The Effect of Antibiotherapy on Prostate-Specific Antigen Levels and Prostate Biopsy Results in Patients with Levels 2.5 to 10 ng/mL

Gokhan Toktas, MD,¹ Murat Demiray, MD,² Erkan Erkan, MD,¹ Ramazan Kocaaslan, MD,³
Ugur Yucetas, MD,¹ and Suleyman Erdinc Unluer, MD³

Abstract

Purpose: This controlled prospective study aims to investigate the possible effects of antibiotic treatment on prostate-specific antigen (PSA) and its derivatives, and consequently on the transrectal biopsy rates, in the diagnosis of prostate cancer.

Patients and Methods: One hundred and forty patients aged 45 to 70 years old, with a PSA level between 2.5 and 10 ng/mL and normal digital rectal examinations (DRE), were included in this study between June 2009 and November 2010. The patients were randomly assigned into two groups. The first group received oral levofloxacin 500 mg 1*1 for 21 days; the second, the control group, was given no treatment. Initially, total PSA, free PSA, a DRE, urinary ultrasonography (including prostate volume, postvoiding residual urine), uroflowmetry, International Prostate Symptom Score, National Institutes of Health Chronic Prostatitis Symptom Index, and International Index of Erectile Function tests were performed. All of these were repeated at the end of 3 weeks of antibiotic treatment. An additional PSA measurement was also performed at day 10 of the treatment. All patients underwent transrectal ultrasonography (TRUS) guided prostate biopsy at day 21, just the day after the final (third) PSA sampling.

Results: The mean age of the patients was 59.6 years. Overall, in 23 patients, prostate cancer was detected, including those found in the rebiopsies. Statistically, there were significant changes in values of PSA and its derivatives in the treatment group (from 5.31 to 4.69 and 4.58 ng/mL, consecutively). Focusing on prostate cancer patients in both the treatment and control groups, however, we did not detect any significant change in the same parameters.

Conclusion: Antibiotic treatment given to the patients with a PSA level between 2.5 and 10 ng/mL can be beneficial, before a decision for TRUS guided prostate biopsy, just in a limited subgroup, by reducing the PSA levels below the threshold value. Considering the large population of patients in the gray zone, however, it still does not provide clear solid evidence for avoiding unnecessary prostate biopsies.

Introduction

PROSTATE CANCER (PCa), THE MOST COMMON CANCER in men, has been a disease that can be scanned biochemically and diagnosed at early stages since the use of prostate-specific antigen (PSA) testing began in the 1980s.¹ Although PSA is a prostate-specific marker, it is not cancer-specific. Serum levels of PSA in healthy persons have been known to vary depending on age, race, prostate volume, and biologic variability. The PSA level can increase for several reasons, including trauma, ejaculation, and rectal and urethral procedures. It can also increase because of diseases such as benign prostatic hyperplasia and prostatitis.²

Approximately 80% of patients with a normal digital rectal examination (DRE) and PSA value between 4 and 10 ng/mL have negative biopsy results for cancer.^{3,4} There is a trend to reduce the threshold value of PSA to 2.5 ng/mL to detect more PCa. The number of unnecessary biopsies, however, will increase during the struggle to detect more cancer. Thus, the next goal should be the reduction of unnecessary biopsies while diagnosing more PCa.^{5–8}

In patients with a PSA value between 2.5 and 10 ng/mL, free/total PSA (f/t PSA) ratio, PSA density (PSAD) and PSA velocity help us to increase the cancer specificity of PSA and avoid unnecessary biopsies. Although the biologic basis has not been fully understood, decreased f/t PSA ratio

¹Department of Urology, Istanbul Teaching and Research Hospital, Istanbul, Turkey.

²Department of Urology, Elbistan Governmental Hospital, Elbistan, Turkey.

