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ROLE OF ANTIBIOTIC IN PREVENTING PROSTATE BIOPSY IN PATIENTS WITH PSA LEVEL 4-10 NG/ML WITH NORMAL DRE

Urology

Dr Ravi Ranjan* Department Of Urology And Transplant, VMMC & Safdarjung Hospital, New Delhi *Corresponding Author

Dr Rakesh Ranjan Department Of Urology And Transplant, VMMC & Safdarjung Hospital, New Delhi

Dr Nabal Kumar Mishra Department Of Urology And Renal Transplant, VMMC & Safdarjung Hospital, New Delhi

ABSTRACT

Objectives- To evaluate the antibiotic treatment in preventing prostate biopsy in patients with PSA level 4-10 ng/ml with normal DRE.
Methods- The study was a prospective randomized open-label trial including 108 patients divided into study group (58patients) and control group (50 patients) done in the department of urology and renal transplant vmmc and safdarjung hospital new delhi, from october 2016 to october 2017.Study Group patients were given ofloxacin 400 mg twice daily for 4 weeks. PSA repeated. Patients again divided into 2 groups- PSA < 4ng/ml and PSA >4 ng/ml. Standard 12-core biopsy was done in all patients. Percentage of patients positive for malignancy were observed and analyzed in both groups. Control Group patients received multivitamin capsules for 4 weeks.
Results- 26 of 58 patients (44.8%) in study group and 8 of 50 patients (16%) in control group had decrease in PSA level below 4ng/ml. Among the study group patients, cancer was found in only 02 of 26 patients (7.6%) whose repeat PSA was below 4ng/ml whereas cancer was diagnosed in 14 of 32 patients (43.7%) whose repeat PSA was above 4ng/ml.
Conclusion- 4 weeks of ofloxacin treatment significantly decreases PSA in patients with levels between 4-10 ng/ml. Biopsy can be avoided in patients with repeat PSA<4ng/ml after antibiotic treatment. Larger randomized blinded control trials are required for arriving at a definitive conclusion.

KEYWORDS

prostate, psa, dre

INTRODUCTION

Prostate specific antigen is a glycoprotein that is serine protease. Secreted primarily by prostate gland .its function may be to facilitate liquefaction of semen it is also marker of prostatic disease.it is measured by immunoassay and normal range can differ a little from laboratory to laboratory. there is no real upper limit. PSA is not cancer-specific. Its levels may be found elevated in the setting of prostate disease (BPH, prostatitis, prostate cancer) and with prostate manipulation (prostate massage, prostate biopsy). the most widely used test to detect and follow prostate cancer patients[1]. PSA elevation may indicate the presence of prostate disease, but not all men with prostate disease have elevated PSA levels[2]. Furthermore, PSA elevations are not always specific for prostate cancer .The PSA range 4-10 ng/ml is commonly referred to as diagnostic grey zone[3]. The incidence of cancer in this grey zone ranges from 20-30%if TRUS biopsy is done in.patients with psa range in this grey zone with normal dre then we are subjecting 70-80% patients to invasive procedure .Subclinical prostatic inflammation or physiological fluctuation in PSA levels have been observed in 20-40 % cases in various clinical trials. In clinical practice, many specialists use empiric antibiotic treatment followed by a repeat PSA in this group of patients; however, scientific evidence is not clear to support this approach [4,5] Many urologists use PSA density, PSA velocity, %free PSA to decide whether to proceed for biopsy or not. In our study we aim to investigate whether use of empirical antibiotic therapy in patients with grey zone PSA and normal DRE can avoid the need for unnecessary biopsies by reducing false positive PSA elevation.

METHODS

This study was conducted at Deparment of urology and renal transplant vmmc and safdarjung hospital new delhiI period from october 2016 to october 2017. Ethical clearance was taken from the Institute Ethics Committee prior to the start of the study. The study was a prospective randomized open-label trial. Patients with age >50 years, initial PSA 4-10 ng/ml with a normal DRE presenting with LUTS symptoms attributable to prostate were included in the study. Other causes of LUTS were ruled out. Exclusion criteria's were - patient presenting with acute urinary retention, patient clinically suspected of prostatitis, patients with active UTI, patients with h/o catheterization/ instrumentation/ prostate surgery or biopsy, recent use of 5-alpha reductase inhibitors/broad spectrum antibiotics and patients with hypersensitivity to fluroquinolones.

