Celecoxib May Lower Risk of Some Skin Ca

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MONTREAL — A twice-daily dose of celecoxib given over a period of 9 months was associated with a 60% reduction in the incidence of nonmelanoma skin cancer, according to the results of a new study.

"Inhibition of COX-2 is an effective means of limiting the development of cutaneous squamous and basal cell carcinomas in humans," said Dr. Craig Elmets at the annual meeting of the Society for Investigative Dermatology.

The findings suggest that pharmaceutical agents such as celecoxib may offer greater protection against skin cancer than do sunscreens, which are only "modestly effective," said Dr. Elmets, professor and chair of the department of dermatology and director of the Skin Disease Research Center at the University of Alabama, Birmingham. "There's only about a 35% reduction in squamous cell carcinomas when sunscreens are used on a regular basis over a 5-year period of time, and there's no reduction in basal cell carcinomas."

The multicenter, randomized, placebo-controlled study was funded by the National Cancer Institute and the National Institute of Arthritis and Musculoskeletal and Skin Diseases, with additional funding from Pfizer through a contractual agreement with the National Institutes of Health, he said. Dr. Elmets did not disclose any personal conflicts of interest.

The study enrolled 238 patients with nonmelanoma skin cancers from eight U.S. centers. The mean age of the patients was 65 years, most were male, and virtually all were white.

"The study was terminated somewhat early because of concerns of cardiovascular effects due to another COX-2 inhibitor," he noted.

Subjects in the study had Fitzpatrick skin types I-III, extensive actinic damage with 10-40 actinic keratoses (AKs), and a prior histologic diagnosis of either AK or nonmelanoma skin cancer. Subjects were excluded if they required treatment with NSAIDs, although cardioprotective doses of aspirin were allowed.

At entry, patients had a mean number of 22 AKs, and between 2.1 and 2.5 nonmelanoma skin cancers, he said.

Patients were randomized to either placebo or celecoxib 200 mg twice daily, which is the approved dosage for arthritis, Dr. Elmets said. "We were concerned about cardiovascular abnormalities and GI abnormalities, and if anything there was a bias towards patients in the celecoxib group having a prior history of that."

A comparison of the number of AKs at baseline and completion showed a lack of effect of celecoxib, compared with placebo, he noted. However, the development of new cutaneous basal and squamous cell carcinomas was much reduced. "We were delighted to find that celecoxib was quite effective, with a 58% reduction compared to placebo-treated controls," he said.

If the two types of lesions are considered separately, celecoxib treatment led to a 58% reduction in squamous cell carcinoma (SCC), and a 62% reduction in basal cell carcinoma (BCC).

"The difference between the [placebo and treated] groups started to become apparent quite rapidly, at 3 months, and persisted throughout the study. We were concerned that there might be one or two outliers that were skewing the results, so rather than looking at the total number of skin cancers, we also looked at the number of individuals who developed BCC or SCC or both. Again we found that patients with celecoxib had fewer BCCs and SCCs than the placebo group."

There were no differences in adverse events including cardiovascular adverse events between the two groups, Dr. Elmets reported. During the question period, he acknowledged that there were higher blood pressures reported in the treatment group.

The data are "very compelling," commented Dr. Maryam Asgari of Kaiser Permanente in Oakland, Calif., in an interview. But she suggested perhaps the study was too short to have such dramatic conclusions. "I know that typically for most cancers you would need a study to last 2-5 years before you would expect to measure an effect," she said. Similarly, adverse events from COX-2 inhibitors would likely need longer to develop.

Dr. Asgari said her research in the same field has produced the opposite results. Her study found no protective effect for all NSAIDs—both selective and nonselective COX inhibitors—on the incidence of squamous cell carcinoma. A previous paper published by her group also found no protective effect of these drugs on melanomas (J. Natl. Cancer Inst. 2008;100:967-71).

Celecoxib's lack of effect on AKs is a puzzling result, she added. "You would think that if COX-2 inhibitors are working to prevent new cancers from arising that they would also have a pretty dramatic effect on actinic keratoses because they both share the same pathway."

