Alfuzosin Slows Progression of Benign Prostatitis

BY JANE SALODOF MACNEIL
Southwest Bureau

PARIS — The α-1 blocker alfuzosin prevented overall clinical progression of benign prostatic hyperplasia but had no impact on acute urinary retention in a 2-year, double-blind, placebo-controlled, multinational study that enrolled 1,522 men at high risk of serious outcomes.

Alfuzosin (Uroxatral) reduced the relative risk for any worsening of lower urinary tract symptoms by 26%, according to data reported by Dr. Claus Roehrborn at the annual congress of the European Association of Urology.

A total of 289 patients in both arms of the study had at least one event signalling progression. Symptom deterioration was the most common, occurring in 215 men, followed by surgery related to benign prostatic hyperplasia (BPH) in 87 men and acute urinary retention in 30 men. The overall incidence of events was 16.3% of 754 men on alfuzosin vs. 22.1% of 761 men on placebo.

Dr. Roehrborn of the University of Texas Southwestern Medical Center at Dallas presented the results on behalf of the Alfuzosin Long-Term Efficacy and Safety Study (ALTESS) study group.

He reported that alfuzosin was associated with a 30% reduction in the relative risk of the International Prostate Symptom Score (IPSS) worsening by at least four points. The cumulative incidence of this measure was 11.7% in the alfuzosin arm vs. 16.8% of placebo patients. Patients on alfuzosin also were 22% less likely to have BPH-related surgery: 5.1% required operative interventions vs. 6.5% of the placebo group.

Only the cumulative incidence of acute urinary retention was similar in the two groups: 2.1% of the alfuzosin group vs. 1.8% of placebo. "This may be attributable to selection of patients with higher risk of retention," Dr. Roehrborn said.

He noted that the study was designed to enroll high-risk patients aged 55 or older. The criteria included an IPSS at or above 13, a Qmax of 5-12 mL/sec for a voided volume of 150 mL or more, postvoid residual urine of 350 mL or more, prostate size of 30 g or more as estimated by a digital rectal exam, and a prostate-specific antigen concentration of 1.4-10 ng/mL.

Patients were enrolled from May 2001 to March 2005 at 148 urology centers in North America, Europe, Australia, the Middle East, and South Africa, according to Dr. Roehrborn's poster. Subjects randomized to alfuzosin took 10 mg daily for 2 years.

About one-third of the patients—513 men—dropped out of the study. Lack of efficacy or disease progression prompted 9.9% of the alfuzosin patients and 14.5% of the placebo group to withdraw from the trial. Adverse events led to 9.4% and 8.1% of withdrawals, respectively.

Alfuzosin had a similar side effect profile to placebo and was well tolerated, according to Dr. Roehrborn. The most common adverse event was dizziness in both arms of the study (alfuzosin, 6.0% and placebo, 4.6%). Only 1.2% of patients in the alfuzosin arm had hypotension or postural hypotension. Ejaculatory disorders were rare as well (0.4%).

Dr. Roehrborn also reported significant improvements in IPSS scores over 2 years and peak flow rate at 12 months for alfuzosin vs. placebo. Over 2 years, prostate-specific antigen levels decreased 0.6% with alfuzosin, but increased 3.6% with placebo.

The results are similar to those for doxazosin in the Medical Therapy of Prostatic Symptoms study, Dr. Roehrborn said. "We have learned the limits and the utilities of α-blockers in the long term for patients with lower urinary tract symptoms and benign prostatic hyperplasia." ■

Postvoid Residual Found Predictive

ALTESS trial investigators were surprised to find that postvoid residual urine could predict progression of benign prostatic hyperplasia symptoms over time, according to Dr. Roehrborn.

He reported that increasing postvoid residual (PVR) scores were associated with a worsening of symptoms in the alfuzosin and the placebo arms of the study.

The predictive power of PVR has been underestimated when patients are observed longitudinally. Guidelines for long-term monitoring of benign prostatic hyperplasia should be recognized, he said.

"We have brushed it [PVR] off as an unreliable and not reproducible value," when in fact the opposite is true.

Dr. Roehrborn reported that age was not a risk factor for any of the study's outcomes, but higher baseline prostate-specific antigen concentration was predictive of surgery and of acute urinary retention. This was true whether patients were taking alfuzosin or placebo.

Analysis of ALTESS data suggests that the severity of baseline symptoms as measured by the International Prostate Symptom Score is unlikely to predict thresholds of symptoms worsening, Dr. Roehrborn added. He reported that patients with lower scores were more likely to have their symptoms worsen, whereas patients with higher IPSSs were more likely to have surgery.

