

Effect of combination treatment on patient-related outcome measures in benign prostatic hyperplasia: clinical utility of dutasteride and tamsulosin

Bob Djavan
Seyed Saeid Dianat
Amir Kazzazi

New York University, Department
of Urology, New York, USA

Background: Benign prostatic hyperplasia, the fourth most commonly diagnosed medical condition in the elderly, is a major underlying cause of lower urinary tract symptoms in men. Medical therapy is usually the first therapeutic option. Combination therapy is increasingly used for better symptom relief and outcome.

Methods: We searched the literature using the MEDLINE database for the efficacy of combination therapy in men with benign prostatic hyperplasia in terms of symptom improvement and impact on quality of life.

Results: Combination therapy with dutasteride and tamsulosin not only provides better symptom improvement and improved urinary flow rate, but is also associated with a more favorable impact on quality of life and patient satisfaction with treatment than monotherapy. Combination therapy also reduces the risk of events related to disease progression, such as acute urinary retention and benign prostatic hyperplasia-related surgery.

Conclusion: Combination therapy with dutasteride and tamsulosin is highly efficacious as medical therapy for benign prostatic hyperplasia in patients with moderate-to-severe lower urinary tract symptoms.

Keywords: benign prostatic hyperplasia, combination therapy, dutasteride, tamsulosin, quality of life, treatment outcome

Introduction

Benign prostatic hyperplasia (BPH), the fourth most commonly diagnosed medical condition in the elderly, affects more than half of men aged older than 50 years and nearly 90% of men over 80 years.^{1,2} BPH is one of the major causes of lower urinary tract symptoms in men. These are categorized into three groups of symptoms, ie, voiding symptoms (reduced urinary stream, intermittency, hesitancy, straining, terminal dribble), storage symptoms (frequency, nocturia, urgency, overflow incontinence), and post-micturition symptoms (sensation of incomplete bladder emptying, postmicturition dribble).³ The goal of treatment is mainly focused on improvement in symptom scores, patient-reported quality of life, patient satisfaction, and reduction of risk of disease progression and need for further surgical interventions.⁴

Treatment of lower urinary tract symptoms suggestive of BPH is initially planned by assessment of severity of symptoms using quantitative indices, such as the International Prostate Symptom Score (IPSS), which is the most widely accepted American Urological Association (AUA) symptom index.⁵

Correspondence: Bob Djavan
Department of Urology, VA University
Hospital, New York University School
of Medicine, New York, NY, USA
Tel +1 64 6825 6335
Fax +1 64 6825 6397
Email bdjavan@hotmail.com

An important issue in the management of lower urinary tract symptoms is to determine the contribution of bladder outlet obstruction to development of symptoms. However, studies have reported that prostate size and severity of symptoms might not be strongly correlated with the degree of bladder outlet obstruction. Therefore, other pathological conditions of the bladder, prostate, other pelvic organs, and possibly other unknown causes, might contribute to this correlation.⁶ Thus, a combination of symptom scores and uroflowmetry assessment might be beneficial for more precise diagnosis of underlying pathology and better planning of treatment. Uroflowmetry is a simple and noninvasive assessment method, but is still not sufficiently specific for clear determination of the underlying etiology of lower urinary tract symptoms.⁶

The gold standard diagnostic test for more accurate determination of the role of bladder outlet obstruction in lower urinary tract symptoms is the detrusor pressure-flow study. One of the main benefits of this diagnostic test is its ability to distinguish men with low urinary flow rate due to poor detrusor contractility from those with bladder outlet obstruction as the underlying cause of low flow rate.⁷

Despite a high yield of data obtained using urodynamic studies, we have no accepted indications for using urodynamics in patients with lower urinary tract symptoms. Based on AUA guidelines, urodynamics should not be considered for initial evaluation of men with lower urinary tract symptoms. The main indications for urodynamic studies are to determine the underlying mechanism of low urinary flow rate in patients with lower urinary tract symptoms who are candidates for invasive therapies. Invasive procedures are usually planned by the results of a pressure-flow study or when the prostate size and anatomical configuration are important factors for a proposed treatment modality.⁸ Therefore, urodynamic study answers the questions arising from standard noninvasive urologic evaluations, including history and physical examination, urinalysis, symptom scores, uroflowmetry, urinary diary, and post-voiding residual urine.⁹

Bladder outlet obstruction can lead to lower urinary tract symptoms, mainly through dynamic and static factors. The dynamic component might be due to smooth muscle tension in the bladder neck and prostate, while the static component is due to the enlarged prostate encroaching upon the prostatic urethra and bladder outlet. Medical treatment is mainly focused on the treatment of both static and dynamic factors.¹⁰

This paper reviews the therapeutic options for lower urinary tract symptoms due to BPH. Combination medical

treatment using dutasteride and tamsulosin is focused in terms of improvement of lower urinary tract symptoms, quality of life, and maximal urinary flow rate, as well as the long-term outcome to reduce the risk of acute urinary retention and need for surgery.

