Common Medications Associated With Reductions in PSA Levels

BY SUSAN LONDON

SAN FRANCISCO — Commonly used medications were associated with clinically important reductions in prostate-specific antigen levels among roughly 2,000 middle-aged and older men in a cross-sectional study.

After 1 year of regular use, PSA levels were 1% lower in users of nonsteroidal anti-inflammatory drugs (NSAIDs), 3% lower in statin users, and—an apparently novel observation—6% lower in thiazide diuretic users, according to data reported at a symposium on genitourinary cancers. The difference in PSA levels among users and nonusers of the common medications increased over time, with reductions of 4%, 13%, and 26% seen with 5 years of regular use of NSAIDs, statins, and thiazide diuretics, respectively.

“If taking these medications alters serum PSA, it could affect the quality of prostate cancer screening,” said lead investigator Dr. Steven L. Chang.

Using data from the National Health and Nutrition Examination Survey (NHANES) for 2003-2006, the researchers assessed associations between medication use and log-transformed PSA levels in 1,846 men aged 40 years or older who had a serum PSA measurement; see PSA Levels page 4.

Second Gene Polymorphism Reduces Activity of Clopidogrel

BY MITCHEL L. ZOLER

ATLANTA — A second, newly recognized type of metabolic polymorphism has been found to reduce the clinical efficacy of the antiplatelet drug clopidogrel in patients with coronary disease.

In contrast, a similar antiplatelet drug, prasugrel, does not require metabolic conversion to its active form and was not associated with a change in its clinical activity related to this polymorphism, Dr. Jessica L. Mega and her associates reported in a poster at the annual meeting of the American College of Cardiology.

Clopidogrel’s activity was previously shown to be affected by a polymorphism in the liver enzyme cytochrome P450, estimated to occur in 2%-14% of the population. This finding formed the basis of a boxed warning imposed by the Food and Drug Administration on clopidogrel’s labeling on March 12.

The newly found polymorphism also limits clopidogrel’s activity and affects a cell membrane protein that controls drug efflux out of intestinal enterocytes. The homozygous polymorphism enhances efflux, thus interfering with metabolic conversion of clopidogrel. The polymorphism occurred in 27% of more than 2,900 patients with acute coronary syndrome (ACS) enrolled in a recent drug study, said Dr. Mega, a cardiologist at Brigham and Women’s Hospital in Boston.

Patients with ACS who are homozygous for the polymorphism, a genotype known as C3435T, “have less platelet inhibition [from clopidogrel] and are at significantly increased risk of recurrent ischemic events,” the researchers said.

The analysis used data collected in the TRITON-TIMI 38 study, which compared affected patients ‘are at significantly increased risk of recurrent ischemic events.’ See Clopidogrel page 3.

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did not have a history of prostate cancer, prostatitis, or recent prostate manipulation; and were not taking 5-alpha reductase inhibitors or hormone therapy.

Statsin topped the list of the 10 medications most commonly used in the study cohort (taken by 20% of the men), according to study results, which were reported in a poster session.

The most commonly used by beta-blockers (13%), angiotensin-converting enzyme (ACE) inhibitors (11%), NSAIDs (9%), proton pump inhibitors (9%), calcium channel blockers (6%), selective serotonin reuptake inhibitors (6%), thiazide diuretics (5%), alpha-blockers (4%), and sulfonlures (4%). In multivariate analyses, PSA levels after 1 year of regular use were 1% lower in NSAID users (P = .03), 3% lower in statin users (P = .01), and 6% lower in thiazide diuretic users (P = .03), relative to those in the respective nonusers. The remaining medications were not independently associated with PSA levels.

The effects of statins and NSAIDs on PSA have been previously reported, but the finding for thiazide diuretics appears to be new and was somewhat surprising in magnitude, Dr. Chang commented in an interview.

Adoption of New, Costlier Therapies For Prostate Cancer Precedes Evidence

BY SUSAN LONDON

SAN FRANCISCO — The use of new, more expensive therapies for prostate cancer increased rapidly during a recent 4-year period, despite a lack of consensus on their effectiveness relative to that of older, less expensive therapies, researchers reported at a symposium on genitourinary cancers. In a cross-sectional sample of 58,581 older U.S. men with nonmetastatic prostate cancer, the use of minimally invasive radical prostatectomy rose 19-fold, of intensity-modulated radiation therapy (IMRT) almost 3-fold, and of the combination of brachytherapy plus IMRT roughly 4-fold. The use of older therapies fell correspondingly.

“Despite limited comparative effectiveness data, there was a rapid increase in utilization of these more expensive therapies for prostate cancer,” said lead investigator Dr. Paul L. Nguyen. “Potential benefits really must be weighed against the added costs as newer, expensive therapies are introduced.”

The researchers used the linked SEER (Surveillance, Epidemiology, and End Results)–Medicare database to identify men aged 65 years or older who received a diagnosis of nonmetastatic prostate cancer between 2002 and 2005 and who were not enrolled in an HMO. Treatments were ascertained by using procedural codes.

The pattern of relative use of treatment modalities remained constant between 2002 and 2005, with external-beam radiation therapy used most commonly, followed by brachytherapy, and then by surgery. But there were major shifts within each modality in the specific therapies used, Dr. Nguyen reported at the symposium, which was sponsored by the American Society of Clinical Oncology, American Society for Radiation Oncology, and Society of Urologic Oncology.

Among men who had surgery, the proportion who had minimally invasive (laparoscopic or robotic) radical prostatectomy increased 19-fold, from 1.5% in 2002 to 28.7% in 2005. Meanwhile, the proportion having open prostatectomy fell.

Among men who had external-beam radiation therapy, the proportion who had IMRT almost tripled, from 28.7% to 81.7%. At the same time, the use of 3D-conformal radiation therapy decreased.

Among men who had brachytherapy, the proportion also treated with IMRT roughly quadrupled, from 8.5% to 31.1%. Meanwhile, the proportion receiving brachytherapy plus 3D-conformal radiation therapy fell, and the proportion receiving brachytherapy alone was unchanged, said Dr. Nguyen, director of prostate brachytherapy at the Dana-Farber Cancer Institute and Brigham and Women’s Hospital, both in Boston.

Compared with men who had open prostatectomy, men who had minimally invasive radical prostatectomy were more likely to be highly educated, reside in a high-income neighborhood, and live in the Northeast or the West; were more likely to have a high tumor grade, a clinical T1 stage, and limited comorbidity; and were more likely to be Asian and less likely to be black or Hispanic.

All of these factors were also associated with receiving IMRT as opposed to 3D-conformal radiation therapy, except for race/ethnicity. IMRT recipients were more likely to be Asian and more likely to be white, but less likely to be black.

“Comparative effectiveness research into these more expensive therapies has been pretty limited. Certainly, there are no randomized trials that tell us that the most expensive therapy is better than the less expensive therapy,” Dr. Nguyen commented. An analysis suggesting that IMRT is cost effective (Int. J. Radiat. Oncol. Biol. Phys. 2006;66:408-15) was published after the use of this therapy was already widespread. “So we have to ask ourselves, did we do these things because we felt the fact that we found it was cost effective,” he said.

“What if we had found out it wasn’t?”

The findings have important implications for guiding the use of future technologies, such as proton therapy, Dr. Nguyen observed. “Even if there is a clinical benefit to these more expensive therapies, it’s still fair to ask whether these benefits [will] outweigh the added costs,” he said.

Disclosures: Dr. Nguyen reported having no conflicts of interest related to the study.