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Combination of calcium, vitamin D reduces melanoma risks in some women

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A combination of calcium and vitamin D may cut the chance of melanoma in half for some women at high risk of developing this life-threatening skin cancer, according to a new study by Stanford University School of Medicine researchers.

Using existing data from a large clinical trial, the study zeroed in on women with a history of non-melanoma skin cancer, as people with this generally non-fatal disease are more likely to develop the more lethal illness — melanoma. The researchers found that women who once had non-melanoma and took the calcium-vitamin D combination developed 57 percent fewer melanomas than women with similar histories who were not given the supplements. Non-melanoma skin cancers, such as basal cell or squamous cell cancers, are the most common forms of skin cancer.

"In preventive medicine, we want to target people most at risk for the disease," said dermatologist Jean Tang, MD, PhD, lead author of the study. "If you previously had a non-melanoma skin cancer, calcium plus vitamin D might reduce your risk of the more deadly melanoma."

Tang added a note of caution. The study found that a daily dose of 1,000 mg calcium plus 400 IU of vitamin D doesn't provide skin cancer protection for everybody. Women without a history of non-melanoma skin cancer who took the supplements did not see any reduction of risk compared with their placebo-group counterparts, according to the research.

The study will be published online on June 27 in the *Journal of Clinical Oncology*.

Vitamin D is well-known for its role in bone growth, but it also affects non-skeletal cells. In many parts of the body, including the skin, vitamin D controls how quickly cells replicate, a process that often goes awry in cancer. Reports from various institutions have suggested that vitamin D is associated with lower risks of colon, breast, prostate and other cancers. Nonetheless, the Institute of Medicine published a report last November saying that more research was needed on vitamin D and calcium, as the evidence was insufficient to prove their having a benefit for conditions other than bone health.

This study is the second to look at the effect of vitamin D supplementation on cancer risk with a randomized, controlled trial.

Tang and colleagues analyzed data from the Women's Health Initiative, a study that followed 36,000 women ages 50 to 79 for an average of seven years. Half of the women took the daily dose of calcium and vitamin D as part of the experiment; the other half took a placebo pill. The WHI calcium plus vitamin D trial was designed to look at the effects of the supplement on hip fractures and colorectal cancers, but its researchers collected data on many other health issues, including other cancers.

Tang and colleagues took advantage of the large and long-term data set provided by the WHI trial to explore whether vitamin D has a protective effect against skin cancer. "Our results include the first positive cancer-reducing effect seen from the calcium plus vitamin D trial," said Teresa Fu, MD, a co-author of the study and a recent graduate of the School of Medicine.

The lack of protective effect in women without a history of non-melanoma skin cancer may be due to the amount of vitamin D given to

the patients in the WHI trial. "The patients in the Women's Health Initiative were given vitamin D at a very low dose, based on today's knowledge — only 400 IU per day," said David Feldman, MD, professor emeritus of endocrinology and a co-author of the study. Furthermore, patients in the placebo group were allowed to take as much vitamin D as patients that were provided the calcium and vitamin D supplements, so the experimental difference between the two groups was small. In light of that small difference, "it's somewhat surprising that there was an effect on melanoma risk, and I think many potential benefits of vitamin D may not have been detected," said Feldman.

Because men were not included in the trial, the researchers cannot be certain whether the protective effect of the supplements would also apply to men with a history of non-melanoma skin cancer. Nonetheless, a 2010 study by Tang demonstrated that elderly men with higher blood levels of vitamin D have fewer non-melanoma skin cancers.

Even in a large study like the WHI, the low frequency of melanomas means that the absolute number of cancers was small. Out of the 36,000 participants, only 176 cases of melanoma were reported. "That just highlights how large a trial needs to be to capture cancer as relatively rare as melanoma," said Marcia Stefanick, PhD, the Stanford WHI principal investigator and senior author of this study.

"These results spur us to do more studies," said Tang. She is planning multiple lines of research to examine the potential relationship between vitamin D and cancer prevention, including a study that will compare blood levels of vitamin D with melanoma outcomes. Another line of research will examine the effect of larger doses of vitamin D on the behavior of skin cells in patients with high skin-cancer risk.

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