Flu Vaccine Found Less Effective in SLE Patients

BY KATE JOHNSON
Montreal Bureau

Influenza vaccination appears to be safe in patients with quiescent systemic lupus erythematosus, although the overall efficacy of the immunization is decreased in them compared to controls, according to a new study.

In addition, there is a trend toward a further decrease in the vaccine's efficacy among systemic lupus erythematosus (SLE) patients taking azathioprine as compared with several other immunosuppressive drugs, reported Dr. A. Holvast from the University of Groningen, the Netherlands, and colleagues.

The study included 56 SLE patients with quiescent disease, defined as an SLE disease activity index (SLEDAI) of ≤5. Patients were divided into groups based on their use of immunosuppressive drugs, with 12 using no drugs, 17 using hydroxychloroquine (≤400 mg/day), 13 using azathioprine (≤50 mg/day) and 14 using prednisone (≤10 mg/day) (Ann. Rheum. Dis. 2006;65:913-8).

All patients, along with 18 healthy controls, were vaccinated in October and November 2003 with Influvac (Solvay Pharmaceuticals Inc.), a trivalent influenza vaccine.

SLEDAI scores measured a mean of 30 days after vaccination did not differ significantly from baseline SLEDAI scores in any of the patient groups, and there were also no significant changes in patient-recorded visual analogue scores—suggesting that vaccination did not induce disease activity. "The immune response to influenza is generated during the first weeks following vaccination," wrote the authors. "If vaccination were to enhance established autoimmunity, this would be expected to occur particularly during this early period."

They noted that compared with controls, SLE patients had more systemic side effects of vaccination—although these were all mild. With respect to vaccination efficacy, the authors concluded that "SLE patients appear to have a decreased immune response, compared to healthy controls."

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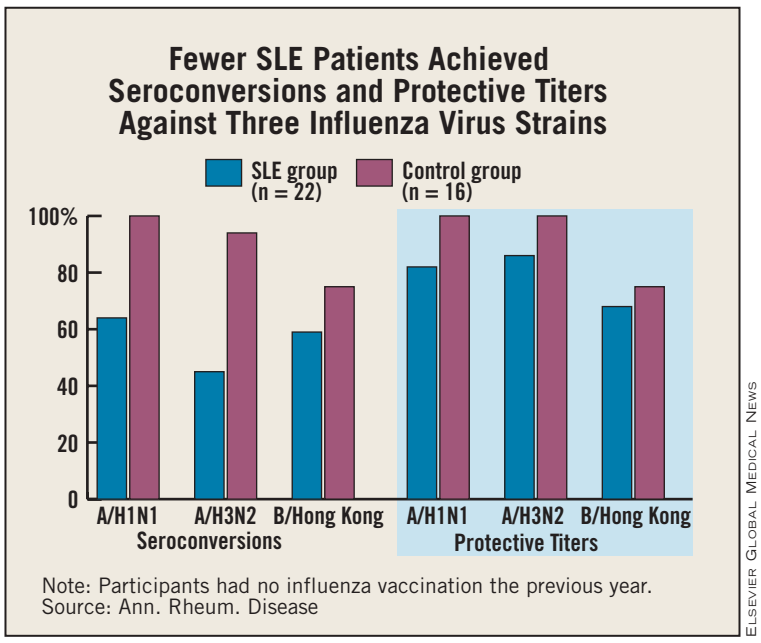

Using blood samples taken at baseline and at the follow-up visit, the subjects' influenza antibody responses to A/H1N1, A/H3N2, and B/Hong Kong were measured in 3 ways: by assessment of a ≤fourfold titer rise (seroconversion); by means of a titer rise to ≤40; and by geometric mean titers (GMT).

Although the GMT increased after vaccination in all subjects and did not differ significantly between patients and controls, the authors suggested this was because prevaccination GMTs were higher in patients than in controls because of the patients' higher rate of vaccination in the previous year (77% vs. 22%).