Methods

We searched the English language literature using the MEDLINE database for studies of medical treatment of lower urinary tract symptoms due to BPH published up to January 2011. We used several keywords, including “benign prostatic hyperplasia”, “combination therapy”, “dutasteride”, “tamsulosin”, “quality of life”, and “treatment outcome”. Combination therapy with dutasteride and tamsulosin was mainly focused on in the literature review in terms of treatment outcome and patient satisfaction.

Overview of available treatments

Surgical treatment

There are two large groups of surgical and medical options for treatment of lower urinary tract symptoms suggestive of BPH. The standard surgical treatment option has been transurethral resection of the prostate (TURP) for a long time.¹¹ TURP has been effective for improvement of symptom scores and urinary flow rate, with low post-voiding residual urine and low retreatment rates in long-term follow-up studies. Despite advances in this field, there are still complications, such as perioperative bleeding requiring blood transfusion, transurethral resection syndrome, prolonged urinary catheterization, and hospital stay, as well as urinary incontinence and retrograde ejaculation.¹²

Novel techniques have been introduced to the clinic, which are grouped as minimally invasive procedures. These modalities use various energy sources for resection, ablation, or vaporization of the gland, which might be beneficial in terms of a lower rate of complications than with TURP. In addition to achieving better efficacy, these novel techniques might be beneficial with regard to cost-effectiveness, reflected by a shorter duration of hospital stay and less need for outpatient treatments.¹³ Some of the new minimally invasive surgical treatment options for BPH include bipolar TURP, bipolar transurethral vaporization, holmium laser enucleation, and potassium-titanyl-phosphate laser vaporization of the prostate.¹⁴

Medical treatment

Two groups of drugs, ie, α -blockers and 5α -reductase inhibitors, are increasingly used as the first option in medical

treatment of symptomatic BPH.¹⁵ The major subtype of α -adrenoceptor for contraction of the prostate is the α_{-1A} receptor. However, the mechanism of the α -blocker effect on symptoms might not be entirely addressed by lowering bladder outlet resistance.¹⁶ Thus, the α_1 -receptors outside the prostate, such as in the bladder and spinal cord, might be the possible mechanism of action and effectiveness. Side effects are mainly mediated by vascular α_1 -receptors, other smooth muscle cells outside the prostate, and the central nervous system.¹⁷

There are four α -blockers on the market that are commonly used, ie, alfuzosin, doxazosin, terazosin, and tamsulosin. The selective α_{-1A} -receptor blocker for which the most experience and data are available is tamsulosin. However, some newer drugs are available, including silodosin and naf-topidil (α_{-1A} and α_{-1D} receptor blockers), but without strong evidence of effectiveness.^{18,19} Using tamsulosin achieves better patient compliance on once daily administration, with a continuous 24-hour pharmacological effect.²⁰

Hyperplasia of stromal and epithelial cells in the transition and periurethral zones of the prostate gland is mediated by two isotypes of the 5α -reductase enzyme. It has been shown that the 5α -reductase inhibitors reduce prostate volume by an average of 15%–25% during treatment.^{21,22} There are two available drugs in this category, ie, finasteride and dutasteride. Combination therapy of dutasteride and tamsulosin is currently the recommended medical treatment in patients with moderate-to-severe lower urinary tract symptoms suggestive of BPH, prostate serum antigen ≥ 1.5 ng/mL, and prostate volume ≥ 30 mL.²³

Phosphodiesterase 5 is an isoenzyme encoded by the phosphodiesterase family of genes that inactivate cGMP. Phosphodiesterase 5 inhibitors are the firstline treatment for erectile dysfunction. Furthermore, phosphodiesterase 5 inhibitors may cause smooth muscle relaxation in the bladder neck, urethra, and prostate.²⁴ Tadalafil, a phosphodiesterase 5 inhibitor, with or without an α -blocker, might be a potential future therapeutic option in patients with lower urinary tract symptoms suggestive of BPH with comorbid erectile dysfunction. However, using this agent, the vasodilatory effect is an adverse drug reaction.²⁵

It appears that storage symptoms are more common than the other components of lower urinary tract symptoms.²⁶ On the other hand, prostate enlargement and overactive bladder syndrome can both lead to bladder outlet obstruction presenting as lower urinary tract symptoms.²⁷ Thus, antimuscarinics are indicated in patients with persistent storage symptoms (overactive bladder type) following α -blocker therapy.²⁵

Subjective outcome and impact on quality of life

Reliable evaluation of the severity of lower urinary tract symptoms and impact on quality of life is an important step in the management of patients with lower urinary tract symptoms suggestive of BPH. There are various validated symptom-scoring questionnaires that are used in both clinical and research settings.²⁸ The American Urological Association Symptom Index (AUASI) is the most widely used and extensively validated symptom-scoring system for BPH.^{29,30} Seven questions concerning incomplete emptying, frequency, intermittency, urgency, weakness of urinary stream, straining, and nocturia are assessed in this questionnaire. Comparison of the AUASI with three self-administered questionnaires, ie, the Maine Medical Assessment Program, Madsen–Iversen, and Boyarsky symptom scores, show a correlation of 0.77–0.93.³¹

There are some questionnaires that are used for quantitative evaluation of symptoms and impact on quality of life. The IPSS consists of AUASI questions plus one question on quality of life, and is one of the most widely used scoring systems for BPH.²⁸ Table 1 shows the items in the IPSS questionnaire.

