EDITORIAL

Prostate cancer detection: beware of the low PSA

Many posters and presentations at the annual meeting of the American Urological Association in Anaheim, California drew attention to instances when caution is needed when interpreting PSA levels to assess prostate cancer risk.

A highlight of the meeting was the debate between Ian Thompson and Patrick C. Walsh regarding the interpretation of the Prostate Cancer Prevention Trial. This trial, published in the *New England Journal of Medicine* in 2003 (Thompson IM et al. *N Engl J Med* 2003;349:215-224), compared the 5-alpha reductase inhibitor finasteride versus placebo and reported a 25% reduction in prostate cancers diagnosed in the treatment arm versus the placebo arm. There were, however, more high-grade tumors among the men taking finasteride, an observation that has led to much debate and search for explanations. Thompson argued that the results of the trial are compelling enough for urologists to prescribe finasteride for the chemoprevention of prostate cancer, while Walsh cautioned against the overly optimistic interpretation of the risk reduction and expressed concern over the increased incidence of high-grade cancers. Both experts artfully dodged some bullets while raising some very pertinent points about the prescription of finasteride.

The speakers drew attention to the fact that this trial reported a surprisingly high cancer incidence (24%) in the placebo group, a level that is only slightly less than the prevalence of prostate cancer reported in autopsy studies. Many of the cancers were discovered at the end-of-study biopsies when the men had normal digital rectal examinations and PSA levels lower than 4 ng/mL. Even men with very low PSA levels were at risk of having prostate cancer. Finasteride is known to decrease PSA levels, and conventional wisdom says that measured PSA values should be multiplied by a factor of 2.0 in order to arrive at "true" PSA values for patients who are taking this drug. In this study, however, this adjustment factor was changed to 2.3 after the men in the treatment arm had taken finasteride for 3 years. One would have to wonder if this adjustment factor should be even higher in men taking 5-alpha-reductase inhibitors for longer periods of time.

The point that low PSA levels cannot rule out prostate cancer was also made in a presentation by Hominger and colleagues (Abstract 607). In their study about screening volunteers for prostate cancer, this cancer was diagnosed in 21% of men with PSA levels below 4 ng/mL and in 14% of men with PSA levels below 2 ng/mL. Leite et al (Abstract 1754) found similar results in men who underwent a schema of extended biopsies, and the researchers reported a positive biopsy incidence that ranged from 29% (in men with PSA levels of 1.1 to 2 ng/mL) to 39% (in men with PSA levels of 3.1 to 4 ng/mL).

Connolly et al (Abstract 1608) cautioned that if a patient with an elevated PSA has the test repeated and it is normal the second time, this patient still has a 12% likelihood of harboring prostate cancer.

During a podium session on prostate cancer epidemiology and natural history, Hamilton and colleagues (Abstract 463) cautioned that statin medications influence PSA levels. Their investigation of 1545 men who were prescribed a statin concluded that statins can influence prostate biology, significantly reduce PSA levels, and complicate cancer detection. Considering the vast number of patients taking such medications, this may indeed be a major factor for urologists to consider, and we should be well aware of the influence of statins on PSA if our patient is being treated for hyperlipidemia.

Similarly, increasing numbers of men are taking over-the-counter dietary supplements, and some of these also affect PSA levels, according to a poster presented by Ide et al (Abstract 1624).

The take-home message is loud and clear. Men continue to be at risk for prostate cancer despite having low PSA levels. An increasing variety of medications — 5-alpha-reductase inhibitors, statins, antibiotics, dietary supplements, and possibly other agents — are emerging as having a profound influence on PSA levels. These medications and dietary supplements may reduce inflammation and alter the prostatic microenvironment, and they could prevent prostate cancer, or simply mask it and delay the diagnosis. The mechanism and kinetics of PSA alteration must be investigated further, but in the meantime, as urologists, we must become more cognizant of the actions of these agents and know when our patients are taking them.

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