ASK THE EXPERT

Managing Immunization in Rheumatic Disease

Infections are a major concern for people with rheumatic disease, in whom they occur more frequently than in the general population. When they occur, infections in this population tend to be more serious, possibly because of an inherent immune dysfunction associated with the disease or as a complication of the drugs used to control it. Despite the increased risk of infection, however, adults with rheumatic disease are underimmunized for preventable infections, including pneumococcal diseases and influenza, according to Dr. Nora G. Singer, associate professor of pediatric and adult rheumatology at Case Western University in Cleveland.

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The strength of the protective response mounted by the body following exposure to immunization might not be as robust among individuals whose immune system has been compromised by their disease or their therapy.

However, most patients with a rheumatic disease will generate some immune response to immunization against influenza and pneumococcal diseases that will at least lessen the severity of subsequent infection with the relevant microbe, Dr. Singer said at the Congress of Clinical Rheumatology in Destin, Fla., earlier this year.

In this Ask the Expert column, Dr. Singer discusses some of the important considerations with respect to immunization in this immune-compromised population.

Rheumatology News: Given their increased risk of infection, why are adults with rheumatic disease not routinely being vaccinated against influenza and pneumococcus?

Dr. Singer: The vaccination rate appears to be between 30% and 40% of those who are candidates for immunization against flu and pneumococcal diseases. Patient and physician factors appear to contribute to undervaccination. Patient issues include worries about side effects, ability to pay, and some patients' perception that they are too healthy to require vaccination. Physician factors include systems problems, such as lack of readily available influenza vaccine at the time it is required, lack of systems to record and track vaccinations within practices, lack of an assigned office support person to routinely offer vaccination to patients, underrecognition of who should be vaccinated, and more individual issues including, but not limited to, concerns that individual patients may not respond to vaccine because of their illness or medication, and that patients may have to pay out of pocket or won't be able to afford the vaccines.

RN: Can patients with rheumatic disease who are on immunosuppressant therapies safely be vaccinated against pneumococcal disease and influenza? What are the most important considerations with respect to vaccination in this population?

Dr. Singer: Yes, these patients can and should be vaccinated against influenza and pneumococcal disease.

Live, attenuated vaccines are considered relatively contraindicated in rheumatic disease patients who are on biologic therapies, so when we talk about vaccines in these patients, we are talking about inactivated vaccines or component vaccines, rather than live, attenuated vaccines.

For pneumococcus, a polysaccharide vaccine is available and recommended; for influenza, the inactivated vaccine flu shot, rather than nasal FluMist, is recommended.

RN: Do biologic therapies affect vaccine responses? What, if any, treatment modifications should be made?

Dr. Singer: Some biologics may reduce the level of immune response to vaccination, but most patients on biologics appear to get some benefit from vaccination, as best we can measure.

Patients on anti–tumor necrosis factor–alpha therapy appear to have protective vaccine responses for the most part. In patients treated with costimulatory blockade or B-cell–depleting agents, the timing of vaccination may be important in maximizing vaccine response. Most measurement of vaccine protection depends on measuring antibodies in the blood, which are a surrogate marker for protection.

For example, a doubling or quadrupling of antibody in the blood might be what is desired based on previous studies. No one, however, would propose vaccinating a patient with flu vaccine and then purposely exposing that person to influenza in order to directly determine whether the vaccine confers immunity.

So instead of challenging patients with the infection against which we are trying to protect them, we measure the antibodies in their blood against the infectious agents.

Although some people who have been immunized against influenza might contract it, the hope is that the antibodies they develop as a result of the vaccine will at least result in milder disease.

RN: Are there published guidelines for immunization specific to this population?

Dr. Singer: The Centers for Disease Control and Prevention has published guidelines that include specific references to immunocompromised hosts (http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5540a10.htm?s_cid=mm5540a10_e).

