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The effect of decreasing the dosage of finasteride in patients with benign prostatic hyperplasia: Our experience in a tertiary hospital

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Abstract
Background: Finasteride, a 5 alpha reductase inhibitor, is an established treatment for benign prostatic hyperplasia. The recommended dosage is 5 mg a day, however case reports have shown effectiveness with lower doses. The objective of the current study was to determine in men with benign prostatic hyperplasia, previously treated for at least one year with finasteride 5 mg daily, if they will maintain subjective and objective improvements in urinary obstruction when treated with 2.5 mg of finasteride daily for one year.
Methods: In an open label, prospective study, 40 men with benign prostatic hyperplasia, previously treated for at least one year with 5 mg of finasteride, took 2.5 mg of finasteride daily for one year. Measurements included AUA symptom score, maximum flow rate, voided volume and PSA.
Results: There were no significant changes in maximum flow rate, voided volume, or AUA symptom score after one year of finasteride 2.5 mg daily therapy. PSA increased significantly, p <. 01, after one year of finasteride 2.5 mg daily, 2.0 +1.4 ng/ml, when compared to finasteride 5 mg daily, 1.4+ 1.0 ng/ml.
Conclusions: The daily dose of finasteride can be reduced to 2.5 mg daily without significant effect on subjective and objective measures of urinary obstruction. Although statistically significant increases in PSA are noted when reducing the daily finasteride dose from 5 mg to 2.5 mg, the clinical significance of a mean. 6 ng/ml increase in PSA is questionable.

Keywords: finasteride; BPH; PSA; AUA

Introduction
Benign prostatic hyperplasia (BPH) is a pathologic process which may contribute to lower urinary tract symptoms in aging men. A common problem among males over 50 years, its prevalence increases with age and many longitudinal studies have demonstrated the progressive nature of the disease.1 Histologically, BPH is characterized by an increased number of both epithelial and stromal cells in the periurethral area of the prostate. There is controversy as to whether this increase is secondary to epithelial and stromal proliferation or impaired apoptosis leading to cellular accumulation. Nevertheless, it is understood that androgens, growth factors, neurotransmitters and other cell interactions play a role in the development of this condition
While alpha-blockers provide rapid relief in the form of improved flow rate, their effects may not reduce the overall risk of BPH-related complications. 5α-reductase inhibitors were therefore introduced to impact underlying disease by inhibiting the enzyme which converts testosterone to dihydrotesterone (DHT), the primary androgen involved in normal and abnormal prostate growth. Through this inhibition, prostate size is decreased, thereby reducing the risk of acute urinary retention and BPH-related surgery while providing symptom control.
Finasteride is a synthetic inhibitor of human 5 alpha reductase, an enzyme that converts testosterone to dihydrotestosterone (DHT) within the prostate (1). Placebo controlled studies have demonstrated improvements in subjective and objective measurements of urinary outlet obstruction in men with benign prostatic hyperplasia treated with finasteride 5 mg daily for one year (2). Comparable reductions in DHT levels noted with 5 mg of finasteride have been observed with dosages as low as 1.5 mg (3, 4). Given the current monthly cost of $63 for 5 mg daily finasteride and the anticipated lifetime requirement for therapy, a less costly maintenance regimen, which is able to control symptoms, would be beneficial.
The current study was undertaken to determine in men with benign prostatic hyperplasia previously treated with finasteride 5 mg daily for at least one year, if 2.5 mg of finasteride daily for an additional year will maintain subjective and objective improvements in urinary obstruction.

Patients and Methods
This was an open label, prospective study involving 40 men with a history of benign prostatic hyperplasia treated for at least one year with 5 mg of finasteride daily. All subjects reported subjective improvement in urinary symptoms with the 5 mg finasteride dose. The study was approved by the institutional review board at Mercy Hospital, San Diego, CA, and all men gave written informed consent.
On day 1 and after one year of therapy with finasteride 2.5 mg a day, subjects completed an American Urological Association Symptom Index form and Quality of Life questionnaire (5), blood

was drawn for prostate-specific antigen (PSA), and maximal urinary flow rate and voided volume were determined using a calibrated Dantec urinary flowmeter. The subjects were given a pill cutter and instructed to cut a 5 mg finasteride tablet in half in order to take 2.5 mg daily. Serum PSA was measured using a Hybritech, immunoradiometric assay.