Finally, patients in the COX-2 study were allowed to take cardioprotective doses of aspirin—an important factor that the analysis did not adjust for, she pointed out. "Even low-dose aspirin inhibits COX, and it could just be that the people in the treatment arm were much more likely to be on aspirin as well." ■

Melanoma Risk Not Lowered By Increased Vitamin D Intake

MONTREAL — Increased vitamin D intake is not protective against melanoma, according to the results of the largest prospective cohort study on the topic.

"If you're worried about melanoma risk, I don't think popping a vitamin D pill is going to help, at least in the standard doses," said Dr. Maryam M. Asgari, of Kaiser Permanente in Oakland, Calif.

In fact, her study, presented at the annual meeting of the Society for Investigative Dermatology, actually suggests a trend toward a greater risk of melanoma with high dietary intake of vitamin D.

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DR. ASGARI

"When we looked at diet alone there was a slightly increased risk, but when we combined diet and supplement use, the risk washed out," she said in an interview. "It's hard to say whether this was an effect of dietary vitamin D itself, or something else—for example, mercury—in the diets of people who consume large amounts of fatty fish, liver, and egg yolk."

The study included a cohort of 68,611 participants in the Vitamins and Cohort Lifestyle (VITAL) study (J. Invest. Dermatol. 2009;129:1675-80). The average age of the cohort was 62 years, and 52% of participants were female.

A food frequency questionnaire was used to determine dietary intake of vitamin D and other nutrients in the preceding year. Data were also collected about vitamin supplement use over the past 10 years. Total vitamin D intake from both dietary and supplemental sources was then calculated for a 10-year period, compared with incident melanoma cases from the Surveillance, Epidemiology, and End Results database.

There was no evidence of an association between overall supplement use or duration of use with either an increased or decreased risk of melanoma, Dr. Asgari reported. However, there was a nonsignificant trend toward a protective effect at the higher supplement doses ($P = .67$). "In our study, we did not have a lot of high-dose supplement users. Most of them were taking an additional 600 IU," she commented.

When supplement use was examined in combination with dietary intake, there was no association with melanoma risk. However, high dietary intake alone was associated with a slightly increased risk of melanoma ($P = .05$).

"These people were just eating their normal diet, but this finding is not inconsistent with what's been published in the past, with regard to cohort studies," she said. Specifically, a Norwegian study of almost 51,000 participants found that cod liver oil consumption was associated with an increased risk of melanoma in women, but not in men (Int. J. Cancer 1997;71:600-4).

In contrast, one case-control study of around 1,000 participants found a protective effect of high dietary vitamin D intake, but no impact when dietary and supplemental intake were examined together (Cancer Epidemiol. Biomarkers Prev. 2004;13:1042-51).

"The overall take-home message of our study is that vitamin D is not associated with decreased melanoma risk," Dr. Asgari said. ■

Melanoma Incidence Had Annual Increase of 3% Over 10-Year Period

MONTREAL — The incidence of melanoma in the United States increased rapidly over a 10-year period, regardless of tumor thickness and socioeconomic status, Dr. Eleni Linos reported.

"This has implications for preventive screening and primary care," she said at the annual meeting of the Society for Investigative Dermatology. "We believe this represents a genuine increase in melanoma cases, not just a sign of better screening."

Dr. Linos and her coinvestigators examined data from the Surveillance, Epidemiology, and End Results (SEER) registry between 1992 and 2004 (J. Invest. Derm. 2009;129:1666-74). They identified 70,596 cases, said Dr. Linos, who declared having no conflicts of interest.

During the study period, the incidence of melanoma of all thicknesses increased from 18 per 100,000 in 1992 to 26 per 100,000 in 2004—an annual increase of 3%, said Dr. Linos of Stanford (Calif.) University. The steepest increase was seen in men aged 65 years and older, in whom the incidence rose from 73 to 126 new cases per 100,000.

"The vast majority of melanomas that are diagnosed are thin, and that is why we have not seen such a dramatic increase in mortality rates," she explained. Overall mortality rose by 0.4% annually, with a 2% annual rise seen in older men.

Melanoma trends were examined according to socioeconomic status to determine whether the findings could be explained by better screening in those with a higher status, resulting in less mortality. Similarly, tumor thickness was examined to determine whether the increased incidence could be explained by more diagnoses of thin, clinically insignificant tumors.

"We found parallel increases across all socioeconomic groups and thicknesses, representing a true increase in clinically significant tumors," she said. ■