Variability of transrectal ultrasound-guided prostate biopsy prophylactic measures

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Introduction: *To assess the variability of pre-prostate biopsy prophylaxis among American urologists.*
Materials and methods: *A survey was electronically mailed to 3355 urologists around the country. Urologists were surveyed on their antibiotic prophylaxis choice, the route and duration of antimicrobial prophylaxis. Additionally they were questioned about their knowledge of local antimicrobial resistance and if rectal enemas were routinely used.*
Results: *There were 679 (21%) responses to the survey. The survey revealed differences in pre-prostate biopsy prophylaxis among urologists. Ten different classes of antibiotics were used orally, 4 classes intramuscular, 5 classes intravenous, and there was also 14 different duration regimens.*
Conclusion: *Despite the initiation of the 2008 American Urological Association Guidelines on this topic, there still is a lack of uniformity in prostate biopsy prophylaxis.*

Key Words: infection, prophylaxis, prostate, biopsy

Introduction

Approximately 800,000 transrectal ultrasound-guided prostate biopsies are performed annually in the United States, making it one of the most commonly performed procedures.[1] Prior to antibiotic prophylaxis, infection rates following prostate biopsy ranged from 16%-100%.[2-5] Following the routine use of prophylactic antibiotics the incidence of post-biopsy urinary tract infections decreased, to as low as 1.7%.[6] However, recent reports have indicated that infections are on the rise.[7] Data from the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial reported an incidence of biopsy-related complications of 69 per 10000 cases.[8] Recently a study by Loeb and colleagues reported a hospitalization rate of 6.9% following prostate biopsy.[9]

Prophylactic techniques are performed with the goal of decreasing biopsy-related infections. Unfortunately, as noted above, infection rates are increasing. To fully understand this problem, it is imperative to first catalog what prophylactic measures are being employed. Shandera et al performed the last major survey on this topic in 1998.[10] The present study surveys American urologists' practice patterns, specifically antibiotic agent of choice, number of antibiotics used, route of delivery, duration of prophylaxis and rectal enema use.

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Materials and methods

Survey administration

An electronic survey was mailed out via Survey Monkey to 3300 urologists in the United States. Urologists from all 50 states and the District of Columbia were randomly chosen to be surveyed. Each potential respondent received a single email containing a unique link to complete the survey. All potential participants were informed of the voluntary nature of their participation and their responses were kept confidential. No financial compensation was given in exchange for participation. The survey was active from November 2011 to December 2011.

Survey design

A previously validated survey on prophylaxis techniques prior to prostate biopsy was used as a model for our survey.[10] Urologists were questioned about their knowledge of local bacterial resistance, their antibiotic prophylaxis choice, the route of administration, the duration of antimicrobial prophylaxis, the time from drug delivery to biopsy, and if rectal enemas were routinely used.

Results

A total of 679 (21%) responses were received. Fifty-five urologists indicated they do not perform prostate biopsies, 20 urologists did not complete the survey, and were excluded from analysis. Respondents were distributed throughout all seven AUA regions. Ninety-one percent of respondents were male. Ninety-eight percent were attending physicians in practice and the majority (66%) of responders had been in practice for more than 10 years. Fifteen percent of respondents reported not being aware of the local bacterial resistance patterns. Seventy-nine percent routinely gave an enema prior to biopsy.

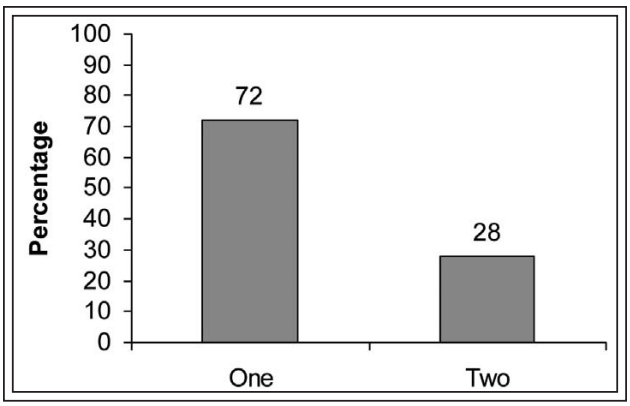

Figure 1. Do you use one or two drugs for prophylaxis?

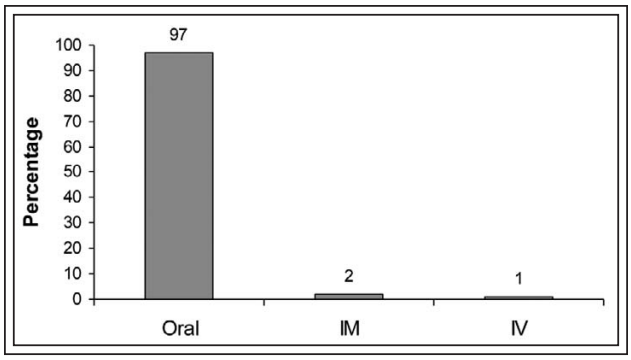

Figure 2. If you give only one antibiotic by which route do you administer it?