The AUA committee has also validated the BPH Impact Index to assess the impact of lower urinary tract symptoms due to BPH on various domains of health.³² The BPH Impact Index is a self-administered questionnaire including four questions on how urinary symptoms during the past month have affected physical comfort, heightened worry about health, severity of symptoms as a bothersome problem, and whether the symptoms are interfering with usual activities.³³ Table 2 summarizes the items included in the BPH Impact Index scoring system.

Use of the AUASI and the BPH Impact Index to determine disease-specific quality of life has also been compared. Two items of the AUASI, including urinary frequency and weak stream, were reported to explain best the disease-specific quality of life in patients with lower urinary tract symptoms.³⁴

It has been suggested that the AUASI and BPH Impact Index are useful indices of outcome in patients with lower urinary tract symptoms before and after treatment. It has also been reported that the slight improvement detected by patients with treatment was associated with a mean decrease in AUASI and BPH Impact Index scores of 3.1 and 0.4 points, respectively. However, baseline scores are an important factor in this relationship.³⁵

The Patient Perception of Study Medication (PPSM) is a 12-item questionnaire for assessment of patient satisfaction with treatment (Table 3). There is now a US English-validated PPSM questionnaire for patients with lower urinary tract symptoms

Table 1 International Prostate Symptom Score questionnaire

In the past month	Not at all	Less than 1 in 5 times	Less than half of the time	About half of the time	More than half of the time	Almost always	Your score
1. Incomplete emptying How often have you had the sensation of not emptying your bladder?	0	1	2	3	4	5	
2. Frequency How often have you had to urinate less than every 2 hours?	0	1	2	3	4	5	
3. Intermittency How often have you found you stopped and started again several times when you urinated?	0	1	2	3	4	5	
4. Urgency How often have you found it difficult to postpone urination?	0	1	2	3	4	5	
5. Weak stream How often have you had a weak urinary stream?	0	1	2	3	4	5	
6. Straining How often have you had to strain to start urination?	0	1	2	3	4	5	
7. Nocturia How many times did you typically get up at night to urinate?	None	1 time	2 times	3 times	4 times	5 times	Your score
Total IPSS score	0	1	2	3	4	5	
Quality of life due to urinary symptoms	Delighted	Pleased	Mostly satisfied	Mixed-equally satisfied and dissatisfied	Mostly dissatisfied	Unhappy	Terrible
If you were to spend the rest of your life with your urinary condition the way it is now, how would you feel about that?	0	1	2	3	4	5	6

Notes: Total IPSS score: 0–7 mildly symptomatic; 8–19 moderately symptomatic; 20–35 severely symptomatic.

Abbreviation: IPSS, International Prostate Symptom Score.

Table 2 Benign Prostatic Hypertrophy Impact Index questionnaire

1. During the last month, how much physical discomfort did any urinary problems cause you?	None (0)	Only a little (1)	Some (2)	A lot (3)	
2. During the last month, how much did you worry about your health because of any urinary problems?	None (0)	Only a little (1)	Some (2)	A lot (3)	
3. Overall, how bothersome has any trouble with urination been during the last month?	Not at all (0)	A little (1)	Some (2)	A lot (3)	
4. During the last month, how much of the time has any urinary problem kept you from doing the kinds of things you would usually do?	None (0)	A little (1)	Some of the time (2)	Most of the time (3)	All the time (4)

to assess their satisfaction with treatment. In this version of the PPSM, total score is the result of summed responses to questions 1–4 and 9–11. Other questions are excluded from the total score. Questions 5–8 are about pain assessment and are excluded due to low prevalence of pain in BPH patients in general. Question 12 assesses the patient's willingness to ask for medication and is not directly related to patient satisfaction or perception of improvement with treatment.³⁶

Combination therapy Before dutasteride and tamsulosin

The PREDICT (PRospective European DoxazosIn and Combination Therapy) trial was designed to determine

the efficacy of combination treatment using doxazosin and finasteride in comparison with monotherapy. It appeared that combination therapy was superior to 5 α -reductase inhibitor monotherapy, but offered no significant advantage over α -blocker monotherapy.³⁷

McConnell et al designed a long-term, double-blind study to investigate the efficacy of doxazosin, finasteride, and combination therapy for more than 4 years. It was identified that combination therapy was superior to α -blocker or 5 α -reductase inhibitor monotherapy for improvement of symptoms and increasing maximal urinary flow rate during long-term follow-up. However, a treatment regimen containing finasteride was effective for reducing the