Mean, standard deviation and paired T tests were performed on the day 1 and one year data using Statgraphics Plus statistical software. All tests of significance were two tailed, and all P values of <. 05 were considered to indicate significance.

Results

Urodynamic, AUA symptom and quality of life scores, and PSA values on day 1 and one year after 2.5 mg of finasteride daily are presented in Table 1. There was no significant change in any urodynamic measurement or AUA symptom and quality of life score after one year of finasteride 2.5 mg a day. There was a statistically significant (p <.01) increase in PSA, mean. 6 ng/ml, observed after one year of finasteride at 2.5 mg a day.

Discussion

The effects of finasteride on prostate size have been studied extensively with maximal reduction of prostate volume achieved within 6 months.8 since the mechanisms underlying finasteride's positive effects on prostate outcomes are thought to be mediated by volume reduction, one can assume that subjects with larger prostates may achieve greater benefit. Therefore, the majority of randomized, placebo-controlled trials have evaluated subjects with larger prostates which creates difficulty in generalizing to a typical patient, with normal-sized prostate.9 The first multicenter, randomized, double-blind, placebocontrolled clinical trial investigating the efficacy of finasteride was performed by Gormley and colleagues in 1992 and is often referred to as the North American Finasteride Trial.8

As mentioned above, the baseline prostate volumes in both the placebo and experimental groups (measured by transrectal ultrasound) were quite large (60 cm3), limiting its application to men with more typical size prostates. Eight hundred and ninety-five subjects with BPH were randomized to receive placebo or 1 or 5 mg of finasteride for 1 year. The primary outcome measures consisted of a modified Boyarsky symptom score and peak flow rate, although measurements of prostate volume were also recorded as a secondary outcome.

The modified Boyarsky symptom score, originally described by Boyarsky and colleagues12 and modified and validated by Bolognese *et al*. 13 was computed as the total sum of scores of nine symptoms: decreased urinary stream, dribbling, interruption in stream, hesitancy, feeling of incomplete emptying, straining to initiate flow, urgency, incontinence, and dysuria. Results demonstrated a mean percentage change in symptom score at 12 months of −2%, 9%, and 21% in the placebo, 1-mg, and 5-mg finasteride groups, respectively. These results were statistically significant when comparing placebo and 5-mg finasteride groups but not for the 1-mg group.

Mean percentage changes in peak flow rate were 8%, 23%, and 22% while the mean percentage changes in prostate volume were −3%, −18%, and –19% respectively. A secondary analysis attempted to correlate symptom score improvement with reduction of prostate size. However, this did not prove to be dose-dependent, suggesting that the efficacy of finasteride may not be exclusively mediated by the reduction of prostate volume

Following this initial study, a second report was published in 1993, termed the International Finasteride Study.10 Known as the Finasteride Study Group, these researchers reported another multicenter, randomized, double-blind, placebo controlled clinical trial which described the effect of finasteride on symptom score, peak flow rate, and prostate volume. Measured via transrectal ultrasound, the mean prostate volume here was also relatively large (47 cm3), including only prostates above 30 cm3. Results were in agreement with the North American Finasteride Trial, demonstrating a prostate volume reduction of 22% (P 0.001), increased peak flow rate by 1.7 mL/sec (P 0.025) and improved symptom score by 3.3 points (P = 0.005). While the above studies were favorable with regard to peak flow rate, prostate size reduction, and symptom score, they also demonstrated bias toward larger prostates, which presents difficulty in generalizing to a more typical patient population. The first study to examine the efficacy of finasteride on smaller prostate size was performed by Andersen and colleagues in 1995.11 unlike prior studies, the mean prostate size in this study was approximately 40 mL. Seven hundred and seven patients were maintained on either placebo or finasteride for 2 years. Primary outcome measures included a modified Boyarsky symptom score, peak flow rate and prostate volume, and these were examined at both 12 and 24 months. The group mean difference from placebo was statistically significant but the mean change was less than that shown in the both the North American Finasteride Trial as well as the International Finasteride Study.

Time-dependent symptom score changes demonstrated a placebo response which returned to baseline by year 2 whereas the finasteride response remained effective throughout the study time period. Mean differences between symptom scores of the placebo and finasteride groups, however, were not markedly different, with –0.3 and 0.6 units change in symptoms between 12 and 24 months, respectively. However, when assessing mean change of symptom score between baseline and month 24, a more dramatic change of symptom score is demonstrated in the finasteride group (2 units) compared to placebo (0.2 units) (P 0.01). Although statistically significant, one may question the clinical application of a small difference between the two groups.

