TITLE: Dutasteride and Finasteride for Men with Benign Prostatic Hyperplasia: Comparative Clinical Effectiveness and Safety

DATE: 07 March 2014

RESEARCH QUESTIONS

1. What is the comparative clinical effectiveness and safety of dutasteride and finasteride for men with benign prostatic hyperplasia?

2. What is the clinical effectiveness and safety of dutasteride versus placebo for men with benign prostatic hyperplasia?

3. What is the clinical effectiveness and safety of finasteride versus placebo for men with benign prostatic hyperplasia?

KEY MESSAGE

Four systematic reviews and six randomized controlled trials were found regarding the clinical effectiveness and safety of dutasteride and finasteride compared to each other or placebo for the treatment of benign prostatic hyperplasia.

METHODS

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2014, Issue 2), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, and randomized controlled trials. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between February 29, 2004 and February 25, 2014. Internet links were provided, where available.

The summary of findings was prepared from the abstracts of the relevant information. Please note that data contained in abstracts may not always be an accurate reflection of the data contained within the full article.

RESULTS

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials.

Four systematic reviews and six randomized controlled trials (RCTs) were found regarding the clinical effectiveness and safety of dutasteride and finasteride compared to each other or placebo for the treatment of benign prostatic hyperplasia (BPH). No health technology assessments were identified.

Additional references of potential interest are provided in the appendix.

OVERALL SUMMARY OF FINDINGS

One systematic review[1] and three RCTs[5,7,10] were found reporting on the clinical effectiveness and safety of dutasteride versus finasteride for BPH (Table 1). The systematic review[1] and one large RCT[7] found no significant differences in clinical improvement or adverse events between groups. The other two RCTs[5,10] reported dutasteride as being superior to finasteride in terms of improved symptom scores, maximum urine flow rate, total prostate volume, bladder residual volume, or quality of life; though it should be noted that both abstracts were unclearly reported.

Three systematic reviews[1-3] and two RCTs[6,8] were identified regarding the clinical effectiveness and safety of dutasteride versus placebo for BPH. The three systematic reviews and one of the RCTs[8] found significant improvements in symptoms and peak urine flow rates in the dutasteride group compared to the placebo group, although the other RCT did not[6] (Table 1). Two of the systematic reviews[1,2] and both RCTs[6,8] reported dutasteride superior to placebo in reducing total prostate volume. Two systematic reviews[1,2] reported more adverse events in the dutasteride group than the placebo group, while two of the RCTs[6,8] reported that adverse event rates were low but did not compare groups within their abstracts.

Two systematic reviews[3,4] and one RCT[9] were identified regarding the clinical effectiveness and safety of finasteride versus placebo for BPH. Both systematic reviews found improved symptoms, maximum urine flow rates, and a lowered risk of BPH progression with the use of finasteride versus placebo, although one[3] included an RCT that found no difference between symptom scores or flow rates between groups (Table 1). Both reviews also reported a higher incidence of sexual adverse events with the use of finasteride. The RCT[9] reported only an improved total prostate volume with the use of finasteride versus placebo.

Table 1: Summary of Study Types, Characteristics, and Conclusions

Author, Year	Study Type	Study Characteristics	Conclusions Result (95% confidence interval) unless otherwise indicated
Dutasteride versus finasteride			
Park et al., 2014[1]	SR with MA	• Men aged 40+ with moderate to severe BPH symptoms on the IPSS. • RCTs of more than 6	• No significant differences in symptom improvement or adverse events.

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		months duration. • Sample size unclear. • 9 RCTs included.	
Li et al., 2013[5]	RCT	• 72 men with BPH. • DUT was 0.5 mg daily, FIN dose improperly reported. • 6 months duration. • Blinding not reported.	• IPSS score DUT: -6.7 +/- 0.9 FIN: -6.0 +/- 1.3, p < 0.01 • Significant differences (p < 0.01) also found in maximum urine flow rate, TPV, and bladder residual volume *Note: direction not specified, though likely in favour of DUT.* • Serum level PSA, rates of effectiveness, and incidence of AEs were not significantly different between groups.
Nickel et al., 2011[7]	RCT	• Multicentre, double blind 12-month trial of men aged 50 and over with clinical BPH. • DUT 0.5 mg (n=813) or FIN 5 mg (n=817). • Optional 24 months open label extension.	• Both DUT and FIN effective at reducing TPV with no significant difference between groups. • Mean AUA-SI scores, peak urine flow rates, and percentage of AEs were also similar between groups.
Ravish et al., 2007[10]	RCT	• Patients with lower urinary tract symptoms and enlarged prostate randomized to 5 mg FIN or 0.5 mg DUT for 12 weeks. • Sample size and blinding not reported.	• DUT significantly improved peak urine flow rate, IPSS score, and quality of life compared to FIN at 12 weeks.
Dutasteride versus placebo			
Park et al., 2014[1]	SR with MA	• Men aged 40+ with moderate to severe BPH symptoms on the IPSS. • RCTs of more than 6 months duration. • Sample size unclear. • 9 RCTs included.	• Improving urinary symptoms (IPSS) DUT superior: -1.78 (-3.01, -0.55) • Peak Urinary Flow (Q max) DUT superior: 1.27 mL/s (0.97,1.57) • Change in TPV DUT superior -17.4 cm^3 (-25.77,-9.02) • Drug-related AEs DUT inferior: RR 1.35 (1.19,1.54)
Wu et al., 2013[2]	SR with MA	• Inclusion criteria unclear. • 4 RCTs included. • N = 6460 DUT, 6475	• Average symptoms (IPSS) DUT superior: -1.98 (-1.77,-2.19) • Average maximum flow DUT superior: 1.16 mL/s (0.63,1.70)

