Analysis Refutes Hepatitis B Vaccine, RA Link

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BALTIMORE — The hepatitis B vaccine does not appear to be associated with an increased risk for rheumatoid arthritis, Dr. Roger P. Baxter and his associates reported at a vaccine research conference sponsored by the National Foundation for Infectious Diseases.

Both acute and chronic arthropathies have been reported in adults vaccinated with the tetanus-diphtheria (Td), hepatitis B (HepB), and measles-mumps-rubella (MMR) vaccines. However, most of the evidence to support or refute a causal relationship between the Td or HepB vaccine and chronic arthritis has come from isolated case reports, uncontrolled observational studies, or studies that lacked sufficient statistical power, said Dr. Baxter, associate director of the Vaccine Study Center at Kaiser Permanente, Oakland, Calif., and his associates.

A case-control analysis designed to overcome the shortcomings of the previous studies included a cohort of continuous enrollees in Northern California Kaiser Permanente's health plan from Jan. 1, 1995, through Dec. 31, 1999, who were aged 15-59 years during Jan. 1, 1997–Dec. 31, 1999.

Individuals who had made clinic visits for rheumatoid arthritis (RA) and other inflammatory conditions prior to their follow-up start date were excluded.

A total of 416 incident cases of RA were identified (based on definitive diagnosis at the time or subsequent assessment by a rheumatologist), and each was matched with three controls based on age and the number of clinic visits made during the year prior to the onset date.

Rates of hepatitis B vaccination among the RA patients were compared with those of controls, with adjustment for sex, age, and exact number of clinic visits. Similar comparisons were made for the tetanus and influenza vaccines.

No statistically significant risk of RA was found for any of the three vaccines. Only 1% of RA patients versus 0.6% of controls had been exposed to the hepatitis B vaccine within 1-90 days of onset of RA symptoms, for an adjusted odds ratio of 1.48.

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Within 1-180 days, the percentages were 1.9% with RA versus 0.9% of controls, giving a still insignificant odds ratio of 2.01.

Within 1 year, 2.4% of RA cases and 1.6% of controls had been exposed to the vaccine, again insignificant at 1.42.

In all, only 10 of the 416 RA patients had received the HepB vaccine within 1 year of symptom onset, suggesting that, "If there is an association, these data would imply that hepatitis B vaccine would only contribute to a small minority of cases," Dr. Baxter and his associates said in their poster.

Results for the other two vaccines were also not significant, with adjusted odds ratios of 0.77-1.06 for tetanus and 0.66-1.11 for influenza.

Health care utilization was higher among those with RA, which was a slight confounder in this study despite the attempt to control for number of visits: Even after adjustment, there was still a significant residual effect for number of visits, with an odds ratio of 1.15.

"Basically, people who get vaccines of all kinds are different from those who don't, and underlying differences may confound the relationship with things like RA. We try to control for these factors by matching and analyses, but still we think there are differences. …

"People who have RA are more likely to be higher utilizers and also more likely to have gotten vaccines than people who don't utilize the system as much," Dr. Baxter commented in a follow-up interview.

However, he added, although the difference in utilization was statistically significant, it probably wasn't that different clinically.

"We thought initially this was an important confounder. But in the end we found that although they were different, in reality we could adjust for the vast majority of the difference," he said. ■