In June 2008, the American College of Rheumatology Guidelines Task Force panel recommended that patients with rheumatoid arthritis who are receiving leflunomide, methotrexate, or sulfasalazine can be immunized with inactive viral vaccines in accordance with CDC's relevant recommendations (http://www.lupus.org/webmodules/webarticlesnet/articlefiles/946-shingles.pdf).

The ACR Guidelines Task Force recommended avoidance of live viral vaccine preparations with "all biologic agents," but provided no directives on whether live vaccines are safe with methotrexate or corticosteroid use.

Additionally, regarding the zoster vaccine, the ACR disseminated the following advice to its members in 2008: "Until more research becomes available, it is still advisable to avoid the zoster vaccine in patients actively receiving TNF inhibitors, as well as abatacept, rituximab, and anakinra. In some, it may be advisable to delay the initiation of biologic therapy until at least 2 weeks after the zoster vaccine is given."

Dr. Singer reported no relevant conflicts of interest. ■

By Diana Mahoney

Switching Anti-TNF Agents Is Common, but Unstudied

BY DENISE NAPOLI

Rheumatoid arthritis patients taking tumor necrosis factor inhibitors switch agents often, resulting in low 2-year continuation rates for these agents, despite the fact that no large, controlled studies have been done on the effects of frequent switching.

"Increased expectations on the part of the patient or the physician could play a role in creating impatience when immediate results are not seen" with given anti-TNF inhibitors, wrote Dr. Yusuf Yazici from the New York University Hospital for Joint Diseases, and colleagues.

And although much of the existing literature does support switching to another anti-TNF agent after initial failure, "these results have been reported mostly in small, short-term studies that focus on efficacy outcomes, not TNF inhibitor survival in the 'real world,' " he added.

In a study to assess anti-TNF treatment patterns, Dr. Yazici and colleagues looked at insurance claims data from 90 managed care organizations on 50 million patients in the United States. They analyzed data on all patients with RA who initiated anti-TNF therapy between Jan. 1, 2000, and July 1, 2005. A subsidiary cohort of the 6,070 patients who started an anti-TNF agent between 2003 and 2005 was also analyzed to assess use of adalimumab, which was not commercially available until 2003.

Patients on infliximab had the highest percentage of continuation on the drug in both cohorts. However, at 2 years, this figure was only 50%.

Furthermore, 40% of patients starting on infliximab needed one or more dose escalation over the study period, which has "important implications, given the drugs and administration costs associated with more medication use," wrote the authors (J. Rheumatol. 2009 March 30 [doi:10.3899/jrheum.080592]).

Additionally, despite the relatively high continuation rate seen with infliximab, the authors found that etanercept was the most commonly prescribed initial anti-TNF agent, used by about 50% of patients in both cohorts who were starting anti-TNF therapy for the first time. However, at 2 years in both cohorts, only about 20% of the initial etanercept patients remained on the drug.

In the subcohort, adalimumab was the initial drug started by 1,365 patients (23% of the cohort); the continuation rates closely mirrored those seen with etanercept.

Dr. Yazici and his colleagues speculated that the flexibility of infliximab scheduling and dosing, and the ability of a majority of patients to increase their dose, may explain why infliximab had higher continuation rates than did the two other agents. Additionally, the authors postulated that because infliximab is an agent that is given by infusion and thus requires regular follow-up, "seeing a physician regularly may encourage a patient to remain" on the regimen.

They recommend that other agents now on the market, like abatacept and rituximab, also be investigated in a real world setting.

"TNF inhibitor use patterns are changing with time, with more frequent changes and shorter duration of treatment before the change," wrote the authors. "Further research needs to be conducted to determine if those tends remain constant with the availability of new biologic treatment options, and how these newer treatments influence the treatment algorithm."

Dr. Yazici has served as a consultant and/or speaker for Bristol-Myers Squibb Co., Celgene Corp., Centocor Inc., Genentech Inc., Hoffmann-La Roche Inc., and UCB SA. One of the authors on the current study is an employee of Bristol-Myers Squibb. ■