The current study has demonstrated, in a select group of men with benign prostatic hyperplasia and symptomatic improvement after treatment with 5 mg a day of finasteride, the dose can be reduced to 2.5 mg daily without significant change in urodynamic measurements of obstruction or worsening of symptoms. The dose of 2.5 mg was selected for the current study because of the relative ease in splitting a 5 mg tablet, but significant improvements in urodynamic measurements and obstructive symptoms have been demonstrated with a 1 mg a day dose (2). The current price of the 1 mg finasteride, approved for alopecia,

is more than the cost of splitting a 5 mg tablet in order to obtain the 2.5 mg dose and the efficacy of reducing the finasteride Maintenance dose from 5 mg daily to 1 mg daily has not been investigated.

Gormley, *et al*., has reported no significant difference in PSA values at one year for men treated with 1 mg or 5 mg finasteride daily (2). There are no published reports on the effect of finasteride on PSA values for treatment periods greater than one year. The significant increase in PSA, noted after one year of finasteride at 2.5 mg daily in the present study, is of questionable clinical importance given a mean increase of only. 6 ng/ml. However, this may represent a regrowth of prostatic tissue, which may affect urodynamic measurements and symptom scores beyond the one year observation period utilized in this study. When utilizing the PSA for prostate cancer detection in a patient receiving finasteride, it is prudent to recheck the PSA 3–6 months after any finasteride adjustments, in order to determine a new baseline for future reference.

The clinical benefits of 5 mg of finasteride with respect to symptom scores, peak urinary flow rates, and prostatic volumes appears to reach a maximum after 6 months of daily therapy (2). Results from the current study would suggest, in those patients with improvement in prostatic symptoms after receiving 5 mg of finasteride daily for 6 months the dose can safely be reduced to 2.5 mg daily.

References

1. Peters D, Sorkin E. Finasteride. Drug, 1993; 46:177-208.
2. Gormley G, Stoner E. *et al*. The effect of finasteride in men with benign prostatic hyperplasia. NEJM, 1992; 327:1185-91.
3. McConnell J, Wilson J. *et al*. Finasteride, an inhibitor of 5 alpha reductase, suppresses prostatic dihydrotesteosterone in men with benign prostatic hyperplasia. JCEM, 1992; 74:505-8.
4. Vermeulen A, Giagulli P. *et al*. Hormonal effects of an orally active 4-azasteroid inhibitor of 5 alpha reductase in humans. The Prostate, 1989; 14:45-53.
5. Barry M, Fowler F. *et al*. The American urological association symptom index for benign prostatic hyperplasia. J Urol, 1992; 148:1549-57.
6. Emberton M, Cornel EB, Bassi PF, Fourcade RO, Gomez JM, Castro R. *et al*. Benign prostatic hyperplasia as a progressive disease: a guide to the risk factors and options for medical management. Int J Clin Pract, 2008; 62:1076-1086.
7. Russell DW, Wilson JD. Steroid 5 alpha-reductase: two genes/two enzymes. Annu Rev Biochem, 1994; 63:25-61.
8. Jenkins EP, Andersson S, Imperato-McGinley J, Wilson JD, Russell DW. Genetic and pharmacological evidence for more than one human steroid 5 alpha-reductase. J Clin Invest, 1992; 89:293-00.
9. Carson C, 3rd, Rittmaster R. The role of dihydrotestosterone in benign prostatic hyperplasia. Urology, 2003; 61:2-7.
10. Norman RW, Coakes KE, Wright AS, Rittmaster RS. Androgen metabolism in men receiving finasteride before prostatectomy. J Urol, 1993; 150:1736-1739.
11. Anderson JB, Roehrborn CG, Schalken JA, Emberton M. The progression of benign prostatic hyperplasia: examining the evidence and determining the risk. Eur Urol, 2001; 39:390-399.
12. McConnell JD, Bruskewitz R, Walsh P. *et al*. The effect of finasteride on the risk of acute urinary retention and the need for surgical treatment among men with benign prostatic hyperplasia. Finasteride Long-Term Efficacy and Safety Study Group. N Engl J Med, 1998; 338:557-563.