Effectiveness of standardized peri-operative protocol with combination of gentamicin and levofloxacin as prophylactic antibiotics on preventing infections after transrectal prostate biopsy: A retrospective study of 577 patients

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Abstract

Purpose

This retrospective study to determine the effectiveness standardized peri-operative protocol in combination with prophylactic gentamicin and levofloxacin in preventing infectious complications after trans-rectal prostate biopsy.

Material and Method

Patients were screened for prostate cancer at our out-patient department, either due to abnormal digital examination or elevated PSA level. Patients who underwent transrectal ultrasound (TRUS) guided prostate biopsy from January 2008 to December 2012 was included in this study. After using surgical code to identify the patients, charts were reviewed, and complications were recorded. Infectious complications were defined as any patient who experienced any signs systemic inflammatory response syndrome (SIRS) within 14 days after undergoing TRUS biopsy. Complications were graded according to Clavien-Dindo classification.

Results

Out of the 577 patients there were 20 patients (3.47 %) with infectious complications. Of the 20 patients with infectious complications, only four patients (0.7%) needed hospitalization due to bacteremia. Minor complications (i.e., hematuria, acute urine retention, hematospermia, etc.) were self-resolving. There were 9 positive urine culture and 4 positive blood culture with Escherichia coli (E. coli) as the predominant species. Three patients had positive urine culture for ciprofloxacin resistant strain, which was susceptible to 2nd an 3rd generation cephalosporin or amikacin. One patient had blood culture positive for extended-spectrum beta-lactamase (ESBL) E. coli infection, which was sensitive to amikacin. The infectious complication rate and number decrease each year without increase in resistant strain.

Conclusion

Our current peri-operative and post-operative protocol appears to be feasible in reducing infection complications after prostate biopsy; our complication and sepsis rate were similar compared to other English literatures. A prospective randomized controlled trial would be needed to determine if a single factor or a combination of several factors are responsible for the reduction in post-biopsy infections.

Background

The number of prostate biopsy performed increases has resulted in a rise of insignificant prostate cancer being diagnosed [1]. This increase of clinically insignificant prostate cancer has raised concern about overtreatment, but overtreatment should not be the only concern for urologist. Complications after prostate biopsy are a major concern, which could lead to severe patient morbidity and even mortality. Post-operative complications of prostate biopsy can range from self-resolving hematuria to life threating

septic shock, which requires intensive care unit. The rate of infectious complications reported in literatures after transrectal ultrasound (TRUS) guided prostate biopsy has been as high as 11% and severe sepsis requiring intensive care being less than 1% [2, 3]. Guidelines and randomized controlled trials recommend the use of fluoroquinolone in prostate biopsy [4, 5], but incidences of quinolone-resistance strain infection has also been on the rise [6–11]. Efforts to reduce post TRUS biopsy infections have led to numerous studies focusing on either peri-operative preparation or prophylactic antibiotics [4, 12–16]. Addressing the problem with increase in quinolone resistance, studies advocate the use of pre-operative anal swab culture guided antibiotic prophylaxis, peri-operative povidone-iodine anal preparation, and formalin disinfection of biopsy needle [8, 10, 12, 13, 15, 17]. In this study, we review the results of our standard protocol in preventing post-biopsy complications.

Method

Patients

Changhua Christian Hospital institutional review board approved retrospective study (IRB number: 141114). A single doctor (PHC) retrospectively identifies all the patients using surgical code (T79401C) at our hospital from January 2008 to December 2012. Medical records were reviewed, and all complications were recorded and analyzed. Infectious complications related to TRUS biopsy is defined as any patient who experience systemic inflammatory response syndrome (SIRS) symptoms within 14 days after biopsy.

Procedure routine and post-operative regimen

A standardized operating room was used for all prostate biopsy and patients will either undergo with local or general anesthesia. After performing “time-out”, the patient will receive a single dose of gentamicin sulfate 80 mg (Ensafe industrial Co. Ltd. Hsin Ying City, Tainan City) intra-muscular injection 30 minutes before procedure. For patients under local anesthesia, we place the patient in lateral decubitus position and lithotomy position for patients under general anesthesia. Peri-anal region is disinfected with povidone-iodine only and intra-rectal cleaning is done with a combination of povidone-iodine mixed with 2% xylocaine jelly (AstraZeneca global). Patient positioning and disinfecting was described in more detail in our previous study [18]. After ultrasound probe is inserted transrectally, local anesthesia was injected at the base of the prostate then 12-core biopsy will be performed. Post-operative regimen after biopsy includes: magnesium oxide tablet 500 mg TID, acetaminophen 500 mg TID, levofloxacin 500 mg QD, and tranexamic acid 500 mg TID (optional, depend on attending physician) is then prescribed for 3 days. Patients were then educated about post-operative complications (hematuria, urine retention, infection, etc.) before leaving the hospital and were told to promptly seek medical attention in case of persistent symptoms with medication use.

