Diet-Acne Association Gains Footing in Literature

ARTICLES BY BRUCE JANCIN
Denver Bureau

WAIKOLOA, HAWAII — Most physicians, taught that diet is unrelated to the pathogenesis of acne vulgaris, dismiss as folklore the frequent questions posed by patients and family members as to whether eating greasy foods, chocolate, or other sweets causes their skin problem.

The diet issue, however, has gained renewed vitality of late in the dermatology literature, with various studies implicating milk, high–glucose-load diets, and low-fiber/high–saturated-fat intake, Dr. Anthony J. Mancini said at the annual Hawaii dermatology seminar sponsored by Skin Disease Education Foundation.

The link between milk consumption and acne has been extensively pursued by investigators at the Harvard School of Public Health, Boston, said Dr. Mancini. In a prospective cohort study of 6,094 girls, aged 9-15 years, who were children of Nurses' Health Study II participants, self-reported greater consumption of milk—whether whole, low-fat, or skim—on food frequency questionnaires was independently associated with acne severity in a multivariate analysis, said Dr. Mancini, head of pediatric dermatology at Children's Memorial Hospital, Chicago.

Those who drank two or more servings of milk per day during the 2-year study period were roughly 20% more likely to have acne than were girls who drank less than one serving per week. The results weren't significantly altered by excluding girls using contraceptives or restricting the analysis to those who were less than 11 years old at baseline (Dermatol. Online J. 2006;12:1).

In a similarly designed study conducted with 4,273 teenage boys, the Harvard group once again found a positive association between milk intake and acne. This time, though, the relationship was significant only for skim milk (J. Am. Acad. Dermatol. 2008; 58:787-93).

The investigators' hypothesis is that hormones and other bioactive agents contained in milk have effects upon acne.

In an editorial accompanying an earlier study by the group, Dr. F. William Danby, a dermatologist at Dartmouth University, Hanover, N.H., noted that 75%-90% of all milk reaching the marketplace comes from pregnant cows. This milk contains progesterone, other dihydrotestosterone precursors, somatostatin, prolactin, insulin, growth factor–releasing hormone, insulinlike growth factors 1 and 2, and numerous other substances that could stimulate pilosebaceous activity (J. Am. Acad. Dermatol. 2005;552:360-2).

Dr. Mancini noted that the link between acne and a high–glycemic-load diet rich in processed carbohydrates was made by Loren Cordain, Ph.D., and coworkers at Colorado State University, Fort Collins. In contrast to the near-universal prevalence of acne in adolescents in modern developed countries, they reported a rate of essentially zero in two non-Westernized populations: the Aché hunter-gatherers of Paraguay and Kitavan Islanders of Papua New Guinea. These subjects also had low serum insulin and high insulin sensitivity.

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In one study, two or more servings of milk daily raised the risk of acne 20%.

Genetic factors were unlikely to be the sole explanation, the investigators argued. They highlighted the subjects' strikingly non-Western diets, which consisted of minimally processed plant and animal foods (Arch. Dermatol. 2002;5138:1584-90).

In pursuit of the hypothesis that low–glycemic-load diets may diminish acne, investigators at RMIT University in Melbourne, conducted a 12-week randomized trial involving a low–glycemic-load diet and a carbohydrate-dense control diet in 43 male acne patients aged 15-25 years, Dr. Mancini said.

Both acne severity and insulin sensitivity improved on the low–glycemic-load diet, but the subjects also lost weight on the diet and the investigators couldn't rule out the possibility that this weight loss played a role in the observed benefits (J. Am. Acad. Dermatol. 2007;57:247-56).

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Two Topical Acne Therapies Slated for Armamentarium

WAIKOLOA, HAWAII — In a regulatory turnaround, it looks like physicians will gain ready access to dapsone gel 5% for the treatment of acne vulgaris after all, Dr. David M. Pariser said at the annual Hawaii dermatology seminar sponsored by Skin Disease Education Foundation.

The favorable results of a phase IV safety study of the topical agent conducted in acne patients with known glucose 6-phosphate dehydrogenase deficiency recently persuaded the Food and Drug Administration to rescind its requirement that all acne patients be tested for G6PD deficiency before prescribing Aczone (dapsone gel).

That requirement, which came as a condition of FDA approval of Aczone in 2005, had convinced the drug's manufacturer, QLT Inc., that topical dapsone was not a marketable drug. Aczone has languished ever since.

Dr. Pariser of Eastern Virginia Medical School, Norfolk, was an investigator in the phase IV safety study, which involved 56 evaluable acne patients with G6PD deficiency and showed no safety problems. Hemolysis is a concern with systemically administered dapsone in G6PD-deficient patients, but there is virtually no systemic absorption of topical dapsone gel, he said.

