CORRELATION BETWEEN HIGHER DOSES OF VITAMIN D SUPPLEMENTS AND TOTAL CANCER INCIDENCE AND MORTALITY

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Introduction.

A good vitamin D (VD) status is proved to be beneficial both in cancer prevention and in the prognosis of several cancers, according to a new research review. Many studies have shown that the VD receptor (VDR) is expressed in almost all tissues of the body.

Many tissues without any obvious relationship with the calcium/phosphorus and/or bone metabolism are able to express the VDR, 1-alpha-hydroxylase, and 24-hydroxylase molecules. 25(OH)D enters these tissues and is locally hydroxylated into calcitriol which binds to the VDRs present in these cells. This "peripheral" production of calcitriol is not regulated by calciotropic hormones (PTH, FGF23, …), but seems dependent on the 25(OH)D concentration in the extra-cellular fluid of these tissues. This is the basis for the "non-classical" genomic effects of VD.

Background.

The anti-cancer effects of VD are especially pronounced in the prevention and treatment of colon cancer and blood cancers.

High VD responsiveness can be linked to a small cancer risk, knowing that this responsiveness varies between individuals, affecting their need for VD supplementation. A low VD status is associated with an increased risk of various cancers in many epidemiological studies, especially colorectal [(1)] and breast [(2)].

VD sufficiency is associated with a delayed mortality not only in prospective observational studies [(3)] but also in international studies [(4)]. These potential "non- classical" effects of VD seem so impressive that a discussion on the level of evidence supporting them is necessary. Since the prevalence of VD inadequacy is high, supplementation with VD has been recommended, especially in high risk and elderly population in many situations. Randomized trial data suggest a stronger benefit of VD on cancer mortality and survival than cancer incidence [(5,6)]

Laboratory and animal studies shown that VD may inhibit carcinogenesis and slow tumor progression, including promotion of cell differentiation, inhibition of cancer cell proliferation, and anti-inflammatory, immunomodulatory, proapoptotic, and antiangiogenic effects [(5,7)]. Several reports have showed that vitamin D has important regulatory roles of mechanisms controlling cellular proliferation, differentiation and growth. For instence, in prostate cancer, the strong anti-proliferative effects of several synthetic analogs known to exhibit less calcemic activity than VD suggest that these compounds potentially may be useful as an additional therapeutic option for the treatment. VD may decrease tumor invasiveness and propensity to metastasize, leading to reduced cancer mortality [(8)]. Higher serum 25(OH)D levels at diagnosis have been linked to longer survival in cancer patients [(9)].

Many studies that associate VD levels with cancer risk measure serum levels of 25(OH)D to determine if the subjects are deficient. For example, a greater proportion of melanoma patients had deficient or insufficient levels of 25(OH)D than healthy controls [(10)]. Similarly, VD levels were lower in patients with thyroid cancer compared to matched controls [(11)]. Women with breast cancer that were deficient in 25(OH)D had larger tumors, more advanced stage and reduced survival than those that were not deficient [(12)]. For glioblastoma, serum 25(OH)D was

inversely associated with risk, although there was no association for non-glioblastoma glioma [13].

Chronic inflammation is considered to be protumorigenic such as for cancer of the prostate, lung, liver and oesophagus [14,15]. VD can temper inflammation and, thus, has been examined for efficacy in inflammation-associated disorders [16,17]. This includes cancer chemoprevention. The immune-modulatory effects of VD in patients with cancer have also been examined. An analysis of the prostate transcriptome showed that VD supplementation (4.000 IU/day) for 2 months prior to undergoing prostatectomy altered expression of inflammatory genes [18].

Conclusion.

Supplemental vitamin D intake could address the high prevalence of vitamin D deficiency in many countries in the world. Many studies indicate that intake or synthesis of vitamin D is associated with reduced incidence and death rates of colon, breast, prostate, and ovarian cancers.

Many laboratories and epidemiological studies have been published concerning the association between vitamin D and its metabolites and cancer. Long-term studies have demonstrated the efficacy of moderate intake of vitamin D in reducing cancer risk. Despite these reassuring studies, up to now, the public health and medical communities have not adopted use of vitamin D for cancer prevention.

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