Therapeutics Letter

Benign prostatic hypertrophy

Update on drug therapy

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Benign prostatic hypertrophy is relatively common and potentially bothersome to aging men. This article updates the evidence of benefit and harm from alpha-blockers and 5-alpha reductase inhibitors.

The goals of drug therapy are symptom relief and prevention of complications. Symptoms are classified as irritative (frequency, nocturia, burning, urgency, or urge incontinence) or obstructive (hesitancy, weak stream, dribbling, incomplete voiding, or retention).

Many trials use the 35-point American Urological Association (AUA) symptom scale. When AUA scores were compared with patient perceptions, men who felt "slightly improved" averaged a 3-point reduction; those "not improved" averaged a 0.7-point reduction. Over 4 years, mean AUA scores fell by 5 points among men receiving placebo.

Alpha-blockers

Five alpha-blockers are available in Canada: alfuzosin, doxazosin mesylate, prazosin, tamsulosin, and terazosin. Alpha-blockers provide modest symptom relief. The most frequent adverse effects of alpha-blockers are dizziness, asthenia, and postural hypotension. Average absolute risk increases for alpha-blockers versus placebo concern dizziness (3% to 8%), postural hypotension (3% to 5%), and asthenia (5% to 6%); number needed to treat to cause 1 harmful event (NNH) is 13 to 33. No consistent evidence shows a therapeutic advantage of one alpha-blocker over another.

5-Alpha reductase inhibitors

Two 5-alpha reductase inhibitors are available in Canada: finasteride and dutasteride.

Finasteride

Finasteride did not significantly reduce symptom scores versus placebo in one 4-year trial. In a second 4-year trial, scores fell by a mean of 1.6 points. In a meta-analysis of 16 randomized controlled trials (17456 patients; maximum 4 years) with at least 1 clinically important health outcome, finasteride reduced acute urinary retention and surgery; it is surprising that total serious adverse effects were not also reduced. Published reports provide insufficient detail to assess rates of other serious adverse effects.

Finasteride versus alpha-blockers

Five randomized controlled trials (0.5 to 4 years) compared finasteride with alpha-blockers. Mortality, serious adverse effects, and withdrawals due to adverse effects did not differ. Finasteride increased sexual dysfunction; alpha-blockers increased dizziness, postural hypotension, and asthenia. Surgery rates did not differ: finasteride 1.6%, doxazosin or terazosin 2.2%. In 4 studies, alpha-blockers reduced AUA symptom scores by 1 to 3 points more than finasteride. Alfuzosin affected scores similarly to finasteride.

Adding finasteride to an alpha-blocker

Adding finasteride did not reduce mean symptom scores as compared with an alpha-blocker alone in 0.5- to 1-year trials: the difference was 0.3 points. In one 4-year randomized controlled trial, the mean symptom score fell by 0.8 points.

Adding an alpha-blocker to finasteride

Combination therapy reduced a combined outcome ("clinical progression") largely driven by symptom scores versus finasteride alone, but did not reduce acute urinary retention (0.4% versus 0.7%) or surgery (1.0% versus 1.6%).

Dutasteride

Dutasteride has been tested less extensively than finasteride. In 3 double-blind trials (combined number=4325), dutasteride reduced AUA scores by 1.3 points more than placebo at 1 year. Dutasteride reduced acute urinary retention (1.8% versus 4.2%) and need for surgery (2.2% versus 4.1%) but increased impotence (7.3% versus 4.0%), ejaculation disorder, and gynecomastia and lowered libido. Mortality and serious adverse effects rates did not differ.

Study conclusions

- Alpha-blockers improve symptoms on average by 2 to 3 points more than placebo (on the 35-point AUA scale), a difference patients perceive as a "slight benefit." Alpha-blockers do not reduce complications, but increase dizziness, postural hypotension, and asthenia (absolute risk increase [ARI] 3% to 8%, NNH 13 to 33).
- 5-Alpha reductase inhibitors reduce acute urinary retention (ARR) by 2%; number needed to treat to

prevent 1 event (NNT) is 50. These agents decrease benign prostatic hypertrophy surgery (ARR 2% to 3%, NNT 33 to 50) but impair sexual function (ARI 3%, NNH 33).

- There is insufficient evidence to suggest that combining the 2 drug classes provides additional benefit.
- Most benign prostatic hypertrophy trials do not report total serious adverse events and mortality. This practice prevents assessment of the overall clinical effect of drug treatment.

Clinical implications

Men with bothersome symptoms who wish a trial of alpha-blocker therapy should set their own treatment goals and weigh the benefits (ie, symptom relief) against side effects (ie, postural hypotension, asthenia). Because all alpha-blockers have relatively short half-lives, maximum concentrations and effect will occur within 4 days. A reasonable approach is to start with a low dose and assess for symptoms during a series of 1-week therapeutic trials at several doses. Neither finasteride nor dutasteride provide symptom relief for most men. Patients considering long-term therapy to prevent complications should be informed of the magnitude of potential benefits and harms, as outlined above.

Source: *Therapeutics Letter* 2006;58:1-2. For the complete text of this report, check the Therapeutics Initiative website **http://www.ti.ubc.ca.**

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