Efficacy and safety of finasteride therapy for benign prostatic hyperplasia: results of a 2-year randomized controlled trial (the PROSPECT Study)

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Abstract • Résumé

Objective: To evaluate the efficacy and safety of 2 years' treatment of moderate benign prostatic hyperplasia (BPH) with finasteride.

Design: Double-blind, parallel-group, placebo-controlled, multicentre, prospective randomized study.

Setting: Outpatient care in 28 centres across Canada.

Participants: Men aged 45 to 80, in good health, with moderate BPH and no evidence of prostate cancer. A total of 613 men were entered into the study; 472 completed the 2 years of treatment.

Intervention: After 1 month of receiving a placebo (run-in period), patients were given either finasteride (5 mg/d) or a placebo for 2 years.

Outcome measures: Efficacy: changes from baseline in BPH symptom scores, maximum urinary flow rates and prostate volume. Safety: onset, course and resolution of all adverse events during the treatment period.

Results: In the efficacy analyses the mean BPH symptom scores decreased 2.1 points (from 15.8 to 13.7) in the finasteride group, as compared with a decrease of 0.7 points (from 16.6 to 15.9) in the placebo group ($p \leq 0.01$). The maximum urinary flow rate increased by a mean of 1.4 mL/s (from 11.1 to 12.5 mL/s) in the finasteride group, as compared with an increase of 0.3 mL/s (from 10.9 to 11.2 mL/s) in the placebo group ($p \leq 0.01$). The mean prostate volume decreased by 21% (from a mean volume of 44.1 cm^3 at baseline) in the treatment group; it increased by 8.4% (from a mean volume of 45.8 cm^3 at baseline) in the placebo group ($p \leq 0.01$). In the safety analysis, the proportion of patients who experienced any adverse event was similar in the two groups (81.0% in the treatment group and 81.2% in the placebo group). However, the incidence of adverse events related to sexual dysfunction were significantly higher in the finasteride group than in the placebo group (ejaculation disorder 7.7% v. 1.7% and impotence 15.8% v. 6.3%; $p \leq 0.01$ for both parameters).

Conclusion: Finasteride is a well-tolerated and effective alternative to watchful waiting in the treatment of moderate BPH.

Objectif : Évaluer l'efficacité et la sûreté d'un traitement d'une durée de 2 ans au finastéride contre l'hypertrophie bénigne modérée de la prostate (HBP).

Conception : Étude randomisée prospective multicentrique à double insu, avec contrôle parallèle et contrôlée par placebo.

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Contexte : Service externe dans 28 centres du Canada.

Participants : Hommes de 45 à 80 ans, en bonne santé, atteints d'hypertrophie bénigne modérée de la prostate sans indication de cancer de la prostate. Au total, 613 hommes ont commencé l'étude et 472 ont terminé les 2 années de traitement.

Intervention : Après avoir reçu un placebo pendant 1 mois (période de rodage), les patients ont reçu du finastéride (5 mg/j) ou un placebo pendant 2 ans.

Mesures des résultats : Efficacité : changements par rapport à la ligne de base des résultats des symptômes d'hypertrophie bénigne de la prostate, débit urinaire maximal et volume de la prostate. Sûreté : apparition, évolution et disparition de tous les événements indésirables au cours de la période de traitement.

Résultats : Dans le cas des analyses d'efficacité, les résultats moyens des symptômes d'hypertrophie bénigne de la prostate ont diminué de 2,1 points (de 15,8 à 13,7) chez ceux qui ont pris du finastéride, comparativement à 0,7 point (de 16,6 à 15,9) chez ceux qui ont pris un placebo ($p \leq 0,01$). Le débit urinaire maximal a augmenté en moyenne de 1,4 mL/s (de 11,1 à 12,5 mL/s) chez les sujets qui ont pris du finastéride, comparativement à 0,3 mL/s (de 10,9 à 11,2 mL/s) chez ceux qui ont pris le placebo ($p \leq 0,01$). Le volume moyen de la prostate a diminué de 21 % (d'un volume moyen à la ligne de base de 44,1 cm^3) chez les sujets traités et a augmenté de 8,4 % (d'un volume moyen à la ligne de base de 45,8 cm^3) chez ceux qui ont pris le placebo ($p \leq 0,01$). L'analyse de la sûreté a révélé que la proportion des patients qui ont connu des événements indésirables était semblable chez les deux groupes (81,0 % chez les sujets traités et 81,2 % chez ceux qui ont pris un placebo). L'incidence des événements indésirables liés au dysfonctionnement sexuel a toutefois été beaucoup plus élevée chez les sujets qui ont pris du finastéride que chez ceux qui ont pris le placebo (troubles éjaculatoires, 7,7 % c. 1,7 % et impotence, 15,8 % c. 6,3 %; $p \leq 0,01$ dans le cas des deux paramètres).

Conclusion : Le finastéride est une solution de rechange bien tolérée et efficace à l'attente attentive pour traiter une hypertrophie bénigne modérée de la prostate.

