CLINICAL UPDATE

Varicella vaccine in clinical practice

Vazquez M, LaRussa P, Gershon A, Steinberg S, Freudigman K, Shapiro E. The effectiveness of the varicella vaccine in clinical practice. *N Engl J Med* 2001;344:955-60.

Background: A live attenuated vaccine for varicella has been available in the United States since 1995 and in Canada since 1998. Because the effectiveness of a vaccine in clinical practice may differ from its efficacy in randomized clinical trials,[1] Vazquez and associates initiated an ongoing observational, practice-based study to assess the effectiveness of the varicella vaccine among children older than 12 months.

Question: In a pediatric practice, what are the odds that children with chickenpox have received varicella vaccine, as compared with healthy control subjects?

Methods: This case–control study was conducted in 15 participating pediatric practices in and around New Haven, Conn. Eligible subjects were nonimmunocompromised children aged between 13 months and 16 years who had not had chickenpox and who had not received the varicella vaccine within 4 weeks of enrolment. Cases of varicella were identified through active surveillance and were assessed at home by a research assistant who had no knowledge of the subjects' vaccination status. Severity was determined using a modified version of the illness severity scale used in earlier clinical trials.[2] In addition, vesicular fluid was collected from a lesion to test for varicella–zoster virus by the polymerase chain reaction (PCR). For each child with suspected varicella, 2 control subjects matched by date of birth and pediatric practice were selected at random from a list generated by the practice's computerized database.

The health records of all study subjects were reviewed to determine vaccination status. Children with chickenpox (or their matched control subjects) who had received varicella vaccination at least 4 weeks before the onset of illness were considered vaccinated. A matched odds ratio for vaccination in cases and controls was calculated and was adjusted for potential confounding variables in a multivariate analysis.

Results: From March 1997 through November 2000, 461 potential cases of varicella were identified. The study's main analysis was based on a comparison between the 202 children with positive PCR results and 389 age-matched control subjects. The groups did not differ significantly in age, sex or ethnic background. Attendance at day-care centres was slightly more prevalent among the case subjects than among the control subjects (14% v. 9%, $p = 0.05$). The difference in vaccination rates, however, was substantial, with 23% of case subjects and 61% of control subjects having been vaccinated (matched odds ratio 0.15, 95% confidence interval [CI] 0.10–0.22, $p < 0.001$). Effectiveness of the vaccine, expressed as 1 minus the matched odds ratio, after adjustment for sex, ethnic background and attendance at a day-care centre, was reported to be 87%. In protecting against moderately severe and severe disease, the vaccine was reported to be 97% effective (95% CI 93%–99%, $p < 0.001$).

Potential bias resulting from differential access to medical care was assessed by comparing rates of measles–mumps–rubella (MMR) vaccination in the case and control groups; in each group the prevalence of MMR vaccination was 100%.

Commentary: There are a number of reasons to suspect that the varicella vaccine might be less effective in clinical practice than in the original randomized trials. These include the lower concentration of virus in the commercially available vaccine (3000 to 9000 plaque-forming units per dose, as compared with 17 000 plaque-forming units per dose in the original trial)[3] and the decline in virus concentration that occurs over time when the thermolabile vaccine is kept frozen. This case–control study suggests, however, that the vaccine's effectiveness in practice is comparable to that shown in earlier clinical trials. The authors have attempted to control for confounding variables and to guard against selection bias. Nonetheless, as with all observational research, the results must be interpreted with caution.

Practice implications: In the short term, varicella vaccine appears to be as effective in clinical practice as it was in earlier clinical trials. Confirmation of its long-term effectiveness in practice awaits further observational study. — *Donald Farquhar*

The Clinical Update section is edited by Dr. Donald Farquhar, head of the Division of Internal Medicine, Queen's University, Kingston, Ont.. The updates are written by members of the division.

References

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2. Gershon A, Steinberg S, Gelb L, Galasso G, Borkowsky W, LaRussa P, et al. Live attenuated varicella vaccine: efficacy for children with leukemia in remission. *JAMA* 1984;252:355-62.
3. Weibel R, Neff B, Kuter B, Guess H, Rothenberger C, Fitzgerald A, et al. Live attenuated varicella virus vaccine. Efficacy trial in healthy children. *N Engl J Med* 1984;310:1409-15.

[A commentary on the chickenpox vaccine appears on page 1454.]