³Department of Urology, Kafkas University Medical Faculty, Kars, Turkey.

has been determined to be more common in prostate cancer patients.^{9,10}

Acute and chronic prostatitis has been a known cause of increased PSA levels. Many studies point out that prostatic inflammation is related to increased serum PSA levels.^{11–14} It has also been acclaimed that most patients with a gray-zone PSA value get out of the PSA pool that necessitates biopsy after antibiotic treatment.^{5,15,16} An elevated PSA level caused by subclinical inflammation is a common reason for negative prostate biopsy results.¹⁷

Some urologists, in daily practice, use antibiotics to treat patients who have high PSA values because of prostatitis. Several studies have shown that receiving antibiotic treatment, before deciding to have a biopsy, can reduce PSA values to normal levels, and biopsy can be avoided.^{5–8} Approximately 15% of patients with a PSA value ≤ 4 ng/mL have prostate cancer, however.¹⁸

This study investigated the effect of antibiotics in avoiding unnecessary biopsies, without missing cancer, in patients with a PSA level of gray zone (2.5–10 ng/mL). The PSA kinetics during and at the end of antibiotic treatment were measured; the cancer detection rates were investigated and compared with those of the control group, who received no therapy to learn if antibiotic treatment can decrease the number of prostate biopsies caused by reasons other than PCa.

Patients and Methods

The study was conducted between June 2009 and November 2010 on 140 patients who had been referred to our outpatient department with lower urinary tract symptoms and shown to have a PSA level between 2.5 and 10 ng/mL and a normal DRE. The mean age of patients was 59 years (range 45–70 years). The exclusion criteria were having signs of acute or chronic prostatitis, a history of prostate biopsy or prostate surgery, a family history of prostate cancer, and history of 5- α reductase inhibitor treatment. The patients with a recent history of instrumentation of the urinary tract were also excluded, along with those who had any nodules, induration, or suspicion of malignancy at DRE, and those with evidence of acute urinary tract infection through urinalysis, such as pyuria and bacteriuria, residual urine measuring over 100 mL, and hypersensitivity to quinolones.

The first visit involved a detailed medical history; an investigator urologist performed a general physical examinations and DRE. International Prostate Symptom Score (IPSS), and International Index of Erectile Function (IIEF), National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI), and Quality of Life (QoL) scores were determined. Complete urinalysis and PSA measurements (tPSA and fPSA) were performed. PSA was measured by electrochemiluminescence immunoassay, using the Modular Analytics™ E170 immunoassay analyzer device. Prostate volume and postvoid residual urine volume were determined. Uroflowmetry was also performed.

Patients were randomized systematically into two groups according to order of admission. Those in the first group were given 500 mg oral levofloxacin once a day for 21 days. The second, the control group, received no treatment. All patients were reevaluated using the same parameters, at the end of 3 weeks. Over the following period, PSA sampling was repeated twice, with an interval of 10 days. Just after the termination of antibiotic treatment and final PSA sampling, all

patients underwent transrectal ultrasonography (TRUS) guided systematic 12-core prostate biopsies regardless of the final PSA value.

An investigator urologist performed TRUS of the prostate, using a biplanar technique with a 7.5 MHz ultrasound probe (GE Health™ Lociq 200 Pro), at a standard 12-core fashion. Specimens were evaluated by a single uropathologist. The histopathology of biopsy was classified as benign, malignant, or prostatitis. In case of atypical small acinar proliferation (ASAP), an immediate second 20-core saturation biopsy was performed.

All statistical evaluations were performed by SPSS 18.0 software. Parametric and nonparametric independent samples *t* test and the Mann-Whitney *U* test were used. Repeated measurements were tested with the Wilcoxon test. Analysis of the proportional data was performed with the chi-square test and Fischer test. Any *P* value less than 0.05 was considered as significant.

Results

There were no differences between the two groups in terms of age, tPSA, f/t PSA, PSAD, transrectal prostate volume (TRPV), IPSS, QoL, and NIH-CPSI scores (Table 1).

In the treatment group, there was a statistical difference between initial and subsequent tPSA, f/t PSA and PSAD levels (Fig. 1). Of the 70 patients in the treatment group, 54 had a lower PSA level in the second sampling (day 10) and 27 in the third (day 21). No statistical difference was detected in the control group (Table 2). Regarding the mean tPSA, antibiotic treatment caused 11% and 13% fall in the first (tPSA1) and second (tPSA2) control, respectively. The change in the mean tPSA was similar in the control group, especially in the second control (5% and 10.5%). Regarding the number of patients with significant change in control tPSA, however, antibiotic treatment decreased tPSA in 22.7% of patients, while only 5.9% of controls had a statistically significant fall in tPSA ($P < 0.05$).

