Antibiotic prophylaxis and complications following prostate biopsies

A systematic review

Klemann, Nina; Helgstrand, John Thomas; Brasso, Klaus; Vainer, Ben; Iversen, Peter; Røder, Martin Andreas

Published in:
Danish Medical Journal

Publication date:
2017

Document version
Publisher's PDF, also known as Version of record

Antibiotic prophylaxis and complications following prostate biopsies – a systematic review

Nina Klemann[1], John Thomas Helgstrand[1], Klaus Brasso[1], Ben Vainer[2], Peter Iversen[1] & Martin Andreas Røder[1]

ABSTRACT

INTRODUCTION: Transrectal ultrasound-guided biopsies (TRUS-gb) are associated with both mild and serious complications. Prophylactic antibiotics reduce the risk of septicaemia and mortality; however, no international consensus exists on the timing and duration of antibiotics, including the optimal drug strategy. We reviewed the current evidence supporting use of prophylactic antibiotics and the risk of complications following prostate biopsies.

METHODS: This review was drafted in accordance with the Prisma Guidelines. The PubMed, Embase and Cochrane databases were searched.

RESULTS: A total of 19 eligible trials were identified. One trial demonstrated a significant reduction in the risk of infection after biopsy and reported that oral ciprofloxacin as either a single-dose or a three-day regimen was superior to oral chloramphenicol and norfloxacin. Of three studies investigating the timing of the first dose of antibiotic, one study found that administration 24 h before biopsy versus administration immediately before reduced the relative risk of post-biopsy infection by 55%. Seven studies compared different durations of antibiotic prophylaxis. None showed any benefit from continuing prophylaxis beyond a single dose or a one-day regimen.

CONCLUSION: Evidence supporting a specific antibiotic regimen for TRUS-gb prophylaxis is scarce. Widespread use of fluoroquinolone prophylaxis may be associated with an increase in resistant *Escherichia coli* strains, posing a potentially major health issue in the future.

During the past three decades, the epidemiology of prostate cancer (PCa) has changed dramatically and, excluding non-melanoma skin cancer, PCa is now the most common male cancer diagnosis in most Western countries [1]. The 4-8% annual increase in PCa incidence observed in high-resource countries is mainly attributed to a growing awareness of PCa and the widespread use of prostate-specific antigen (PSA) testing. Prostate biopsy remains the mainstay in the diagnosis of PCa, and systematic transrectal ultrasound-guided biopsies (TRUS-gb) of the prostate is the gold standard technique. The procedure may be associated with mild or serious adverse events, most importantly infectious complications [2-4], but no international consensus exists on the use of antibiotics prior to and after TRUS-gb. In Denmark (DK), approximately 10,000 TRUS-guided biopsy sets are performed annually, but the frequency of complications and infections remains unknown. We systematically reviewed the current evidence of post-biopsy complications and the use of prophylactic antibiotics and discussed the use of antibiotic regimens in DK.

METHODS

This review was drafted in accordance with the Prisma Guidelines [5]. Three different searches in the PubMed, Embase and Cochrane databases were performed using the search strings:

1: biopsy AND prostate AND (prophylaxis OR prophylactic) AND antibiotic
2: biopsy AND prostate AND infection AND bacteria
3: biopsy AND prostate AND resistance.

In PubMed, the limits set were “adult: 19+ years”, and “humans”. In Embase, limits were “humans”, “adult 18 to 64” and “Aged 65+ years” and publication year 2005-2015.

In the PubMed and Cochrane databases, publication year was limited to the period from 2005 to the present was used. Only randomised controlled trials (RCT) reported in English and full-text articles were included, but prospective trials originating from Europe were screened in order to further examine regimens and recommendations of countries in relative proximity to DK. Finally, we identified the literature originating from DK.

Based on titles, all relevant abstracts were read, and the selected articles were evaluated for eligibility. A flow chart is presented in **Figure 1**. All retrospective studies, reviews and case reports were excluded, unless originating from DK, as were papers deemed irrelevant because of their subject, e.g. papers on other cancer forms than PCa.