In a pooled analysis of more than 3,000 patients, 40.5% of acne patients were clear or almost clear after 12 weeks of twice-daily dapsone dosing. Both inflammatory and noninflammatory lesion counts were significantly reduced, with inflammatory lesions responding within the first 2 weeks.

FDA marketing approval is anticipated for another novel topical acne therapy: the combination of the retinoid adapalene 0.1% and benzoyl peroxide 2.5% in a fixed-dose gel formulation applied once daily, according to Dr. Pariser.

The combination, known as Epiduo, showed rapid efficacy in a 517-patient, double-blind, 12-week Galderma-sponsored randomized trial in which it outperformed each of its separate constituents as well as vehicle alone.

At 12 weeks, 42.5% of patients in the fixed-dose combination therapy group were clear or almost clear, the primary study end point required by the FDA. That was significantly better than the 34.5% rate with adapalene only, 34.9% with benzoyl peroxide only, and 14.5% with vehicle. Fifty-three percent of patients on Epiduo experienced at least a 50% reduction in total lesion count, compared with about 35% with either agent alone and 25% with vehicle (J. Am. Acad. Dermatol. 2007;57:791-9).

Dr. Pariser led a 12-month safety and efficacy study of the fixed-dose combination in 452 acne patients. The study showed clinically significant reductions in both inflammatory and noninflammatory lesions as early as week 1, with sustained reductions of 75%-80% at 1 year. Only 2% of subjects discontinued the therapy because of adverse events (J. Drugs Dermatol. 2007;6:899-905).

He disclosed that he is a consultant to QLT and has been paid to conduct research by Galderma. SDEF and this news organization are wholly owned subsidiaries of Elsevier. ■

Removal May Not Alter Outcome

AKs *from page 1*

visit for a mean of 3.5 years (maximum 6 years). None of the AKs were treated. Lesions were biopsied only when they developed some concerning sign suggesting progression to malignancy.

During the study period, the 169 patients had 7,784 AKs documented on their face and ears, one-quarter of which were present at baseline. Fifty-five percent were not present 1 year after diagnosis. Thirty-two percent of those present 1 year after initial diagnoses were absent at the 6-month visit but were noted again 6 months later. Four years after initial diagnosis, 31% of AKs were still present; however, 87% of them had disappeared for one or more interim examinations.

"There are a lot of these things coming and going," Dr. Weinstock said at a meeting of the European Society for Dermatological Research, the Japanese Society for Investigative Dermatology, and the Society for Investigative Dermatology.

Biopsies were obtained on 411 suspicious lesions. Thirty percent proved to be SCCs, 18% were BCCs, 39% were AKs, and 13% were seborrheic keratoses or other lesions.

Overall, 0.6% of clinically diagnosed AKs progressed to SCC at 1 year and 2.6% at 4 years. Three-quarters were invasive and the remainder in situ SCCs. This progression rate is nearly 10-fold greater than the often-quoted 0.075%/year progression rate from a 20-year-old British study, the dermatologist observed (Lancet 1988;8589:795-7).

AKs present at the initial examination had a higher rate of progression to SCC.

AKs also progressed to BCC at a rate of 0.5% in 1 year and 1.6% at 4 years. That was unexpected, said Dr. Weinstock. Dermatologic dogma holds that AKs give rise to SCCs. It's unlikely these lesions were predominantly BCCs that had initially been misdiagnosed as AKs because a steady increase in BCC risk over the follow-up period was noted. Had it been largely a matter of misdiagnosed BCCs, the risk of developing BCC would likely have increased sharply early in the study and then remained stable, he said.

Two-thirds of SCCs and one-third of BCCs on the face and ears of study participants arose in lesions diagnosed clinically as AKs in prior examinations.

Dr. Joel M. Gelfand of the University of Pennsylvania, Philadelphia, pronounced the new insights into the natural history of AKs gained through this study "really important," particularly since there are no persuasive data to show any of the modalities used to treat AKs actually lower the risk of developing SCC. That observation prompted Dr. Weinstock to note that a new VA chemoprevention trial, this one involving topical 5-fluorouracil for AKs, is now underway.

Audience members said a key limitation of the Oklahoma City study is the reliability of clinical diagnosis of AKs. Dr. Weinstock agreed that the reliability of clinical diagnosis is poor—"better than flipping a coin, but not what anyone would hope for clinical judgments"—based upon a comparison of AK counts by seven dermatologists participating in the tretinoin trial that showed substantial discrepancies. The point is, he stressed, that patient management decisions in routine practice are typically based upon clinical diagnosis of AKs. ■