

New Study Confirms The Value of Vitamin D Supplementation In The Adjunctive Treatment Of Prostate Cancer

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In recent years a number of epidemiological, experimental, and intervention trials have suggested that vitamin D-based compounds may be important in the prevention and treatment of prostate cancer. Epidemiological studies indicate that higher blood levels of vitamin D (25-hydroxycholecalciferol) are associated with a lower risk of developing prostate cancer. Experimental evidence has shown that prostate cells contain vitamin D receptors, which allow for the uptake of 25- hydroxycholecalciferol from the blood stream. Once inside prostate cells, an intracellular hydroxylase enzyme readily converts 25-hydroxycholecalciferol into 1,25, dihydroxycholecalciferol (calcitriol). This form of vitamin D (calcitriol) exerts a number of cancer preventive effects on prostate cells, including slowing the rate of cell division and promoting cellular differentiation.

Experimental studies also show that prostate cancer cells respond to calcitriol by slowing their rate of replication. Vitamin D metabolites have also been shown to increase differentiation and apoptosis (programmed cell death), and decrease proliferation, invasiveness and metastasis of human prostate cancer cell lines, in laboratory studies. Although prostate cancer cells have a more limited ability to produce their own 1,25 dihydroxycholecalciferol (calcitriol) than do non cancerous prostate cells, studies show that many prostate cancer cells continue to express vitamin D receptors on their cell surface, extract vitamin D (25-hydroxycholecalciferol) from the blood stream and convert some 25- hydroxycholecalciferol into calcitriol.

Evidence suggests that prostate cancer cells could also be affected by calcitriol synthesized by neighboring prostate cell as well as the calcitriol made in the kidneys (the kidneys convert 25-hydroxycholecalciferol into calcitriol, which is the principle source of blood calcitriol levels).

To date, intervention studies with prostate cancer patients have shown that administration with 0.5-2.5 micrograms of calcitriol daily tends to slow the rise in PSA levels in these patients, helping to control the disease process to a very significant degree.

Unfortunately, this dosage of calcitriol is well in excess of physiological levels and puts patients at risk for toxicity, including hypercalcemia with the likelihood of calcification of soft tissues and internal organs.

However, more recently, the administration of cholecalciferol, at physiological doses, was shown to decrease or slow the rise in PSA levels in men with prostate cancer without risk of vitamin D toxicity.

The indication from these recent experimental and clinical studies suggests that taking vitamin D in its native form, known as cholecalciferol (this is the over-the-counter form of vitamin D that one would purchase in a drug store or health food store), at a daily dosage of 2,000 IU (50 ug) per day, provides the body with sufficient raw material to convert much of the cholecalciferol into 25-hydroxycholecalciferol (this conversion occurs in the liver). The resulting increase in blood levels of 25-hydroxycholecalciferol, in turn, helps to drive a greater amount of this vitamin D metabolite into existing prostate

cancer cells. Experimental evidence indicates that 25-hydroxycholecalciferol, itself, exerts many similar anti-cancer effects on prostate cancer cells, as those produced by calcitriol. The good news is that the ingestion of 2,000 IU of vitamin D (cholecalciferol) is non toxic and the associated blood level rise in 25-hydroxycholecalciferol resulting from the ingestion of this dosage of vitamin D supplementation, which is usually in the range of 50 nmol/L, is well within normal limits (vitamin D toxicity occurs only when blood levels of 25-hydroxycholecalciferol levels are above 225-250 nmol/L, which does not occur with supplementation at 2,000 IU per day of cholecalciferol).

The most recent study to investigate the use of cholecalciferol in the treatment of prostate cancer was published in the journal *Nutrition and Cancer*, in 2005, by TCS Woo and fellow researchers (volume 51, number 1). In this study 15 prostate cancer patients were given 2,000 IU (50 ug) of cholecalciferol daily and monitored prospectively every 2-3 months.

In 9 patients, the PSA level decreased or remained unchanged (no further rise) and these results were sustained during the 21-month course of vitamin D administration. Analysis also showed that there was a statistically significant decrease in the rate of PSA rise after administration of cholecalciferol compared with that before cholecalciferol administration. The median PSA doubling time increased from 14.3 months prior to cholecalciferol administration to 25 months after commencing cholecalciferol. In fact, 14 of the 15 patients showed a prolongation of the PSA doubling time after cholecalciferol supplementation was introduced to this group. There were no side effects reported by any patient.

The marked prolongation of PSA doubling time is an extremely important outcome to the administration of cholecalciferol in these patients, according to the recent work of Partin and fellow researchers (*J Urol*, 2003). Partin and fellow researchers showed that the risk of distal metastasis of prostate cancer (with respect to relapse after prostate cancer surgery) at 5 years was 65% to 75% when PSA doubling time was less than 10 months compared with 10-20% when PSA doubling time was greater than 10 months.

As such, researches working in this field point out that agents such as cholecalciferol that lengthen PSA doubling time or decrease the rate of PSA increase might be clinically useful in the treatment of prostate cancer cases, with respect to affecting (slowing) the clinical course of the disease, and improving survival rates and quality of life, even if they do not reset the PSA levels into the normal range.

The key aspect of the work presented by TCS Woo and fellow researchers is that the common form of vitamin D (cholecalciferol), which is readily available from retail outlets and other sources, may be the most useful form of vitamin D to use in the prevention and treatment of prostate cancer. It is nontoxic when used at the doses required to exert the beneficial effects noted above, provides a multitude of anti-cancer effects that are similar to that of calcitriol and related vitamin D-drugs (deltanoid drugs) and is highly affordable. As cholecalciferol is a nonproprietary molecule, the cost of providing 2,000 IU of this form of vitamin D is less than \$1.50 month US. Further studies are required to confirm these findings, however, health care practitioners should be aware of the potential benefits of recommending the use of cholecalciferol supplementation as one part of the complementary management of prostate cancer.

It has the potential to slow the rate of prostate cancer cell replication, induce apoptosis (programmed cell death of existing prostate cancer cells), encourage cellular differentiation (reversing some cancerous morphological features of the cell), reduce invasiveness and metastasis, and slow the doubling time of PSA or lower the PSA concentrations in the blood.

References:

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2. Partin AW, Pound CR, and Rootselaar CV. Natural history of progression after PSA elevation following radical prostatectomy: Update. *J Urol*. 2003, 169 (4 suppl): 935