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Research Article

Effect the Dosage of Finasteride in Patients with Benign Prostatic Hyperplasia

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Abstract: ***Background:*** Benign prostatic hyperplasia, the noncancerous enlargement of the prostate gland, is the most common benign tumor in men. Benign prostatic hyperplasia (BPH) is a pathologic process which may contribute to lower urinary tract symptoms in aging men. Finasteride, a 5 alpha reductase inhibitor, is an established treatment for benign prostatic hyperplasia. 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:*** This was an open label, prospective study was carried out at Department of Surgery, BSMMU, Dhaka, Bangladesh from June 2013 to July 2014 of involving 40 men with a history of benign prostatic hyperplasia treated for at least one year with 5mg of finasteride daily. 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, 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, the noncancerous enlargement of the prostate gland, is the most common benign tumor in men. Benign prostatic hyperplasia (BPH) is a pathologic process which may contribute to lower urinary tract symptoms in aging men. Finasteride, a 5 alpha reductase inhibitor, is an established treatment for benign prostatic hyperplasia. Like prostate cancer, BPH is more common in Western countries than in Eastern countries such as Japan and China, and may be more common among blacks [1]. A recent study found a possible genetic association of BPH in men under 65 years of age with very enlarged prostates. Their male relatives were four times more likely to undergo surgery for BPH in their lifetime, and their siblings were six times more likely to undergo surgery for BPH in their lifetime, compared with other men. Risk. Histologically, BPH is characterized by an increase in the number of epithelial and stromal cells in the periurethral region of the prostate [2]. It is controversial whether this increase is due to epithelial and stromal proliferation or impaired apoptosis leading to cell aggregation. Nevertheless, it is known that androgens, growth factors, neurotransmitters, and other cellular interactions are involved in the development of this disease. Although alpha-blockers provide rapid symptomatic relief in the form of improved blood flow, their effect may not reduce the overall risk of BPH-related complications [3, 4]. Therefore, 5α-reductase inhibitors have been introduced to target the underlying disease by inhibiting the enzyme that converts testosterone to dihydrotestosterone (DHT), the primary androgen involved in normal and abnormal prostate growth. This inhibition reduces the size of the prostate, reducing the risk of acute urinary retention and BPH-related surgery while controlling symptoms. Nevertheless, it has been reported that finasteride may increase the risk of decreased libido and ejaculatory dysfunction [3, 4]. Dutasteride is also a 5α-R inhibitor. Dutasteride in the treatment of BPH has been found to offer benefits in relieving symptoms associated with BPH and reducing acute urinary retention [5,6]. 5α-R inhibitors reduce dihydrotestosterone (DHT) levels, which are involved in prostate growth. Finasteride reduces circulating DHT levels by 70%, while dutasteride reduces serum and prostate DHT levels almost completely. One study found that dutasteride

showed a greater reduction in prostate-specific antigen (PSA) and International Prostate Symptom Score (IPSS) compared with finasteride in the treatment of BPH [7]. The results of Yin et al. suggested that there was no significant difference between dutasteride and finasteride in the treatment of BPH, except that dutasteride improved BPH symptoms in the IPSS [8]. This study was conducted to determine whether subjective and objective improvement in urinary retention would be maintained with an additional year of finasteride 2.5 mg daily in men with benign prostatic hyperplasia who had been treated with finasteride 5 mg daily for at least 1 year.

METHODS

This was an open label, prospective study was carried out at Department of Surgery, BSMMU, Dhaka, Bangladesh from June 2013 to July 2014 of involving 40 men with a history of benign prostatic hyperplasia treated for at least one year with 5mg 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

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. 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, 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. 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.