Benign prostatic hyperplasia (BPH) is characterized by a proliferation of prostatic tissue, particularly in the periurethral zone,[1] leading to anatomic obstruction of the urethra and diverse but characteristic urinary tract symptoms. The clinical manifestations of BPH fall into two categories: symptoms of obstruction, related to impaired flow (e.g., poor stream, hesitancy or urinary retention), and symptoms of irritation, related to alterations in the bladder response to filling (e.g., frequency, nocturia or urgency).[2] Although these symptoms are linked to prostate enlargement, the correlation between symptom intensity and the degree of prostate enlargement is complex and poorly understood. The presence of symptoms does not always correlate with objective measurements of voiding function (e.g., maximum or mean urinary flow rate, prostate volume or residual urine volume).[3–5]

The natural history of BPH is variable but slowly progressive.[6] Some patients tolerate mild to moderate symptoms for a long time without any treatment.[5,6] Nonetheless, symptoms affect quality of life: they are bothersome, interfere with daily activities and can affect psychological well-being.[7] Moreover, the serious complications of BPH, such as infection, urinary retention and upper tract sequelae, may constitute medical emergencies.

Until recently, the sole treatment for severe symptoms of BPH involved surgery (e.g., transurethral resection of the prostate [TURP]), with surveillance (watchful waiting) the only alternative.[8] Although TURP is associated with a very low mortality rate (0.2%), the morbidity is substantial (18%) and includes failure to void (6.5%), postoperative bleeding requiring transfusion (3.9%), clot retention (3.3%) and infection (2.3%).[9] In addition, following TURP there is a variable incidence of urethral stricture, loss of ejaculation (55%) and impotence (13%). Therefore, it is not surprising that many patients who seek treatment for their BPH symptoms consider medical therapy before surgery. Two types of medication have proven beneficial: α-adrenergic blockers and 5α-reductase inhibitors.

Alpha-adrenergic blockers inhibit excitatory a-receptors in the smooth muscle of the hyperplastic prostate. These receptors stimulate smooth muscle in the prostate and dynamically modulate urethral flow, an effect manifested by "functional" obstruction[10] and fluctuating symptoms.[6] By reducing adrenergic tone, the blocking agents may provide temporary relief of BPH symptoms[11] but would not affect the underlying hyperplasia of the prostate gland and the natural course of the disease.

Finasteride, a potent prostatic 5α-reductase inhibitor, helps to alleviate symptoms by reducing the size of the hyperplastic prostate.[12] The androgen dependence of the prostate was first demonstrated over 200 years ago;[13] more recently, investigators realized that the absence of BPH in men with congenital 5α-reductase deficiency demonstrated the essential role of dihydrotestosterone, and thus of 5α-reductase, in BPH.[14] Finasteride prevents the intraprostatic conversion of circulating testosterone to dihydrotestosterone and thus induces gland involution.[15]

In previous double-blind, placebo-controlled studies — one of 6 months' duration[16] and two of 1 year's duration[17] — finasteride was shown to be well tolerated and effective in alleviating symptoms, reducing prostate size and improving urinary flow rates. The beneficial

effect persisted in an open-label 3-year extension of one of the 1-year trials;[18] however, the 1-year double-blind portion of the trial was too short to allow the long-term effects of finasteride on disease progression to be rigorously assessed. The persistence of therapeutic gains could not be confirmed in a controlled fashion, and a marked placebo effect on BPH symptoms was observed, which confounded interpretation of the therapeutic efficacy of finasteride.[12]

In March 1992 we undertook a 2-year double-blind, prospective, placebo-controlled, randomized study of the safety and efficacy of finasteride in the treatment of BPH in men with moderate symptoms. Our goal was to determine the longer-term safety and efficacy of finasteride and to document the placebo effect beyond 1 year.

Methods

Protocol and assignment

Study population

A total of 613 patients in 28 centres across Canada were enrolled in the study. All centres obtained approval from their respective ethics committees, and all patients gave informed consent before participating. Eligible subjects were men 45 to 80 years old with moderate symptomatic BPH (Table 1). Patients were ambulatory and in generally good health, as judged by their medical history, findings on physical examination and laboratory test results. Patients with a prostate-specific antigen (PSA) level of 10 ng/mL or greater and those with a postvoiding residual urine volume of more than 150 mL were excluded because of concerns about prostate cancer and potential increased risk of urinary retention. Other exclusion criteria are listed in Table 1.

Intervention

Patients who met the inclusion criteria at screening were given 1 month of placebo therapy. Baseline values were obtained after this run-in period. Patients were then randomly assigned, according to a computer-generated schedule, to receive either finasteride (5 mg/d) or placebo for 2 years. Investigators evaluated patients 1 month after randomization and then every 4 months until the end of the study period, for a total of 10 visits.

Study treatment was stopped if a patient required alternative therapy for BPH, if prostate cancer was diagnosed or suspected, if a severe reaction to the study drug was postulated or if the patient did not wish to continue the protocol.