All Danish urology departments performing TRUS-gb were identified and contacted to obtain information about biopsy technique and use of prophylactic antibiotic strategy, including antibiotic dose and duration used. For information about development of resistant bacterial strains in DK, we reviewed the DANMAP, a

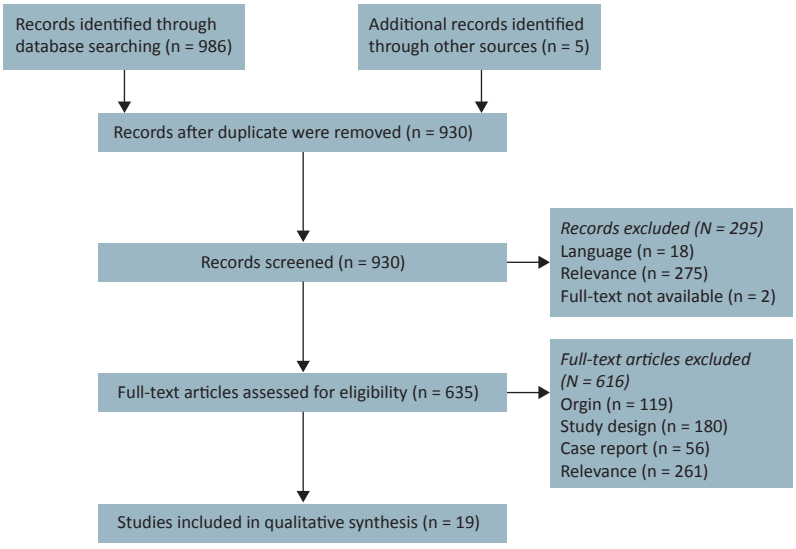
SYSTEMATIC REVIEW

1) Copenhagen Prostate Cancer Center, Department of Urology, Rigshospitalet
2) Department of Pathology, Rigshospitalet, Denmark

Dan Med J 2017;64(1):A5323

FIGURE 1

Flow chart presenting the literature selection process.



KEY POINTS

Transrectal ultrasound-guided biopsy (TRUS-gb) of the prostate is considered the mainstay in the diagnosis of men at risk of harbouring prostate cancer.

Both the annual number of biopsy sets and the number of biopsy cores per biopsy set have increased over time in Denmark.

TRUS-gb is associated with both mild and serious complications, ranging from dysuria to sepsis and death.

Prophylactic antibiotics reduce the risk of infectious complications after TRUS-gb, but no national or international consensus on the use of antibiotic prophylaxis exists.

Frequent use of antibiotics in the general population, development of resistant bacteria and the fact that many patients undergo re-biopsies complicate the introduction of a uniform, prophylactic antibiotic strategy.

Danish programme for surveillance of antibiotic consumption and bacterial resistance in humans.

RESULTS

We identified 19 eligible trials: ten randomised trials, seven prospective trials and two retrospective trials. Four of the randomised trials originated from Europe, two from Asia, one from North America, two from South America and one from Canada. Two retrospective studies from DK were identified. A total of 295 papers were excluded; 18 were not available in English, 275 were irrelevant (e.g. case reports) and two papers were not available in full text. The study characteristics are listed in **Table 1**.

Post-biopsy complications were described in all of the included trials. *Non-infectious* complications, regardless of study type, included haematuria (14.3-62.3%), haemospermia (17.8-59.1%) and rectal bleeding (4.8-21%) [6-13]. The post-biopsy *infectious* complications ranged from post-bioptic positive urine cultures (0.9-18.1%), urinary tract infection (UTI) (0.8-9.3%), prostatitis (0.67-0.7%), epididymitis (0.4%) and dysuria (0.4-13.3%), to more severe complications such as fever (0.3-8.6%), need for hospitalisation (0.4-3.1%), sepsis (0.17-5.7%), septic shock (0.2-0.45%) and death (0.2%) [6, 7, 9-22].

Type of antibiotic

Five trials comparing different prophylactic antibiotic regimens were identified. In these regimens, the administration of antibiotics was initiated between 30 minutes and 24 hours prior to biopsy.

All of the five trials were RCTs. The first study randomised patients to either tosufloxacin or levofloxacin orally, both in a two-day administration [9]. The second study randomised patients into three groups receiving either a single dose of ceftriaxone i.m., a single dose of ciprofloxacin (CFLX) orally or a three-day course of CFLX orally [11]. The third study randomised patients into four arms receiving CFLX or levofloxacin as either single doses or as a three-day regimen [8]. The fourth study randomised patients to receive CFLX with or without the addition of a periprostatic injection of cephalosporin [12]. None of the studies demonstrated any differences in the infectious or non-infectious complication rates following TRUS-gb. However, the fifth study showed that quinolones are superior to chloramphenicol in reducing infectious complications [22]. The trial randomised patients in a four-armed study comparing oral CFLX as either a single-dose or a three-day regimen to chloramphenicol and norfloxacin orally, both as three-day regimens. The study found a significant reduction in the risk of post-biopsy infections favouring CFLX both as single-dose and as three-day regimen compared with chloramphenicol ($p = 0.0003$) and norfloxacin ($p = 0.03$).

Route and timing of administration of prophylaxis

No studies have compared intravenous to oral administration of prophylactic antibiotics prior to TRUS-gb. We identified three studies investigating the importance of the timing of the initial dose of antibiotic. A prospective trial evaluated two different antibiotic strategies during two consecutive years. In the first year, the first dose of antibiotic was administered immediately before the biopsy procedure, and in the second year the antibiotic was administered 24 hours before biopsy. The study concluded that administration 24 hours before biopsies resulted in a relative risk reduction for post-biopsy infection of 55% compared with antibiotics just prior to the procedure [15].