Patient evaluation

Detailed pre-operative medical records and any post-operative complications within 14 days were recorded and analyzed. Clavien-Dindo grading system was used to grade post-operative complications.

Results

Patient Characteristics and peri-operative data

Five hundred seventy-seven patients who underwent TRUS prostate biopsy at our hospital in the 5 years span from 2008 to 2012 were identified. Most of our patients (498) underwent local anesthesia (Table 1). Two hundred forty-eight patients were diagnosed with prostate cancer (43%) with the average Gleason score of 7.17.

Table 1

Basic data (n = 577)	Average
Age (year)	72.76
Weight (kg)	66.49
Height (cm)	166.96
BMI	24.46
Form of anesthesia	
Local	498
IVGA	79
Average PSA	166.01
Averaga prostate volume	40.01
Average transitional zone volume	18.75
Average number of biopsy cores	11.39
Benign : Malignant	329 : 248
Average Gleason score	7.17

Complications

Complications were divided into minor (Clavien-Dindo grade 1) and major (Clavien-Dindo grade 2 or higher) complications which are shown in separate tables (Tables 2 and 3). Eighty-seven patients had minor complications (15%, Table 2) and 21 patients had major complications (3.6%, Table 3). The most common minor complications were hematuria, urine retention and dysuria (6.9%, 2.6%, and 2.1% respectively). All minor complications were either self-resolving or easily managed with medication or temporary urine catheter. One patient experienced severe anal bleeding needing blood transfusion and

hospital admission and was discharged 2 days later without further morbidities. Of the 20 patients (3.4%) with infectious complications, twelve (2.1%) were managed at ER with intravenous antibiotics, four (0.69%) required hospital admission due to severe sepsis bacteremia, two (0.35%) were treated as outpatient with oral antibiotics and two (0.35%) were in-hospital consultation cases for cancer survey due to elevated PSA. Thirteen of twenty infectious complications (65%) showed positive urine and/or blood culture. Eight patients (40%) have both positive urine and blood culture. E. coli is the predominant species (5 urine culture and 3 blood culture, Table 4). Four patients had quinolone resistant E. coli in including 1 patient with ESBL (extended spectrum Beta-Lactamase) E. coli. The quinolone resistant strain E. coli was sensitive to amikacin and 2nd or 3rd generation cephalosporin. The incidence rate for E. Coli bacteremia after transrectal ultrasound-guided prostate biopsy in our series is 0.52% (3 of 577 patients) and quinolone resistance bacteremia is 0.17% (1 of 577 patients). The number and incident rate infectious complications has decrease after instilling our standardized protocol (Fig. 1). Post-biopsy number and incident rate decrease throughout the years even with the increase in the number of biopsy core and number of biopsies. None of our patients had infectious related mortality.

Table 2
minor complications (Clavien-Dindo grade 1)

Minor complications (n = 87)	Incident	Incident rate
Hematuria	40	6.93%
Acute urine retention	15	2.60%
Dysuria	12	2.08%
Anal bleeding, self resolving	9	1.56%
Hematospermia	6	1.04%
Perineal / anal pain	2	0.35%
Frequency	1	0.17%
Insomnia	1	0.17%
Painful stool passage	1	0.17%

Table 3
Major complications (Clavien-Dindo grade 2 or higher)

Major complications (n = 21)	Incident	Incident rate
Severe anal bleeding, requiring transfusion	1	0.17%
Infectious complications (n = 20)		3.47%
ER observation	12	2.08%
Ward admission	4	0.69%
OPD treatment	2	0.35%
In-hospital consultation	2	0.35%
Sepsis with bacteremia	4	0.69%
Prostatitis	2	0.35%
Epididymitis	1	0.17%
(+) Blood culture	4	0.69%
(+) Urine culture	10	1.73%

Table 4
Positive culture results in infectious complications

Urine culture	N	Incident rate
E. Coli (no FQ resistance)	2	10%
E. Coli (FQ resistance)	3	15%
KP	1	5%
Enterococcus	1	5%
GNB	2	10%
Blood culture	N	
E. Coli (no FQ resistance)	2	10%
E. Coli (FQ resistance)	1	5%
KP	1	5%