Evaluation and follow-up

At baseline, 1 year and 2 years, patients underwent a complete physical examination: DRE, measurement of postvoiding residual urine volume and transrectal ultrasonographic measurement of prostate volume. Also performed at these intervals were serum PSA measurements and laboratory tests for drug safety (liver function tests, routine hematologic tests and urinalysis). The three main outcome measures were (a) changes in symptoms attributable to BPH, (b) changes in urinary flow rates and (c) changes in prostate volume.

To document and quantify BPH symptoms, a validated, self-administered questionnaire, as described by Boyarsky and associates[2] and later modified by Bolognese and collaborators,[19] was completed by patients at every visit. Nine categories of symptoms were assessed: (1) impairment of size and force of the urine stream, (2) hesitancy or delay in starting urination, (3) dribbling, (4) interruption in urine stream, (5) feeling of incomplete emptying of bladder, (6) straining or pushing to start urine flow, (7) urgency, (8) wetting of clothes and (9) dysuria. Patients were asked to rate their symptoms using a Likert-type scale, from 0 (never, or no symptoms) to 6 (always, or severest symptoms), for a possible

Table 1: Main inclusion and exclusion criteria in the PROSPECT Study — a 2-year double-blind, randomized controlled trial of the safety and efficacy of finasteride therapy for moderate benign prostate hyperplasia (BPH)

Inclusion criteria
Age ≤ 80 yr
Maximum urinary flow rate of 5–15 mL/s at screening or start of placebo run-in period* or both, with total voided volume of at least 150 mL
At least two moderate symptoms of BPH (e.g., increased frequency of urination or difficulty urinating), but no more than two severe symptoms
Enlarged prostate gland detected by digital rectal examination (DRE)
Serum prostate-specific antigen (PSA) level ≤ 10 ng/mL
Postvoiding residual urine volume ≤ 150 mL
Exclusion criteria
Evidence or suggestion of prostate cancer
Neurogenic bladder dysfunction
History of acute urinary retention necessitating two or more catheterizations in the previous 2 years
History of prostate surgery or other invasive procedure (e.g., transurethral microwave thermotherapy, urethral stenting, balloon urethroplasty)
History of condition predisposing patient to urethral strictures
Chronic bacterial prostatitis
Serum creatinine level > 150 mmol/L, or results of liver function tests > 50% above upper limit of normal
Use of drugs with antiandrogenic properties
Hematuria associated with untreated active urinary tract infection, prostatitis or bladder cancer
Any condition jeopardizing patient's ability to complete the study

*Participants were given placebo for 1 month before being randomly assigned to either the treatment or placebo group.

total score of 54. The sum of scores in the first five categories constituted the score for symptoms related to obstruction (range 0 to 30). The results of the questionnaire were also used to develop a quasi International Prostate Symptom Score (IPSS). The IPSS, commonly called the American Urological Association Symptom Score, is calculated from seven 5-point scales.[4,6] For our study, the seven items from the questionnaire by Boyarsky and associates that corresponded to the IPSS questionnaire were selected, and the two highest values on the 6-point Likert scale were condensed into a single option.

Urinary flow rates were assessed using a uroflow meter (Urodyn 1000; Dantec, Mahwah, NJ) equipped with a filter to eliminate flow artifacts and linked to an integral printer. Residual urine volume was measured using a portable ultrasonic scanner (Bladderscan BVI; Diagnostic Ultrasound Corporation, Kirkland, Wash.) linked to a dedicated printer.

Prostate volume was determined by measuring, in triplicate, the diameter of the prostate along the cephalocaudal, anteroposterior and transverse axes with postvoiding transrectal ultrasonography (in the 25 centres where it was available [562/613 patients]). Every effort was made to use the same radiologist and urologist to perform all measurements throughout the study. An average was calculated from the triplicate measurements for each parameter, and an average prostate volume was then calculated as follows: $3.1416/6 \times \text{length} \times \text{width} \times \text{anteroposterior diameter}$.

The serum PSA level was measured at a central laboratory (MDS Laboratories, Etobicoke, Ont.) using the Tandem—E PSA immunoRadioMetric assay (Hybritech Inc., San Diego). Investigators were not told the PSA level, since such knowledge might let them infer a patient's treatment. As a safety measure, the central laboratory was given the randomization schedule and directed to notify investigators if a patient's PSA level increased by more than a preset value (more than 1 ng/mL for treatment patients and more than 2 ng/mL for control patients) during the study period. Any investigator notified by the laboratory was obliged to measure the PSA level again and perform another DRE. If abnormal findings persisted, a focal biopsy or a blind four-quadrant biopsy of the prostate was performed to rule out cancer.

To determine the incidence of prostate surgery and urinary retention in the entire study population during the 2 years after randomization, all patients who dropped out before completing the study were followed up by their physicians.

