Acne Controversies: An Update Based on Recent Findings

Definitive answers still elude medical professionals, but data offer some suggestions regarding the role of diet in acne and relationship of isotretinoin to IBD.

Insights from Bari B. Cunningham, MD

Despite its prevalence—or perhaps because of it—acne can be a source for confusion and misinformation, not only among affected individuals but also among the medical professionals who manage patients with the disease. Some myths and misconceptions arise from obvious misinformation. Sometimes, science simply has not provided a clear answer on the matter.

Two areas of current controversy in acne management are the role of diet in causing or exacerbating the condition and the relationship between oral isotretinoin therapy and the development of irritable bowel disease. While definitive answers elude medical professionals, the data seem to provide some strong indications. Speaking at the Winter Clinical Dermatology Conference in Koloa, HI in January, Bari Cunningham, MD, of Comprehensive Dermatology Group in Encinitas, CA, reviewed the available data related to these two controversies.

Diet and Acne

The controversial association between acne and diet continues to generate debate among patients and among clinicians. A recent review of the published data offered some insights but did not settle the debate. The review included 27 relevant articles, 21 of which were observational studies and six of which were clinical trials. Among the studies, there were 15 cross-sectional, two case-control, and four prospective cohort designs. Following are highlights of findings from the analysis.

Acne prevalence is lower in rural populations than in industrialized ones, and according to at

Take-Home Tips. The controversial association between acne and diet continues to generate debate among patients and among clinicians. Several studies have elucidated interactions between glycemic load, insulin sensitivity, hormonal mediators, and acne, indicating that a low-glycemic load diet may lead to reduction of acne lesions compared to controls. Some evidence appears to support a role for hormones in milk to influence acne. Although risk for IBD has been added to the isotretinoin label, an analysis of published data concluded that these isolated case reports are not sufficient evidence of an association between isotretinoin and irritable bowel disease.
At least two studies, acne prevalence increases as populations adopt a Western diet, whether through migration or cultural change. A western diet consists of high proportions of food with a high glycemic index (see below), as well as more processed foods, soda, beef, and dairy, according to these reviews, while non-Western diets emphasize fruits, vegetables (including root vegetables) and only a small proportion of flour, sugar, and meat.

The issue of milk consumption and acne has been an area of debate. The current analysis highlighted three large studies that reported a positive association between milk intake and acne. Milk consumption was associated with increased risk for acne as well as increased acne severity. The fat content of milk (skim versus whole) has not been found to influence its association with acne, suggesting that hormones in milk may therefore play a role in mediating the skin disease. Hormones in milk—IGF-1, 5α-reduced steroids, and α-lactalbamin—can survive processing and may affect the pilosebaceous unit. Milk consumption increases IGF-1 production, which has been associated with increased ovarian androgen production.

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Chocolate was not associated with exacerbation of acne in two studies that were reviewed in the recent analysis.

Isotretinoin Updates
The package insert for isotretinoin now has a warning for inflammatory bowel disease (IBD): Inflammatory Bowel Disease: [isotretinoin] has been associated with inflammatory bowel disease (including regional ileitis) in patients without a prior history of intestinal disorders. In some instances, symptoms have been reported to persist after [isotretinoin] treatment has been stopped. Patients experiencing abdominal pain, rectal bleeding or severe diarrhea should discontinue Accutane immediately.

IBD is also listed as a possible adverse reaction to isotretinoin. FDA ordered IBD risk be added to the label in 2005. Nonetheless, the association between IBD and isotretinoin has been controversial.

Recently, a New Jersey court awarded $12.9 million to three patients who developed IBD after being treated with isotretinoin. The settlement in this case generated significant media attention, although other suits preceded it, and numerous law offices continue to actively recruit potentially affected patients.

A 2009 analysis sought to assess the risk of IBD associated with isotretinoin. The analysis uncovered 12 relevant case reports and one case series from seven countries published in the preceding 23 years. No prospective studies had been published. The identified publications all reported an association between isotretinoin use and subsequent development of IBD, however, they differed with respect to reported isotretinoin dose, duration of treatment, the onset of disease in relation to therapy (whether on or off medication), and the clinical presentation of IBD. The authors concluded that these isolated case reports are not sufficient evidence of an association between isotretinoin and IBD. Assuming no increased risk for IBD, estimates predict 59 coincident cases of IBD each year in the population of patients using isotretinoin.

The authors speculate that the natural course of IBD could contribute to an apparent temporal association between IBD and isotretinoin. IBD is most commonly diagnosed in individuals under
age 35, and frequent bouts of abdominal pain and diarrhea in childhood are often reported by patients. A genetic basis of IBD is suspected. IBD is a chronic disorder, and symptoms are known to wax and wane.3

Given these features of IBD, it seems possible that patients with subclinical disease could be prescribed isotretinoin. As IBD flares, isotretinoin may be assumed by the patient and/or physician to have incited the incident and may be withdrawn. By the time treatment is withdrawn, IBD may naturally be entering a non-symptomatic phase, further implicating isotretinoin in the development of GI symptoms. As such, chance, confounding bias, and misrepresentation of the natural course of IBD could contribute to an apparent association between isotretinoin and IBD.2

More recently, the same group reported results of a case-control study of isotretinoin and IBD using a large insurance claims database. Researchers identified incident cases of IBD and matched to three controls on the basis of age, gender, geographical region, health plan, and length of enrollment. Conditional logistic regression was used to adjust for matching variables. In total, 8,189 cases of IBD were identified (3,664 Crohn’s disease (CD), 4,428 ulcerative colitis (UC), and 97 IBD unspecified) and matched to 21,832 controls. A total of 60 subjects (24 cases and 36 controls) were exposed to isotretinoin.

While UC was strongly associated with previous isotretinoin exposure (odds ratio (OR) 4.36, 95% confidence interval (CI): 1.97, 9.66), there was no apparent association between isotretinoin and CD (OR 0.68, 95% CI: 0.28, 1.68). Increasing dose of isotretinoin was associated with elevated risk of UC (OR per 20 mg increase in dose: 1.50, 95% CI: 1.08, 2.09). Overall, the study concluded the absolute risk of developing UC after taking isotretinoin “is likely quite small.”4

Another area of study involving isotretinoin is its use in toddler acne, which has been reported to be safe and effective.5,6 Although the etiology of infantile acne is not fully understood, androgen influence on sebaceous glands is thought to be the primary driver of the presentation.6 Typical dosage of isotretinoin for infants and toddlers is 0.2mg/kg/day to 1.5mg/kg/day. Isotretinoin tablets can be split, and half a tablet can be pressed into a slice of a soft-centered candy bar (such as a Milky Way) so that a child can easily consume it.