A total of 108 patients were included and divided randomly into 2 groups- a Study Group comprising 58 patients and a control group comprising 50 patients. After completing all basic investigations, a baseline initial PSA was obtained. Study Group patients were given ofloxacin 400 mg twice daily for 4 weeks. After 4 weeks, PSA was repeated. The patients were again divided into 2 groups-those with PSA <4ng/ml and those with PSA > 4 ng/ml. All patients were subjected to standard 12 core TRUS guided prostate biopsy. The Control Group patients were given only multivitamins for 4 weeks. PSA was repeated. Patients were again divided into 2 groups as done in study group. TRUS guided biopsy was done in all patients. Statistical analysis was done by analyzing 2x2 contingency tables using chi-square test and one-tailed p- value was obtained

STUDY DESIGN Prospective Randamoised Open Label Trial(total=108 patients)	
Study Group Control Group	
58 patients Ofloxacin 400 mg bd for 4 weeks	50 patients Multivitamin capsules for 4 weeks
PSA <4 ng/ml PSA <4 ng/ml	PSA >4 ng/ml PSA >4ng/ml
(26 patients) (08 patients)	(32 patients) (42 patients)
All patients subjected to standard 12 core TRUS Biopsy Results Analysed	

RESULTS

In the Study Group the Mean Age, Mean Prostate Volume, Mean PSA and Mean PSA density of the patients was 64.24 years, 46.12 cc, 7.26 ng/ml and 0.157 respectively whereas in the Control Group the values were 65.34 years, 45.16 cc, 7.08 ng/ml and 0.156 respectively. Both the groups were comparable statistically

Table 2

Variables	Study group	Control group	P value
Mean Age	64.24yrs	65.34yrs	0.3068
Mean prostate volume	46.12cc	45.16cc	0.3566
Mean PSA	7.26ng/ml	7.08cc	0.4023
Mean PSA Density	0.157	0.156	0.3723

On repeat PSA after 4 weeks, 26 of 58 patients (44.8%) in the Study Group and 08 of 50 patients (16%) in the Control Group had a drop in PSA level below 4ng/ml. The difference in drop of PSA level in Study Group as compared to Control Group was statistically significant with

a p-value of 0.0479 (calculated using chi-square test)

Table-3

	STUDY GROUP	CONTROL GROUP
Total patients	58	50
Repeat PSA <4 ng/ml	26(44.8%)	08(32%)
P-Value	0.0479(statistically significant)	

On analyzing TRUS biopsy results in the Study Group, cancer was present in only 02 of 26 patients (7.6%) among those who had a drop in PSA < 4 ng/ml after 4 weeks. Those patients whose PSA remained above 4 ng/ml, biopsy showed malignancy in 14 of 32 patients (43.7%). The decrease in the incidence of cancer in PSA<4 subgroup was statistically significant with a p-value of 0.0475.

Table-4 STUDY GROUP (58 PATIENTS)		
PSA <4 ng/ml	PSA>4ng/ml	
Total patients	26	32
Positive for cancer	02(7.69)	14(43.75%)
P- Value	0.0475(statistically significant)	

On analyzing TRUS biopsy results in Control Group, cancer was present in 02 of 08 patients (25%) among those patients who had a drop in PSA < 4 ng/ml after 4 weeks. Those patients whose PSA remained above 4 ng/ml, biopsy showed malignancy in 10 of 42 patients (23.8%).