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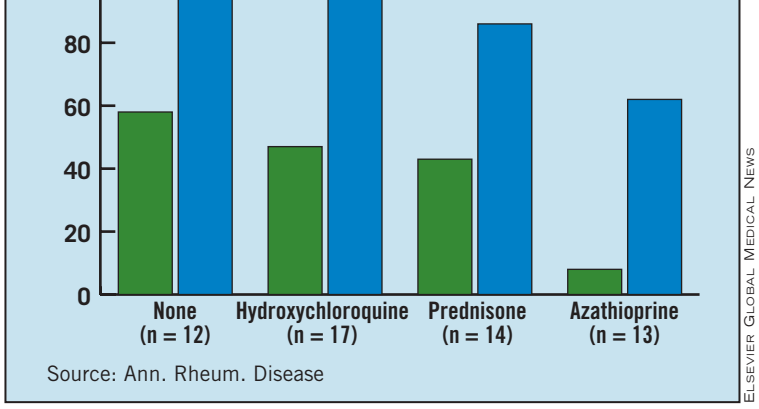
Compared with controls, SLE patients had significantly fewer seroconversions against A/H1N1 and A/H3N2 (43% vs. 94% and 39% vs. 88%, respectively). SLE patients also had fewer seroconversions to B/Hong Kong, compared with controls (41% vs. 71%), although this difference was marginally significant.

No significant differences could be found overall between patients and controls in terms of the percent of people achieving a postvaccination titer of ≤40 for separate influenza strains—although there was a trend toward fewer SLE patients achieving this. Additionally, fewer SLE patients achieved protective titers for both influenza A strains combined (75%, compared with 100% of controls).

After excluding all subjects who had been vaccinated the previous year, they found that significantly fewer SLE patients achieved seroconversions and protective titers to A/H1N1 and A/H3N2. (See seroconversion graph.)

"It is conceivable that SLE patients have an intrinsic [immunologic] defect that results in decreased responsiveness to vaccination," wrote the authors, adding that the use of immunosuppressive drugs may further decrease the vaccination response in these patients. "SLE patients receiving azathioprine showed a trend towards a decreased immune response against influenza A/H3N2, compared with the other patient groups," they wrote. "For A/H3N2, SLE patients receiving azathioprine had fewer fourfold titre rises than [did] the other patient groups ($P = .041$). Furthermore, a smaller proportion of the azathioprine group achieved titres of 40 or greater against A/H3N2 ($P = .030$), compared with the other patient groups."(See immune response graph.)

The authors suggested that virosomal vaccines, which generate better cellular immune responses and enhance humoral immune responses, might improve the efficacy of vaccination in SLE patients. ■



Lupus Nephritis Responds to Low-Dose Cyclophosphamide

BY BRUCE JANCIN
Denver Bureau

AMSTERDAM — A European-style low-dose intravenous cyclophosphamide regimen achieves long-term outcomes similar to the high-dose regimen popularized in National Institutes of Health–sponsored trials for the treatment of proliferative lupus nephritis, Dr. Frederic Houssiau reported at the annual European Congress of Rheumatology.

He presented mean 100-month follow-up data from the European Lupus Nephritis Trial (Euro-Lupus), in which 90 patients with proliferative lupus nephritis were randomized to low- or high-dose cyclophosphamide followed in either case by azathioprine maintenance. The 2006 Euro-Lupus report confirms the trial's standing within the lupus field as a study featuring singularly lengthy and complete follow-up.

The first Euro-Lupus analysis showed that patients on a low-dose regimen experienced half as many serious infections as did those on the high-dose NIH-type regimen. The second report identified two key variables that, when assessed 6 months into therapy, predicted which patients would have good renal outcome at 7 years follow-up: a marked drop in serum creatinine and a decline in 24-hour proteinuria to less than 1 g.

Low-dose regimen patients had half as many serious infections as did those on the high-dose regimen.

DR. HOUSSIAU

The 2006 report concluded that at 8.3 years of follow-up, 5% of participants have developed cancer, 8% have cardiovascular disease, 7% have developed end-stage renal disease, and 6% have died. Rates of all of these outcomes were similar in the high- and low-dose cyclophosphamide arms.

That would give the advantage to the low-dose regimen, which consisted of a fixed dose of 500 mg of cyclophosphamide every 2 weeks for 3 months. In addition to fewer serious infections, other advantages of low-dose therapy are its lower cost, administration via an outpatient 30-minute drip infusion, no need to monitor the nadir WBC count, and fewer side effects, said Dr. Houssiau, professor of rheumatology at the University of Louvain (Belgium) and Euro-Lupus coordinator.

A further advantage favoring the low-dose regimen were the nine live births in that study arm, a rate threefold greater than in the high-dose group, he said.

Nevertheless, cyclophosphamide—even in low-dose form—is far from an ideal therapy. One-third of Euro-Lupus participants have experienced one or more major renal flares. It seems likely that cyclophosphamide will eventually be replaced altogether by mycophenolate mofetil or other novel agents, he predicted. ■