THE EFFECT OF POVIDONE IODINE INTRARECTAL TO REDUCE BACTERIURIA, BACTEREMIA, AND SIRS AFTER TRUS PROSTATE BIOPSY

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ABSTRACT

Objective: *To compare the incidence of bacteruria, bacteremia, and Systemic Inflammatory Response Syndrome (SIRS) after Transrectal Ultrasound (TRUS) of prostate biopsy for the patients whom given intrarectal povidone iodine, enema, prophylactic antibiotic with given enema and prophylactic antibiotic.* ***Material & Methods:*** *A Randomised, experimental study, 20 samples of men with suspicious of prostate cancer were divided into two groups, first group (control) were given enema (dulcolax supp 10 mg) and prophylactic antibiotic (ciprofloxacin 1000 mg), second group (treatment) were given enema (dulcolax supp 10 mg) prophylactic antibiotic (ciprofloxacin 1000 mg), and intrarectal povidone iodine befotre TRUS of prostate biopsy. Urine and rectal swab culture examination were performed before biopsy then urine, blood culture, and blood leucocyte 2 days after biopsy. To assess any bacterial translocation from rectum to urinary tract, we match the post biopsy urine culture antibiogram and rectal swab culture antibiogram before biopsy. Complications and serious adverse effects were also monitored. Outcomes were assessed using Unpaired T Test and Mann Whitney depends on the data distribution and homogeneity.* ***Results:*** *There was no significant difference bacteriuria between groups (p=0.26). Bacteremia and SIRS were not found within two groups 2 days after prostate biopsy. Post biopsy bacteriuria positive patients antibiogram were compared with pre biopsy swab rectal culture antibiogram, there was no significant difference between two groups. But, significant correlation of pre biopsy rectal swab culture with post biopsy urine culture (p=0.04) were noted.* ***Conclusion:*** *Intrarectal povidone iodine before TRUS of prostate biopsy were not needed as part of rectal preparation, since enema and prophylactic antibiotic was proven to decrease the incidence of bacteriuria, bacteremia, and SIRS after TRUS of prostate biopsy. The occurrance of bacteriuria were caused by bacterial translocation from rectum to urinary tract.*

Keywords: *Prostate biopsy, povidone iodine, prophylactic antibiotic, enema, bacteriuria, bacteremia, Systemic Inflammatory Response Syndrome.*

ABSTRAK

Tujuan: *Membandingkan angka bakteriuria, bacteremia, dan Systemic Inflammatory Response Syndrome (SIRS) pasca Transrectal Ultrasound (TRUS) biopsi prostat pada pasien yang diberikan povidone iodine intrarektal, enema, dan antibiotika profilaksis dengan yang diberikan enema dan antibiotika profilaksis saja.* ***Bahan & cara:*** *Penelitian eksperimental dengan desain penelitian randomisasi acak, 20 orang penderita kecurigaan kanker prostat dibagi kedalam 2 kelompok, yaitu kelompok I (kontrol) diberikan enema (Dulcolax supp 10 mg) dan antibiotika profilaksis (Ciprofloxacin 1000 mg) saja dan kelompok II (perlakuan) diberikan enema (Dulcolax supp 10 mg), antibiotika profilaksis (Ciprofloxacin 1000 mg), dan povidone iodine intrarektal. Pemeriksaan kultur urin dan swab rektum dilakukan sebelum biopsi, lalu pemeriksaan kultur urin, kultur darah, dan leukosit darah dilakukan 2 hari setelah biopsi. Pemeriksaan antibiogram kultur urin pasca biopsi dicocokkan dengan kultur swab rektum prebiopsi untuk menilai adanya translokasi bakteri. Dilakukan monitoring efek samping selama penelitian. Hasil penelitian dianalisa dengan menggunakan Unpaired T Test atau Mann Whitney sesuai dengan normalitas dan homogenitas sebaran data.* ***Hasil:*** *Tidak didapatkan perbedaan angka bakteriuria antara kedua kelompok (p=0.26). Sementara bakteremia dan SIRS tidak didapatkan pada kedua kelompok pada 2 hari pasca biopsi prostat. Pada pemeriksaan antibiogram kultur urin pada pasien dengan bakteriuria positif pasca TRUS biopsi prostat didapatkan adanya kecocokan dengan swab rektum prebiopsi prostat, namun hasil ini tidak bermakna secara signifikan diantara kedua grup. Tetapi, saat dilakukan uji korelasi antara swab rektum prebiopsi prostat dan kultur urin pasca biopsi prostat didapatkan hasil yang signifikan (p=0.04).* ***Simpulan:*** *Povidone iodine intrarektal tidak dibutuhkan sebagai prosedur tambahan preparasi rektum sebelum TRUS biopsi prostat dikarenakan pemberian enema dan antibiotika profilaksis saja sudah cukup untuk menurunkan angka bakteruria, bacteremia, dan SIRS pasca TRUS biopsi prostat. Terjadinya bakteriuria disebabkan oleh karena translokasi bakteri dari rektum menuju saluran kemih pasca TRUS biopsi prostat.*

