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Prostate Cancer and Vitamin E

The week I was on vacation, two studies were published that called into question the use of dietary supplements. I wrote about the first a couple of weeks ago; see *10-22-2011 Supplements and Mortality* on the Messages page at drchet.com. The prostate cancer study is the second and as the title indicates, it was about taking the supplement vitamin E and how it affected the rate of prostate cancer in men over 50. From the news media reports, you would think that men were dropping in the streets. As you've come to expect, what grabs headlines doesn't always match what is in the actual study. Let's take a look.

The SELECT Study

The Selenium and Vitamin E Cancer Prevention Trial (SELECT) is a large study with 35,533 men from 427 study sites in the United States, Canada, and Puerto Rico (1). The requirements of the study were a PSA less than 4.0 ng/ml, normal digital rectal exam (DRE), normal blood pressure, and not using aspirin or other types of blood thinning medications; these requirements ruled out the men most likely to get prostate cancer soonest.

There were four groups in the study: placebo, selenium only, vitamin E only, and selenium and vitamin E together. Subjects in the vitamin E group were given 400 IU of all-RAC-alpha-tocopherol acetate, which is synthetic vitamin E. The study had a rolling start beginning 2001 with all subjects participating by 2003. The supplementation portion of the study was terminated in 2008 when the initial report showed a slight increase in prostate cancer among the vitamin E group that was not statistically significant.

They continued to track the subjects through 2011 and updated the results in each group. The newsworthy part of the study was that there was a 17% greater risk of getting prostate cancer in the vitamin E group when compared to the placebo group. This time, the results were statistically significant. The researchers reported that the use of vitamin E as a dietary supplement increased the risk of prostate cancer in healthy men.

So what should you do? Quit taking vitamin E? Let's take a closer look.

Digging Down

In this type of study, it's usually a good idea to examine what the numbers mean in terms of risk. They reported a 17% increased risk of getting prostate cancer. The question is how many men get prostate cancer out of the total population of men? If you take the number of subjects in each group of the study and divide that into the number of men diagnosed with prostate cancer in that group, that gives you the percentage. There were 529 subjects diagnosed with prostate cancer out of the 8,696 subjects in the placebo group; that's a percentage of 6%. There were 620 subjects diagnosed with prostate cancer out of 8,737 in the vitamin E group; that's a percentage of 7.1%. So essentially, one more man for every 100 men will be diagnosed with prostate cancer over eight years. That's important if you're that one man.

But I thought I should check a little further. How many men are diagnosed with prostate cancer every year in the United States? Turns out that this year it's estimated to be 240,890 men based on information from the National Cancer Institute (NCI). Okay. How many men are there in the demographic that they targeted—men 50 and older if they were black and 55 and older if they were white? I checked the Census report for the latest year available, 2009, and added up all the men that fit that demographic. There were 96,137,000 men in that group.

Doing that math, those diagnosed with prostate cancer by the age-specific population used as subjects comes to 0.25%—roughly one out of every 5,000 men in that age group every year. To be fair, multiplying 0.25 per year by eight would bring it up to 2% but the estimate by the NCI included every age group who were diagnosed including those under 50. Also, the general population would include men who were at risk with PSAs and DRE that exceeded the guidelines for subject selection for the study—the men even more likely to get prostate cancer. The diagnosed rate in the study for the placebo group should have been much less than 0.25% per year rather than the 0.75% per year that they obtained.

Therefore, the real question the researchers need to answer is why did their randomly-selected group of subjects have such a high rate of prostate cancer compared to national statistics? Something just wasn't right.

Synthetic Versus Natural

Putting the unexplained statistics aside, the real problem with the study is that the researchers used synthetic vitamin E, and they used it at a high level. Synthetic vitamin E is actually eight different isomers of the vitamin-E molecule. All are absorbed into the bloodstream, but only one form actually mimics natural vitamin E. What do the other forms do? No one knows for sure based on what I've read. Either the researchers in this huge study didn't know that, or they assumed that the synthetic vitamin E would have no negative effect.

What if the seven isomers that are not chemically identical to natural vitamin E have a negative effect on the body? There's no evidence of that to date, but that's at least as good an explanation for the increased risk of prostate cancer as any other. Lumping all forms of alpha-tocopherol—natural and synthetic—together and saying vitamin E is to blame doesn't seem accurate based on the way they did the study.

But there's another problem. They based this study on the ATBC Study that was stopped early because cigarette smokers who took beta-carotene had a slightly increased risk of getting lung cancer. (If you were wondering whether it was synthetic beta-carotene, it was.) But while the negative part of the study hit the press, what was overlooked was that those men who took 50 IU of the same synthetic vitamin E used in the SELECT study had a reduced risk of developing prostate cancer. The recommended amount is 22.5 IU per day; in my interpretation of what the researchers stated as their reason for using 400 IU, they felt that because this was a Phase-3 Clinical Trial, they needed an amount that could provide a benefit. But why that much higher? That amount was used in other trials but in examining them, most were observational and there was no way of knowing what type of vitamin E was used—natural or synthetic.

The Bottom Line

Is there are relationship between healthy men taking vitamin E and increasing their risk of prostate cancer? This Phase-3 Trial was done to definitively determine whether vitamin E could prevent prostate cancer. The researchers reported that it would increase the risk, not lower it. But to me, it revealed that the researchers didn't understand that the vitamin E they were using in the clinical trial was not chemically identical to what you might get from food or from a natural vitamin E supplement.

The only thing that this study reveals in my opinion is that when you do research, you must ask the right questions about every factor that could influence the outcome. Most won't make a difference, but some could be crucial and could affect the results. They didn't consider whether there was a difference between natural and synthetic vitamin E dietary supplements, and that's a basic problem with this study.

They also didn't examine some basic statistics to see if the cancer rate for their subjects was different from the statistics of the general population. Without a good explanation for that, the results are suspect.

This study really raises more questions than it answers. The only problem is that the researchers really don't seem to understand that.

I'll keep taking my natural vitamin E supplement. I don't see any reason why you shouldn't either—not based on this study.

What are you prepared to do today?

Dr. Chet

Reference: JAMA 2011;306(14):1549-1556.