Another study randomised patients to oral levofloxacin 500 mg given either 30-60 minutes before TRUS-gb or immediately after the bioptic procedure, but found no differences in infectious complications [7]. Finally, a prospective trial compared a single dose of oral CFLX 750 mg given either two hours before or in conjunction with the biopsy procedure, but failed to demonstrate a significant impact on the risk of infectious complications [13].

Duration of prophylaxis

Several studies have compared the duration of antibiotics during TRUS-gb administered either as a single dose, a one-day regimen or a three-day regimen. One study [14] compared a single dose of 400 mg norfloxacin with a regimen of 400 mg immediately before the biopsies followed by three days of 400 mg norfloxacin twice daily. No statistically significant difference in the risk of complications (p = 0.07) was demonstrated. An additional six studies compared different durations of antibiotic prophylaxis for TRUS-gb procedures, but none were able to show a benefit of continuing prophylaxis for more than a single dose [6, 10, 11, 16, 22] or a three-day [8] regimen.

Isolated bacteria

Bacteria isolated from blood or urine were *Escherichia coli* in 30-100% of the affected cases, *Klebsiella* spp. in 4-15% and *Pseudomonas* spp. in up to 14%, but also *Enterococcus, Enterobacter, Staphylococcus aureus*,

TABLE 1

Study characteristics.

Reference	Design	Result
Type of antibiotic		
Tobias-Machado et al [22]	Ciprofloxacin for 1 day Ciprofloxacin for 3 days Chloramphenicol for 3 days Norfloxacin for 3 days	Ciprofloxacin (1 and 3 days) significantly reduces post-procedural infection rates
Yamamoto et al [9]	Tosufloxacin for 2 days Levofloxacin for 2 days	No difference in rates of infectious complications
Cam et al [11]	Ceftriaxon i.m. single dose Ciprofloxacin single dose Ciprofloxacin for 3 days	No difference in rates of infectious complications
Sabbagh et al [8]	Ciprofloxacin single dose or for 3 days Levofloxacin single dose or for 3 days	No difference in rates of infectious complications
Pace et al [12]	Ciprofloxacin ± cephalosporin injection	No difference in rates of infectious complications
Timing of administration of prophylaxis		
Manecksha et al [15]	Ofloxacin 400 mg immediately before biopsy + 200 mg BID for 3 days Ofloxacin 200 mg BID for 3 days, 1st dose 24 h prior to biopsy	Administration 24 h before biopsy yields a 55% relative risk reduction for post-biopsy infection
Argyropoulos et al [7]	Levofloxacin 500 mg 30 min prior to biopsy Levofloxacin 500 mg immediately after prostate biopsy	No difference in rates of infectious complications
Lindstedt et al [13]	Ciprofloxacin 750 mg 2 h before biopsy Ciprofloxacin 750 mg in direct conjunction with biopsy	No difference in rates of infectious complications
Duration of prophylaxis		
Petteffi et al [14]	Norfloxaxin 400 mg single dose Norfloxacin 400 mg for 3 days	No difference in rates of minor post-bioptic complications
Aron et al [6]	Placebo for 3 days Ciprofloxacin 500 mg + tinidazole 600 mg single dose Ciprofloxacin 500 mg + tinidazole 600 mg single dose, BID for 3 days	No difference in rates of infectious post-bioptic complications between groups 2 and 3 Significantly higher incidence of infection in group 1: placebo
Briffaux et al [10]	Ciprofloxacin 1 g single dose Ciprofloxacin 500 mg BID for 3 days	No difference in rates of post-bioptic complications
Cam et al [11]	Ceftriaxone 1 g i.m. single dose Ciprofloxacin for 3 days Ciprofloxacin 500 mg single dose	No difference in rates of post-bioptic complications
Schaeffer et al [16]	Ciprofloxacin 1 g single dose Ciprofloxacin 1 g for 3 days	No difference in rates of post-bioptic complications
Tobias-Machado et al [22]	Ciprofloxacin for 1 day Ciprofloxacin for 3 days Chloramphenicol for 3 days Norfloxacin for 3 days	No difference between a single-dose and a 3-day regimen of ciprofloxacin
Sabbagh et al [8]	Ciprofloxacin single dose or for 3 days Levofloxacin single dose or for 3 days	No difference in rates of post-bioptic complications

BID = 2 × daily; i.m. = intramuscularly.

Proteus mirabilis and *Streptococcus* were found. One trial reported infections to be caused by Gram-negative species (e.g. *E.coli, Enterobacter* and *Klebsiella*) in 81% of cases, but did not name the isolated bacteria strains [5, 8-21].

