MMRV Approval Should Boost Immunization Rate

BY DIANA MAHONEY
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The Food and Drug Administration's recent approval of the first combination vaccine designed to protect children against measles, mumps, rubella, and varicella is raising expectations of improved immunization rates, but is also eliciting some concerns.

The quadrivalent MMRV vaccine Proquad, developed by Merck and Co., Inc., is a combination of the company's measles, mumps, and rubella (MMR II) and varicella (Varivax) vaccines.

"Right now, at the 1-year visit, we're giving kids four or five shots. That's a lot. Anything that gets the number down while providing the same protection is a good thing. It's not revolutionary, but it's beneficial," said Robert W. Frenck Jr., M.D., a member of the American Academy of Pediatrics' Committee on Infectious Diseases and a professor of pediatrics at the University of California, Los Angeles.

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The need for one less shot, and potentially one fewer office visit, might close the gap between vaccination rates for varicella and for measles, mumps, and rubella. "It's likely that use of the combination vaccine will help get the varicella vaccination numbers up," said Jay Lieberman, M.D., of the UCLA Center for Vaccine Research in Torrance, California.

In 2004, the immunization rate for varicella was estimated to be 87.5%, compared with 93% for measles, mumps, and rubella, according to a press release issued by Merck.

Dr. Lieberman coauthored one of a handful of studies comparing the immunogenicity of the MMVR injection with the standard two-shot MMR II and varicella immunizations.

The Merck-funded study showed that seroconversion rates were similar in children receiving the one- and two-shot regimens, as well as among children who received different lots of the MMRV vaccine. The latter measure, which was necessary for FDA approval, demonstrated the ability to manufacture the vaccine consistently, said Dr. Lieberman.

In this and similar studies, children injected with the MMRV vaccine suffered more fevers following the inoculations than those who received the independent MMR and varicella vaccines; however, "the fevers were mild and not clinically relevant," according to Dr. Lieberman. There was no statistically significant difference in the incidence of more worrisome adverse febrile events, including febrile seizures, he said, noting that overall the one- and two-shot regimens appear to be similarly tolerated.

The FDA approved the quadrivalent vaccine for children between the ages of 12 months and 12 years, including those in need of a second dose of the MMR II vaccine.

Because the recommendation for MMR II has been to give two doses—the first at age 12-15 months and the second prior to school entry at age 4-6 years—adoption of the quadrivalent vaccine would make the ongoing debate over the need for a second dose of the varicella vaccine irrelevant, said Richard K. Zimmerman, M.D., of the department of family medicine at the University of Pittsburgh, Pennsylvania, and a voting member of the Centers for Disease Control and Prevention Advisory Committee on Immunization Practices (ACIP).

"A second dose of varicella vaccine should reduce the number of breakthrough cases of chickenpox that we've seen, but the ACIP has not yet recommended a second dose," Dr. Zimmerman said. In fact, in June of this year, the ACIP rejected a proposal recommending children be given booster shots of the varicella vaccine after age 4. "This was due in part to questions about cost and waiting for a combination vaccine such as MMRV to make it more feasible."

If the ACIP recommends a second dose of varicella vaccine, "then MMRV should be easily accepted, although cost could be a barrier," said Dr. Zimmerman.

According to Merck, the price for Proquad is $114.61 per shot, compared with $104 for the combination of the MMR II and Varivax vaccines, which cost $38 and $66, respectively.

Some immunization watchdog groups are urging caution. "Combining this many live viruses into one vaccine is something that has never been done before, and there is not enough information about possible long-term effects," said Barbara Loe Fisher, president of the National Vaccine Information Center.

"There may be some concerns about delivering more antigens in a single shot, but there is no scientific evidence that this is a problem," said Dr. Frenck. "These viruses are all attenuated, and four is nothing compared to the number of viruses and bacteria that we are all exposed to every day." ■

MMRV Efficacy Similar To MMR II Plus Varivax

BY HEIDI SPLETE
Senior Writer

A quadrivalent measles, mumps, rubella, and varicella vaccine was well-tolerated and effective in children aged 12-23 months, according to data from a pair of studies conducted by Henry Shinefield, M.D., of the University of San Francisco, California, and his colleagues.

