-June.

In 2008, the onset of rotavirus activity occurred in late February, peaked at the end of April, and continues to decline. The proportion of acute gastroenteritis patients aged younger than 3 years who had fecal specimen tests that were positive for rotavirus declined from a median of 41% for the previous 15 seasons: In 2008, 13.5% of tests were positive at week 12 of the season, and 17.8% were positive at the season's peak in April, said the MMWR.

The number of rotavirus tests done from Jan. 1 to May 3 in 2008, was 37% lower than that of the seven previous seasons, and the number of tests that were positive for rotavirus was lower by a median 78.5%.

Similarly, in a separate analysis of data from the prospective New Vaccine Surveillance Network of children aged younger than 3 years with acute gastroenteritis, 405 children were enrolled in the January-April 2006 period, and 481 in the same period of 2007, compared with 283 in 2008. Of those, the proportions with positive rotavirus tests were 51%, 54% and 6%, respectively, Ms. Panozzo said.

Data from eight sentinel U.S. sites suggest a mean 56% of infants aged 3 months received one dose of RotaTeq, and a mean of 33.7% infants aged 13 months received three doses. But because most children aged 2 years and older would have been too old to start the series when the vaccine was licensed in February 2006, the changes in rotavirus activity seem more pronounced than would be expected based on the protective effects of the vaccine alone. Thus, vaccinating some of the population may be conferring some degree of herd immunity, thereby reducing transmission to unvaccinated children, the CDC said. ■

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