Resistance/sensitivity of bacteria

Several the bacterial strains isolated from the blood and/or urine of patients admitted with complications following TRUS-gb were found to be resistant to the most commonly used antibiotics, i.e. quinolones, ceph-

TABLE 2

Prophylactic antibiotics used for transrectal ultrasound-guided biopsy in Denmark.

Capital Region of Denmark Rigshospitalet: 10 cores Amoxicillin/clavulanic acid 500/125 mg orally and mecillinam 400 mg orally the evening before and again 2 h prior to the scheduled appointment The dose is to be repeated 3 × a day for a total of 2 days after the biopsy procedure
Herlev: 10-12 cores Amoxicillin/clavulanic acid 500/125 mg orally and mecillinam 400 mg orally the evening before and again 2 h prior to the scheduled appointment The dose is to be repeated 3 × a day for a total of 2 days after the biopsy procedure
Frederiksberg: 12 cores Amoxicillin/clavulanic acid 500/125 mg orally and mecillinam 400 mg orally the evening before and again 2 h prior to the scheduled appointment The dose is to be repeated 3 × a day for a total of 2 days after the biopsy procedure
Region Zealand Roskilde: 10-12 cores Ciprofloxacin 500 mg orally and metronidazol 1 g orally taken at the time of biopsy, 6 h after and again the following morning
Næstved: 12 cores Ciprofloxacin 500 mg orally and metronidazol 500 mg orally at the time of biopsy repeated on the evening of the procedure and again the following morning
Rønne: 10 cores Ciprofloxacin 1 g 1 h before the procedure, repeated 6 h after the procedure In case of diabetes or surgically implanted foreign bodies, a further 500 mg orally BID for 3 days is added
Region of Southern Denmark Fredericia: 12 cores Ciprofloxacin 500 mg orally and metronidazol 500 mg orally at the time of biopsy and repeated 6-8 h after the procedure
Odense: 12 cores Ciprofloxacin 500 mg orally at the time of biopsy repeated on the evening of the procedure
Esbjerg: 12 cores Ciprofloxacin 500 mg orally before the procedure, repeated 8-10 h later In case of repeat biopsies or if seed implantation is planned within 6 mo.s, the prophylaxis is expanded to ciprofloxacin 1 g × 2 and amoxicillin/clavulanic acid 500/125 mg orally BID for a total of 3 days
Sønderborg: 12 cores Ciprofloxacin 500 mg orally The 1st dose shortly before the procedure and repeated the same evening
Svendborg: 12 cores Ciprofloxacin 500 mg orally at the time of biopsy, repeated on the evening of the procedure and in the morning and evening on the following day
Central Denmark Region Aarhus University Hospital: 10 cores Ciprofloxacin 1 g orally 1 h before the procedure
Randers: 10 cores Ciprofloxacin 1 g as a single dose 1 h before the procedure
Horsens: 10 cores Ciprofloxacin 1 g orally before the procedure If the patient has diabetes the prophylaxis is extended to ciprofloxacin 500 mg orally BID for 3 days
Viborg: 12 cores Ciprofloxacin 500 mg orally The 1st dose shortly before the procedure and repeated the same evening
Holstebro: 12 cores Ciprofloxacin 500 mg p.o. The 1st dose shortly before the procedure and repeated the same evening
North Denmark Region Aalborg: 12 cores Ciprofloxacin 500 mg before and 6 h after the biopsy procedure
Frederikshavn: 12 cores Ciprofloxacin 1 g as a single dose before the procedure
Thisted: 12 cores Ciprofloxacin 500 mg before and 6 h after the biopsy procedure

BID = 2 × daily; p.o. = orally.

alosporins, aminopenicillins (i.e. ampicillin, amoxicillin) and aminoglycosides [9, 10, 12, 15, 17-21]. Bacterial sensitivity towards the most commonly used antibiotics was demonstrated in several studies, including cephalosporins, carbapenem/imipenem/meropenem, and amikacin [9, 12, 15, 17, 20, 21]. In one study, rectal swabs were performed immediately prior to the prostate biopsy. Among 236 rectal cultures obtained, 58 contained bacteria resistant to CFLX; of these, 52 were *E. coli* [21]. Another trial also obtained rectal swabs immediately before the biopsy procedure and found that 19% of patients were colonised with extended spectrum beta-lactamase (ESBL)-producing *E. coli* (ESBL-PE) [18].

