Corticosteroids Confer Highest Infection Risk

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Patients with rheumatoid arthritis are at an increased risk of contracting infections that are severe enough to require hospitalization, compared with people without rheumatoid arthritis, and the use of oral corticosteroids exacerbates that risk, according to results from a recent study.

The results further emphasize the notion that patients should be adequately informed about the heightened risk of infection with glucocorticoids.

"Patients should be routinely vaccinated against influenza, [and also] receive a pneumococcal vaccine," Dr. Mark Hochberg, coinvestigator and head of the division of rheumatology and clinical immunology at the University of Maryland, Baltimore, said in an interview.

The researchers conducted a retrospective cohort study based on records from 61 health plans across the United States from Jan. 1, 1999, through July 31, 2006.

A total of 24,530 patients were included in the RA cohort (inclusion criteria for this group were age over 18 years with at least two physician visits more than 2 months apart for RA with an ICD-9-CM diagnosis code of 714), and a random sample of 500,000 people were included in the non-RA cohort (age over 18 years and no RA diagnosis code at follow-up).

Patients in the RA cohort were more likely to be female than in the non-RA cohort, and a greater portion of RA patients were aged 45-64 years than in the non-RA cohort (66% vs. 39%, respectively).

During the study period, "there were 1,993 cases of a first hospitalized infection in the RA cohort, while 11,977 cases were observed in the non-RA cohort," wrote the authors.

This translated to 3,864 cases per 100,000 person-years in the RA cohort and 1,250 cases per 100,000 years in the non-RA cohort and—adjusted for age, sex, and calendar year—gave a hazard ratio of 2.31 for hospitalized infection (95% confidence interval, 2.20-2.43).

Adjusted again for comorbid conditions and for prescription medication use, the hazard ratio was still 2.03 (95% CI, 1.93-2.13).

The most common infection in both groups was pneumonia, followed by urinary tract infections and after that, skin infections (J. Rheumatol. 2008;35:387-93).

There was also a slightly increased risk of hospitalized infection when the patients were taking biological disease modifying antirheumatic drugs.

The study investigators then performed a nested case-control analysis using all 1,993 hospitalized infection cases in the RA cohort and 9,965 RA controls, to ascertain whether the use of RA drugs further increased the patients' risk of infection.

Adjusted for age, sex, other current RA medication use, and a number of other chronic conditions, as well as the number of hospitalizations between the cohort entry and the index date, the researchers found a slightly increased risk when patients were taking biological disease modifying antirheumatic drugs (DMARDs).

These drugs included infliximab, etanercept, adalimumab, and anakinra (rate ratio 1.21, 95% CI 1.02-1.43).

However, the greatest risk for infection was conferred by current use of oral corticosteroids, and that risk was dose related.

Use of the drugs at less than or equal to 5 mg/day (in prednisone equivalents) was associated with a 1.32 relative risk of infection; use of between 6 mg/day and 10 mg/day, with a 1.94 relative risk.

And use of greater than 10 mg/day had a relative risk for infection of 2.98 (95% CI, 2.41-3.69).

In conclusion, the researchers wrote that methotrexate and hydroxychloroquine were actually associated with decreased risk of hospitalized infection, "whereas for sulfasalazine, leflunomide, and other traditional DMARDs, there was no association."

The authors wrote that their study was limited by the possibility of misclassification of patients into the RA cohort and also by their inability to assess disease severity and patients' history of prior events.

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