October 22, 2011 – Grand Rapids, MI

Supplements and Mortality

While I was on vacation, the *Archives of Internal Medicine* published a study that suggested that elderly women who use dietary supplements had a higher death rate than those who did not (1). Needless to say, that concerned many of you and you let me know it. I've read the study, checked the references, and I'll tell you what I think in this message.

One comment before I begin. I always try to let the science stand on its own merit regardless of my personal bias. I favor the use of dietary supplements, a position I've made clear. But if a study clearly indicated that supplements are not healthy for you or me, I would let you know that without reservation. I don't pick a position and defend it; I let it all stand on its own. I just wanted you to know that.

The Study

Researchers used 41,836 respondents to a mail survey sent to almost 100,000 women in Iowa in 1986 who were 55 to 69 years of age. Of those who responded to the original survey, 38,772 women returned questionnaires that asked for diet and supplement use. Those respondents with a mean age of almost 62 years became the subjects in the Iowa Women's Health Study.

Diet and supplement use was assessed in 1986, 1994, and 2004. Through the end of 2008, 15,594 deaths occurred in this population. After statistically adjusting for possible confounding factors, researchers reported an increase in mortality for those women who used a multivitamin, vitamin B6, folic acid, magnesium, iron, zinc, and copper when compared to non-users of supplements. The analysis showed a decrease in mortality to those women who supplemented with calcium.

The researchers concluded that supplement use may be associated with an increased mortality risk, and the risk was highest for iron supplementation.

The Problems

I specifically did not read any other people's or group's analysis of this study because I didn't want to influence my interpretation. Here's what I found.

Subject Loss
One of the problems with the study is the huge loss of potential subjects. Only 43% responded to the original mail survey. The assumption is that the respondents reflect the characteristics of the entire group. The original study showed that there were differences in age, weight, and where they lived (2). How did they know? They used the information from driver's licenses—and nobody lies about their weight on drivers licenses, do they? Further, the researchers lost another 10% of the potential subjects when the dietary questionnaires were not returned. In that case, they don't know what the reasons were.

This part of research design is often ignored but when you consider the potential subject pool, getting only 38% of them to provide information about supplement use is really a significant loss of data. Everyone believes that with such large numbers it can't affect the outcome. To me, even a 3% difference in responders could have completely changed the outcome when they reported out of 38,772 women, only 509 used folic acid, 229 used copper, and 2,738 used iron, which was identified as the supplement with the highest associated mortality rate.

The Questionnaire
I've commented enough about food-frequency questionnaires so if you're a regular reader, you know I'm not a fan. This was a long questionnaire; 127 items plus some questions about supplements. If you've ever done this type of questionnaire, you know it's tedious.

My real issue is that the supplement questionnaire was never validated; validation is important to see if it measures what it's supposed to measure. The authors made a comment that similar instruments reported a validity of about 0.8 (3). I read that study, and it never says that. In fact, it suggests that there's a lot of research to be done before they even get close to setting a standard for a supplementation questionnaire. On top of that, a validity correlation of 0.8 is low for this type of survey instrument.

Another problem is that the researchers didn't report the amounts of supplements in quartiles or quintiles. Logically, there should be an increase in mortality as the subjects take more of the supplement if it's indeed hazardous. While the researchers suggest that amounts were derived from the questionnaire, it's odd that they didn't perform this common analysis. It makes me wonder why not.

Statistical Significance
What got lost in translation was that most of the relationships the researchers reported as reflecting increased mortality were not statistically significant—that's the yardstick for whether a study's results mean anything or not. Multivitamin and iron use was found to increase mortality while calcium decreased mortality. None of the other supplements were significant. And the significance in mortality occurred only when numerous potential confounding factors were accounted for statistically.

The Bottom Line

There's a lot more that I could say about the problems in this study, but it wouldn't change my evaluation: there's just too much wrong with the study to change your supplementation plan based on its findings.

Let's use some common sense. For instance, whether the study's findings are valid or not, base your iron intake on blood tests that indicate you need it because of anemia—once women stop menstruating, they often don't need extra iron; don't waste your money on a supplement you don't need. And as I've said before, don't buy your multivitamin at the dollar store. Invest in the best quality you can afford.

At its core, this study found one thing: the older the population, the more people die, whether they use supplements or not. Duh. Remember, the women averaged 62 when it began; that means that they were an average of 84 when researchers stopped collecting mortality data in 2008, so close to 60% of the women were still alive.

If you're a woman over 55 years of age, I wouldn't hesitate to take dietary supplements based on this study. My wife Paula falls into that demographic, and I would rather lose a limb than do anything to harm her or any other member of my family. She still takes the same supplements as she always has and will continue to do so. So will I. Your body, your choice, but we're betting on supplementation.

What are you prepared to do today?

Dr. Chet

References:
1. Arch Intern Med. 2011;171(18):1625-1633.
2. Cancer Research 1989; 49:6828-6831.
3. Am J Epid. 2002; 156:669–675.