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Kata kunci: *Biopsi Prostat, Povidone iodine, Antibiotik profilaksis, Enema, Bakteriuria, Bakteremia, Systemic Inflammatory Response Syndrome.*

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INTRODUCTION

Prostate cancer is the most common cancer among elderly in Europe, approximately 200 among 100.000 men.[1] The incidence in Asia, especially in Japan more than 31.6 among 100.000 men are suffered from Prostate cancer.[2] The increasing survival years and decreasing mortality rate maybe related to the more accuratediagnosis of prostate cancer nowadays.[3-5] Suspicious of Prostate cancer are noted when serum Prostate Specific Antigen (PSA) are more than 4 ng/ml or nodule in digital rectal examination.[3]

Transrectal Ultrasound (TRUS) guided prostate biopsy is the gold standart for the diagnosis of Prostate Cancer. Complications of this procedure are reported including haematuria, bacteriuria, bacteremia, and sepsis.[6] Bacteriuria positive is defined by more than 105 cfu/ml colony in urine.[7] According to Crawford and Otrock, urinary tract infection after TRUS prostate biopsy 2-6%, 30-50% of the patients suffered from bacteremia.[8,9]

While the technique of needle biopsy has been refined over time, becoming more accurate and associated with fewer complications, so have methods for detecting and reporting these adverse sequelae. Urinary tract infection after prostate biopsy occurred because of direct inoculation of the bacteria from rectum through periprostatic, parenchyme, blood stream, and urinary tract.[10] Prophylactic antibiotics are reported to reduce the incidence of infection from 25% to 8%.[11] European Association of Urology (EAU) recommends Fluoroquinolone and Trimethoprim-Sulfamethoxazole single dose as prophylactic agents.[1] Enema and prophylactic antibiotics reported by Lindert et al, there was differences of urinay tract infection incidence between of enema and without enema 4% : 28%.[10] Povidone iodine as part of rectal preparation was reported by Huang et al, that combination of phosphate based enema and povidone iodine are effective against infection after prostate biopsy.[12]

The standardization of rectal preparation before prostate biopsy in Dr Soetomo Hospital in preventing urinary tract infection is important, so we are interested to study the role of enema and prophylactic antibiotics as part of rectal preparation.

OBJECTIVE

To compare the incidence of bacteruria, bacteremia, and SIRS after TRUS of prostate biopsy for the patients whom given intrarectal povidone iodine, enema, prophylactic antibiotic with given enema and prophylactic antibiotic.

MATERIAL & METHODS

All 20 men diagnosed by suspicious of prostate cancer from September until November 2016 in Dr Soetomo Hospital Hospital were invited to participate the study. This was a prospective experimental by treatment group design trial of the patients who will be performed TRUS of Prostate Biopsy given Ciprofloxacin 1000 mg (10 men control group) and enema Dulcolax intrarectal suppositoria (10 men treatment group). Indications for biopsy included an increased PSA (more than 4 ng/ml) and/or abnormal DRE. Men with sterile prebiopsy urine culture were included. Men were excluded from study if they were unable to provide informed consent, had an allergy to ciprofloxacin or iodine. At the start of the study period men were also excluded if they had received ciprofloxacin for another reason within 3 months preceding TRUS biopsy, if they had a history of bladder or prostate infection within 3 months preceding TRUS biopsy, if they had a history of UTI or sepsis after TRUS biopsy, if the had history of Diabetes Mellitus, immunosuppresif disease, renal failure, electrolyte imbalance, bowel obstructions, diarrhea, instru-mentations or DJ Stent, and positive prebiopsy urine culture.