Table 3 Patient Perception of Satisfaction with Medication questionnaire

	0	1	2	3	4	5	6
1. Since you began taking the study medication, how has control of your urinary problems changed?	Much improved	Improved	Somewhat improved	No change	Somewhat worse	Worse	Much worse
2. How satisfied are you with the effect of the study medication on control of your urinary problems?	Very satisfied	Satisfied	Somewhat satisfied	Neutral	Somewhat dissatisfied	Dissatisfied	Very dissatisfied
3. Since you began taking the study medication, how has the strength of your urinary stream changed?	Much improved	Improved	Somewhat improved	No change	Somewhat worse	Worse	Much worse
4. How satisfied are you with the effect of the study medication on the strength of your urinary stream?	Very satisfied	Satisfied	Somewhat satisfied	Neutral	Somewhat dissatisfied	Dissatisfied	Very dissatisfied
5. Since you began taking the study medication, how has your pain prior to urinating changed?	Much improved	Improved	Somewhat improved	No change	Somewhat worse	Worse	Much worse
6. How satisfied are you with the effect the study medication has on your pain prior to urinating?	Very satisfied	Satisfied	Somewhat satisfied	Neutral	Somewhat dissatisfied	Dissatisfied	Very dissatisfied
7. Since you began taking the study medication, how has your pain during urination changed?	Much improved	Improved	Somewhat improved	No change	Somewhat worse	Worse	Much worse
8. How satisfied are you with the effect the study medication has on your pain during urination?	Very satisfied	Satisfied	Somewhat satisfied	Neutral	Somewhat dissatisfied	Dissatisfied	Very dissatisfied
9. Since you began taking the study medication, how has the way your urinary problems interfere with your ability to go about your usual activities changed?	Much improved	Improved	Somewhat improved	No change	Somewhat worse	Worse	Much worse
10. How satisfied are you with the effect the study medication has on your ability to go about your usual activities without interference with your usual activities?	Very satisfied	Satisfied	Somewhat satisfied	Neutral	Somewhat dissatisfied	Dissatisfied	Very dissatisfied
11. Overall, how satisfied are you with the study medication and its effect on your urinary problems?	Very satisfied	Satisfied	Somewhat satisfied	Neutral	Somewhat dissatisfied	Dissatisfied	Very dissatisfied
12. Would you ask your doctor for the medication you received in this study?	Yes	No	Not sure				

long-term risk of acute urinary retention necessitating invasive procedures.³⁸

Introduction of dutasteride

The CombAT (Combination of Avodart and Tamsulosin) study generated some very useful and valuable information on the efficacy of combination therapy using dutasteride and tamsulosin in patients with moderate-to-severe lower urinary tract symptoms secondary to BPH and an enlarged gland (≥ 30 mL). Combination therapy was shown to be superior to monotherapy in terms of reduction in storage symptoms with dutasteride from month 3, and better than tamsulosin after 12 months of treatment. In addition, reduction in voiding subscore was greater in the combination group than in the dutasteride group from month 3 and in the tamsulosin group from month 6. However, there was no difference in reduction of storage symptoms between the dutasteride and tamsulosin groups in the 2-year data. Tamsulosin was more effective for improvement of voiding symptoms than dutasteride at months 3, 6, and 9, but the difference was no longer significant by month 12. However, dutasteride was more effective than tamsulosin for reduction of voiding scores from month 18 onwards.³⁹

Reduction in storage subscores was shown to be significantly greater with combination therapy than either monotherapy in the lower baseline prostate volume tertiles (30–42 mL and 42–58 mL) after 2 years, whereas in men with the highest baseline prostate volume tertile (≥ 58 mL), reduction in storage subscores was significantly greater with a dutasteride-containing regimen than with tamsulosin monotherapy. Combination therapy was also more effective than either monotherapy for improvement of voiding symptoms in patients with a prostate volume of 30–42 mL.³⁹ The authors also showed that combination therapy was associated with significantly greater improvement in patient-reported disease-specific quality of life and treatment satisfaction than both monotherapies after treatment for 2 years.⁴

The 4-year results of CombAT have also been promising. Symptom relief, based on IPSS data, was significantly greater with combination therapy than with tamsulosin or dutasteride monotherapy (mean IPSS change of -7.3 , -4.9 , and -6.4 , respectively). A significantly greater decrease in IPSS quality of life score was also detected for the combination treatment (-1.5) compared with tamsulosin (-1.1) or dutasteride (-1.3). Furthermore, peak urinary flow rate was significantly increased on combination treatment (2.4 mL/second) compared with tamsulosin (0.7 mL/second) or dutasteride (2 mL/second). Symptom deterioration was the

most common disease progression event in each treatment group. Combination therapy reduced the risk of symptom deterioration on the IPSS by at least four points, ie, 41.3% and 35.2% when compared with tamsulosin and dutasteride, respectively. Combination therapy was also persistently beneficial compared with monotherapy for symptom relief during the study period, and was compatible with uroflowmetry results. Although it appeared that combination therapy significantly reduced the time to first episode of acute urinary retention or BPH-related surgery, combination therapy was associated with a reduced risk of acute urinary retention and BPH-related surgery compared with the other treatment groups. This difference appeared from eight months onwards, with a higher incidence of acute urinary retention or BPH-related surgery in the tamsulosin arm compared with the combination and dutasteride arms.⁴⁰

