Department of Veterans Affairs
Health Services Research & Development Service

Evidence Synthesis Pilot Program

HSR&D

Comparative Effectiveness Review

Benign Prostatic Hyperplasia (BPH) Management in Primary Care – Screening and Therapy

EXECUTIVE REPORT

Final Report
February 2007

Mark Helfand, MD, MPH, FACP
Staff Physician
Portland VA Medical Center
Portland, OR

Tara Muzyk, Pharm.D.
Clinical Pharmacist
VA Southern Nevada Healthcare System
Las Vegas, NV

Mark Garzotto, MD
Staff Physician, Urology Section
Portland VA Medical Center
Portland, OR

The purpose of this report is to make available information regarding the comparative effectiveness and safety profiles of different drugs within pharmaceutical classes. Reports are not usage guidelines, nor should they be read as an endorsement of, or recommendation for, any particular drug, use or approach.

Portland VA Medical Center does not recommend or endorse any guideline or recommendation developed by users of these reports.

EXECUTIVE SUMMARY

Background

Benign prostatic hyperplasia (BPH) causes urinary hesitancy and intermittency, weak urine stream, nocturia, frequency, urgency, and the sensation of incomplete bladder emptying. These symptoms, collectively called "lower urinary tract symptoms," or LUTS, can significantly reduce quality of life. Men with no symptoms or mild symptoms (AUA Symptom Index [SI] score of <7 points), and those who tolerate moderate symptoms well, may be managed without pharmacotherapy ("watchful waiting"). For those who have moderate or severe symptoms, medical treatments include alpha-1-selective adrenergic receptor (a-1-AR) antagonists, 5-alpha-reductase inhibitors (5-aRIs), or a combination therapy with one drug from each of these classes.

This report addresses the following questions about treatment for BPH:

1. For patients with BPH, what are the comparative benefits, harms, and efficacy of combination therapy with a 5-alpha-reductase inhibitor plus an alpha blocker versus either treatment alone?

2. What are the comparative efficacy and harms of alpha-1-adrenergic antagonists?

3. Are there subgroups of patients based on demographics (age, racial groups), other medications, or co-morbidities for which one treatment is more effective or associated with fewer adverse events?

Results

Combination therapy versus an alpha blocker or 5-ARI alone.

In the first year of treatment, alpha blockers are more effective than finasteride in improving symptoms. Combination therapy and an alpha blocker alone have similar effects on quality of life in the first year and a half of treatment.

For men who have BPH and have a large prostate or a high PSA at baseline, combination therapy can prevent about 2 episodes of clinical progression per 100 men per year over 4 years of treatment. There is no additional benefit within the first year of treatment. Most men who take combination therapy will have no additional benefit, and about 4 additional patients per 100 will become impotent who would not have taking an alpha blocker alone. Combination therapy can also be instituted after clinical progression occurs, but this strategy, while used widely, has not been studied.

There is considerable uncertainty about how best to monitor PSA in whom to choose to take finasteride or combination therapy and who are otherwise candidates for PSA screening. Candidates for combination therapy—patients who have large prostates and at least moderate

symptoms—tend to have higher PSA levels than other patients who have BPH. Finasteride reduces prostate size and PSA levels, making detection of prostate cancer more difficult. Alpha-blockers do not affect PSA levels. Expanding access to combination therapy as an initial option would require higher utilization of ultrasound and PSA testing in BPH patients to assess the risk of progression. The consequences of such a program in a primary care setting have not been studied.

Choice of Alpha Blocker.

Previous, good-quality systematic reviews found that the alpha blockers, including alfuzosin prolonged-release and doxazosin GITS, have similar efficacy in improving symptoms and urinary flow rate. Observational studies of doxazosin, terazosin, and tamsulosin in selected patients indicate that in most patients who respond to an alpha blocker and who tolerate it well initially, the drug continues to work and to be well-tolerated for many years.

Head-to-head trials of alpha-blockers are few, small, and have serious limitations. They do not adequately test commonly held beliefs about differences in the side effect profiles of the alpha blockers. Specifically, they do not prove that, when used in practice, tamsulosin causes fewer cardiovascular adverse effects than other alpha-blockers because it does not reduce blood pressure. In placebo-controlled trials, tamsulosin caused higher rates of sexual ejaculation abnormalities than other alpha blockers. The placebo-controlled trials do not adequately test the hypothesis that use of tamsulosin as initial therapy reduces the risk of symptomatic hypotension.

For combination therapy, doxazosin is the best-studied alpha blocker.

Treatment of BPH in subgroups of patients.

Long-term observational studies establish that BPH can be treated safely with alpha blockers in patients taking other medications for hypertension. Alpha blockers should not be used as initial treatment for patients with hypertension, even those with BPH, because they are associated with poorer long-term outcomes than other choices. Data on the safety of alpha blockers in patients taking erectile dysfunction drugs are sparse.

Recently, the FDA issued a notice that intraoperative Floppy Iris Syndrome (IFIS) has been observed during phacoemulsification cataract surgery in some patients currently or recently treated with tamsulosin.