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		PL)	• Change in TPV DUT superior: 1.86 mL (12.76,14.96) • Acute Urinary Retention DUT superior: OR 0.35 (0.27,0.47) • Sexual Dysfunction (AE) DUT inferior: OR 0.41 (0.31,0.54) *Note, OR for sexual dysfunction appears to be placebo relative to DUT rather than DUT relative to placebo as reported for AUR.*
McNicholas et al., 2011[3]	SR without MA	• Included SRs and RCTs. • Maximum follow-up was 48 months.	• One RCT found DUT improved AUA-SI scores and peak urinary flow rate after 24 months compared to PL.
Na et al., 2012[6]	RCT	• Chinese adults with symptomatic BPH. • 0.5 mg DUT daily. • Randomized and blinded duration of 6 month with further 12 month open label extension.	• Mean TPV reduction of 17.14% in DUT group versus 3.71% in PL group ($p<0.05$). • Differences in peak urinary flow and AUA-SI did not reach statistical significance. • Low incidence of treatment emergent AEs over 18 months reported.
Tsukamoto et al., 2009[8]	RCT	• Double-blind. • 378 Japanese men with BPH having IPSS scores ≥ 8, TVP ≥ 30 mL, and maximum urinary flow rate ≤ 15mL/s. • 52 weeks in duration. • Subjects were stratified by concomitant use of tamsulosin (242 using versus 136 not).	• DUT improved IPSS, peak urine flow rate, and TPV compared to placebo at 52 weeks. • Drug-related sexual AEs were infrequent in the DUT group and generally not treatment limiting.
Finasteride versus placebo			
McNicholas et al., 2011[3]	SR without MA	• Included SRs and RCTs. • Maximum follow-up was 48 months.	• Included SR found FIN 5 mg improved total symptom score, maximum urinary flow rate, and TPV compared with placebo. FIN was associated with higher incidence of sexual adverse events. • One RCT found no significant differences in IPSS or peak urinary flow rate over one year.

Table 1: Summary of Study Types, Characteristics, and Conclusions			
Author, Year	**Study Type**	**Study Characteristics**	**Conclusions Result (95% confidence interval) unless otherwise indicated**
			• Another RCT found FIN reduced the risk of clinical progression, AUR, and need for invasive therapy versus placebo. Sexual AEs occurred significantly more frequently in the FIN group.
Tacklind et al., 2010[4]	SR without MA	• Included RCTs of at least 6 months duration of FIN versus placebo or active control.	• FIN consistently improved urinary symptom scores in trials longer than one year and significantly lowered the risk of BPH progression (AUR, risk of surgical intervention, ≥ 4 point increase in AUA-SI/IPSS) versus PL. • Drug-related AEs were reported as rare, though FIN increased the risk of sexual AEs versus PL.
Kaplan et al., 2008[9]	RCT	• 3,047 patients with BPH and lower urinary tract symptoms received FIN 5mg, doxasosin, FIN + doxasosin, or PL for an average of 4.5 years.	• Long-term treatment with FIN lead to an approximately 25% reduction in TPV compared to PL regardless of baseline TPV.

AE = adverse events; AUA-SI = American Urological Association Symptom Index; AUR = acute urinary retention; BPH = benign prostatic hyperplasia; DUT = dutasteride; FIN = finasteride; IPSS = International Prostate Symptom Score; MA = meta-analysis; OR = odds ratio; PL = placebo; RCT = randomized controlled trial; RR = relative risk; SR = systematic review; TPV = total prostate volume.

REFERENCES SUMMARIZED

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-analyses

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Randomized Controlled Trials

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APPENDIX – FURTHER INFORMATION:

Other Outcomes of Potential Interest

Systematic Review

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Randomized Controlled Trials

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Combination Therapy

Finasteride plus Tamsulosin versus Dutasteride versus Tamsulosin

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Dutasteride plus Tamsulosin versus Tamsulosin Alone

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