Risk factors

Several risk factors were associated with post-biopsy infections, including diabetes, a history of prostatitis, previous biopsies, fluoroquinolone consumption within two months prior to biopsy, pre-biopsy bacteriuria and faecal carriage of fluoroquinolone resistant *E. coli* [13, 16, 18, 21]. One trial demonstrated that faecal carriage of ESBL-PE was associated with symptoms of UTI without microbiological evidence [18]. However, no association between faecal ESBL carriage and post-procedure symptomatic UTI was found. Also, prior use of quinolones or other antibiotics, as well as diabetes, were associated with a risk of carrying ESBL-PE before biopsy in multivariate analysis [18]. A second trial found that chronic prostatitis and fluoroquinolone consumption within six months before biopsy were risk factors associated with faecal carriage of fluoroquinolone-resistant *E. coli* strains [21]. A further two trials found no correlation between infection and either the number of core samples taken or the procedure being a re-biopsy [16, 21].

Two Danish reports on prophylactic antibiotics and post-biopsy infectious complications have been published. A retrospective analysis demonstrated a post-biopsy sepsis incidence of 0.91% (n = 4) among 438 patients who underwent TRUS-gb biopsies in the 2009-2011 period. The antibiotic prophylaxis used was 500 mg of CFLX and 500 mg of metronidazole taken before, six hours after, and the day after the procedure. *E. coli* with resistance towards CFLX was described as the causative pathogen in patients who experienced a post-bioptic septic complication [23].

The second study considered patients who underwent TRUS-gb at a single hospital in DK in the 2010-2013 period, and who were administered three different prophylactic antibiotic regimens, namely CFLX or the combination of pivmecillinam and amoxicillin/clavulanic acid for either one or three days [24]. Overall, the admission rates due to infectious complications were 1.8%, and the most commonly isolated pathogens were *E. coli, Klebsiella pneumoniae* and *Enterococcus faecalis*. Of these, 12.1-55.3% were found to harbour resistance towards CFLX and 12.1-21.1% towards cephalosporins. Among the *E. coli* isolates, up to 15.8% were ESBL-PE. When changing the prophylaxis from CFLX to the pivmecillinam and amoxicillin/clavulanic acid combination, a reduction in CFLX resistance from 55.3 to 12.1% was seen.

Prophylactic antibiotic strategies in Denmark

We identified 19 departments of urology in DK that perform TRUS-gb (**Table 2**). All facilities reported taking out 10-12 needle cores per biopsy set, and all had a standard prophylactic regimen prescribed to patients before biopsy. The most prevalent regimen was monotherapy with CFLX, which was reported by 13 facilities. CFLX in combination with metronidazole and amoxicillin + clavulanic acid in combination with mecillinam was reported by three and two facilities, respectively. There was much variation in the duration of prophylaxis, ranging from a single dose to a three-day regimen.

DISCUSSION

Complications following biopsy of the prostate range from mild and self-limiting to life-threatening conditions requiring prompt medical attention. Antibiotic prophylaxis is necessary to reduce the risk of serious infectious complications, but the evidence supporting specific regimens remains scarce.

The most commonly reported non-infectious complications following TRUS-gb were haematuria and haemospermia, both with occurrence rates reaching 60%. Rectal bleeding was also a frequent complication seen in up to 20% of patients. UTI and dysuria were the most common infectious complications with occurrence rates reaching 9.3% and 13.3%, respectively, whereas sepsis, septic shock and death were reported in rates of up to 5.7%, 0.45% and 0.2%, respectively. The differences in the reported incidence of complications may be attributed to different follow-up regimens, different disease definitions and different methods of data collection.

Risk factors associated with septic complications have not been rigorously defined, although comorbidity and previous use of antibiotics seem to be predisposing risk factors. Only quinolones and chloramphenicol have been tested in a randomised trial.

The fact that CFLX is superior to chloramphenicol and norfloxacin may not seem surprising when reviewing drug pharmacokinetics. At least 50-70% of CFLX is excreted in the urine as unmetabolised drug, which is twice as much as for norfloxacin and chloramphenicol. Chloramphenicol is not active against a number of Gram-negative strains, some *E. coli* strains are even spontaneously resistant to the drug, and a relatively high concentration of chloramphenicol is needed to achieve a minimum inhibitory concentration in *E. coli*

bacteria [22]. Interestingly, only one study reported a difference in rates of infectious complications between quinolone-treated groups [22]. Also, no trials were able to demonstrate that administration of several doses of antibiotics is superior to a single dose and thus prolonged use of antibiotics following TRUS-gb remains controversial [6, 8, 10, 11, 16, 22]. This is in line with the findings by Zani et al from 2011 [25]. It remains unknown whether a single dose compared with several doses is associated with an increase in bacterial resistance mechanisms, which could potentially influence the risk of infectious complications if patients are scheduled for re-biopsy procedures. Consequently, current guidelines on antibiotic prophylaxis in association with TRUS-gb must primarily be based on empirical evidence and knowledge about rectal bacterial culture as well as the typical response to known antibiotics.

