Treatment of lower urinary tract symptoms in benign prostatic hypertrophy with α-blockers

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Clinical question

Are α-blockers effective in reducing lower urinary tract symptoms in benign prostatic hypertrophy (BPH)?

Bottom line

As a first-line therapy, α-blockers are effective. Compared with placebo, around 1 in 10 patients have improved BPH symptoms or avoid symptom progression, while about 1 in 50 patients experience hypotension or dizziness. Mainly indirect comparisons suggest doxazosin and terazosin are slightly more effective but have increased risk of adverse events.

Evidence

- In a systematic review of 26 RCTs of α-blockers versus placebo, peak urinary flow (Q_{max}) improved by 1.32 mL/s and International Prostate Symptom Score (IPSS) decreased by 1.92.[1]
- Meta-analysis of 124 RCTs comparing doxazosin, terazosin, alfuzosin, and tamsulosin found improvement in Q_{max} (by 1.95, 1.21, 1.07, and 1.07 mL/s, respectively) and symptoms (changes in IPSS of -3.67, -3.37, -2.13, and -2.07, respectively).[2]
  -Doxazosin performed statistically significantly better for both outcomes. There was a statistically significant increase in adverse events with doxazosin and terazosin.
- A systematic review of 23 RCTs (20 821 patients) compared α-blockers to finasteride[3] and found it was inferior to doxazosin and terazosin for Q_{max} and IPSS at 1 year, but noninferior to tamsulosin. Finasteride and dutasteride are similarly effective.[4]
- An RCT of 3047 men compared placebo with doxazosin, finasteride, and a combination.[5] Compared with placebo, doxazosin reduced symptom progression (number needed to treat [NNT] of 15 over 4 years) and increased hypotension (number needed to harm [NNH] of 58) and dizziness (NNH=48).
- In 3 pooled RCTs (955 patients),[6] more men taking alfuzosin (76%) had a 3-point improvement or greater in IPSS than men taking placebo did (62%; NNT=7).

Context

- Guidelines recommend α-blockers as first-line therapy in men with symptomatic BPH.[7]
- Clinically meaningful improvement of IPSS is 2 to 6 points or more, depending on baseline score.[8]
- Transurethral resection of the prostate improves Q_{max} about 10 mL/s and decreases IPSS by 16.7.[9]
- The α-blockers are associated with increased risk of falls (NNH=589) and fracture (NNH=1667).[10]
- A 2013 systematic review comparing α-blockers to combination therapy with α-reductase inhibitors showed that combination therapy was effective for enlarged prostates and treatment for longer than 1 year.[11]

Implementation

Observational data suggest BPH is correlated with obesity and reduced physical activity.[12] Predicting progression to urinary retention is difficult, although high prostate gland volume, elevated prostate-specific antigen level, and older age might increase risk.[7] In higher-risk patients, it might be reasonable to add α-reductase inhibitors, as they have reduced urinary retention (NNT=60) and surgical intervention (NNT=32) over 4 years.[5] Side effects including adverse sexual effects (NNH=15) should be discussed.[3]

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Competing interests
None declared

References

1. Nickel JC, Sander S, Moon TD. A meta-analysis of the vascular-related safety profile and efficacy of alpha-adrenergic blockers for symptoms related to benign prostatic hyperplasia. *Int J Clin Pract* 2008;62(10):1547-59.
2. Yuan JQ, Mao C, Wong SY, Yang ZY, Fu XH, Dai XY, et al. Comparative effectiveness and safety of monodrug therapies for lower urinary tract symptoms associated with benign prostatic hyperplasia: a network meta-analysis. *Medicine* (Baltimore) 2015;94(27):e974.
3. Tacklind J, Fink HA, Macdonald R, Rutks I, Wilt TJ. Finasteride for benign prostatic hyperplasia. *Cochrane Database Syst Rev* 2010;(10):CD006015.
4. Nickel JC, Gilling P, Tammela TL, Morrill B, Wilson TH, Rittmaster RS. Comparison of dutasteride and finasteride for treating benign prostatic hyperplasia: the Enlarged Prostate International Comparator Study (EPICS). *BJU Int* 2011;108(3):388-94.
5. McConnell JD, Roehrborn CG, Bautista OM, Andriole GL Jr, Dixon CM, Kusek JW, et al. The long-term effect of doxazosin, finasteride, and combination therapy on the clinical progression of benign prostatic hyperplasia. *N Engl J Med* 2003;349(25):2387-98.
6. Roehrborn CG, Van Kerrebroeck P, Nordling J. Safety and efficacy of alfuzosin 10 mg once-daily in the treatment of lower urinary tract symptoms and clinical benign prostatic hyperplasia: a pooled analysis of three double-blind, placebo-controlled studies. *BJU Int* 2003;92(3):257-61.
7. Nickel JC, Méndez-Probst CE, Whelan TF, Paterson RF, Razvi H. 2010 Update: guidelines for the management of benign prostatic hyperplasia. *Can Urol Assoc J* 2010;4(5):310-6.
8. Barry MJ, Williford WO, Chang Y, Machi M, Jones KM, Walker-Corkery E, et al. Benign prostatic hyperplasia specific health status measures in clinical research: how much change in the American Urological Association symptom index and the benign prostatic hyperplasia impact index is perceptible to patients? *J Urol* 1995;154(5):1770-4.
9. Milonas D, Verikaite J, Jievaltas M. The effect of complete transurethral resection of the prostate on symptoms, quality of life, and voiding function improvement. *Cent European J Urol* 2015;68(2):169-74.
10. Welk B, McArthur E, Fraser LA, Hayward J, Dixon S, Hwang YJ, et al. The risk of fall and fracture with the initiation of a prostate-selective α antagonist: a population based cohort study. *BMJ* 2015;351:h5398.
11. Füllhase C, Chapple C, Cornu JN, De Nunzio C, Gratzke C, Kaplan SA, et al. Systematic review of combination drug therapy for non-neurogenic male lower urinary tract symptoms. *Eur Urol* 2013;64(2):228-43.
12. Lin PH, Freedland SJ. Lifestyle and lower urinary tract symptoms: what is the correlation in men? *Curr Opin Urol* 2015;25(1):1-5.

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