The 4-year results showed that patients in the dutasteride-containing arms had persistently stable satisfaction with their treatment during the follow-up period, while the tamsulosin-containing arms experienced decreased satisfaction from nine months onwards. The improvement in BPH Impact Index reached the threshold for marked improvement at 30 months for the combination group, which was maintained out to 48 months.⁴¹

Montorsi et al have also investigated the effect of combination therapy on patient-reported quality of life and treatment satisfaction using the same measurements and questionnaires. Combination therapy was associated with significantly better symptom improvement based on the BPH Impact Index and IPSS question 8 than monotherapy. Combination therapy was more advantageous than dutasteride from three months onwards, and from nine months (BPH Impact Index) or 12 months (IPSS question 8) onwards compared with tamsulosin. The PPSM questionnaire showed that a significantly higher proportion of patients on combination therapy were satisfied with treatment and would request its continuation.⁴¹ Although there were more drug-related adverse events in the combination group, withdrawal rates were similar between the treatment arms. Also, there was no difference in overall cardiovascular event rates. This study provides strong evidence for the beneficial long-term use of dutasteride and tamsulosin combination therapy in patients with moderate-to-severe lower urinary tract symptoms suggestive of BPH and prostatic enlargement at increased risk of progression.⁴⁰ The results of the major efficacy studies of 5α -reductase inhibitor and α -blocker combination therapy in comparison with monotherapy or placebo are summarized in Table 4.

Table 4 Results of trials on efficacy of combination therapy with an α -blocker and a 5 α -reductase inhibitor

Reference	Duration (weeks)	Intervention (n)	Symptom change (% IPSS)	Change in Q _{max} (mL/sec)	Change in TPV (%)
Lepor et al ⁴⁷	52	Placebo (n = 305)	-16.5 ^a	+1.4	+1.3
		Terazosin 10 mg/day (n = 305)	-37.7 ^{a,b,d}	+2.7 ^{b,d}	+1.3
		Finasteride 5 mg/day (n = 310)	-19.8 ^a	+1.6	-16.9
		Combination therapy (n = 309)	-39 ^{a,b,d}	+3.2 ^{b,d}	-18.8 ^{b,c}
Debruyne et al ⁴⁸	26	Alfuzosin 5 mg bid (n = 358)	-41.2 ^d	+1.8	-0.5
		Finasteride 5 mg/day (n = 344)	-33.5	+1.8	-10.5 ^c
		Combination therapy (n = 349)	-39 ^d	+2.3	-11.9 ^c
Kirby et al ⁴⁹	52	Placebo (n = 253)	-33.1	+1.4	-
		Doxazosin 1-8 mg/day (n = 250)	-49.1 ^{b,d}	+3.6 ^{b,d}	-
		Finasteride 5 mg/day (n = 239)	-38.6	+1.8	-
		Combination therapy (n = 265)	-49.7 ^{b,d}	+3.8 ^d	-
McConnell et al ³⁸	234	Placebo (n = 737)	-23.8 ^a	+1.4 ^a	+24 ^a
		Doxazosin 1-8 mg/day (n = 756)	-35.3 ^{a,b,d}	+2.5 ^{a,b}	+24 ^a
		Finasteride 5 mg/day (n = 768)	-28.4 ^{a,b}	+2.2 ^{a,b}	-19 ^{a-c}
		Combination therapy (n = 786)	-41.7 ^{a-d}	+3.7 ^{a-d}	-19 ^{a-c}
Roehrborn et al ⁵⁰	104	Tamsulosin 0.4 mg/day (n = 1611)	-27.4	+0.9	0
		Dutasteride 0.5 mg/day (n = 1623)	-30.5	+1.9	-28 ^c
		Combination therapy (n = 1610)	-39.2 ^{c,d}	+2.4 ^{c,d}	-26.9 ^c
Roehrborn et al ⁴⁰	208	Tamsulosin 0.4 mg/day (n = 1611)	-23.2	+0.7	+4.6
		Dutasteride 0.5 mg/day (n = 1623)	-32.3	+2.0	-28 ^c
		Combination therapy (n = 1610)	-38 ^{c,d}	+2.4 ^c	-27.3 ^c

Notes: ^aSignificant compared with baseline; ^bSignificant compared with placebo; ^cSignificant compared with α -blocker monotherapy; ^dSignificant compared with 5 α -reductase inhibitor monotherapy.

Abbreviations: Q_{max}, maximal urinary flow rate; IPSS, International Prostate Symptom Score; TPV, total prostate volume.

