What Is the Dose-Response Relationship Between Vitamin D and Cancer Risk?

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Background: An inverse association of serum 25-hydroxyvitamin D with risk of cancers of the colon and breast has been reported in several well-designed observational studies. This study describes the dose-response gradient between serum 25(OH)D and risk of these cancers. It also projects dose-response gradients for cancers of several other sites, based on age-standardized cancer incidence and ultraviolet B irradiance among 177 countries.
Methods: Combined data from observational studies of the inverse association of serum 25-hydroxyvitamin D [25(OH)D] with breast and colon cancer were analyzed to obtain dose-response gradients. A similar approach was used for ovarian cancer, based on more limited data. For several other cancers, dose-response gradients were estimated based on modeled or reported winter serum 25(OH)D levels and estimated age-standardized incidence rate estimates for 177 countries from the IARC GLOBOCAN database. Serum 25(OH)D levels in each country were obtained from previous studies or modeled based on winter solar ultraviolet B irradiance by country, adjusted for winter cloud cover data obtained from NASA international climatology (ISCCP) satellites.
Results: There was an inverse dose-response relationship between serum 25(OH)D and risk of colon, breast, and ovarian cancer. The asymptotic portion on the left side of the dose-response curve was shortest for colon cancer (0–11 ng/ml) and longer for breast (0–20 ng/ml) and other cancers. The slope of the active part of the curve did not differ greatly by cancer. According to observational studies, approximately 50% of colon cancer incidence could be prevented by lifelong maintenance of a serum 25(OH)D level of $\geq$ 35 ng/ml. Prevention of 50 percent of breast cancer incidence potentially would be achievable by maintenance of $\geq$ 55 ng/ml. In North America and Europe, a projected 50 percent reduction in colon cancer incidence would require universal oral intake of 1,500 IU/day of vitamin D_3, while a similar reduction in incidence of breast cancer would require 3,500 IU/day. The latter is above the 2,000 IU/day upper limit established by the National Academy of Sciences. These gradients for cancer risk suggest that the upper limit should be revised upward. In the meantime, 2,000 IU/day would be practical for general intake, with routine advice to consume 175–225 ml/day of water or other fluids.
Conclusions: According to observational studies, there was an inverse dose-response gradient between serum 25(OH)D and cancers of the colon and breast. More research would be worthwhile to better define the dose-gradient of 25(OH)D with ovarian and other cancers. Additional research would be desirable on appropriate levels of 25(OH)D in childhood, which is arguably the most critical period for breast cancer. In the meantime, the dose-response gradients reported in this study would be useful in designing new studies and in making cancer prevention recommendations to the public. Pending future research, it would be prudent to measure serum 25(OH)D annually in winter or early spring in all persons, and when possible, seek to maintain a serum 25(OH)D level, at all ages beyond infancy, of not less than 55 ng/ml.