Discussion

Since every invasive procedure carries the risk of complications, surgeons must take steps to minimize the chances of complications whenever possible. From the early 2000 to early 2010, there have been

several studies focusing on emergence of infectious complications with resistant strain species after prostate biopsy [6–9]. As infection rate with drug resistant strain bacteria increases, several studies have been conducted to reduce post biopsy infections [10, 12, 13, 15–17]. These studies can be group into pre-operative anal culture, prophylactic antimicrobials (either pre-operative and/or post-operative), and peri-operative preparations (i.e., beta-iodine rectum cleaning, formalin disinfection of biopsy needle). Taylor et. al demonstrated that patients with targeted prophylactic antibiotics using pre-biopsy rectal swab culture had a lower incidence of infectious complications compared to empirical prophylactic antibiotics group [17]. The reported incidence of sepsis from prostate biopsy ranges from 0.1 to 2% with Young, et al reported an incidence rate of quinolone resistance E. Coli to be < 1% [11]. Even though Taylor et. al demonstrated that pre-operative anal swab culture is useful in lowering medical cost, routine wide-spread use of anal swab culture might take a toll on the ever-growing laboratory department due to the current COVID pandemic. In combination with the low incidence rate of quinolone-resistance E. coli bacteremia in our current series and previous studies, we recommend anal swab culture directed prophylactic antibiotics in patients with known risk factors for post-biopsy infection [7, 11, 18, 19]. AbuGhosh et. al saw a 42% relative risk reduction of infectious complications with povidone-iodine rectal cleaning [13]. Bacterial inoculum on biopsy needle is also a concern and Issa et. al address the concern with their study of formalin disinfection of biopsy needle which resulted in 2 infectious complications out of 1642 patients [15]. In our previous study of 2 different era of prostate biopsy at our department, we noticed a decreased in infectious complications from 11–1% using a standardize protocol of anal cleaning and prophylactic antibiotics [18]. Pre-operative cleaning of anal mucosa with povidone-iodine with the combination of peri-operative cleaning of biopsy needle seems to be safe and effective in preventing infectious complications. In the recent years, trans-perineal prostate biopsy (TPPB) has been emerging as the approach of choice due to low incidence of sepsis (0.1 vs 0.9%) [20, 21]. Even though TPPB offers lower incident rate for infection, TPPB is not without limitations [22–24]. Since most urologist initially learn transrectal biopsy, TPPB procedure will be less familiar and re-education on the procedure will be required. Part of re-education include investing in new equipment for TPPB, such as brachytherapy grids. As opposed to most TPPB which requires general anesthesia, transrectal biopsy are often performed during office setting and under local anesthesia. General anesthesia has its associated cost and complications. Even though TPPB has lower incident of infectious complications, TPPB is more associated with lower urinary tract complications mainly urine retention [25]. TPPB is not 100% free of infectious complications, the reported sepsis rate of < 1% [22–25]. Diagnostic rate for prostate cancer is another concern for TPPB. In randomized trials, the detection rate differences does not reach statistically significant but the detection rate is lower for trans-perineal group [22, 23]. Recent advances in technologies can help improve detection rate with either approach, such as pre-biopsy MRI, cognitive biopsy, MRI fusion, but at an added cost for the patient and the hospital. Due to the vast combination of clinical scenario and patient conditions, there is no single approach or method that can prevent all these vast range of combinations from infectious complications. Initially, we can assess the current state of antimicrobial resistance in hospital and region. Also need to assess the patient's risk for antimicrobial resistance. If the region is more prone to quinolone resistance and/or patient has risk factors for quinolone resistance strains, a smart bomb-like strategy with anal swab culture targeted prophylactic

antibiotics prior to trans-rectal biopsy seem reasonable. If doctor is proficient and/or facility has access to perineal biopsy, these high-risk patients would also benefit from the lower risk of infection. Peri-operative disinfection with povidone-iodine also provide a safe, cost efficient and effect form of infection prevention. The standardized protocol of pre- and post-operative antibiotics with combination of intra-operative preparation, we achieved decreasing incidence of infectious complications each year.

Conclusion

In this study, we offer a standardized protocol for trans-rectal biopsy that helps in lowering post-biopsy infectious complications. With a standardized protocol in place, clinical urologists also need to be adaptive to different situation and offer different approach methods to minimize risks of post-biopsy infection. In high-risk patients, a targeted biopsy or trans-perineal biopsy will be helpful in lowering infectious complications. Longer retrospective data might reveal if our standardized protocol can withstand the test of time. A randomized controlled trial would also offer insight into whether one or multiple factors are responsible for reduction in infectious complications.

Abbreviations

TRUS: transrectal ultrasound

SIRS: systemic inflammatory response syndrome

IRB: institutional review board

ESBL: extended spectrum Beta-Lactamase

Declarations

Ethics approval and consent to participate

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Due to the retrospective nature of the study, informed consent has been waived for this study but all patients were informed about the surgical intervention consent form during out-patient clinics.

Changhua Christian Hospital Institutional Review Board approved the study (IRB reference number: 141114).