For the safety analysis, investigators assessed patient well-being, incidence of adverse events and treatment compliance during an open-ended interview at each visit. An adverse event was defined as any unexpected and unfavourable change in the patient's health during the study period, whether considered to be related to treatment or not. The onset, course and resolution of all such adverse events were documented as comprehensively as possible. In each case, the investigator was required to give his or her opinion on the relation between the adverse event and the study drug. In accordance with Canadian Health Protection Branch guidelines, adverse events that were fatal or life-threatening, that necessitated admission to hospital or that were associated with substantial disability were reported on an urgent basis to the investigator's ethical review board and the government regulatory agency.

Data analysis

The data were compiled and analysed using SAS software, version 6.08. (SAS Institute Inc., Cary, NC). The primary analysis was completed on an intention-to-treat basis. Intention-to-treat analyses are generally thought to minimize reporting bias.[20] A per-protocol analysis, involving only patients who completed the study according to the protocol, was done as a quality-control measure to confirm that the results for the intention-to-treat cohort were similar to those obtained for the patients who adhered to the protocol.

Analysis of variance (ANOVA) models were used to compare the two groups in terms of symptom scores (total and obstruction), maximum and mean urinary flow rates, prostate volume, PSA levels and laboratory safety parameters. The following factors were included: treatment, study centre and treatment-by-study centre interaction.

All analyses of variance were performed using both parametric and nonparametric methods. The parametric analyses used the actual recorded values, and the nonparametric analyses used the ranks of the values across treatment groups and centres. Where the data distribution was appropriate for parametric analysis, the parametric results were considered to be primary. Where the data distribution did not meet the conditions required for parametric analysis, the nonparametric results were adopted. All tests of significance for between-group differences were two-tailed, and a p value of 0.05 or less was considered to be significant.

Blinding

The study was double-blind. Patients and investigators were blind to treatment allocation. The placebo tablets were made to be identical in appearance and taste to the finasteride tablets. Patients and investigators were also blind to the patients' PSA levels, since changes in these levels are characteristic of finasteride therapy. To ensure that the blind could be broken under potentially urgent circumstances, investigators were issued masked envelopes containing the treatment allocation for each

patient. However, in the course of the study, none of these envelopes was opened.

Bias in the data analysis was minimized by defining primary and secondary endpoints prospectively, and by "freezing" the database (i.e., closing the database to any further revisions or modifications) before releasing the allocation schedule to the investigators and before carrying out any data analysis.

Results

Participant flow and follow-up

The profile of the study is summarized in Fig. 1. Of the 613 patients, 310 were randomly assigned to the finasteride group and 303 to the placebo group. The baseline symptom scores, maximum and mean urinary flow rates, and the prostate volumes did not differ significantly between the two groups (Table 2) and were within limits expected for a patient population with moderate BPH.

A total of 472 patients (77.0%) completed the study: 246 (79.4%) in the finasteride group and 226 (74.6%) in the placebo group. There were no outstanding differences between the two groups in the reasons given for withdrawal (Fig. 1). Follow-up data regarding prostate-related problems was obtained for all but 17 of the 141 patients who dropped out; thus, follow-up data were available for a total of 596 patients (97.2%).

Analysis

The results of the primary intention-to-treat analysis and the secondary per-protocol analysis were comparable. In this article, we report only the results of the primary analysis.

