Isotretinoin Use May Increase Risk of IBD

BY SHERRY BOSCHERT

SAN DIEGO — Isotretinoin use was associated with a 68% increased risk for subsequent development of inflammatory bowel disease, particularly ulcerative colitis, in a retrospective case-control study of 30,021 patients.

The odds ratio of 1.68 for inflammatory bowel disease (IBD) in isotretinoin users compared with nonusers had a 95% confidence interval (CI) of 0.98-2.86, Dr. Seth Crockett and his associates reported in a poster presentation at the annual meeting of the American College of Gastroenterology.

The findings add to ongoing controversy that IBD risk with isotretinoin may have been a factor in the decision by Roche to pull the best-known brand of isotretinoin, Accutane, off the market in June 2009.

The current study examined a large administrative claims database with records on 55 million patients from more than 70 U.S. health plans. The investigators compared 8,189 patients with at least 12 months of continuous health plan enrollment and diagnoses of ulcerative colitis, Crohn's disease, or indeterminate IBD with three non-IBD control patients per IBD patient, matched by age, gender, and geographic region. They looked at exposure to isotretinoin in the 21,832 control patients during the first 12 months of health plan enrollment.

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Results pointed to a possible dose-response effect: The risk for IBD increased with the number of isotretinoin prescriptions. Having four or more isotretinoin prescriptions was associated with an odds ratio of 2.67 for development of IBD (CI, 1.32-5.41), reported Dr. Crockett of the University of North Carolina, Chapel Hill.

Subgroup analyses showed a strong association between isotretinoin use and ulcerative colitis (odds ratio, 4.36; CI, 1.98-9.66) but no association between isotretinoin exposure and Crohn's disease (odds ratio, 0.68).

"The flip side of all this is that there are patients who desperately need isotretinoin," Dr. Stephen P. Stone commented in an interview. "Those of us who care for people with acne and are aware of the physical and psychosocial aspects of it find it an indispensable drug," said Dr. Stone, chair of the American Academy of Dermatology's task force on retinoids and professor at Southern Illinois University, Carbondale. The drug also is helpful for less common problems such as cutaneous lupus that do not respond to other treatments, he added.

The possible association between isotretinoin and IBD has long been included in label warnings, but it drew increased interest after a 2006 study by gastroenterologists at the University of Chicago. That study looked at all 85 cases of IBD in isotretinoin users reported to the Food and Drug Administration in 1997-2002 and graded the strength of causality using the Naranjo adverse drug reaction probability scale. Mean scores suggested that the oral retinoid was a "probable" cause of IBD (Am. J. Gastroenterol. 2006;101:1569-73). Some dermatologic experts criticized the study's methodology, saying that a one-point adjustment for accuracy in the probability ratings would downgrade the mean score to "possible."

A separate study by gastroenterologists at the University of Manitoba, Winnipeg, found no significant association between isotretinoin use and IBD. Using a large government database and drug registry, they found that 1.2% of patients with IBD and 1.1% of matched patients without IBD used isotretinoin before IBD diagnosis, an insignificant difference (Am. J. Gastroenterol. 2009;104:2774-8).

Dr. Crockett and his associates reported having no conflicts of interest related to their study. Dr. Stone reported no conflicts of interest. ■