E. coli, Klebsiella spp. and *Enterobacter* spp. – all Gram-negative, facultatively anaerob bacteria – seem to be the most commonly isolated bacteria in symptomatic patients, and an antibiotic strategy should target these species. However, since anaerob culturing of urine or blood was not performed systematically, the prevalence of strict anaerob bacteria may be underreported. The study performing rectal swabs prior to the prostate biopsy demonstrated that almost one fourth of the patients were carriers of CFLX-resistant bacteria [21]. Thus, for patients with increased risk of post-bioptic infections (i.e. diabetes, chronic prostatitis and prior use of antibiotics), performing a rectal swab that allows for diagnosis of resistant bacterial strains may prove valuable in creating a targeted antibiotic strategy.

Recent studies suggest that an increase in infectious complications after prostate biopsies has occurred over time [26]. In Canada, an increased risk of hospitalisation 30 days after TRUS-gb was demonstrated between 1996 and 2005 (odds ratio = 3.74; 95% confidence interval (CI): 2.0-7.0; $p < 0.0001$) [27]. Similarly, an increase in the frequency of hospitalisation due to infectious complications after TRUS-gb of the prostate over a study period from 1991 to 2007 (p for trend 0.001) has been reported [28]. Repeat biopsies during active surveillance have been argued to increase the risk of post-biopsy infectious complications. One trial found the odds of infectious complications after TRUS-gb to increase by 1.33 with each additional previous biopsy (95% CI: 1.01-1.74; $p = 0.041$) [29]. On the other hand, previous biopsies have also been found not to be related to a higher risk of post-bioptic complications [21].

A range of different measures have been applied to the TRUS-gb procedure in an attempt to minimise the number and severity of post-bioptic complications, i.e. cleansing of the biopsy needle between each biopsy [30], pre-bioptic assessment of urine bacterial culture [31], the transperineal biopsy technique [32] and the use of enemas with or without an added antibiotic. The evidence for an improved outcome for these regimens, however, remains low.

The Danish perspective

According to Danish guidelines, population-based PSA screening is not recommended and the PSA test is reserved for symptomatic patients, patients who have findings on clinical examination that raise suspicion of PCa, or patients with at least two close relatives who have suffered from early-onset Pca [33]. Current Danish guidelines advocate a set of ten biopsies preceded by the administration of prophylactic, but otherwise unspecified, antibiotics [34].

During the past 20 years, DK has witnessed a dramatic increase in the incidence of prostate cancer with an expected, corresponding increase in the number of TRUS-gb performed each year and, accordingly, an increased use of prophylactic antibiotics. According to DANMAP, a monitoring programme of the antimicrobial resistance in DK, the overall use of antimicrobial agents in Danish patients has increased by 20% since 2004, but the use of fluoroquinolones has increased by more than 40%. At the same time, CFLX-resistance in *E. coli* isolates from urine has increased from 3% to 12% among hospitalised patients [35]. Whether this is associated with the use of fluoroquinolones when performing TRUS-gb is unknown. With CFLX monotherapy being the most commonly used prophylaxis for TRUS-gb in DK, the increase in CFLX-resistant *E. coli* raises concern whether a concomitant increase in post-biopsy infectious complications may follow.

Local clinical guidelines on the use of antibiotics with TRUS-gb are not uniform in DK and there seems to be considerable variation among the drugs of choice even within hospitals of close proximity. CFLX remains the most widely used prophylactic antibiotic for TRUS-gb in DK, but also metronidazole, amoxicillin/clavulanic acid and mecillinam are commonly used. Whether the risk of complications varies between institutions is unknown.

It has been shown that different types of antibiotics penetrate differently into the prostate tissue, and the mode of administration is also important for the concentration of the antibiotic that is reached in the prostatic tissue [36-38]. International guidelines, such as the European Association of Urology Guidelines, recommend oral or intravenous administration of a quinolone prior to biopsy [39]. The American Urological Association recommends oral fluoroquinolones or intravenous or intramuscular administration of cephalosporins or trimethoprim-sulfamethoxazole as first-choice prophylactic antibiotic [40]. If, however, a rectal swab is performed, the antimicrobial prophylaxis can be adjusted

towards the growth result [40], which, according to previous studies appears highly efficient in reducing infectious complications [41, 42]. Minimising the antimicrobial spectrum, the dose and the duration of the antibiotic are important when taking into account the ecological consequences of antimicrobial use (e.g. the development of resistant bacterial strains). Furthermore, with regard to optimal use of antibiotic, the peak serum concentration of CFLX is reached 1-3 hours after oral intake, which may therefore possibly be considered the ideal time for biopsy [6].