There was statistically significant improvement in IPSS, QoL, and NIH-CPSI scores but not in Qmax and IIEF with the antibiotic treatment. No difference was detected in the control group as expected (Table 3).

As a result of pathologic examination, prostatitis was found in 38.6% ($n = 27$), BPH in 47.1% ($n = 33$), and PCa in 14.3% ($n = 10$) in the treatment group. The distribution was similar in the control group (prostatitis 35.7% ($n = 25$), BPH 45.7% ($n = 32$), and PCa 18.6% ($n = 13$). Overall, of the 140 cases, 18 received a diagnosis of PCa and 9 ASAP in the initial biopsy. Those with ASAP underwent 20-core rebiopsy. After rebiopsy, five of these nine patients were found to have PCa. Prostate cancer rates were 14.3% ($n = 10$) in the treatment group and 18.6% ($n = 13$) in the controls ($P > 0.05$).

In the treatment group, there was no statistical difference in terms of age, f/t PSA and TRPV levels between the patients with or without PCa, but the levels of f/t PSA and PSAD were higher in the patients with PCa. The PSA derivatives (f/t PSA and PSAD) of patients with and without PCa, however, showed no statistically significant difference in the control group.

The mean decrease of tPSA and PSAD in patients without PCa was statistically significant after antibiotic treatment ($P = 0.007$ and $P = 0.015$, respectively), while change in f/t PSA

TABLE 1. COMPARISON OF MEAN BASELINE VALUES OF THE STUDY GROUPS

	Group	Mean $\pm$ SD	Range	P
Age (year)	Treatment control	59.16 $\pm$ 6.33 60.09 $\pm$ 6.17	48–70 45–70	0.381*
tPSA (ng/ml)	Treatment control	5.31 $\pm$ 1.76 4.95 $\pm$ 1.78	2.64–9.55 2.69–8.99	0.079**
fPSA (ng/ml)	Treatment control	0.60 $\pm$ 0.98 0.49 $\pm$ 0.61	0.07–2.40 0.36–2.97	0.694**
%f/t PSA	Treatment control	19.03 $\pm$ 7.84 22.06 $\pm$ 8.70	2–39 11–59	0.069**
PSAD (ng/ml ²)	Treatment control	0.16 $\pm$ 0.08 0.14 $\pm$ 0.07	0.06–0.49 0.05–0.36	0.054**
TRPV (ml)	Treatment control	36.06 $\pm$ 12.86 39.81 $\pm$ 18.81	14–72 17–100	0.170*
IPSS	Treatment control	10.99 $\pm$ 8.10 12.79 $\pm$ 7.24	0–33 2–33	0.068**
QoL	Treatment control	2.71 $\pm$ 1.50 3.09 $\pm$ 1.76	0–6 0–6	0.168**
Qmax (ml/s)	Treatment control	14.44 $\pm$ 7.01 14.06 $\pm$ 7.68	5–44 5–44	0.422**
IIEF	Treatment control	19.20 $\pm$ 9.38 16.84 $\pm$ 9.17	1–29 2–29	0.092**
NIH-CPSI	Treatment control	10.46 $\pm$ 7.98 11.80 $\pm$ 7.05	0–18 1–17	0.430**

t* test.Mann-Whitney *U* test.