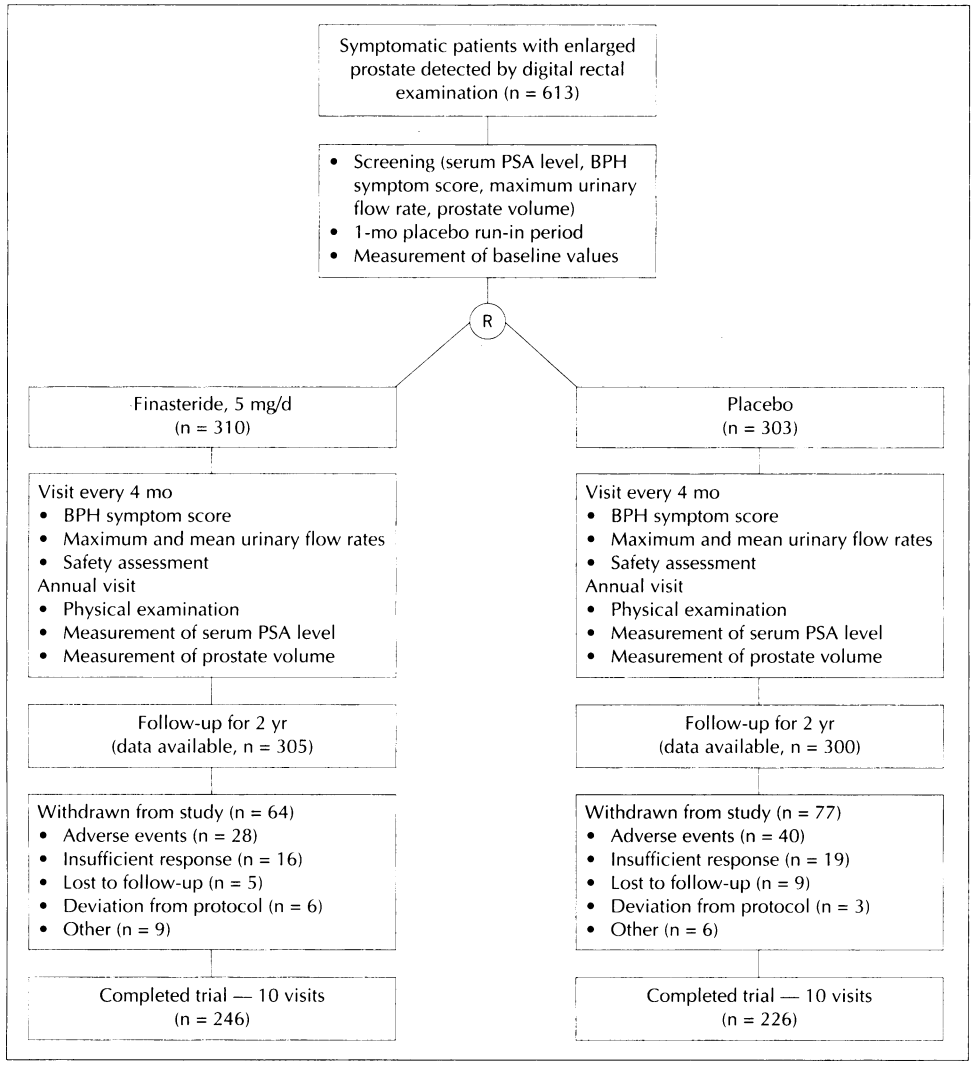

Fig. 1: Trial profile. After screening, eligible patients were given 1 month of placebo therapy, followed by measurement of baseline symptom scores, urinary flow rates and prostate volumes, and then randomization (R). At every visit questionnaires were completed, urinary flow rates were measured and interviews to determine adverse events were held; physical examination and measurement of prostate volumes and serum prostate-specific antigen (PSA) levels were performed at baseline and at 1 year and 2 years.

Effect on outcome measures

For the first 8 months the total symptom scores decreased in both the placebo and finasteride groups (Fig. 2, top). After 8 months the scores in the finasteride group continued to decrease, while those in the placebo group began to increase. The total scores in the finasteride group were significantly improved over baseline at every visit throughout the study. The placebo group, too, had significantly improved total symptom scores for up to 20 months of treatment. The between-group difference was significant at 12 months ($p \leq 0.05$); this difference was more marked at 16 months ($p \leq 0.01$). The obstruction symptom scores (Fig. 2, middle) and the quasi-IPSS (Fig. 2, bottom) followed patterns similar to the total symptom scores.

The maximum urinary flow rate in the finasteride group was significantly better than baseline at every visit (Fig. 3, top). In the placebo group the flow rate showed significant improvement at 4 months, but from 8 months onward it was not statistically different from baseline. After 12 months the flow rate was significantly better in the finasteride group than in the placebo group ($p \leq 0.05$); the difference was even more significant at 20 months ($p \leq 0.01$). The mean flow rate followed a similar pattern of changes (Fig. 3, bottom); however, the between-group difference was significant earlier, at 8 months. The postvoiding residual urine volume did not change in either group (data not shown).

Changes in the mean prostate volume at 1 year and 2 years are shown in Fig. 4. The mean volume decreased progressively in the finasteride group and was 21% lower than the baseline volume after 2 years. In the placebo group, on the other hand, the volume increased progressively and was 8.4% higher than baseline after 2 years. These between-group differences were highly significant, as were the within-group changes from baseline values.

The serum PSA levels in the placebo group rose significantly over the course of the study. The median increase was 5.5% over baseline at 1 year, increasing to 13.3% over baseline after 2 years. In the finasteride group, on the other hand, the median PSA level was 50% of baseline at 1 year and at 2 years. All of these changes were highly significant within and between the two groups.

Table 2: Baseline characteristics of patients in the finasteride and placebo groups

Parameter	Group; mean (and standard deviation*) Finasteride *n = 310*	Placebo *n = 303*
Age (and range), yr	63.0 (46–79)	63.5 (47–80)
Total symptom score	15.8 (7.6)	16.6 (7.2)
Obstruction symptom score	10.2 (4.8)	10.7 (4.5)
Maximum urinary flow rate, mL/s	11.1 (3.7)	10.9 (3.5)
Mean urinary flow rate, mL/s	5.7 (2.0)	5.6 (1.9)
Prostate volume, cm^3	44.1 (23.5)	45.8 (22.4)

*Unless otherwise stated.