Cost-effectiveness: dutasteride versus finasteride

There may be a higher treatment cost with dutasteride than with finasteride. However, it has been shown that patients receiving dutasteride incurred \$20.50 less per month in prostate-specific charges than those taking finasteride (\$105.67 versus \$126.17, $P = 0.0007$) because dutasteride treatment is associated with fewer inpatient hospitalization charges compared with finasteride.⁴² Furthermore, it is more likely that dutasteride allows us to discontinue a α -blocker during treatment, which can lead to cost savings in health care plans and fewer drug-related side effects.⁴³

Planning of medical treatment

Initial evaluations to plan treatment of BPH include urinalysis and serum prostate serum antigen level, as well as asking the patient to complete a validated symptom index. Watchful waiting is usually suggested in patients with mild symptoms or moderate-to-severe but not bothersome symptoms. Surgical management is used in cases of refractory bothersome symptoms despite medical treatment and complications of BPH, including refractory urinary retention, recurrent urinary retention, recurrent hematuria refractory to medical treatment with a 5 α -reductase inhibitor, renal insufficiency,

and bladder stones. Medical treatment with α -blockers is usually the first option, providing a rapid onset of action. The 5 α -reductase inhibitors are usually prescribed for long-term treatment and alleviation of symptoms. These agents are also sometimes recommended for prevention of disease progression in patients with mild symptoms but with an enlarged prostate.²⁵ Patients usually prefer a long-term symptom-free period, and it is essential to assess the patient's preference and satisfaction with BPH treatment, to optimize drug compliance.⁴⁴

Duodart[®], a fixed-dose combination of dutasteride 0.5 mg and tamsulosin 0.4 mg, is a recent development in medical treatment for BPH. GlaxoSmithKline (GSK) has received European approval for Duodart[®] for the treatment of moderate-to-severe symptoms of BPH via the decentralized procedure, with Germany acting as a Reference Member State.⁴⁵ In June 2010, the US Food and Drug Administration also approved Jalyn[™], a single-capsule combination of dutasteride 0.5 mg and tamsulosin 0.4 mg, to treat symptomatic BPH in men with an enlarged prostate.⁴⁶

Conclusion

Combination therapy with dutasteride and tamsulosin in men with moderate-to-severe lower urinary tract symptoms

suggestive of BPH is strongly supported, and reduces the risk of clinical progression, acute urinary retention, and BPH-related surgical interventions. The available data suggest that combination therapy is also associated with better symptom relief and patient satisfaction in long-term follow-up. The fixed-dose combination formulations may also achieve higher compliance and possibly a better outcome.

Disclosure

The authors report no conflicts of interest in this work.