SD=standard deviation; tPSA=total prostate-specific antigen; fPSA=free prostate-specific antigen; f/t PSA=free/total prostate-specific antigen; PSAD=prostate-specific antigen density; TRPV=transrectal prostate volume; IPSS=International Prostate Symptom Score; QoL=quality of life; Qmax=maximal flow rate; IIEF=International Index of Erectile Function; NIH-CPSI=National Institutes of Health Chronic Prostatitis Symptom Index.

ratio was not. The patients who were later found to have PCa did not have a remarkable PSA variation. Thus, there was no significant difference between initial and following tPSA levels after antibiotherapy (Table 4). In the treatment group, patients with PCa were shown to have a steady PSA kinetics

FIG. 1. Total prostate-specific antigen (tPSA) trend in the study groups. There is a statistically significant decrease of tPSA in the treatment group ($P < 0.05$). The treatment group showed a prominent decline (from 5.33 to 4.69 and 4.58 ng/mL, respectively), compared with control, that is more remarkable in between the first and second PSA controls (PSA, ng/mL).

similar to the control group. As expected, there were no significant changes in PSA and its derivatives among patients in the control group, with or without PCa.

In subgroup analysis of the patients according to initial PSA levels (Table 5), after antibiotherapy, a downward shift from gray zone can be seen. This was not evident, however, in the control group. Although tPSA levels dropped below 2.5 ng/mL in eight of the patients, tPSA was observed as higher than 10 ng/mL in two after antibiotherapy. Furthermore, one of three patients who had a subsequent tPSA level below 2.5 ng/mL in the control group had a diagnosis of PCa, while none of the eight patients with PSA below 2.5 ng/mL and a mean decrease of 57% had a diagnosis of PCa after treatment.

Discussion

The risk of PCa is 25% when PSA levels are between 4.0 and 10 ng/mL. This means that three of four biopsies in this group of patients are unnecessary. Therefore, we need a more accurate assessment of PSA levels for the biopsy decision.

Previous observations have suggested that histopathologically confirmed chronic prostatitis might accompany biopsies that prove negative for cancer.¹⁹ These authors found that prostatic inflammation and deterioration of the basement membrane unit in secretory cells can cause high PSA levels.^{11,20} Kwak and associates,²¹ however, have found no correlation between inflammation and serum PSA levels. Therefore, reevaluation of the PSA level is a common daily practice to decide on TRUS biopsy even if the patient is asymptomatic to prevent unnecessary interventions that have

TABLE 2. COMPARISON OF MEAN TOTAL PROSTATE-SPECIFIC ANTIGEN, % FREE/TOTAL PROSTATE-SPECIFIC ANTIGEN, AND PROSTATE-SPECIFIC ANTIGEN DENSITY LEVELS IN THE STUDY GROUPS

	1 st	2 nd	3 rd	P ¹	P ²
Group 1 (Treatment)					
tPSA	5.31 ± 1.76	4.69 ± 2.74	4.58 ± 1.93	0.001	0.113
% f/t PSA	19.03 ± 0.84	20.47 ± 0.13	20.74 ± 11.76	0.003	0.319
PSAD	0.16 ± 0.08	0.14 ± 0.08	0.14 ± 0.06	0.001	0.853
Group 2 (Control)					
tPSA	4.9 ± 1.78	4.66 ± 2.06	4.43 ± 2.08	0.065	0.052
% f/t PSA	22.06 ± 8.70	22.59 ± 12.89	21.01 ± 11.00	0.053	0.583
PSAD	0.14 ± 0.07	0.13 ± 0.07	0.13 ± 0.07	0.059	0.123

PSA (ng/mL); PSAD (ng/mL²).

P¹ = P for comparison of first and second prostate-specific antigen (PSA); P² = P for comparison of second and third PSA.

tPSA = total prostate-specific antigen; f/t PSA = free/total prostate-specific antigen; PSAD = prostate-specific antigen density.

risk of complication. Also, some urologists prefer using antibiotics to control PSA levels by minimizing the effect of inflammation beforehand, so-called normalization of PSA. This behavior that had been applied by many urologists has been evaluated widely, and the influence of antibiotics on the PSA level has been investigated.^{5,8,22,23} Although some studies have suggested a possible decrease in PSA levels after anti-biotherapy, there is no consensus when deciding about TRUS biopsy. Therefore, we conducted a prospective randomized, controlled study that has never been performed before to meet the demand about this issue. Superior to the previous studies, we performed TRUS biopsy on all patients, even those with a decreased PSA level <2.5 ng/mL.