Adverse events

The incidence rates of adverse events overall and in the main categories studied were similar in the two groups (Table 3). However, when sexual dysfunction was specifically assessed, significantly more men in the finasteride group than in the placebo group had complaints

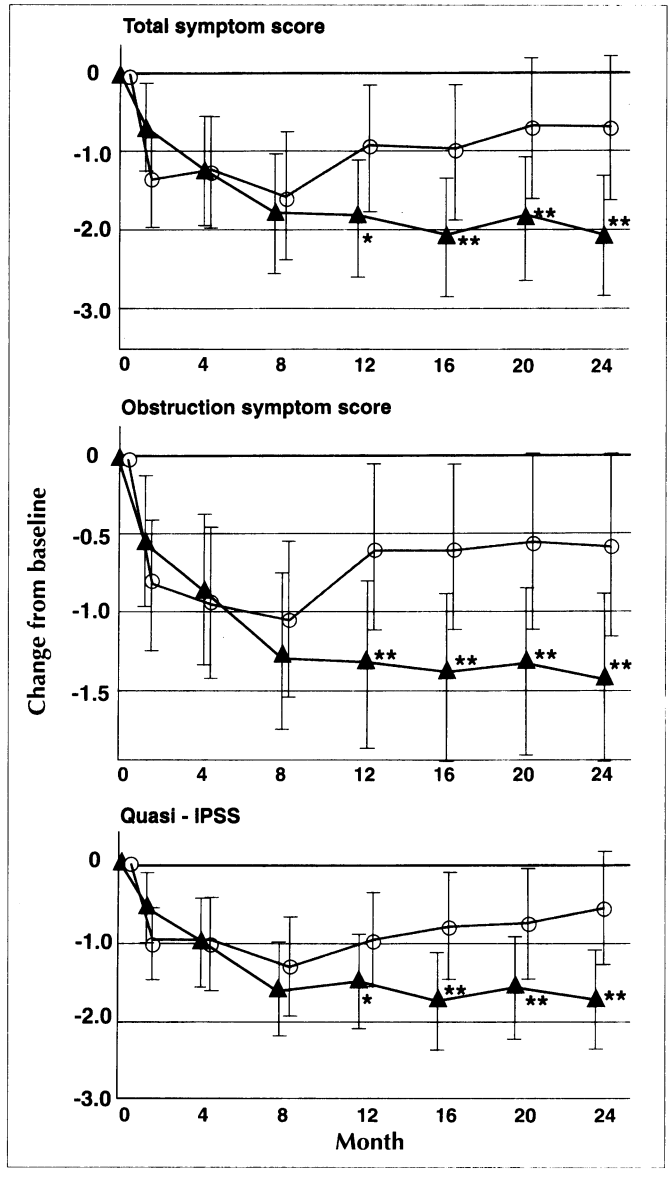

Fig. 2: Changes from baseline in total symptom scores (top), obstruction symptom scores (middle) and quasi International Prostate Symptom Scores (quasi-IPSS) (bottom). Error bars represent 95% confidence intervals of within-group means; if error bars do not cross baseline, within-group change from baseline is statistically significant at $p \leq 0.05$. Asterisks indicate significance of between-group differences: * = $p \leq 0.05$, ** = $p \leq 0.01$. ▲ = finasteride group, ○ = placebo group.

of ejaculatory disorders and impotence (Table 4). Regardless of the treatment group, the symptoms of sexual dysfunction tended to be of long duration and to arise earlier rather than later in the study period.

Other clinical endpoints

During the study period significantly fewer patients in the finasteride group than in the placebo group experienced urinary retention or had some kind of urological intervention (e.g., TURP, thermotherapy or balloon dilatation) to treat BPH-related symptoms (19 [6.1%] v. 31 [10.2%]; $p = 0.08$).

Eight men died during the study period: five in the finasteride group and three in the placebo group. None of the investigators treating these patients considered the deaths to be related to the study drug. Prostate cancer was diagnosed in nine men: three in the finasteride group and six in the placebo group.

Clinical impact of the study therapy

We assessed the impact of the study therapy in terms likely to be meaningful to the patient. For each of the outcome measures, we calculated the proportion of patients in the finasteride group in whom improvements were recorded after the 2-year study period (Table 5). These improvements were clinically meaningful. These findings suggest that a physician prescribing finasteride for moderate BPH can expect, with a 66% likelihood, that the patient will have an alleviation of symptoms that, on average, is clinically meaningful after 2 years of treatment.

