Varicella Vaccine Not Tied to Stroke, Study Finds

BY JEFF EVANS

Vaccination with live, attenuated varicella zoster virus was not associated with an increased risk of ischemic stroke in pediatric patients in the year after they received their vaccination, according to a retrospective, population-based study of children registered in the Vaccine Safety DataLink.

The study is the first to systematically examine the association between varicella zoster virus (VZV) vaccination and ischemic stroke. In previous studies, infection with the wild-type VZV has been associated with ischemic stroke in adults following herpes zoster ophthalmicus and in children following primary infection with the virus (chickenpox).

Suspicion of an association between varicella vaccination and ischemic stroke initially arose because of case reports of children with signs and symptoms of ischemic strokes who had been vaccinated with live, attenuated VZV.

In the study of approximately 3.25 million children who were members of eight medical care organizations that participate in the Centers for Disease Control and Prevention's Vaccine Safety DataLink project, strokes were diagnosed in a significantly lower percentage of children who received at least one varicella vaccination than in those who did not receive the vaccine (0.003% vs. 0.008%), James G. Donahue, D.V.M, Ph.D., of the Marshfield (Wisc.) Clinic Research Foundation and his colleagues reported (Pediatrics 2009;123:e228-34).

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Although unvaccinated children in the cohort had a significantly older mean age than did vaccinated children (7.9 years vs. 1.9 years) because the vaccine was not widely distributed until the late 1990s, adjustment for age did not alter the results of the analysis.

Dr. David Kimberlin, a member of the American Academy of Pediatrics Committee on Infectious Diseases who specializes in varicella, called the study "definitive."

The study "really shows the power of the Vaccine Safety DataLink. It is a phenomenal means by which complications of vaccinations can be assessed, and in this case, ruled out," Dr. Kimberlin, of the division of pediatric infectious diseases at the University of Alabama, Birmingham, said. He was not involved in the study.

The study included children older than 11 months but younger than 18 years, excluding those diagnosed with infantile cerebral palsy or those who were diagnosed before 11 months of age with stroke, hemiplegia, or hemiparesis. The investigators noted that they analyzed the 12-month period after vaccination because "reports have suggested that the incidence of stroke rarely exceeds 1 year after VZV infection."

Within the study period of 1991-2004, the investigators identified 39 children with an inpatient diagnosis of ischemic stroke out of roughly 1.14 million children in the cohort who had received at least one varicella vaccination, compared with 164 diagnoses of stroke in unvaccinated children. There was no evidence of temporal clustering of the 39 patients who had strokes after vaccination. The risk of stroke was not significantly elevated at any point in time during the 12-month period after vaccination.

Of the 203 children who suffered a stroke, 87 had risk factors for the event.

The study was funded entirely by the Centers for Disease Control and Prevention. Three of the investigators reported that they served as a consultant to or received research support from Merck Pharmaceuticals. One of these investigators also has received research support from Novartis, GlaxoSmithKline, Sanofi Pasteur, and MedImmune. ■

Expert Reviews Outpatient Treatment Options for MRSA

BY DOUG BRUNK

SAN DIEGO — Clindamycin and trimethoprim-sulfamethoxazole are the most commonly used agents to treat community-acquired methicillin-resistant *Staphylococcus aureus* on an outpatient basis, but neither is perfect, according to one expert

"The issue with clindamycin is that if you have big loads of bacteria, inducible resistance can develop," Dr. Alice L. Pong said at a meeting sponsored by Rady Children's Hospital and the American Academy of Pediatrics. "So even though the bug might be susceptible on paper, over time it might develop resistance."

Other strikes against clindamycin include its poor palatability—"most kids will throw it up," she said—and the potential for gastrointestinal side effects, especially vomiting and diarrhea.

The recommended dosage is 20-40 mg/kg per day IV divided every 6-8 hours, and 10-30 mg/kg per day orally divided every 6-8 hours.

Trimethoprim-sulfamethoxazole is more convenient than clindamycin because it requires twice-a-day administration, and "it doesn't taste too bad," said Dr. Pong of the division of infectious diseases at Rady Children's Hospital, San Diego. However, it's not effective for group A streptococci, "so if you don't have a culture and you don't know whether it's group A streptococci or *S. aureus*, you might run into trouble."

There are limited data regarding trimethoprim-sulfamethoxazole's efficacy in treating MRSA, but "in many cases it probably works as well as anything else," Dr. Pong said.

The recommended dosage is 8-12 mg/kg per day trimethoprim/40-60 mg/kg per day sulfamethoxazole given every 12 hours.

Doxycycline is another outpatient option for treating MRSA, "and it works well for acne, too," she said. Approved for use in children aged 8 years and older, it has limited efficacy against group A streptococci.

The recommended dosage is 2-4 mg/kg per day given every 12 hours.

Rifampin is yet another treatment option, but it cannot be used alone as rapid resistance will ensue. The recommended dosage is 10-20 mg/kg per day IV or orally every 12-24 hours.

Quinolones such as levofloxacin are widely used for the treatment of MRSA in adults but are not approved for use in children in this situation. Dr. Pong said that she and her colleagues have used quinolones for treating MRSA in children "only in situations where there is no other antibiotic available."

Linezolid, a member of the new oxazolidinone class of drugs, is an expensive treatment option that is active at the ribosomal binding site of the bacterial cell.

"If you're going to give it for a prolonged period of time, you need to watch the complete blood count because linezolid can cause bone marrow suppression," Dr. Pong warned. "But it works pretty well. We occasionally put kids on this as a drug when they are discharged home from the hospital and they've improved on vancomycin or when their organism comes back as resistant to clindamycin and trimethoprim-sulfamethoxazole."

Dr. Pong reported that she had no financial conflicts to disclose. ■

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