Although some studies advocate that there is no need to perform TRUS biopsy for patients with a PSA level <4 ng/mL,^{5-7,23} in fact, there is a 15% risk of PCa.¹⁸ Baltaci and colleagues²⁴ reported that there were still some PCa patients with PSA levels <4 ng/mL after an antibiotic course, while in contrast, no PCa was found in some studies.^{8,15,25} Many studies have reported a decline in PSA levels ranging from 7.1% to 43% after antibiotic treatment.^{8,14,15,23,25}

The PSA variability may also be because of diurnal biologic fluctuation.^{22,26} It is known that there can even be a 20% to

46% difference between two consecutive PSA levels in one person. This physiologic fluctuation rate is 10% to 20% in the normal population.²⁶ The results of our study showed that decreases in PSA levels were statistically similar in both treatment and control groups (mean 13% vs 10.5%). Regarding the individual patient characteristics, however, 22.7% of patients in the treatment arm vs 5.9% in controls had a statistically lower tPSA at the second control. This suggests that the individual change was not because of normal diurnal fluctuation.

Bulbul and coworkers⁶ reported that, among 48 patients, 42% showed PSA decline after 2 weeks of antibiotic treatment, and TRUS biopsy was not performed on those patients. PCa was detected in 39% of the remaining pool of patients. Although this strategy reduced the number of TRUS biopsies, they were not able to show if any PCa was missed or not in the spared group.

Similarly, Bozeman and colleagues⁵ found that 46.3% of the PSA levels of patients with chronic prostatitis decreased below 4 ng/mL after 2 months of antibiotic treatment. Patients with a control PSA >4 ng/mL showed moderately a mean decline of 20.2%, which was statistically insignificant. Prostate cancer was detected in 25.5% of those patients. They concluded that the patients with a decreased PSA <4 ng/mL stay stable and may be followed without a need for biopsy. Because Bozeman and associates⁵ did not perform TRUS biopsy on any patients who showed decreases in PSA levels <4 ng/mL, the PCa rate was uncertain in this study. Supporting these data, however, we did not detect any PCa in patients with PSA levels that decreased below the level of 2.5 ng/mL (n=8), whereas, the cancer detection rate was higher than ours regarding the group with a PSA >4 ng/mL after antibiotics (25.5% vs 12.8%).

In our study, PCa was detected in 14.3% (n=10) and 18.6% (n=13) of the patients in the antibiotherapy treatment and control groups, respectively. Overall, our study was not able to demonstrate a difference in prostate cancer rate in both groups. Thus, antibiotic treatment seemed to be beneficial on only a very limited subgroup of patients but still cannot be offered routinely in cases with no symptom of prostatitis. The histopathologic distribution of our cases was similar to the literature about conducting TRUS biopsy for elevated PSA. When we used a threshold of PSA level 2.5 ng/mL, PCa was detected in 16.1% (10/62), although this rate was only 12.8% (5/39) when we adopted a threshold of PSA level 4 ng/mL.

TABLE 3. COMPARISON OF MEAN INITIAL AND CONSEQUENT MAXIMAL FLOW RATE, INTERNATIONAL PROSTATE SYMPTOM SCORE, QUALITY OF LIFE, NATIONAL INSTITUTES OF HEALTH CHRONIC PROSTATITIS SYMPTOM INDEX VE INTERNATIONAL INDEX OF ERECTILE FUNCTION SCORES IN STUDY GROUPS

	Group1 (treatment)	Group 2 (control)	P*
Qmax1	14.44 ± 7.01	14.06 ± 7.68	0.422
Qmax2	15.88 ± 7.35	14.99 ± 7.87	0.272
IPSS1	10.99 ± 8.10	12.79 ± 7.24	0.068
IPSS2	9.43 ± 7.95	11.23 ± 7.67	0.057
QoL1	2.71 ± 1.50	3.09 ± 1.76	0.168
QoL2	2.29 ± 1.61	2.67 ± 1.73	0.208
NIH-CPSI1	10.46 ± 7.98	11.80 ± 7.05	0.430
NIH-CPSI2	8.19 ± 7.45	9.14 ± 7.43	0.057
IIEF1	19.20 ± 9.38	16.84 ± 9.17	0.092
IIEF2	18.09 ± 9.98	16.33 ± 9.34	0.246

Qmax = maximal flow rate; IPSS = International Prostate Symptom Score; QoL = quality of life; NIH-CPSI = National Institutes of Health Chronic Prostatitis Symptom Index; IIEF = International Index of Erectile Function.