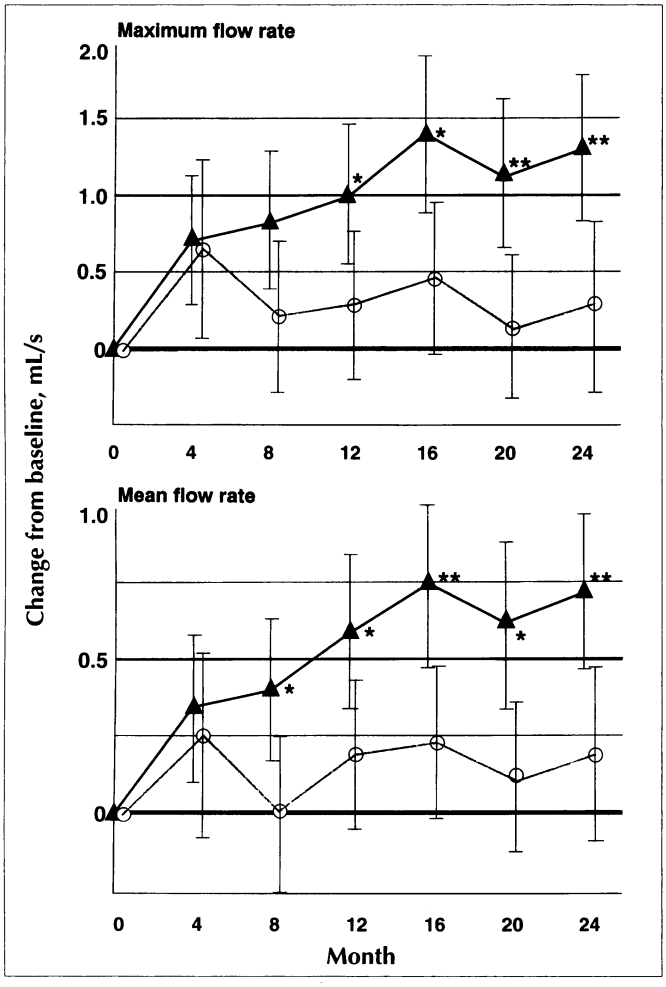

Fig. 3: Changes from baseline in maximum (top) and mean (bottom) urinary flow rates. Descriptions of symbols, error bars and asterisks as in Fig. 2.

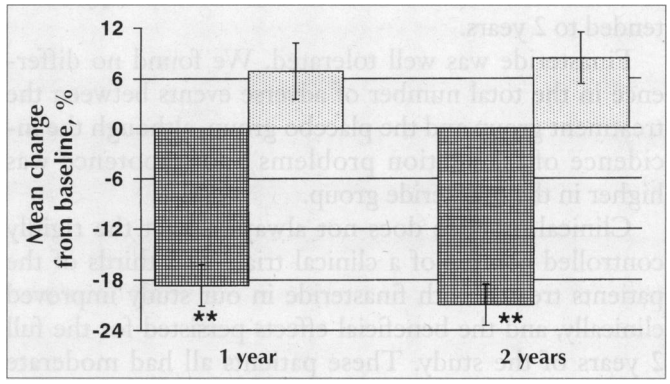

Fig. 4: Change in prostate volume at 1 year and at 2 years. Dark bars = finasteride group, light bars = placebo group. Descriptions of error bars and asterisks as in Fig. 2.

Table 3: Adverse events reported by patients*

Category of adverse event	Group; no. (and %) of patients: Finasteride	Placebo
Urogenital	124 (40.0)	122 (40.3)
Neurologic other than special sense	87 (28.1)	82 (27.1)
Respiratory	80 (25.8)	76 (25.1)
Musculoskeletal	72 (23.2)	82 (27.1)
Cardiovascular	69 (22.3)	51 (16.8)
Digestive	69 (22.3)	71 (23.4)
Body as a whole	64 (20.6)	59 (19.5)
Dermal/appendages	40 (12.9)	38 (12.5)
Metabolic/nutritional/immunologic	23 (7.4)	20 (6.6)
Special sense	22 (7.1)	20 (6.6)
Endocrine	11 (3.5)	7 (2.3)
Hematic/lymphatic	4 (1.3)	1 (0.3)
Any adverse event	251 (81.0)	246 (81.2)

*Percentages do not total 100 because patients may have reported more than one adverse event and not necessarily in the same category.

Table 4: Adverse events related to sexual dysfunction

Adverse event	Group; no. (and %) of patients: Finasteride	Placebo
Ejaculation disorder*	24 (7.7)	5 (1.7)
Impotence*	49 (15.8)	19 (6.3)
Libido decreased	31 (10.0)	19 (6.3)

*$p < 0.01$ between groups.

Discussion

In this double-blind, placebo-controlled, randomized study involving patients with moderate BPH, finasteride therapy led to a continuous improvement in symptom scores, urinary flow rates and prostate volumes during the 2 years of treatment. Our results confirm observations from previous double-blind studies of finasteride of 6, 12 and 24 months' duration[16,17,21] and suggest that the difference between finasteride therapy and placebo is maintained, and in fact increased, when therapy is extended to 2 years.

Finasteride was well tolerated. We found no difference in the total number of adverse events between the treatment group and the placebo group, although the incidence of ejaculation problems and impotence was higher in the finasteride group.

Clinical practice does not always reflect the rigidly controlled context of a clinical trial. Two thirds of the patients treated with finasteride in our study improved clinically, and the beneficial effects persisted for the full 2 years of the study. These patients all had moderate symptoms of BPH. A physician in the clinic may observe better or worse results than these, depending on their patient population. If treated patients have predominantly "functional" symptoms and relatively small prostates, treatment results may be less favourable. The use of finasteride in patients with more severe symptoms or in those with larger prostate glands may have more favourable results, but this needs confirmation.

Pronounced and persistent placebo effects have been observed with many therapies for BPH. In our study, significant placebo effects on symptom scores and urinary flow rates were noted early in the follow-up period, and even at 2 years the mean symptom score and urinary flow rate in the placebo group had not crossed the original baseline values. This complicates the analysis of any medical treatment of BPH. However, prostate volume was not affected in the placebo group, whereas it decreased by about 20% in the finasteride group by the end of the study.