Consent for publication

Not applicable

Availability of data and materials

The datasets for this article are available in the Changhua Christian Hospital (Changhua City, Taiwan) Medical Records Room data base repository. The datasets analyzed in this study is available from the corresponding author upon request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Treatment of patients, data collection and assessment: HCC, JL, MYY, CCC, JTC, PHC

Data collection and statistical analysis: PHC

Manuscript written, discussion, revision: PHC, HCC, JL, MYY, CCC, JTC

Study coordination: HCC, JL, MYY, CCC, JTC, PHC

Study conception and design: PHC, HCC

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Disclosures

This manuscript has not been previously published or submitted elsewhere for publication and will not be sent to another journal until a decision is made concerning publication

Conflict of interest

None of the authors has conflict of interest

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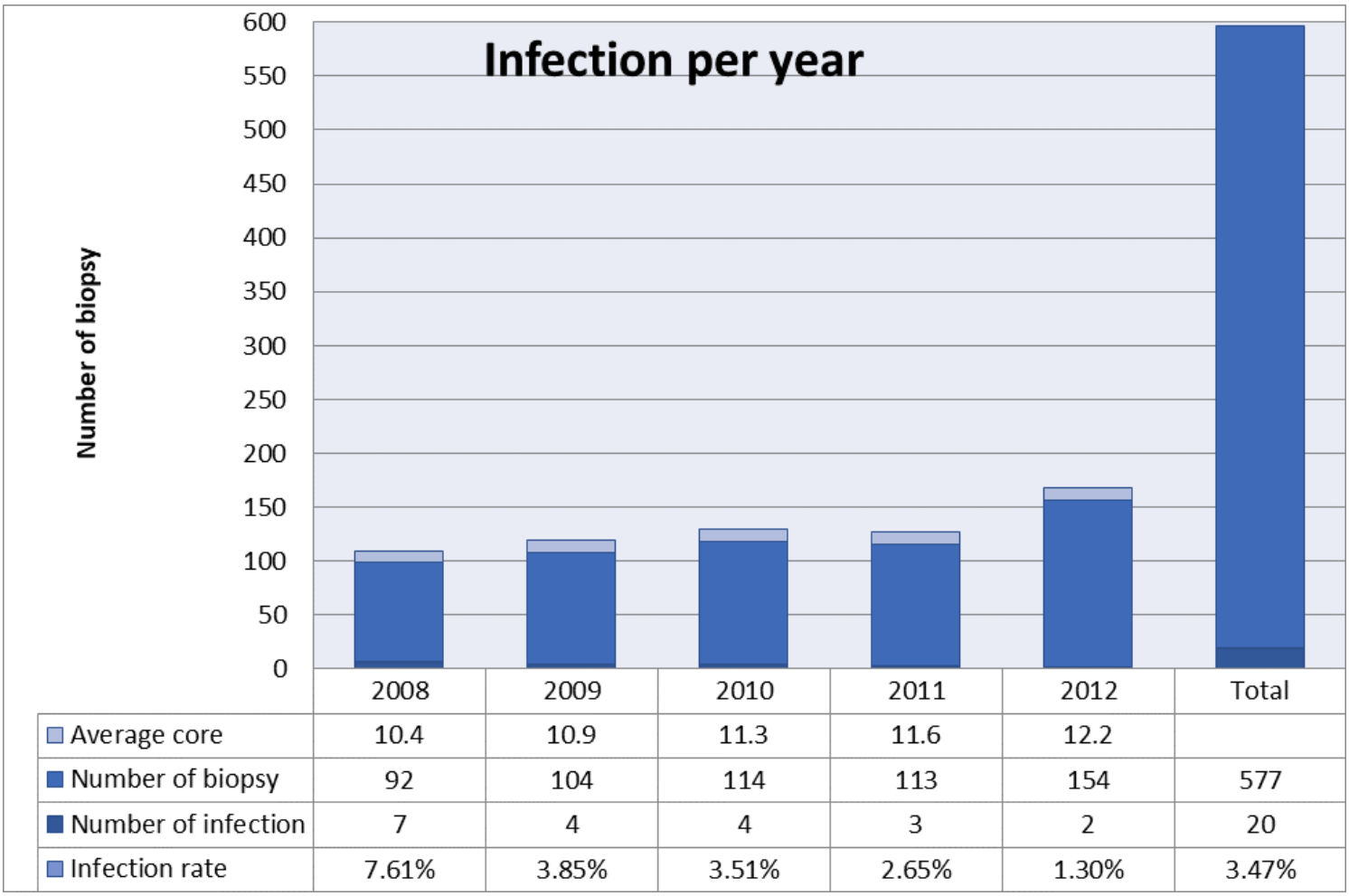
Figures



	2008	2009	2010	2011	2012	Total
Average core	10.4	10.9	11.3	11.6	12.2	
Number of biopsy	92	104	114	113	154	577
Number of infection	7	4	4	3	2	20
Infection rate	7.61%	3.85%	3.51%	2.65%	1.30%	3.47%

Figure 1

infection complications per year