

WEB EXCLUSIVES

Preventing Prostate Cancer: Drugs or Diet?

BY ELIZABETH WHITTINGTON

Prostate cancer is one of the most common cancers in men; over 232,000 will be diagnosed with the disease this year. Fortunately, because of screening tests, many cancers will be caught early. Five-year survival rates have jumped from 67 percent in the mid 1970s to 98 percent in the past decade because of early detection. Although survival has improved dramatically, side effects caused by treatment can impact the patient's quality of life, including incontinence and impotence. And for 30,000 men each year, the disease is fatal.

While the best treatment for any disease is prevention, clinical studies have been difficult to perform. Cancer prevention trials are hard to design, data are difficult to interpret and large-scale studies are very costly. The main three prevention areas—diet, exercise and chemoprevention, which is medication to prevent the disease from developing or progressing—are being researched as possible avenues, but many of the past studies have produced inconclusive results, especially in regards to diet and exercise.

“Chemoprevention looks a little more promising to me,” says Eric Klein, MD, head of urologic oncology at the Cleveland Clinic in Ohio.

Although lifestyle modifications are beneficial for a person's overall health, there has been no firm evidence that diet and exercise change the risk of prostate cancer. Intake of antioxidants, soy, selenium, vitamin E and lycopene are among the many dietary supplements that have been researched with positive, although not conclusive, results. But in the field of chemoprevention, there are several large clinical trials, including one completed study involving finasteride, which produced positive results.

Prostate Cancer Prevention Study with Finasteride

After surviving three wars, retired Air Force colonel Charles Lysaght wasn't going to be brought down by prostate cancer. When he heard that another retired colonel, Ian M. Thompson, MD, at the University Texas in San Antonio was conducting a prostate prevention trial with Proscar (finasteride), Lysaght joined for the benefits of long-term preventative care. After seven years on the study, Lysaght says taking the daily finasteride pill wasn't difficult, especially if it helped prevent prostate cancer.

“A lot of my friends have had prostate cancer and I haven't,” Lysaght says. “People I've known through the years have had it. It's pretty well saturated the male community.”

Finasteride blocks 5-alpha reductase, an enzyme needed to convert testosterone to dihydrotestosterone (DHT), a male hormone that promotes growth of prostate cells that can lead to benign prostate enlargement and prostate cancer. Because finasteride has a similar structure to testosterone, the 5-alpha reductase enzyme binds to finasteride instead of testosterone, preventing the overabundance of DHT.

In the large, phase III Prostate Cancer Prevention Trial (PCPT), finasteride was found to lower the risk of prostate cancer by 24.8 percent from 24.4 to 18.4 percent when compared with placebo. Over 18,000 men with a normal digital rectal exam (DRE) and PSA levels were enrolled in the trial and given finasteride or placebo daily over seven years.

It also appeared that men who did develop prostate cancer while being treated with finasteride had a higher risk of having an aggressive form of the disease, but Dr. Klein says that it may not be a cause-and-effect relationship.

“With finasteride, we’re more likely to find cancer because it shrinks the prostate,” says Dr. Klein. During the trial, men with abnormal PSA levels had a biopsy performed. The smaller the prostate, the more likely a biopsy will find cancer, which may also make PSA testing more reliable when finasteride is used.

Trial data also showed that men on finasteride had an increased risk of sexual side effects, but lowered the risk of urinary retention.

Dr. Thompson, the principal investigator for the trial, says their next step is to find methods to identify men who are predisposed to prostate cancer and who will most likely benefit from finasteride.

“For a man who is having a PSA (screen) performed regularly for prostate cancer—that is over 50 percent of the U.S. male population—it is essential that they know about the potential for finasteride to reduce their risk of disease,” Dr. Thompson says.

The Next Generation of Chemoprevention

A second-generation 5-alpha reductase inhibitor, Avodart® (dutasteride) is currently being studied in the REDUCE trial, an international study involving over 8,000 men. Dutasteride blocks both type 1- and 2-specific 5-alpha reductase enzymes, while finasteride blocks only type 2. Dutasteride reduces DHT production, relieves symptoms and decreases testosterone faster than finasteride. Final results of the REDUCE trial are expected in 2009.

Because of the potential for side effects with finasteride and dutasteride, it is not recommended as a prevention tool for every man over 50. Rather, researchers would like to find a biomarker they could use to identify men who are at high risk for prostate cancer.

Predicting Prostate Cancer

Prostate intraepithelial neoplasia (PIN), a condition when epithelial cells in the prostate have an abnormal growth rate, is a predictor of adenocarcinoma, but only half of prostate cancer patients who have high-grade PIN will develop prostate cancer in ten years. PIN increases with age and many men who have high-grade PIN will never develop prostate cancer. Although PIN would be an adequate biomarker, it can only be detected through biopsy or another invasive procedure. Attempts to find a gene or protein have been unsuccessful, but

research is ongoing.

“In the big picture, there are men who are more susceptible (to prostate cancer),” Dr. Klein says. “It seems to be related to the ability of cells to fight off oxidative stress. That’s the current reigning hypothesis.” DNA mutations caused by chronic inflammation and environmental agents could cause cancer if the cells’ ability to react to those mutations is impaired.

Determining a Dietary Prevention Strategy

Although chemoprevention looks more promising in regards to data, dietary and lifestyle changes may have fewer side effects and be more cost efficient. The fastest accruing trial for its size with over 35,000 men, the SELECT trial is studying whether vitamin E and selenium, alone and together will lower prostate cancer risk. Dr. Klein speculates that if the SELECT trial shows positive benefits, vitamin E and selenium may be added to the food change, such as fluoride in tap water. “That’s not possible with finasteride,” he says, because of potential side effects and cost.

Identifying specific genotypes could determine which dietary prevention strategy would work best for individual patients. For example, a study has shown that men with a certain gene can reduce their risk of prostate cancer by half if their diet is high in broccoli. Men with the gene deletion, however, did not show a risk reduction.

While early detection has made prostate cancer a very curable disease, preventing cancer is the next step. “Never having it in the first place removes the anxiety of knowing that you have the disease, and you can’t have the side effects of treatment if you never need treatment in the first place,” says Dr. Thompson.

Lysaght says he is interested in what the studies find. In the meantime, he says he had such a good experience with the PCPT study, that he has since joined another study under Dr. Thompson. “It’s a mind set—you keep getting checked and if you don’t have it, you have the attitude you’re not going to get it. You’re going to be free of prostate cancer.”