New Meningococcal Vaccine Immunogenic, Tolerated in Infants

A new tetravalent meningococcal vaccine proved to be immunogenic and well-tolerated in infants in a phase II study, investigators reported in JAMA.

The tetravalent meningococcal vaccine that is currently licensed in the United States is recommended for all 11- to 18-year-olds, but was found to be poorly immunogenic in infants so is not licensed for use in children under age 2 years.

Because infants are the age group at highest risk for meningococcal disease, a new vaccine was developed and tested in an open-label, randomized controlled trial involving 421 infants in England and Canada.

The new vaccine—MenACYW—covers serogroups A, C, W-135, and Y. It was developed by Novartis Vaccines and Diagnostics, which funded this phase II study.

Two different primary three-dose schedules were evaluated: a single dose at 2, 3, and 4 months of age, and a single dose at 2, 4, and 6 months of age.

A two-dose schedule (a single dose at 2 and 4 months) was also assessed. This was to examine the vaccine’s safety and efficacy when given according to the different routine immunization schedules in different countries, said Dr. Matthew D. Snape of the Oxford Vaccine Group, University of Oxford (England), and his associates.

A subset of infants also received a booster dose at 12 months of age, since some waning in antibody titers was expected, has been observed after immunization against serogroup C alone. Another subset of subjects received a reduced dose of vaccine at 12 months as a probe for immunologic memory.

One month after the immunization series was complete, 92% of the infants who had received the 2-, 3-, and 4-month schedule showed human complement serum bactericidal antibody (HCSBA) titers of 1:4 or better against all four serogroups, which is considered protective. Similar results were obtained with the 2-, 4-, and 6-month schedule, except that the proportion of infants with protective HCSBA titers against serogroup A was lower, at 81%, Dr. Snape and his associates said (JAMA 2008; 299:173-84).

The infants who received MenACYW only at 2 and 4 months had less of a response. About 80% showed HCSBA titers of 1:4 or better for serogroups C and W-135, and 50% of infants who received a booster at this time showed a “reassuring” increase in titers.

All serogroups showed a waning in antibody titers by 12 months of age. The subjects who received a booster at this time showed a ‘reassuring’ increase in titers. The first was a brief episode of idiopathic thrombocytopenic purpura after the booster dose, which occurred in a child who had had a viral-like illness with oral ulcers and rash 2 weeks previously.

The second was an episode of supraventricular tachycardia, and it was found that this child had a history of the arrhythmias and had been entered in violation of the study’s exclusion criteria.

The most important limitation in this study was that the number of subjects was “too small to draw firm conclusions regarding the safety of this vaccine, and therefore further studies will be required,” Dr. Snape and his associates noted.

Nevertheless, in an editorial comment accompanying this report, Dr. Lee H. Harrison of the infectious diseases epidemiology research unit of the University of Pittsburgh, said the study “represents a substantial advance in the vaccine prevention of meningococcal disease.”

It is not yet known whether the new vaccine prevents pneumococcal carriage of meningococcal organisms, “a major public health benefit” that has been noted in other conjugate vaccines such as those against pneumococcal disease and Haemophilus influenzae type b.

Given that the MenACYW vaccine “behaves immunologically like a conjugate vaccine,” it would be expected to prevent pneumococcal carriage, which would in turn prevent transmission among the unimmunized population and thus promote herd immunity.