One antibiotic

Seventy-two percent of respondents reported giving only one antibiotic prior to biopsy, Figure 1. The overwhelming majority (97%) reported oral dosing. Two percent administered the antibiotic intramuscularly (IM) and 1% intravenously (IV), Figure 2. The oral antibiotic most frequently used was a fluoroquinolone (94%). Gentamicin was the most commonly administered IM (63%) and IV (50%) antibiotic.

Two antibiotics

Twenty-eight percent reported using two antibiotics. Eighty-seven percent used IM and oral routes of delivery, while 13% used IV and oral, Figure 3. For patients receiving IM and oral prophylaxis, the most popular combinations were gentamicin IM and an oral fluoroquinolone (68%). Twenty percent were given a third generation cephalosporin IM and an oral fluoroquinolone. Thirteen percent of urologists used IV and oral prophylaxis, with the most popular combination (43%) being an IV and oral fluoroquinolone. Thirty-three percent were given gentamicin IV and an oral fluoroquinolone.

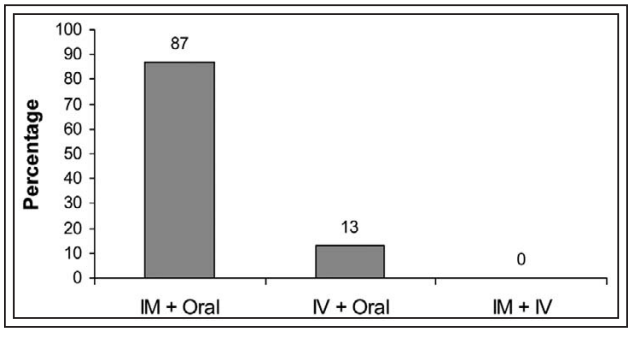

Figure 3. If you give two antibiotics by which route do you administer it?

Duration of prophylaxis

Five hundred sixty- eight (94%) of urologists reported using oral antibiotics. Of these 568 urologists, 63% reported starting antibiotics the day prior to biopsy and 37% reported starting the day of the biopsy. Three hundred seventy-five (66%) reported giving antibiotics in the days following the procedure. Post procedure, 221 (59%) reported giving it for 1 day, 71 (19%) for 2 days, 53 (14%) for 3 days, and 30 (8%) for more than 4 days. The majority of urologists overall 59%, 356 reported waiting greater than 60 minutes after prophylaxis administration before performing the prostate biopsy.

Discussion

The incidence of infection following prostate biopsy has been increasing. Nam and colleagues[11] found the 30 day hospitalization rate following prostate biopsy increased from 1% to 4.1% between 1996 and 2005. Loeb and colleagues examined a 5% random sample of Medicare participants in the Surveillance, Epidemiology and End Results database from 1991 to 2007 and found that men who had received a prostate biopsy within 30 days had an overall hospitalization rate of 6.9%.[9] This represented a 2.65 fold increased risk over a control population (2.7% hospitalization rate). They also observed a steady, yet significant, increase in prostate biopsy-related infections over the course of the study period.

In addition to the morbidity of prostate biopsy-related infections, the associated healthcare costs should also be considered. In a study by Adibi and colleagues, the authors estimated the cost of a hospital admission for a post-biopsy infection to be $5900.[12] If the hospitalization rate is 6.9% following prostate biopsy, as outlined in Loeb's study[9], then the potential burden to the healthcare system would exceed $300 million dollars annually based on an average of 800,000 annual biopsies.[1] In light of this rise in prostate biopsy infections we sought to evaluate urologists' prophylaxis choices prior to prostate biopsy.

Regarding class of antibiotic, 68% of respondents reported using only an oral fluoroquinolone. The American Urological Association (AUA) Best Practice Statement on Urologic Surgery Antimicrobial Prophylaxis recommends fluoroquinolones as the antimicrobial agent of choice.[13] However, the AUA's recommendation was largely based on randomized control studies published over 10 years ago.[14,15] More recent studies have found that many post-biopsy infections are due to fluoroquinolone resistant organisms. Feliciano and colleagues found that half of their recorded infections following prostate biopsy were due to fluoroquinolone resistant bacteria.[16] Similarly, Zaytoun and colleagues reported that 28% of the patients who had a post-prostate biopsy infection had a culture positive for fluoroquinolone resistant *Escherichia coli*.[17] Mosharafa et al found that prior fluoroquinolone use was the most significant risk factor for acute prostatitis following a prostate biopsy.[7] In addition, 85.7% of isolated gram-negative organisms in urine and/or blood cultures from prostatitis patients were fluoroquinolone resistant.

