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Effects of Finasteride on Prostate Volume and Prostate-specific Antigen

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Background. Finasteride was introduced to treat patients with benign prostatic hyperplasia (BPH) recently, and it has shown its effects in reduction of prostate volume and decrease of prostate-specific antigen (PSA). We want to know how and how much does finasteride affect prostate volume as well as PSA and prostate-specific antigen density (PSAD), since PSA and PSAD are widely used as screening tools for early detection of prostate cancers.

Methods. Among 166 men with the diagnosis of BPH who received finasteride (5 mg/day) for 6 months, the serum PSA levels were measured. The prostate volumes before and after medication for a subgroup of 86 patients were measured by transrectal ultrasonography (TRUS). Paired *t*-test was used for the statistical analysis. The median percentage change in PSA of total 166 men and the median percentage changes in prostate volumes and PSAD of 86 men were also calculated.

Results. Among 166 men, the average serum PSA level was 2.48 ± 2.02 ng/mL at baseline and 1.57 ± 1.47 ng/mL at 6 months later. The median percentage change of serum PSA level was -44.26%. For 86 patients who underwent TRUS evaluation the average prostate volume changed from 39.83 ± 21.10 mL to 33.62 ± 20.52 mL. The median percentage change of prostatic volume was -17.80%. Also, the median percentage change in PSAD for these 86 patients after medication was -38.67%.

Conclusions. Finasteride does decrease the serum PSA level and PSAD as well as prostate volume in men with BPH treated with it for 6 months. Physicians prescribing finasteride for patients with symptomatic BPH should always keep in mind its effect on PSA and PSAD levels in order not to miss potential prostate cancers.

Prostate-specific antigen (PSA) is a glycoprotein with serum protease-like activity secreted by the glandular epithelium of the prostate,[1,2] and it has become the single most valuable method to detect prostate cancer earlier.[2] Although the amount of PSA released into the blood stream by *per* gram prostate adenocarcinoma is 10 times as much as that *per* gram by benign prostatic hyperplasia (BPH),[3] there is a considerable degree of overlap between PSA distributions in men with localized prostate cancer and in men with BPH.[2] Therefore, efforts have been made to adjust serum PSA level accounting for the prostate volume in order to improve the separation of PSA levels between men with prostate cancer and BPH, for example, PSA density (PSAD), which is defined as serum PSA level divided by prostate volume.[4,5]

Finasteride, a specific 5α-reductase inhibitor, has been introduced to reduce prostate size and improve the urodynamic status in men with symptoms of BPH.[6-10] In the meantime, finasteride has also shown its effect in decreasing serum PSA levels in men with BPH[11,12] and prostate cancer.[13] Since PSA has become an important tool for early detection of the prostate cancer, it seems we should reconsider the value of interpretation PSA as well as PSAD in men with BPH treated with finasteride. The purpose of this analysis was to evaluate the magnitude and distribution of change in PSA among men having symptomatic BPH treated with finasteride in a teaching hospital in central Taiwan.

METHODS

From January 1996 to December 2000, 166 men who came to the outpatient clinics of the urology division of

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Taichung Veterans Hospital with the symptoms of BPH were enrolled in this study. The mean age of these patients was 72 ± 5.35 years old (ranged from 57 to 86). Oral finasteride, 5 mg/day, was prescribed for all of the patients for 6 months. Serum PSA level of these patients was measured before and after 6-month medication using the assay of CIS Bio, International, Bagnols Sur Ceze Cedex, France. Among those 25 men with baseline serum PSA levels greater than 4 ng/mL, prostate cancer was ruled out by digital rectal examination (DRE) and transrectal ultrasound (TRUS) sextant biopsies using diagnostic ultrasound system of B-K Medical, Inc. Herlev, Denmark.

The prostate volume of a subgroup of 86 patients out of the total 166 men was measured at baseline and after 6-month medication. The method of measurement is also the same as the TRUS method used for sextant biopsy. The PSAD of these patients at baseline and 6 months after medication were calculated as serum PSA (ng/mL) divided by prostate volume (mL), respectively.

The method used for the statistical analyses of change of PSA, prostate volume and PSAD was paired *t*-test.

RESULTS

The average serum PSA level for total 166 patients was 2.48 ± 2.02 ng/mL at baseline and 1.57 ± 1.47 ng/mL 6 months later (Table 1). After 6-month treatment with finasteride, the median percentage change of serum PSA level was -44.26%.

For patients with baseline serum PSA level ≤ 4 ng/mL (141 men), the median percentage change of PSA after medication was -46.50%. Meanwhile, the median percentage change of PSA for those baseline PSA levels > 4 ng/mL (25 men) was -47.36%. There was no statistical significance of the effect on PSA caused by finasteride between these 2 groups of patients.

In the subgroup of 86 men who underwent TRUS before and after the treatment, median percentage change of prostate volume for these patients was -17.80% (from 39.83 ± 21.10 to 33.62 ± 20.52 mL) (Table 1). The median percentage change of PSAD in these patients was -38.67% (from 0.077 ± 0.049 to 0.055 ± 0.040) (Table 1). There were 57 out of 86 patients (66.3%) who had prostate volume decreasing greater than 10% after the medication.