Table 1: Distribution of patients according to their age groups

Age group (years)	Frequency n (%)	p-value
41-50	1 (2. 5)	0.001
51-60	5 (12.5)	
61-70	14 (35.0)	
71-80	15 (37.5)	
81-90	4 (10.0)	
>90	1 (2.5)	

Table 2: Mean and standard deviation for maximal flow rate, total voided volume, PSA, AUA score on day 1 and one year after 2.5 mg of finasteride daily

	Day 1	1 Year
Maximal flow rate cc/sec n = 38	13.7 ± 5.4	13.6 ± 6.4
Voided Volume 283 cc n = 38	283 ± 93	282 ± 98
PSA ng/ml n = 28	1.4 ± 1.0	2.0 ± 1.4
AUA score		
Part A Urinary symptoms n = 40	9.6 ± 5.9	9.3 ± 5.0
Part B Problems due to symptoms n = 39	6.4 ± 5.5	6.1 ± 4.3
Part C Quality of life due to urinary problems n = 39	4.2 ± 3.2	4.5 ± 3.3

DISCUSSION

Benign prostatic hyperplasia (BPH) is a common condition in men over the age of 50, and its incidence increases with age (18). Benign prostatic hyperplasia (BPH) is a health problem that becomes more common with age. It is also called enlarged prostate. The prostate is a small gland that helps produce semen. It is located just below the bladder. And it often gets bigger with age. Prostate enlargement can cause bothersome symptoms, such as obstruction of urine flow from the bladder. It can also cause problems with the bladder, urinary tract, and kidneys.[9] The effect of finasteride on prostate size has been studied extensively, with maximum reduction in prostate volume achieved

within 6 months.8 Because the mechanism underlying finasteride's beneficial effect on the prostate is thought to be mediated by volume reduction, individuals with larger prostates would likely derive greater benefit. Therefore, the majority of randomized placebo-controlled trials have been conducted on individuals with larger prostates, making generalization to the typical patient with a normal-sized prostate difficult.[10] As noted above, baseline prostate volume values (measured by transrectal ultrasound) in the placebo and experimental groups were quite large (60 cm3), limiting use in men with more typical prostate sizes. 895 men with benign prostatic hyperplasia were randomized to receive placebo or 1-5 mg finasteride for one year. Primary outcomes consisted of modified Boyarsky symptom scores and peak flow rates, but prostate volume measurements were also recorded as secondary outcomes. 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. Following this initial study, a second report was published in 1993, termed the International Finasteride Study [11]. 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 Trail, demonstrating a prostate volume reduction of 22% (p-0.001), increased peak flow rate by 1.7 mL/sec (P-0.0025). and improved symptom score by 3.3 points (P = 0.005). 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 [12]. 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 (0.2units) (P-0.01).

Although statistically significant, one may question the clinical application of the small difference between the two groups. In this study, we demonstrated that in a selected group of men with benign prostatic hyperplasia whose symptoms improved after treatment with finasteride 5 mg per day, the dose could be reduced to 2.5 mg per day without significant changes in urodynamic measures of obstruction or worsening symptoms. The 2.5 mg dose was chosen in this study because 5 mg tablets are relatively easy to divide, but a dose of 1 mg per day demonstrated significant improvements in urodynamic measures and obstructive symptoms [13]. The current price of finasteride 1 mg, which is approved for alopecia, is higher than the cost of dividing a 5 mg tablet to obtain a dose of 2.5 mg, and the efficacy of reducing the maintenance dose of finasteride by 5 mg per day to 1 mg per day has not been studied. Gormley et al. reported that there was no significant difference in PSA levels after 1 year in men receiving finasteride 1 mg or 5 mg daily [14]. There are no published reports on the effect of finasteride on PSA levels over a treatment period longer than 1 year. The significant increase in PSA seen in this study after 1 year of finasteride 2.5 mg/day is of questionable clinical significance given that the mean increase was only 6 ng/ml. However, this may represent regrowth of prostate tissue, which may affect urodynamic measurements and symptom scores beyond the 1-year observation period used in this study. When using PSA to detect prostate cancer in patients receiving finasteride, it is recommended that PSA be retested 3-6 months after each finasteride adjustment to establish a new baseline for future reference.

CONCLUSIONS

The daily finasteride dose can be reduced to 2.5 mg per day without significant effects on subjective and objective measures of urinary retention. Although a statistically significant increase in PSA is observed when the daily dose of finasteride is reduced from 5 mg to 2.5 mg, the clinical significance of the mean PSA increase of 6 ng/mL is questionable.

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