CONCLUSION

Evidence supporting a specific antibiotic prophylaxis strategy for TRUS-gb is scarce. Furthermore, the frequent use of antibiotics in the population in general, the surfacing of many resistant bacteria and the fact that many men undergo re-biopsies means that is seems difficult to introduce a uniform, prophylactic antibiotic regimen for TRUS-gb. Patients who develop post-biopsy sepsis often harbour bacteria with complex resistance patterns; thus, the available microbiological expertise should be applied when initiating therapy.

CORRESPONDENCE: *Nina Klemann.* E-mail: ninakhp@gmail.com

ACCEPTED: 15 November 2016

CONFLICTS OF INTEREST: Disclosure forms provided by the authors are available with the full text of this article at www.danmedj.dk

LITERATURE

1. Center MM, Jemal A, Lortet-Tieulent J et al. International variation in prostate cancer incidence and mortality rates. Eur Urol 2012;61:1079-92.
2. Crawford ED, Haynes AL, Story MW et al. Prevention of urinary tract infection and sepsis following transrectal prostatic biopsy. J Urol 1982;127:449-51.
3. Kapoor DA, Klimberg IW, Malek GH et al. Single-dose oral ciprofloxacin versus placebo for prophylaxis during transrectal prostate biopsy. Urology 1998;52:552-8.
4. Fahmy A, Rhashad H, Mohi M et al. Optimizing prophylactic antibiotic regimen in patients admitted for transrectal ultrasound-guided prostate biopsies: a prospective randomized study. Prostate Int Asian Pacific Prost Soc 2016;4:113-7.
5. Liberati A, Altman DG, Tetzlaff J et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. PLoS Med 2009;6:e1000100.
6. Aron M, Rajeev TP, Gupta NP. Antibiotic prophylaxis for transrectal needle biopsy of the prostate: a randomized controlled study. BJU Int 2001;85: 682-5.
7. Argyropoulos AN, Doumas K, Farmakis A et al. Time of administration of a single dose of oral levofloxacin and its effect in infectious complications from transrectal prostate biopsy. Int Urol Nephrol 2007;39:897-903.
8. Sabbagh R, McCormack M, Péloquin F et al. A prospective randomized trial of 1-day versus 3-day antibiotic prophylaxis for transrectal ultrasound guided prostate biopsy. Can J Urol 2004;11:2216-9.
9. Yamamoto S, Ishitoya S, Segawa T et al. Antibiotic prophylaxis for transrectal prostate biopsy: a prospective randomized study of tosufloxacin versus levofloxacin. Int J Urol 2008;15:604-6.
10. Briffaux R, Coloby P, Bruyere F et al. One preoperative dose randomized against 3-day antibiotic prophylaxis for transrectal ultrasonography-guided prostate biopsy. BJU Int 2009;103:1069-73,discussion 1073.
11. Cam K, Kayikci A, Akman Y et al. Prospective assessment of the efficacy of single dose versus traditional 3-day antimicrobial prophylaxis in 12-core transrectal prostate biopsy. Int J Urol 2008;15:997-1001.
12. Pace G, Carmignani L, Marenghi C et al. Cephalosporins periprostatic injection: are really effective on infections following prostate biopsy? Int Urol Nephrol 2012;44:1065-70.
13. Lindstedt S, Lindström U, Ljunggren E et al. Single-dose antibiotic prophylaxis in core prostate biopsy: impact of timing and identification of risk factors. Eur Urol 2006;50:832-7.
14. Petteffi L, Toniazzo GP, Sander GB et al. Efficiency of short and long term antimicrobial therapy in transrectal ultrasound-guided prostate biopsies. Int Braz J Urol 28:526-32.
15. Manecksha RP, Nason GJ, Cullen IM et al. Prospective study of antibiotic prophylaxis for prostate biopsy involving >1100 men. Sci World J 2012; 2012:650858.
16. Schaeffer AJ, Montorsi F, Scattoni V et al. Comparison of a 3-day with a 1-day regimen of an extended-release formulation of ciprofloxacin as antimicrobial prophylaxis for patients undergoing transrectal needle biopsy of the prostate. BJU Int 2007;100:51-7.
17. Carmignani L, Picozzi S, Spinelli M et al. Bacterial sepsis following prostatic biopsy. Int Urol Nephrol 2012;44:1055-63.
18. Tukenmez Tigen E, Tandogdu Z, Ergonul O et al. Outcomes of fecal carriage of extended-spectrum β-lactamase after transrectal ultrasound-guided biopsy of the prostate. Urology 2014;84:1008-15.