All patients were asked to supply urine for routine culture at the time the biopsy was scheduled (before starting antibiotic prophylaxis). Patients received extended release ciprofloxacin (1.000 mg) orally at the day of biopsy. They were also instructed to instill a Fleet® enema at home approximately

1 day before the biopsy. Immediately before the biopsy, a rectal swab was taken and sent for routine culture. Patients were randomized into 2 groups. In the treatment group the anterior rectal wall over the prostate was cleansed using a thin layer of gauze soaked in povidone iodine. The examiner used his/her index finger to wipe across the prostate at least 5 times from one lateral margin to the other. Two minutes were allowed to pass between this cleansing and the start of the biopsy. The control group underwent DRE without cleansing. There was no blinding. All prostate biopsies were performed transrectally 10 core biopsy using an 18 gauge Tru-Cut® needle under ultrasound guidance after local infiltration of Lidocaine. All patients were discharged home after the biopsy and post-biopsy urine sample for culture after 48 hours. An interview was conducted 2 days after the biopsy to ascertain whether any infectious or noninfectious complications had occurred, vital sign and physical examination assessment. If a patient received medical attention in the intervening 7 days, the medical records were obtained and reviewed. The primary end point of this study was the rate of infectious complications, which was defined as a composite of 1 or more of fever, UTI and sepsis. Fever was defined as oral temperature 38^0C or greater within 48 hours after biopsy. UTI was defined as more than 100 million cfu/L in urine culture obtained 48 hours after biopsy, associated with any clinical symptoms of UTI. Sepsis was defined by the American College of Chest Physicians/ Society of Critical Care Medicine Consensus Conference as positive urine or blood culture plus 2 or more of the following criteria within 1 week of biopsy, that is temperature 38^0C or greater, or less than $36.^0$C; heart rate greater than 90 beats per minute; respiratory rate greater than 20 breaths per minute; white blood cell count greater than 12.0 or less than 4.0 109/Lm. Antibiogram results of the prebiopsy rectal culture were compared with post biopsy urine culture.

Differences between treatment groups in terms of complication rates were assessed using the Fisher exact test. Univariate analysis was performed using an unpaired t test for continuous variables and Pearson's exact 2-tailed Chi-square test for categorical variables. Variables determined to have a p 0.20 on univariate analysis were further evaluated in multivariate analysis, using logistic regression to assess for independent risk factors associated with infectious complications.

RESULTS

Total of 20 men were invited to participate in the study, of whom 10 men (50%) were in control group and 10 men (50%) were in the treatment group.

Patient characteristics are summarized in table, mean PSA was 20.84 ng/ml, and mean prostate size was 42.46 ml. There were no statistical differences between the treatment and control groups.

Table 1. Samples characteristic.

	Control group	Treatment group	Overall	p value
Mean pt age	66.54	63.51	65.02	0.07
Mean PSA	24.17	17.51	20.84	0.39
Mean prostate volume	44.37	40.56	42.46	0.35
Mean pulse	79.78	81.00	80.39	0.49
Mean temperature	36.65	36.72	36.68	0.49
Mean blood leucocyte	9.31	9.74	9.52	0.45

Table 2. Presence of bacteriuria between groups.

Bacteriuria	Group		Total (%)	p value
	Control (%)	Treatment (%)		
Positive	3 (30)	1 (10)	4	
Negative	7 (70)	9 (90)	16	0.26
Total	10	10	20	

Table 3. Results of urine culture after biopsy.

Culture results (CFU/ml)	Group		Total (%)
	Control (%)	Treatment (%)	
E coli $>10^5$	2 (20)	0	2 (10)
E coli 10^4	1 (10)	1 (10)	2 (10)
Enterobacter cloaca $>10^5$	1 (10)	0	1 (5)
Klebsiella Pneumonia $>10^5$	0	1 (10)	1 (5)
Klebsiella Pneumonia 10^4	0	1 (10)	1 (5)
Sterile	6 (60)	7 (70)	13 (65)

The clinical parameter or vital sign pre-biopsy also were not statistically differences between 2 groups, pulse (p=0.49), temperature (p=0.49), blood leucocyte (p=0.45). There were nor SIRS sign before biopsy.

The amount of more than 105 CFU/ml bacteria in urine culture 2 days after biopsy indicated positive bacteriuria. Otherwise, the presence of less than 105 CFU/ml bacterias or sterile in urine culture indicated negative bacteriuria. There were vo statistically differences of bacteruria between two groups (p=0.26).

DISCUSSION

Cleansing the rectum with povidone iodine is a safe and well tolerated intervention that is inexpensive, easy to perform and takes little additional time. However, in this prospective, we did not demonstrate a statistically significant reduction in infectious complications in patients undergoing TRUS biopsy with rectal cleansing. From the three parameters at 2 days after biopsy, there were no significant results on pulse between 2 groups (p=0.13) and (p=0.68); temperature (p=0.36) and (p=0.17); blood leucocyte (p=0.26) and (p=0.06).

According to the urine culture 2 days after biopsy, positive bacteriuria were found on control group 30% compared with 10% on treatment group, but the results were not statistically significant (p=0.26). Colonies found on positive bacteria results were E.coli 105, Enterobacter cloaca 105, and Klebsiella pneumonia 105.