TABLE 4. COMPARISON OF THE TREND IN PROSTATE-SPECIFIC ANTIGEN AND DERIVATIVES IN PATIENTS WITH AND WITHOUT PROSTATE CANCER IN STUDY GROUPS (GROUP 1 TREATMENT, GROUP 2 CONTROLS)

	1st	2nd	PCa		No PCa	
			<i>p</i> *	1st	2nd	<i>P</i> *
Group1						
tPSA	5.78±3.98	5.13±3.64	0.315	5.24±3.47	4.62±5.72	0.007
%f/t PSA	19.40±19.6	18.8±18.62	0.971	18.97±15.14	20.75±15.92	0.382
PSAD	0.19±0.12	0.19±0.12	0.579	0.15±0.15	0.13±0.15	0.015
Group 2						
tPSA	5.09±2.20	4.60±4.46	0.545	4.92±3.42	4.68±4.08	0.165
%f/t PSA	18.38±15.34	24.31±41.74	0.579	22.89±17.54	22.19±21.04	0.456
PSAD	0.16±0.14	0.1±0.14	0.362	0.13±0.12	0.13±0.13	0.557

Wilcoxon test.

PSA, ng/mL; PSAD, ng/mL².

PCa = prostate cancer; tPSA = total prostate-specific antigen; f/t PSA = free/total prostate-specific antigen; PSAD = prostate-specific antigen density.

Therefore, 40 additional biopsies were performed when the tPSA cutoff value was defined as 2.5 ng/mL. Of those patients, six had a diagnosis of PCa, which means that there was a 35% increase in detection, but unfortunately 40% of the biopsies performed had been unnecessary.

Kaygisiz and colleagues⁸ demonstrated that decrease in PSA levels after antibiotics was similar in patients with and without prostatitis, expressed by prostatic secretions.⁸ They detected PCa in 10.8% of the patients, and all of these patients had a PSA level > 4 ng/mL. The study concluded that there was still a high risk for PCa in patients who have PSA levels > 4 ng/mL after antibiotics, even if they have been diagnosed with prostatitis clinically. Overall, they recommended 3 weeks of anti-biotherapy before making the TRUS biopsy decision.

Serratta and coworkers²⁵ found that there was a PSA reduction in 59% of patients after a 3-week course of antibiotics. They reported that 40% and 20.3% of patients diagnosed with PCa had unchanged and decreased PSA levels, respectively.²⁵ In addition, no cancer was detected in patients with a PSA level below 4 ng/mL, and the study suggested that biopsy could be postponed if PSA levels decreased more than 50% or below 4 ng/mL. Inclusion of patients with a previous history of biopsy and variability in the number of cores, ranging from 12 to 21, limit this study, however.

The results of our study showed that the PSA level of patients with a diagnosis of PCa had a variable pattern. Eight of 54 (14.8%) patients who had responded to antibiotics with a PSA fall were shown to have PCa while 2 of 16 with an increased PSA had PCa.

TABLE 5. NUMBER OF CASE DISTRIBUTION ACCORDING TO SEQUENTIAL TOTAL PROSTATE-SPECIFIC ANTIGEN LEVELS

<i>t</i> PSA (ng/mL)	Treatment		Control	
	<i>t</i> PSA1 (<i>n</i> = 70)	<i>t</i> PSA2 (<i>n</i> = 70)	<i>t</i> PSA1 (<i>n</i> = 70)	<i>t</i> PSA2 (<i>n</i> = 70)
<2.5	0	8	0	3
2.5–4.0	13	23	27	31
4.01–10.0	57	37	43	34
>10.01	0	2	0	2

tPSA = total prostate-specific antigen.

