Changes in Serum Prostate-Specific Antigen after Treatment with Antibiotics in Patients with Lower Urinary Tract Symptoms/Benign Prostatic Hyperplasia with Prostatitis

Yoon-Soo Kyung, Hyeoung-Cheol Lee, Hyung-Jee Kim

Department of Urology, Dankook University College of Medicine, Cheonan, Korea

Purpose: Many urologists have performed prostate biopsy in men with a high level of prostate-specific antigen (PSA) alone. However, high levels of PSA may be induced by infection. We studied the effects of antibiotics on serum total PSA and PSA density (PSAD) in men with total PSA between 4 and 10 ng/ml and normal digital rectal examination (DRE) and transrectal sonographic findings.

Materials and Methods: From January 2005 to October 2009, a total of 107 patients with complaints of lower urinary tract symptoms (LUTS) or benign prostatic hyperplasia (BPH) were evaluated. To be included in this study, patients had to be at least 50 years old, have a palpably normal DRE, have infection in the prostate, have a total serum PSA of 4 to 10 ng/ml, and have transrectal ultrasound findings that did not show a hypoechoic lesion in the prostate. Only patients in whom the PSA level was rechecked after short-term antibiotics administration (8 weeks) were included. Serum PSA and PSAD were measured before transrectal ultrasound or EPS and after 8 weeks of treatment with antibiotics (quinolone). Age, prostate volume, serum PSA, PSAD, and PSA rate of change were compared.

Results: The mean age of the patients was 66.3 years. The mean prostate size was 48.8±24.9 g. Forty patients had a high level of PSAD. Total PSA and PSAD significantly decreased after treatment (p <0.05). In 45 of the 107 men, total PSA after antibiotics treatment was normalized (less than 4 ng/ml). PSAD after treatment was normalized (less than 0.15 ng/ml/cm³) in 23 of the 40 patients with a high level of PSAD.

Conclusion: Antibiotics treatment for at least 8 weeks in BPH patients with an increased PSA level (4-10 ng/ml), infection, and normal DRE and transrectal sonographic findings may decrease serum PSA significantly. However, because the PSA level was not decreased to the normal range (less than 4 ng/ml) in all patients, it seems that antibiotics therapy before prostatic biopsy is not necessary.

Key Words: Prostate-specific antigen; Antibiotics

Introduction

The elderly population is gradually increasing in Korea, and more of the population eats a Western diet. The incidence of prostate cancer also increases with age; more than 75% of diagnosed cancers are in men older than 65 years of age [1,2]. When prostate cancer is diagnosed too late, the course of the prostate cancer will have a poor progression [3]. However, patients diagnosed with...
early prostate cancer have a significantly better survival rate. Thus, effort was made for the early detection of prostate cancer [4]. Currently, tests for the early diagnosis of prostate cancer include the digital rectal examination (DRE), transrectal prostate ultrasound, and serum prostate-specific antigen (PSA). Catalona et al. concluded that the use of PSA in conjunction with DRE enhances early prostate cancer detection, and prostatic biopsy should be considered if either the PSA level is greater than 4 micrograms/L or the DRE is suspicious for cancer, even in the absence of abnormal transrectal ultrasonography findings [5]. Also, the PSA test has a higher reproducibility and a relatively lower cost and is simple for the early diagnosis of prostate cancer. However, isolated serum PSA levels in individuals have not demonstrated sufficient sensitivity and specificity to be useful in the routine evaluation of prostate disease [8-10]. Many studies have reported that an elevated PSA level is related to prostatitis [6-9]. However, in a recent study, it was reported that although antibiotics therapy will decrease serum total PSA, it will not decrease the risk of prostate cancer even if the PSA decreases to less than 4 ng/ml [10]. Therefore, the aim of this study was to evaluate the effects of antibiotics on serum total PSA and PSA density (PSAD) in men with PSA between 4 and 10 ng/ml and normal DRE and transrectal ultrasound findings.

**Materials and Methods**

Form January 2005 to October 2009, a total of 107 patients with complaints of lower urinary tract symptoms (LUTS) or benign prostatic hyperplasia (BPH) were evaluated in this study. To be included in the present analysis, patients had to be at least 50 years old, have a palpably normal DRE, have a total serum PSA of 4 to 10 ng/ml, and have transrectal ultrasound findings that did not show a hypoechoic lesion in the prostate. Only patients in whom the PSA level was rechecked after short-term antibiotics use (8 weeks) were included. Patients with symptoms of acute prostatitis were excluded. Also, patients with a history of acute urinary retention, pyuria, an indwelling catheter, or previous prostate surgery or who had taken 5-alpha reductase enzyme inhibitors were excluded from the study.

Chronic nonbacterial prostatitis is diagnosed by normal findings in urinalysis and more than 20 white blood cells in smear expressed prostatic secretion (EPS) under microscope with a high magnification view ($\times$400). Serum PSA and PSAD were measured before transrectal ultrasound or EPS and after 8 weeks of treatment with antibiotics (quinolone). Age, prostate volume, serum PSA, PSAD, and PSA rate of change were compared. PSA relative change (%) was defined as first serum PSA/ (first serum PSA - PSA after antibiotics treatment) $\times$ 100. These data were analyzed statistically by using SPSS 8.0. The results were expressed as means±SD. Student’s t-test was used to compare the mean values of continuous variables. A p-value less than 0.05 was considered significant.