References

- Issa MM, Fenter TC, Black L, Grogg AL, Kruep EJ. An assessment of the diagnosed prevalence of diseases in men 50 years of age or older. *Am J Manag Care*. 2006;12:S83–S89.
- Naslund MJ, Issa MM, Grogg AL, Eaddy MT, Black L. Clinical and economic outcomes in patients treated for enlarged prostate. *Am J Manag Care*. 2006;12:S111–S116.
- Gravas S, Melekos MD. Male lower urinary tract symptoms: How do symptoms guide our choice of treatment? *Curr Opin Urol*. 2009;19:49–54.
- Barkin J, Roehrborn CG, Siami P, et al. Effect of dutasteride, tamsulosin and the combination on patient-reported quality of life and treatment satisfaction in men with moderate-to-severe benign prostatic hyperplasia: 2-year data from the CombAT trial. *BJU Int*. 2009;103:919–926.
- Barry MJ, O'Leary MP. Advances in benign prostatic hyperplasia. The developmental and clinical utility of symptom scores. *Urol Clin North Am*. 1995;22:299–307.
- Chapple CR, Roehrborn CG. A shifted paradigm for the further understanding, evaluation, and treatment of lower urinary tract symptoms in men: Focus on the bladder. *Eur Urol*. 2006;49:651–658.
- Abrams P, Chapple C, Khoury S, Roehrborn C, de la Rosette J. Evaluation and treatment of lower urinary tract symptoms in older men. *J Urol*. 2009;181:1779–1787.
- American Urological Association Education and Research I. Chapter 1. AUA guideline on the management of benign prostatic hyperplasia: Diagnosis and treatment recommendations. Available at: http://www.auanet.org/content/guidelines-and-quality-care/clinical-guidelines/main-reports/bph-management/preface_toc.pdf. Accessed March 9, 2011.
- Mehdizadeh JL, Leach GE. Role of invasive urodynamic testing in benign prostatic hyperplasia and male lower urinary tract symptoms. *Urol Clin North Am*. 2009;36:431–441.
- Roehrborn CG. Clinical management of lower urinary tract symptoms with combined medical therapy. *BJU Int*. 2008;102 Suppl 2:13–17.
- Madersbacher S, Marberger M. Is transurethral resection of the prostate still justified? *BJU Int*. 1999;83:227–237.
- Reich O, Gratzke C, Bachmann A, et al. Morbidity, mortality and early outcome of transurethral resection of the prostate: A prospective multicenter evaluation of 10,654 patients. *J Urol*. 2008;180:246–249.
- Burke N, Whelan JP, Goeree L, et al. Systematic review and meta-analysis of transurethral resection of the prostate versus minimally invasive procedures for the treatment of benign prostatic obstruction. *Urology*. 2010;75:1015–1022.
- Ahyai SA, Gillling P, Kaplan SA, et al. Meta-analysis of functional outcomes and complications following transurethral procedures for lower urinary tract symptoms resulting from benign prostatic enlargement. *Eur Urol*. 2010;58:384–397.
- Naslund M, Eaddy MT, Hogue SL, Kruep EJ, Shah MB. Impact of delaying 5- α reductase inhibitor therapy in men on alpha-blocker therapy to treat BPH: Assessment of acute urinary retention and prostate-related surgery. *Curr Med Res Opin*. 2009;25:2663–2669.
- Barendrecht MM, Abrams P, Schumacher H, de la Rosette JJ, Michel MC. Do alpha1-adrenoceptor antagonists improve lower urinary tract symptoms by reducing bladder outlet resistance? *Neurourol Urodyn*. 2008;27:226–230.
- Oelke M, Bachmann A, Descazeaud A, et al. Conservative treatment of non-neurogenic male LUTS. Available at: <http://www.uroweb.org/?id=217&tyid=2>. Accessed March 1, 2011.
- Cantrell MA, Bream-Rouwenhorst HR, Hemerson P, Magera JS Jr. Silodosin for benign prostatic hyperplasia. *Ann Pharmacother*. 2010;44:302–310.
- Garimella PS, Fink HA, Macdonald R, Wilt TJ. Naftopidil for the treatment of lower urinary tract symptoms compatible with benign prostatic hyperplasia. *Cochrane Database Syst Rev*. 2009:CD007360.
- Michel MC, Korstanje C, Krauwinkel W, Kuipers M. The pharmacokinetic profile of tamsulosin oral controlled absorption system (OCAS®). *Eur Urol Suppl*. 2005;4:15–24.
- Keam SJ, Scott LJ. Dutasteride: A review of its use in the management of prostate disorders. *Drugs*. 2008;68:463–485.
- Rittmaster RS, Norman RW, Thomas LN, Rowden G. Evidence for atrophy and apoptosis in the prostates of men given finasteride. *J Clin Endocrinol Metab*. 1996;81:814–819.
- Djavan B, Handl MJ, Dianat S. Combined medical treatment using dutasteride and tamsulosin for lower urinary tract symptoms suggestive of benign prostatic hyperplasia. *Expert Opin Pharmacother*. 2010;11:2535–2547.
- Wang C. Phosphodiesterase-5 inhibitors and benign prostatic hyperplasia. *Curr Opin Urol*. 2010;20:49–54.
- Djavan B, Margreiter M, Dianat SS. An algorithm for medical management in male lower urinary tract symptoms. *Curr Opin Urol*. 2011;21:5–12.
- Irwin DE, Milsom I, Hunskaar S, et al. Population-based survey of urinary incontinence, overactive bladder, and other lower urinary tract symptoms in five countries: Results of the EPIC study. *Eur Urol*. 2006;50:1306–1314.
- Abdel-Aziz KF, Lemack GE. Overactive bladder in the male patient: Bladder, outlet, or both? *Curr Urol Rep*. 2002;3:445–451.
- Cambio AJ, Evans CP. Outcomes and quality of life issues in the pharmacological management of benign prostatic hyperplasia (BPH). *Ther Clin Risk Manag*. 2007;3:181–196.
- Barry MJ, Fowler FJ Jr, O'Leary MP, et al. The American Urological Association symptom index for benign prostatic hyperplasia. The Measurement Committee of the American Urological Association. *J Urol*. 1992;148:1549–1557.
- MacDonald D, McNicholas TA. Drug treatments for lower urinary tract symptoms secondary to bladder outflow obstruction: Focus on quality of life. *Drugs*. 2003;63:1947–1962.
- Barry MJ, Fowler FJ Jr, O'Leary MP, Bruskewitz RC, Holtgrewe HL, Mebust WK. Correlation of the American Urological Association symptom index with self-administered versions of the Madsen-Iversen, Boyarsky and Maine Medical Assessment Program symptom indexes. Measurement Committee of the American Urological Association. *J Urol*. 1992;148:1558–1563.
- Barry MJ, Fowler FJ Jr, O'Leary MP, Bruskewitz RC, Holtgrewe HL, Mebust WK. Measuring disease-specific health status in men with benign prostatic hyperplasia. Measurement Committee of The American Urological Association. *Med Care*. 1995;33:AS145–AS155.
- Angalakuditi M, Seifert RF, Hayes RP, O'Leary MP, Viktrup L. Measurement properties of the benign prostatic hyperplasia impact index in tadalafil studies. *Health Qual Life Outcomes*. 2010;8:131.
- Marklund-Bau H, Edell-Gustafsson U, Spangberg A. Bothersome urinary symptoms and disease-specific quality of life in patients with benign prostatic obstruction. *Scand J Urol Nephrol*. 2007;41:32–41.
- Barry MJ, Williford WO, Chang Y, 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;154:1770–1774.