Rising of the colony forming unit were count as delta CFU. Delta CFU were found in 4 patients (control groups) and 3 patients (treatment groups), but not statistically significant (p=0.49).

Antibiogram or Antibiotics sensitivity test analized the matchness of urine colony after biopsy and rectal colony before biopsy. The similar charac-

Table 4. Vital sign and laboratory examination before and after prostate biopsy.

Variable	Group	Before biopsy	After biopsy	p
Pulse (x/m)	Control	79.72 ± 4.32	83.24 ± 2.34	0.06
	Treatment	81.01 ± 3.46	81.69 ± 2.67	0.68
Temperature (^{0}c)	Control	36.65 ± 0.33	36.61 ± 0.28	0.36
	Treatment	36.74 ± 0.15	36.75 ± 0.16	0.17
Blood Leucocyte (x10 ^{3}/mm ^{2})	Control	9.37 ± 0.84	8.92 ± 1.14	0.26
	Treatment	9.74 ± 1.12	8.87 ± 0.79	0.06

Table 5. Antibiogram matchness between rectal swab before biopsy and urine culture after biopsy.

Translocations	Group		Total (%)	p
	Control (%)	Treatment (%)		
Yes	2 (20)	0	2	
No	8 (80)	10 (100)	18	0.14
Total	10	10	20	

teristic indicates translocations of the bacterias from rectum to the urinary tract.

Despite the translocations of the bacteria during the biopsy were not statistically significant (p=0.14). However, the correlations between the translocations and urine culture after biopsy was statistically significant (p=0.04).

CONCLUSION

There were no differences of bacteriuria, bacteremia, and SIRS sign 2 days after prostate biopsy, but from our study we conclude that during the biopsy, urinary tract infection was caused by bacteria translocations from rectal into the urinary tract. Rectal cleansing using povidone iodine before prostate biopsy was safe but not statistically significant to reduce the complication. The urinary tract infection after biopsy can be reduced as long as the application of enema and prophylactic antibiotics.

REFERENCES

1. Mottet N, Bellmunt J, Briers E. EAU Guidelines on prostate cancer. Eur Urol. 2015; 53: 68-80.
2. Suzuki K. Epidemiology of prostate cancer and benign prostatic hyperplasia. JMAJ. 2009; 52(6): 478–83.
3. Steuber T, Slawin KM, Lilja H. Screening and early detection of prostate cancer. Comprehensive Textbook of Genitourinary Oncology. 3rd Ed. Lippincot Williams & Wilkins. 2006; 3: 102-5.
4. Costa, Joseph. Prostate cancer screening in the PSA Era. Northeast Florida Medicine. 2007; 2: 92-94.
5. Ramey J, Halpern E, Gomella L. Ultrasonography and biopsy of the prostate. Campbell Walsh Urology. 9th Ed. Philadelphia; Saunders Elsevier. 2007; Chap 92: 2735-50.
6. Raajimakers R, Kirkels WJ, Roobol MJ, WIldhagen MF, Schrder FH. Complication rates and risk factors of 5802 transrectal ultrasound-guided sextant biopsies of the prostate within a population-based screening program. Urology. 2002; 60: 826-30.
7. Klein, Eric A, Platz, Elizabeth A & Thompson, Ian M. Epidemiology, etiology, and prevention of prostate cancer. Campbell-Walsh Urology, 9th Ed. Philadelphia; Saunders-Elsevier. 2007; Chap 90: 2704-10.
8. Crawford ED, Haynes AL Jr, Story MW, Borden TA. Prevention of urinary tract infection and sepsis following transrectal prostate biopsy. J Urol. 1982; 127; 449-51.
9. Otrock ZK, Oghlakian GO, Salamoun MM, Haddad M, Bizri AR. Incidence of urinary tract infection following transrectal ultrasound guided prostate biopsy at a tertiary care medical centre in Lebanon. Infect Control Hosp Epidemiol. 2004; 25; 873-7.
10. Lindert AK, Kabalin NJ, Terris KM. Bacteremia and bacteriuria after transrectal ultrasound guided prostate biopsy. J Urol. 2000; 164: 76-80.
11. Taylor KA, Zembower RT, Nadler BR. Targeted antimicrobial prophylaxis using rectal swab cultures in men undergoing transrectal ultrasound guided prostate biopsy is associated with reduced incidence of postoperative infectious complications and cost of care. J Urol. 2012; 187: 1275-9.
12. Huang Y, Ho D, Wu C. Modified bowel preparation to reduce infection after prostate biopsy. Chang Gung Medical Journal. 2006; 29(4): 395-400.