Table-5

CONTROL GROUP (50 patients)		
PSA<4ng/ml	PSA>4ng/ml	
Total patients	08	42
Positive for cancer	02(25%)	10(23.8%)
P-Value		0.4841

DISCUSSION

Serum PSA is the most commonly used marker for prostate cancer and can rise in conditions other than cancer. The use of other parameters such as PSAV, PSAD, and % free PSA has been studied to avoid unnecessary biopsies. Prostate biopsy should be performed in patients with abnormal DRE findings, regardless of other parameters. When the PSA level is between 4-10 ng/ml, the risk of cancer in the biopsy is approximately 20-30%. There is a high percentage of patients with normal DRE in the PSA gray zone, subjected to unnecessary biopsy. This is still a problem to overcome. The purpose of our study was to determine the effect of antibiotic use in lowering PSA levels below threshold and its role in preventing unnecessary prostate biopsies. The strength of the present study is its randomized, controlled, prospective design. There are numerous studies that show that inflammation in the prostate can lead to an increase in the PSA levels and support the use of antibiotics. Carver et al. have reported 32% chronic prostatitis cases in a randomly chosen group of 300 men. Anim et al. have evaluated 331 patients and observed subclinical prostatitis in 40%. In the study of Kaygisiz et al .antibiotics were administered to 48 patients who underwent to prostate biopsies. The PSA levels decreased below 4 ng/mL in 18 (37%) of them and the biopsies of these men were negative for malignancies. In the subgroup of other 30 men prostate cancer was found in 10.8%. The Authors suggested a long course of antibiotic treatment (at least 3weeks), regardless of inflammation findings, when PSA levels are mildly high (i.e.4-10 ng/mL), in order to decide whether or not to carry out the biopsy on the basis of the subsequent re-dosed PSA results. In present study, we obtained similar results as 13 of 29 (44.8%) patients treated with antibiotics had their PSA dropped below 4 ng/ml. In the subgroup (PSA<4 ng/ml) the incidence of malignancy was only 7.6%, whereas it was 43.7% in subgroup (PSA>4 ng/ml). Bozeman et al. reported that when serum PSA had been normalized with treatment there was no longer an indication for TRUS biopsy in almost half of their 95 patients diagnosed with elevated PSA and chronic inflammation, suggesting that chronic prostatitis is an important cause of elevated PSA and that, when identified, treatment can decrease the percent of negative biopsies.n 377 patients. They showed a significant overall decrease in PSA after antibiotic treatment. Okada et al. concluded that subclinical inflammation could cause PSA elevation, and emphasized the fact that nearly half of all clinically asymptomatic men with elevated PSA levels have laboratory signs of prostatitis. They suggest that the use of antibiotics would result in a decrease in PSA levels in almost 50% of patients, thereby avoiding biopsy. This approach, however, requires careful follow-up, especially for patients whose PSA levels fail to decrease to within the normal range. Serretta et al. found no cancer present if PSA levels decreased to below 4ng/mL, or more than 70%, and postulated that biopsy can be postponed, with only a small risk of failing to detect cancer. Hochreiter et al. showed a PSA reduction in 63% of patients following antibiotic therapy, with PSA returning to normal values in 9% of cases, thus avoiding prostate biopsy. After antibiotic treatment, Potts et al. documented PSA normalization in 42% of patients. Stopiglia et al. in a prospective randomized and double-blind trial with placebo, demonstrated that PSA reduction occurred after antibiotic and placebo application, and suggested that a decrease in PSA does not indicate the absence of cancer. There are other studies which are not in favor of antibiotic use or does not show any benefit in preventing biopsies.tages associated with this approach, such as costs, toxicity, and the promotion of resistant bacterial species development that would have exposed the biopsied patient to more resistant and aggressive sepsis. Faydaci et al. demonstrated that antibiotic therapy given to patients with PSA levels higher than the threshold value has not led to a significant change in prostate needle biopsy decisions, and suggested that biopsy should be considered without the use of antibiotics in patients with high PSA values if a suspicion of prostatitis does not exist.

CONCLUSION

From the results of the present study, we conclude that 4 weeks of ofloxac in therapy decreases PSA significantly in patients with PSA levels between 4 to 10 ng/ml. PSA decreases significantly more in patients without prostate cancer. So antibiotic therapy may help select patients who have decreased probability of harboring cancer by effectively lowering PSA level below 4 ng/ml. But we should also be precocious of the adverse effects, development of bacterial resistance and increase in incidence of post biopsy sepsis with resistant bacteria. So patient should be carefully selected for antibiotic therapy.

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