19. Wagenlehner FME, Van Oostrum E, Tenke P et al. Infective complications after prostate biopsy: outcome of the Global Prevalence Study of Infections in Urology (GPIU) 2010 and 2011, A prospective multinational multicentre prostate biopsy study. Eur Urol 2013;63:521-7.
20. Campeggi A, Ouzaid I, Xylinas E et al. Acute bacterial prostatitis after transrectal ultrasound-guided prostate biopsy: epidemiological, bacteria and treatment patterns from a 4-year prospective study. Int J Urol 2014; 21:152-5.
21. Steensels D, Slabbaert K, De Wever L et al. Fluoroquinolone-resistant E. coli in intestinal flora of patients undergoing transrectal ultrasound-guided prostate biopsy – should we reassess our practices for antibiotic prophylaxis? Clin Microbiol Infect 2012;18:575-81.
22. Tobias-Machado M, Corrêa TD, De Barros EL et al. Antibiotic prophylaxis in prostate biopsy. A comparative randomized clinical assay between ciprofloxacin, norfloxacin and chloramphenicol. Int Braz J Urol 29:313-9.
23. Hayatzaki K, Menne S, Nielsen K. Prophylactic antibiotics reduce sepsis after biopsy of the prostate. Dan Med J 2014;61(11):A4963.
24. Antsupova V, Nørgaard N, Bisbjerg R et al. Antibiotic prophylaxis for transrectal prostate biopsy – a new strategy. J Antimicrob Chemother 2014;69:3372-8.
25. Zani EL, Clark OAC, Rodrigues Netto N. Antibiotic prophylaxis for transrectal prostate biopsy. Cochrane Database Syst Rev 2011;5:CD006576.
26. Loeb S, Vellekoop A, Ahmed HU et al. Systematic review of complications of prostate biopsy. Eur Urol 2013;64:876-92.
27. Nam RK, Saskin R, Lee Y et al. Increasing hospital admission rates for urological complications after transrectal ultrasound guided prostate biopsy. J Urol 2013;189:S12-S17,discussion S17-S18.
28. Loeb S, Carter HB, Berndt SI et al. Complications after prostate biopsy: data from SEER-Medicare. J Urol 2011;186:1830-4.
29. Ehdaie B, Vertosick E, Spaliviero M et al. The impact of repeat biopsies on infectious complications in men with prostate cancer on active surveillance. J Urol 2014;191:660-4.
30. Koc G, Un S, Filiz DN et al. Does washing the biopsy needle with povidone-iodine have an effect on infection rates after transrectal prostate needle biopsy? Urol Int 2010;85:147-51.
31. Bruyère F, d'Arcier BF, Boutin J-M et al. Is urine culture routinely necessary before prostate biopsy? Prostate Can Prostatic Dis 2010;13:260-2.
32. Suzuki M, Kawakami S, Asano T et al. Safety of transperineal 14-core systematic prostate biopsy in diabetic men. Int J Urol 2009;16:930-5.
33. Clinical guidelines. http://ducg.dk/fileadmin/www.ducg.dk/Prostatacancer/Kl._retningslinjer/2016/5._Diagnosticering-MB.pdf (7 Nov 2016).
34. http://ducg.dk/fileadmin/www.ducg.dk/Prostatacancer/Kl._retningslinjer/4__Screning_praehospitalsfase_symptomer_og_diagnose_mb29_09_13.pdf (1 Aug 2016).
35. Agersø Y. Danmap 2013. report 2014:1-108. www.danmap.org/~/media/Projekt sites/Danmap/DANMAP reports/DANMAP 2013/DANMAP 2013.ashx (26 Jun 2015).
36. Wagenlehner FME, Weidner W, Sörgel F et al. The role of antibiotics in chronic bacterial prostatitis. Int J Antimicrob Agents 2005;26:1-7.
37. Kataoka N. [Concentration of antimicrobial agents in male genital organs]. Hinyokika Kiyo 1983;29:1219-30.
38. Wagenlehner FME, Pilatz A, Waliszewski P et al. Reducing infection rates after prostate biopsy. Nat Rev Urol 2014;11:80-6.
39. Mottet N, Bellmunt J, van den Bergh RCN et al. Guidelines on Prostate Cancer. 2015 https://uroweb.org/wp-content/uploads/09-Prostate-Cancer_LR.pdf (1 Aug 2016).
40. AUA Quality Improvement Summit 2014: Conference Proceedings on Infectious Complications of Transrectal Prostate Needle Biopsy. www.auanet.org/common/pdf/practices-resources/quality/white-papers/QI-Summit.pdf (21 Jul 2015).
41. Summers SJ, Patel DP, Hamilton BD et al. An antimicrobial prophylaxis protocol using rectal swab cultures for transrectal prostate biopsy. World J Urol 2015;33:2001-7.
42. Duplessis CA, Bavaro M, Simons MP et al. Rectal cultures before transrectal ultrasound-guided prostate biopsy reduce post-prostatic biopsy infection rates – Clinical Key. Urology 2012;79:556-63.