Baltaci and associates²⁴ reported on 100 patients with normal DRE and PSA levels between 4 and 10 ng/mL who had been given 3 weeks of antibiotics. An overall decrease of 7.15% in PSA value was detected. The study also reported PCa in 29.4% (5/17) of the patients with PSA levels < 4 ng/mL, after antibiotic treatment.²⁴ The authors claimed that antibiotic therapy might decrease serum tPSA significantly, although it will not decrease the risk of PCa. Therefore, they did not recommend antibiotics for asymptomatic patients with increased PSA values. Similarly, we detected PCa in 14.3% of the antibiotic group and 18.6% of the control group, respectively, and found no difference in PCa detection. We did not detect PCa in patients with a PSA level that decreased more than 50%, nor in those below 2.5 ng/mL (*n* = 8) after antibiotic treatment. For this subgroup of patients, biopsy can be postponed, with close follow-up.

Recently, Heldwein and colleagues²⁷ investigated the effect of a 30-day trial of levofloxacin in asymptomatic patients with a raised PSA. They compared the treatment group with a considerable smaller control group without randomization and concluded that the PSA variation caused by antibiotic treatment has a limited predictive performance regarding biopsy results and thus antibiotic treatment should not be discouraged to be used in this manner.

There is still an ongoing controversy about the effect of antibiotics on f/t PSA ratio. Serretta and coworkers²⁵ showed no prominent change in f/t PSA ratio on consequent PSA levels before and after antibiotic treatment. Another study, however, demonstrated that the f/t PSA rate increased after antibiotics.⁸ On the other hand, Baltaci and colleagues²⁴ observed a general increase in the f/t PSA ratio with antibiotics except the patients who later received a diagnosis of PCa and had shown no difference in f/t PSA after antibiotics.²⁴ In our study, the f/t PSA ratio increased moderately with antibiotics compared with controls, while this change was significant in patients with benign histopathology. Therefore, the present study showed a risk for malignancy in patients without significant f/tPSA increase, even if the tPSA decreased after anti-biotherapy. Unfortunately, we were not able to predict a cutoff value for f/tPSA because of the limited number of patients measured for fPSA data. It seems clear that further large randomized studies are needed to look at the use of fPSA in clinical practice.

Conclusions

In daily practice, a remarkable number of patients with a gray-zone PSA visit urology departments. Urologists often tend to give antibiotic treatment to these patients and recheck the PSA level to avoid unnecessary biopsies. This clinical behavior, however, is still under debate. We aimed at illuminating the issue by presenting this randomized controlled prospective study.

Although we determined significant decreases in PSA levels after antibiotic treatment, the cancer detection rate is not different than controls. A decrease in PSA does not point to a decreased rate of PCa and does not support the idea of giving up the decision of biopsy. Therefore, it does not help to avoid unnecessary biopsies.

Biopsy can be postponed in a small group of patients whose tPSA values decrease below 4 ng/mL, accompanying a reduction of more than 50%. For a precise conclusion, however, larger studies are needed.

Administering antibiotics before deciding biopsy is not helpful to avoid unnecessary biopsies. Every urologist must decide, by adapting previous experience to the clinical situation of each patient individually, to make the best practice concerning biopsy, without confronting the patients with possible side effects of antibiotics.

Disclosure Statement

No competing financial interests exist.

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Address correspondence to:

Ramazan Kocaaslan, MD
Department of Urology
Kafkas University Medical Faculty
36100 Kars
Turkey

E-mail: ramizkoca@gmail.com

Abbreviations Used

ASAP = atypical small acinar proliferation
DRE = digital rectal examination
fPSA = free prostate-specific antigen
f/t PSA = free/total prostate-specific antigen
IIEF = International Index of Erectile Function
IPSS = International Prostate Symptom Score
NIH-CPSI = National Institutes of Health Chronic Prostatitis Symptom Index
PCa = prostate cancer
PSA = prostate-specific antigen
PSAD = prostate-specific antigen density
Qmax = maximal flow rate
QoL = quality of life
tPSA = total prostate-specific antigen
TRPV = transrectal prostate volume
TRUS = transrectal ultrasonography