**Results**

A total of 107 patients were enrolled in this study. The mean age of the patients was 66.3 years (range, 50 to 83 years). The mean prostate size was 48.8±24.9 g (range, 22-110 g). Of these patients, the mean total PSA was 6.3±1.9 ng/ml and 4.8±2.4 ng/ml before and after treatment, respectively. There was a significant difference in the total PSA (p<0.05). In the same period, PSAD changed from 0.15±0.08 ng/ml/cm$^3$ to 0.11±0.07 ng/ml/cm$^3$ before and after treatment, respectively, which also showed a significant difference (p<0.05). The mean PSA rate of change was -23.8% at the same time. After 8 weeks of quinolone administration, the elevated total PSA level of 45 patients (42.1%) was normalized. Forty patients had a PSAD above 0.15 ng/ml/cm$^3$. Of these, PSAD was normalized in 23 cases (57.5%) after 8 weeks of quinolone administration. After 8 weeks of antibiotics treatment, in patients with a total PSA level of more than 4 ng/ml, 25 patients wanted more medication, but after four more weeks of treatment, the total PSA was decreased to 4 ng/ml in 8 cases (32%) (Table 1).
Table 1. Changes in pre- and post-treatment parameters

<table>
<thead>
<tr>
<th>No. of Patients</th>
<th>107</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age</td>
<td>66.3 years old</td>
</tr>
<tr>
<td>Prostatic size</td>
<td>48.8±24.9 g</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Pre</th>
<th>post</th>
<th>normalized patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>tPSA (ng/ml)</td>
<td>6.3±1.9</td>
<td>4.8*±2.4</td>
<td>45/107</td>
</tr>
<tr>
<td>PSAD (ng/ml/cm³)</td>
<td>0.15±0.08</td>
<td>0.11*±0.07</td>
<td>23/40</td>
</tr>
</tbody>
</table>

The results were expressed as means±SD.
* expressed significant difference (p<0.05).

Discussion

After Hara et al identified PSA as a gamma-semiino protein from the seminal plasma [11], Wang et al. reported the possibility that PSA might be a tumor marker for prostate cancer [12] and Papsidero et al. applied PSA to the clinical diagnosis of early prostate cancer and the follow-up of prostate cancer patients [13].

However, because PSA is a serine protease secreted by prostate epithelial cells [14] as well as primary gastric, mammary gland, and breast cancer tissue [15], PSA is nonspecific to the prostate. Moreover, the PSA level is increased by prostate cancer as well as by BPH, prostatitis, and other circumstances such as prostate biopsy, DRE, and acute urinary retention [16,17]. This leads to potentially unnecessary biopsy procedures [18]. Another study revealed that the lack of specificity of PSA measurement as the only biopsy indicator is most easily pointed out by the observation that in only 20% to 30% of biopsied men with a PSA value greater than 4.0 ng/mL is prostate cancer detected thus, approximately 70% to 80% of these men have a false-positive test result [19].

After Dalton et al. reported [20] that the PSA level of patients with acute prostatitis was increased and normalized after antibiotics use, Neal et al. reported [21] that chronic prostatitis results in changes in PSA. In another study, prostate volume and inflammation were reported to be the most important factors contributing to serum PSA elevation in men without clinically detectable prostate cancer [6]. Prostatitis must be considered when using PSA as a tumor marker because the PSA level decreases to normal after effective antibiotics therapy in most patients with bacterial prostatitis [7,8]. However, little is known about the relationship between the serum PSA level and the inflammatory state in BPH, and there are few Korean reports on the analysis of PSA changes in asymptomatic or mild symptomatic patients. According to a Korean study of middle-aged and older men with prostatitis, among 39 men, serum PSA and PSAD values returned to the normal range after antibiotics treatment in 22 (56.4%). It was suggested that prostatitis was one of the most important factors in serum PSA and PSAD elevation in men without clinically detectable prostate cancer and that a decrease in PSA and PSAD after antibiotics treatment can help to avoid unnecessary prostate biopsies [22].

However, in a recent study, there was no significant difference in the PSA levels of men with and without prostate inflammation [23]. Baltaci et al. reported that although antibiotics therapy will decrease serum total PSA, it will not decrease the risk of prostate cancer even if the PSA decreases to less than 4 ng/ml therefore, prescribing antibiotics for asymptomatic men with a newly increased PSA may not be an appropriate method of management [10].

The duration of antibiotics treatment was between 20 and 28 days in other studies [10,22]. Because the duration of antibiotics treatment has not been confirmed, we treated for 8 weeks based on the fact that in chronic bacterial prosta-
titis and inflammatory CPPS, a total treatment period of 4 to 6 weeks has been recommended [24].

In our study, even though total PSA was decreased significantly after 8 weeks of treatment with antibiotics, and total PSA and PSAD were normalized in approximately 50% of patients, the total PSA and PSAD of all patient were not decreased to the normal range (less than 4 ng/ml). Thus, it seems that antibiotics therapy is not necessary.

Conclusions

Antibiotics treatment for at least 8 weeks in BPH patients with an increased PSA level (4-10 ng/ml), prostatitis, and normal DRE and transrectal sonographic findings may decrease serum PSA significantly. However, because total PSA and PSAD were not decreased to the normal range (less than 4 ng/ml) in all patients, it seems that antibiotics therapy is not necessary.

References

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