He called the finding paradoxical and attributed it to a ceiling effect. "In other words, it is more difficult for symptoms to worsen by 4 points or more in the highest symptom group score," he explained.

Unnecessary PSA Screening Of Elderly Men Occurs Often

BY PATRICE WENDLING
Chicago Bureau

CHICAGO — Despite recommendations to the contrary, prostate-specific antigen screening is being performed in many elderly men who are not in good health and have limited life expectancies.

That conclusion was drawn from an analysis of data collected during a cohort study of 597,824 veterans aged 70 years and older who were seen at 104 Veterans Health Administration centers during fiscal years 2002 and 2003. The subjects did not have a history of prostate cancer, elevated prostate-specific antigen (PSA) levels, or prostate symptoms.

Most guidelines recommend that PSA screening should not be performed in elderly men who have a life expectancy of fewer than 10 years—the majority of those over age 80 years and men aged 70 years or older in poor health—because the known harms outweigh the potential benefits, Dr. Louise Walter and associates reported at the annual meeting of the American Geriatrics Society.

PSA levels are often inaccurate, leading to unnecessary biopsies because of false-positive results. This can cause psychological distress as well as treatment of irrelevant cancers, which may lead to incontinence or impotence. "The benefit of PSA screening remains unproven, and even if some benefit is ultimately proven, it is estimated that a life expectancy of 10-20 years would be needed for any chance of receiving such a survival benefit," said Dr. Walter, of the geriatrics division at the University of California, San Francisco, and a staff physician at San Francisco VA Medical Center.

The mean age of the men in the VA-supported study was 77 years, and 333,041 (56%) had a PSA test performed in 2003. Health status was measured with the Charlson-Deyo index using VA and Medicare claims in 2002. The scores were used to stratify the men into three groups, ranging from best health (score of 0) to worst health (score of 4 or more).

PSA screening rates decreased significantly with advancing age, ranging from 64% in men aged 70-74 years to 27% in men aged 90 or older. But screening rates did not decline substantially with worsening health, she said. Among men aged 85-89 years, 36% in the best-health group had a PSA test, compared with 37% in the worst-health group.

Although men aged 80 years or older in the worst health have less than a 10% chance of living 10 years, 11,391 (41%) of these men had a PSA test. ■

Three-Year Testosterone Regimen Didn't Improve Cognition in Healthy Older Men

BY PATRICE WENDLING
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CHICAGO — Exogenous testosterone, taken either alone or with finasteride for 36 months, did not significantly improve cognition in a randomized, placebo-controlled trial involving healthy older men.

The findings do little to settle the debate over the effect of hormone therapy on cognition in elderly men. About half of randomized, controlled trials of testosterone therapy in older men have shown positive effects on cognitive function, particularly spatial cognition, Dr. Camille Vaughan said at the annual meeting of the American Geriatrics Society.

She presented data from a study in which 70 healthy men, ages 65-83 years, with low levels of testosterone (less than 350 ng/dL) and normal performance on the Mini-Mental State Examination (MMSE) were randomly assigned to receive one of three regimens: 200 mg of IM testosterone enanthate every 2 weeks with placebo pills; 200 mg of IM testosterone enanthate every 2 weeks with 5 mg of finasteride daily; or placebo injections and placebo pills.

At baseline, there were no significant differences in hormone levels between groups. Their mean age was 72 years. All patients had an MMSE score of 28 or higher, out of 30, reported Dr. Vaughan, an internal medicine resident at Emory University in Atlanta, and colleagues.

Cognitive testing performed at baseline, 4 months, and 36 months included a comprehensive battery assessing attention, executive function, visuospatial skills, and visual and verbal memory skills. Serum hormone levels also were measured at the indicated intervals.

Sixty-nine men completed baseline testing, 65 completed at least 4 months, and 46 completed all 36 months of the study.

Serum total testosterone, bioavailable testosterone, and estradiol levels increased significantly in the treatment groups throughout the study period. Hormone levels did not change for the placebo group at any time.

The three groups didn't demonstrate significant differences in cognitive performance on any of the tests at the 4- or 36-month evaluations, Dr. Vaughan said. There was a trend in the active treatment groups toward improved performance in the Benton Visual Retention Test and in visuospatial skills on the Visual Patterns Test. But scores were not significantly different from the placebo group at any time.

Further studies are warranted to determine if hormone therapy in men with preexisting cognitive impairment is beneficial, Dr. Vaughan concluded. ■