The studies, which were sponsored in part by Merck & Co., indicated that either a one- or two-dose vaccine containing antibodies to all four diseases was similar in safety and efficacy to a combination of the previous measles, mumps, and rubella vaccine (MMR II) and a separate dose of the varicella virus vaccine (Varivax).

In a randomized, multicenter study, 480 healthy children received either MMR II plus Varivax (VV) or the quadrivalent vaccine (MMRV) plus a placebo. Children in the MMRV group had significantly higher rates of elevated temperature from 5-12 days after vaccination, compared with the MMR-plus-VV group (28% vs. 19%), but the fevers were generally mild and averaged less than 2 days' duration. Adverse events were not significantly different between the two groups at 42 days after vaccination (Pediatr. Infect. Dis. J. 2005;24:665-9).

A measles-like rash was the most common adverse event in both groups; the rashes averaged 6 days' duration and were mild to moderate. The incidence of pain and redness at the injection sites and the proportion of children with at least one adverse event were similar between the groups.

In a separate study of 1,559 healthy children, antibody responses from the MMRV were equal to those from a combination of MMR plus VV (Pediatr. Infect. Dis. J. 2005;24:670-5).

The children were randomized to one of four treatment groups and received a quadrivalent vaccine with a low, middle, or high varicella-zoster virus (VZV) potency or a dose of MMR plus VV. Those in the quadrivalent groups received a second MMRV injection 90 days after the first injection.

The antibody rates in all three MMRV groups after the second injection were at least as high as the MMR-plus-VV group, and most of the children who had not responded to the VZV in the first injection did so after the second injection.

After the second injection, the observed response rates for measles in the low, middle, and high potency groups were 99.4%, 99.7%, and 100%, respectively, compared with 99.7%, in the MMR-plus-VV group. The observed response rates for varicella in the low, middle, and high potency groups were 99.7%, 100%, and 99%, respectively, compared with 93.1% in the MMR-plus-VV group. Similar response rates to those of measles and varicella were seen in the low, middle and high potency groups for mumps and rubella.

The incidence of measles-like rashes was similar in all groups, and the incidence of both varicella-like and measles-like rashes was lower in the MMRV group after the second MMRV injection, compared with the MMR-plus-VV group.

Approximately 70% of the children in any of the MMRV groups as well as the combination group reported at least one systemic adverse event, including fever, irritability, and upper respiratory tract infection. A febrile seizure suffered by a child in the middle potency group was the only severe adverse event thought to be vaccine related.

Febrile seizures might indeed be a cause for concern when using the quadrivalent vaccine, said Margaret Rennels, M.D., the American Academy of Pediatrics' coliaison to the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices.

But on the whole, the quadrivalent vaccine is a public health achievement, she said in an interview.

"Many of us believe that we should be giving a second dose of varicella and this [quadrivalent vaccine] would make that very easy," said Dr. Rennels, clinical chief of infectious diseases at the University of Maryland, Baltimore.

'Herd Immunity' Keeps Varicella Hospitalizations Down in Wake of Vaccine

Hospitalizations for varicella have declined 88% since 1994-1995, with the biggest decrease seen among infants.

Because infants are not eligible to receive the vaccine, "The decline reflects reduced force of varicella infection in the population (i.e., herd immunity)," as do declining rates among adults and adolescents, reported Dr. Fangjun Zhou, Ph.D., and associates (JAMA 2005;295:797-802).

Dr. Zhou, of the Centers for Disease Control and Prevention, examined varicella treatment codes extracted from a national health plan database of about 4 million consumers, from 1994-2002. He found an overall decline in varicella hospitalization, from 2.3/100,000 to 0.3/100,000 (88%).

Hospitalization rates declined for every age group: 100% for infants; 91% for children aged 9 years and younger; 92% for children aged 10-19 years; and 78% for adults aged 20-49 years.

Ambulatory visits for varicella also decreased significantly, declining 59% over the period. Again, the decrease was most apparent among infants (90%). The rate declined 63% for children aged 9 years and younger; 42% for those aged 10-19 years; and 60% for adults aged 20-49 years.

National spending on varicella hospitalizations and ambulatory visits declined from $85 million in 1994 and 1995 to $22 million in 2002, a 74% decrease.

—Michele G. Sullivan