



To Pee or Not to Pee: Combination agents for benign prostatic hypertrophy

CLINICAL QUESTION

For patients with benign prostatic hypertrophy (BPH) is combination therapy with alpha-blockers and 5-alpha reductase inhibitors (5ARI) more efficacious than alpha-blockers alone?

BOTTOM LINE

At best, adding 5ARIs to alpha-blockers reduces the number of men with clinical progression (5% compared to 10% on alpha-blocker alone), and the number needing BPH surgery (2% compared to 8% on alpha-blocker alone). Drug related adverse effects are increased from 19% on alpha-blockers alone to 28% on combination.

EVIDENCE

- Systematic review¹ identified 6 RCTs, 2 with >1 year follow-up.^{2,3} Enrolled patients were symptomatic white males receiving additional testing (example transrectal ultrasound) and specialist care.^{2,3} Four-year outcomes reported below.
- Doxazosin (1mg titrated up to 8mg), doxazosin plus finasteride (5mg), or placebo (n=3,047):²
 - Clinical progression: Composite of worsening symptoms [>4 point change on 35-point American Urological Association Score], acute retention, incontinence, or recurrent urinary tract infection (UTI). Symptom progression contributed ~80% of the composite.

- Doxazosin 10%, combination 5%: Number needed to treat (NNT)=20 (placebo 17%).
 - BPH surgery:
 - Doxazosin 3%, combination 1%: NNT=50 (placebo 5%).
 - Adverse effects, statistics not reported:⁴
 - Decreased erectile function: Doxazosin 13%, combination 17% (placebo 13%).
- Tamsulosin (0.4mg) or tamsulosin plus dutasteride (0.5mg) (n=4,844):³
 - Clinical progression: Composite of worsening symptoms [\geq 4-point change on 35-point International Prostate Symptom Score], acute retention, incontinence, recurrent UTI, urosepsis or renal insufficiency. Symptom progression contributed ~65% of the composite.
 - Tamsulosin 22%, combination: 13%: NNT=12.
 - BPH surgery:
 - Tamsulosin 8%, combination 2%: NNT=23.
 - Adverse effects:
 - Any drug related adverse effect: Tamsulosin 19%, combination 28%; number needed to harm=12.
 - Erectile dysfunction: Tamsulosin 5%, combination 9%, not statistically different.
 - Dizziness: No difference.

CONTEXT

- 5ARI may decrease prostate cancer incidence, but cancers found may be higher grade.^{5,6}
 - 17-year follow-up: No difference in prostate cancer mortality.⁷
- 5ARI decreases prostate serum antigen (PSA) levels by ~50%,⁸ which might delay prostate cancer diagnosis.⁹
 - If following, PSA should be multiplied by 2-2.3 for patients on 5ARI.^{5,6}
- Canadian guidelines recommend:¹⁰
 - Alpha-blockers: First line.
 - Combination: If prostate enlargement.

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