The increase in fluoroquinolone resistance has led some to advocate a more intensive antibiotic regimen. Cormio and colleagues compared IV piperacillin/tazobactam to ciprofloxacin and found the piperacillin/tazobactam group had a lower rate of bacturia following biopsy.[18] Batura and colleagues studied adding IV amikacin to their antibiotic regimen and found a significantly decreased bacteremia rate.[19] In our study when multiple antibiotics were used the most frequent were IM gentamicin and oral fluoroquinolones or IV fluoroquinolones and oral fluoroquinolones.

Multiple studies have addressed how long antibiotics should be given following prostate biopsy. Aron et al found that a single dose of a fluoroquinolone was equivalent to a 3 day regimen.[15] Two randomized trials compared fluoroquinolone use the day of biopsy versus the day of biopsy and 48 hours after and found no difference in infection rates.[20,21] In the present survey, 77% of urologists gave antibiotics beyond the day of biopsy (59% 1 day after and 41% more than 1 day after).

Seventy-nine percent of urologists reported using rectal enemas prior to prostate biopsy. The data on their efficacy is equivocal. Multiple studies have shown no benefit.[22,23] Mosharafa and colleagues observed a non-significant trend ($p = 0.61$) towards decreased prostatitis with an enema use.[7] Two publications reported a decreased risk of bacteremia and bacteriuria with pre-biopsy enema.[24,25]

There have been two previous studies regarding antibiotic prophylaxis by American urologists. Shandera and colleagues published the results of a survey completed by 568 urologists in 1998.[10] Ninety-three percent of urologists only used oral antibiotics, 4% only IM, and 3% both oral and IM prophylaxis. Fluoroquinolones, either alone or in combination, were used by 92% of urologists. Sixty-four percent of respondents reported an antibiotic duration of more than 1 day. Fleet enemas were used by 81% of urologists. Davis and colleagues published the results of a similar survey in 2002.[26] Of the 88 respondents,

TABLE 1. **Comparison of prior surveys on pre-prostate biopsy prophylaxis to this survey**

Study	Shandera et al[10]	Davis et al[26]	Present survey
N respondents	568	88	624
Use of exclusive oral antibiotics (%)	93	83	70
Exclusive use of oral fluoroquinolones (%)	*	67	66
IM + oral (%)	*	15	24
IV + oral (%)	*	0	4
Use of antibiotics greater than 1 day post-procedure (%)	64	41	41
Rectal enema use (%)	81	79	79

*not reported
IM = intramuscular; IV = intravenous

83% reported giving only an oral antibiotic prior to biopsy, with 81% giving a fluoroquinolone. Fifteen percent reported giving a combination of a fluoroquinolone and an aminoglycoside. Forty-one percent of respondents reported giving antibiotics for more than 1 day and 79% of respondents gave an enema prior to biopsy.

A comparison of those studies and the present survey is summarized in Table 1. In the present survey, fewer urologists reported giving oral antibiotics alone and the use of broad spectrum IV or IM antibiotics in combination with an oral increased. Additionally, despite no clear evidence of efficacy in the literature, the use of rectal enemas remained consistently high.

The results of the present survey revealed that 10 different classes of antibiotics were used orally, 4 classes IM, 5 classes IV, and there was also 14 different duration regimens. This extreme variability despite existing guidelines on the topic may be directly attributed to the recent rise in post prostate biopsy infections and sepsis. Furthermore, as compared to previous surveys on the topic there is an increase in the use of broad spectrum IV and IM antibiotics.

This study was limited by the fact it was designed to give an overview of the antibiotic choice of American urologists and cannot comment on the efficacy of any of the reported regimens. Additionally, the survey had a low response rate of 21%. This likely reflects the limitations of using an electronic medium of distribution to a large dataset of contact information that may be outdated. Due to the anonymous nature of the electronic distribution, we could not ensure that the survey reached its intended recipient. Subsequently, our sample of respondents may represent a non-response bias. However, our sample was distributed throughout all AUA sections and the number of respondents was high (679). Therefore, we believe that this study may be extrapolated to represent the diverse population of urologists nationwide despite the stated potential response bias.

Conclusion

The AUA guidelines on antimicrobial prophylaxis were released in 2008. Since their publication the infection rates following prostate biopsy have increased. The present study found that there continues to be a wide array of prophylactic regimens being used by American urologists, with the majority incorporating fluoroquinolones despite rising resistance rates. □

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