36. Black L, Grove A, Morrill B. The psychometric validation of a US English satisfaction measure for patients with benign prostatic hyperplasia and lower urinary tract symptoms. *Health Qual Life Outcomes*. 2009;7:55.
37. Kirby RS, Roehrborn C, Boyle P, et al. Efficacy and tolerability of doxazosin and finasteride, alone or in combination, in treatment of symptomatic benign prostatic hyperplasia: The Prospective European Doxazosin and Combination Therapy (PREDICT) trial. *Urology*. 2003; 61:119–126.
38. McConnell JD, Roehrborn CG, Bautista OM, 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;349:2387–2398.
39. Becher E, Roehrborn CG, Siami P, Gagnier RP, Wilson TH, Montorsi F. The effects of dutasteride, tamsulosin, and the combination on storage and voiding in men with benign prostatic hyperplasia and prostatic enlargement: 2-year results from the Combination of Avodart and Tamsulosin study. *Prostate Cancer Prostatic Dis*. 2009;12:369–374.
40. Roehrborn CG, Siami P, Barkin J, et al. The effects of combination therapy with dutasteride and tamsulosin on clinical outcomes in men with symptomatic benign prostatic hyperplasia: 4-year results from the CombAT study. *Eur Urol*. 2010;57:123–131.
41. Montorsi F, Henkel T, Geboers A, et al. Effect of dutasteride, tamsulosin and the combination on patient-reported quality of life and treatment satisfaction in men with moderate-to-severe benign prostatic hyperplasia: 4-year data from the CombAT study. *Int J Clin Pract*. 2010;64:1042–1051.
42. Fenter TC, Runken MC, Black L, Eaddy M. Finasteride versus dutasteride: A real-world economic evaluation. *Am J Manag Care*. 2007; 13 Suppl 1:S23–S28.
43. Naslund M, Black L, Eaddy M, Batiste LR. Differences in alpha blocker usage among enlarged prostate patients receiving combination therapy with 5 ARIs. *Am J Manag Care*. 2007;13 Suppl 1:S17–S22.
44. Emberton M. Medical treatment of benign prostatic hyperplasia: Physician and patient preferences and satisfaction. *Int J Clin Pract*. 2010;64:1425–1435.
45. GlaxoSmithKline. The first fixed dose combination medicine for benign prostatic hyperplasia. Available at: http://www.gsk.com/media/pressreleases/2010/2010_pressrelease_10036.htm. Accessed March 9, 2011.
46. GlaxoSmithKline. FDA approves Jalyn™, a fixed-dose combination of dutasteride and tamsulosin, for symptomatic BPH in men with an enlarged prostate. Available at: http://www.gsk.com/media/pressreleases/2010/2010_us_pressrelease_10035.htm. Accessed March 9, 2011.
47. Lepor H, Williford WO, Barry MJ, et al. The efficacy of terazosin, finasteride, or both in benign prostatic hyperplasia. Veterans Affairs Cooperative Studies Benign Prostatic Hyperplasia Study Group. *N Engl J Med*. 1996;335:533–539.
48. Debruyne FM, Jardin A, Colloi D, et al. Sustained-release alfuzosin, finasteride and the combination of both in the treatment of benign prostatic hyperplasia. European ALFIN Study Group. *Eur Urol*. 1998;34: 169–175.
49. Kirby RS. A randomized, double-blind crossover study of tamsulosin and controlled-release doxazosin in patients with benign prostatic hyperplasia. *BJU Int*. 2003;91:41–44.
50. Roehrborn CG, Siami P, Barkin J, et al. The effects of dutasteride, tamsulosin and combination therapy on lower urinary tract symptoms in men with benign prostatic hyperplasia and prostatic enlargement: 2-year results from the CombAT study. *J Urol*. 2008;179:616–621.

Patient Related Outcome Measures

Publish your work in this journal

Patient Related Outcome Measures is an international, peer-reviewed, open access journal focusing on treatment outcomes specifically relevant to patients. All aspects of patient care are addressed within the journal and practitioners from all disciplines are invited to submit their work as well as healthcare researchers and patient support groups. Areas covered will

Submit your manuscript here: <http://www.dovepress.com/patient-related-outcome-measures-journal>

include: Quality of life scores; Patient satisfaction audits; Treatment outcomes that focus on the patient; Research into improving patient outcomes; Hypotheses of interventions to improve outcomes; Short communications that illustrate improved outcomes; Case reports or series that show an improved patient experience; Patient journey descriptions or research.

Dovepress