DISCUSSION

The lifespan of man has increased due to remarkable progress of social health status and medical care in recent years, and the diseases that mainly insult aged people have become a major task for modern doctors. Since the trend of disease treatment has been toward minimally invasive in recent years, medical therapy still plays a major role in treating people suffered from BPH.[7] Moreover, for those patients who suffer from the lower urinary tract symptoms, it is important for the clinical doctor to distinguish benign origins from malignant ones.

Early detection of prostate cancer is a major task, since there is no specific symptom in patients with early-stage prostate cancer. Recently, PSA was introduced as a powerful method for screening of prostate cancer. However, 1 of the difficulties in using PSA as a tool for early detection of prostate cancer among men with BPH is relatively poor sensitivity and specificity due to substantial overlap in PSA levels between men with BPH and prostate cancer.[11,12] Significant improvement in positive prediction can be achieved by using other detection methods such as DRE and TRUS along with serum PSA level, as well as age-specific PSA nor-

Table 1. The differences of average serum PSA level, prostate volume, and PSA density at baseline and six months after finasteride, respectively

	Serum PSA level *(ng/mL)*	***Prostate volume*** *(mL)*	***PSA density***
Baseline	2.48 ± 2.02	39.83 ± 21.10	0.077 ± 0.049
Six months	1.57 ± 1.47	33.62 ± 20.52	0.055 ± 0.040
p* value	< 0.001	< 0.001	< 0.001

*Tested by paired *t*-test.

mal ranges and PSAD.[2,4,5,11]

The management of BPH should be individualized to patients' circumstances and personal choices. Subjective symptoms, bothersomeness and negative impact on the quality of life are the main reasons for the patient to seek treatment for BPH.[14] Among various medical treatment options, finasteride has gained its role in first-line therapy for those patients with uncomplicated symptomatic BPH.[6-8] It opens another window for the medical therapy of BPH and has shown its clinical ability to decrease prostatic size and relieve the obstructive symptoms subsequently.[6-9] A multi-center, double-blind, placebo-controlled study revealed finasteride could effectively increase the flow rate and decrease the obstructive symptoms as well as prostate volume in patients with symptomatic BPH treated with it for 12 months.[11] This study from North America disclosed finasteride could increase serum luteinizing hormone concentrations and decrease PSA levels (median decrease was 50%). Another domestic study conducted in northern Taiwan also showed the ability of finasteride in deceasing prostate size (-15%) as well as symptom score (-37%) and serum PSA level (-44%) for patients treated with finasteride for 12 months.[10] Our study again outlined the clinical effect of finasteride on serum PSA level. All these results remind the clinical physicians to pay much attention to serum PSA level for patients having finasteride for symptomatic BPH to prevent delayed diagnosis of possible prostate cancer.

The patients included in this study were prescribed with only finasteride but not alpha-blockers. However, in this group of patients, the incidence of having alpha-blockers at the same time for other medical problems is higher. Thus, we couldn't make sure that all the patients included were not taking alpha-blockers. Since this study is mainly discussing the effects of finasteride on PSA and prostate volume but not the flow rate and alpha-blockers have been shown to improve flow rate without any effects on the above 2 categories,[15] the possible effect of alpha-blockers on the outcome can be neglected. Our results clearly show the clinical benefit of finasteride on the treatment of BPH in decreasing prostate volume.

It is well known that finasteride affects PSA in a highly predictable way.[12,16-18] Our data showed the same effect; that the median percentage serum PSA level of patients with BPH treated with 6-month finasteride is approximately -45%. Some authors even suggest that we should multiply the serum PSA levels of men treated with finasteride by 2 and compare the results to either age-independent or age-specific upper limits of normal for serum PSA in untreated men with BPH.[19,20] However, there is no available data to date on whether the normal range of PSA velocity of men with BPH treated with finasteride should be modified.

Our results indicated there was no difference of median percentage PSA change between the 2 groups of patients treated with finasteride using the cutoff value of serum PSA level as 4 ng/mL, although recent efforts have shown that there are more pronounced differences for all of the bothersome symptoms of BPH for men with baseline PSA > 4 ng/mL.[17,21] Further efforts should be made to define the difference of median percentage change in PSA for patients with early or unsymptomatic prostate cancer.

Some authors have proved finasteride will decrease the PSAD in patients with BPH.[18,20,21] Our data indicated decrease of PSAD level after oral finasteride for 6 months. Gormley *et al.* have reported that PSAD could be used to provide additional reassurance from PSA levels without requiring adjustment after treatment with finasteride.[20] Their report did show differential changes in separation of patients with and without prostate cancer, but an optimal cut-point between the groups could not be established because of small case number.[22] The question of the superiority of PSAD to PSA in patients taking finasteride needs to be studied further in a patient cohort sufficiently large to evaluate this issue definitively.

In conclusion, our study found finasteride did have its effect on reducing prostate volume. Physicians should have a heightened level of suspicion about the possible existence of malignancy in patients who are taking finasteride if the PSA does not fall to the expected degree. Regular follow-up of PSA level in these patients is highly recommended.

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