For symptomatic relief in men with moderate symptoms of BPH and obstruction, finasteride should be considered an effective alternative to watchful waiting. Future studies are needed to see whether preselecting appropriate patients would improve the response rate and whether finasteride would reduce the need for surgery.

Table 5: Clinical impact of 2 years of finasteride therapy

Clinical response	% of finasteride patients	Mean change from baseline value*
Improvement in total symptom score	65.6	−5.7 points
Increase in maximum urinary flow rate	60.7	+3.6 mL/s
Decrease in prostate volume	85.3	−26.8%

*Following 1 month of placebo therapy.

Clinical relevance: This randomized placebo-controlled study has demonstrated the long-term efficacy of finasteride in alleviating symptoms, improving urinary flow rates and reducing prostate volume in men with moderate symptoms of BPH. The study has also shown a prolonged placebo effect and confirms that long-term randomized controlled trials of medical therapy for BPH are necessary.

Study limitations: The study had neither the design nor the power to allow preselection of the subgroup of men with moderate BPH who would benefit the most from finasteride therapy.

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Dec. 4–7, 1996: 3rd International Conference on Long-term Care Case Management — Bridging the Many Worlds of Case Management

San Diego

American Society on Aging, 511–833 Market St., San Francisco CA 94103-1824; tel 415 974-9600, fax 415 974-0300

Dec. 8–11, 1996: 2nd National Canadian Conference on Immunization

Toronto

Mr. Chuck Schouwerwou, conference and committee coordinator, Childhood Immunization Division, Laboratory Centre for Disease Control, PL # 0603E1, Tunney's Pasture, Ottawa ON K1A 0L2; fax 613 998-6413

Feb. 1–4, 1997: 23rd Annual Predoctoral Education Conference

Orlando, Fla.

Ray Rosetta, meetings and programs director, Society of Teachers of Family Medicine, 8880 Ward Pkwy., PO Box 8729, Kansas City MO 64114; tel 816 333-9700 or 800 274-2237, ext. 4512; fax 816 333-3884; admstaff@stfm.org; website: http://stfm.org

Feb. 12–14, 1997: 1997 Review Course in Pain Medicine (held in conjunction with the American Academy of Pain Medicine 13th Annual Conference)

Scottsdale, Ariz.

AAPM Review Course and Conference, PO Box 682, Glenview IL 60025-0682; tel 847 375-4731, fax 847 375-4777

Feb. 14–16, 1997: American Academy of Pain Medicine 13th Annual Conference — Controversies in the Practice of Pain Medicine

Scottsdale, Ariz.

AAPM Review Course and Conference, PO Box 682, Glenview IL 60025-0682; tel 847 375-4731, fax 847 375-4777

Mar. 5–9, 1997: 17th Annual Family in Family Medicine Conference

Kiawah Island, SC

Ray Rosetta, meetings and programs director, Society of Teachers of Family Medicine, 8880 Ward Pkwy., PO Box 8729, Kansas City MO 64114; tel 816 333-9700 or 800 274-2237, ext. 4512; fax 816 333-3884; admstaff@stfm.org; website: http://stfm.org

Mar. 20–21, 1997: Rotman Research Institute 7th Annual Conference — Memory Disorders: Advances in Science and Clinical Practice

Toronto

Poster deadline: Dec. 13, 1996

Rotman Research Institute, Baycrest Centre for Geriatric Care, 3560 Bathurst St., Toronto ON M6A 2E1; tel 416 785-2500, ext. 3550; fax 416 785-2862; rotman@psych.utoronto.ca

Apr. 4–5, 1997: American College of Physicians–Ontario Chapter Annual Meeting

North York, Ont.

Dr. Jay Silverberg, Sunnybrook Health Science Centre, Suite H-149, 2075 Bayview Ave., North York ON M4N 3M5; tel 416 480-4761, fax 416 480-6191

May 3–7, 1997: Society of Teachers of Family Medicine 30th Annual Spring Conference

Boston

Ray Rosetta, meetings and programs director, Society of Teachers of Family Medicine, 8880 Ward Pkwy., PO Box 8729, Kansas City MO 64114; tel 816 333-9700 or 800 274-2237, ext. 4512; fax 816 333-3884; admstaff@stfm.org; website: http://stfm.org

May 7–10, 1997: North American Society of Pacing and Electrophysiology 18th Annual Scientific Sessions

New Orleans

Abstract deadline: Dec. 4, 1996

North American Society of Pacing and Electrophysiology, Natick Executive Park, 2 Vision Dr., Natick MA 01760-2059; tel 508 647-0100, fax 508 647-0124

May 8–10, 1997: Critical Issues in Rural Obstetrics (cosponsored by the Department of Family Practice, University of British Columbia)

Victoria

British Columbia Reproductive Care Program, 207–1909 W Broadway, Vancouver BC V6J 1Z3; tel 604 737-7270, fax 604 737-2517

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