

Prophylactic antibiotics reduce sepsis after biopsy of the prostate

Khalilullah Hayatzaki¹, Sveinar Menne¹ & Karsten Nielsen²

ABSTRACT

INTRODUCTION: Prostate cancer is the most common form of cancer in Danish men, and the incidence is rising. The diagnosis is made by transrectal prostate biopsy guided by ultrasound. This procedure has several complications, the most severe being sepsis. In our department, this is sought prevented by administering the prophylactic antibiotics metronidazol and ciprofloxacin. This study examined the rate of sepsis in patients who had the procedure performed at our department.

METHODS: The electronic patient records of all patients who had transrectal ultrasound of the prostate with biopsies performed at the Department of Urology at Naestved Hospital in the period from 1 May 2009 to 31 May 2011 were examined, and all admissions to our Department (or any department in the same region) due to sepsis within two weeks of the procedure were registered.

RESULTS: A total of 438 patients had the procedure performed, some multiple times, which resulted in a total of 511 procedures. In all, four patients were later admitted due to sepsis, corresponding to 0.91%. Three of the patients had positive blood and urine cultures in which *Escherichia coli* resistant to ciprofloxacin were found, the last had been prescribed antibiotics by a general practitioner the previous day, and no bacteria could be cultured.

CONCLUSION: The frequency of sepsis after transrectal needle biopsies from the prostate at our department was found to be below 1% in this study, which is comparable to international findings. Most of the cases of sepsis were related to ciprofloxacin-resistant bacteria. Further randomised studies are needed to investigate the ideal prophylactic regime.

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Prostate cancer is the most common cancer in Danish men with an incidence of 146/100,000 in 2010 [1]. The incidence is increasing and varies internationally from 1 to 156/100,000 with the highest incidence being observed in the USA and Northwest Europe. In Denmark, more than 4,000 cases are diagnosed annually. The established diagnostic methods are digital rectal exploration, serum value of prostate-specific antigen (PSA) and transrectal ultrasound of the prostate (TRUS) with multiple biopsies, in Denmark usually a minimum of ten needle biopsies. With TRUS, the echoic pattern of the

prostate is examined, and the volume of the prostate is estimated. Furthermore, the needle biopsies are guided to the different areas of the prostate (**Figure 1**).

In Denmark, 10,000-15,000 biopsies of the prostate are performed annually [1]. The most common complications are pain, dysuria, haematuria, haemospermia, rectal bleeding and infection. The most important and most serious complication is infection with sepsis. International experience with infectious complications ranges from 1.5% to 12.9% for any infectious complication, and from 0.09% to 3.1% for serious infectious complications requiring hospitalisation [2-7]. However, there are differences in the definitions of infectious complications and the collection of data in these studies. There are no prior Danish studies.

It is agreed that antibiotic prophylaxis should be a part of the procedure [8], but there is no consensus about the prophylactic regime to be used. A Cochrane analysis [9] and multicentre studies in Europe including many patients [10] and studies in the US [11] using aminopenicillin, ciprofloxacin, cefuroxim and cefotaxim were inconclusive as the studies included in the Cochrane analysis and the multicentre studies were non-randomised studies.

In Denmark, different regimes are used, e.g. Bioclavid and pivmecillinam at Herlev Hospital, Bioclavid and metronidazol at Rigshospitalet, and ciprofloxacin alone at Aalborg, Skejby and Odense Hospitals. Ciprofloxacin and metronidazol are used in Naestved and Roskilde Hospitals. The aim of this study was to investigate the incidence of sepsis at the Department of Urology, Naestved Hospital.

METHODS

The study is a retrospective investigation of all records of all patients who had TRUS with multiple needle biopsies done at the Department of Urology, Naestved Hospital, in the period from 1 May 2009 to 31 May 2011. All patients had 12 needle biopsies taken with disposable equipment size 18 gauges BARD 22 mm. All patients received the same regime of antibiotic prophylactics consisting of tablet ciprofloxacin 500 mg and tablet metronidazol 500 mg two hours before the biopsy procedure, six hours after the biopsy procedure and the following morning.

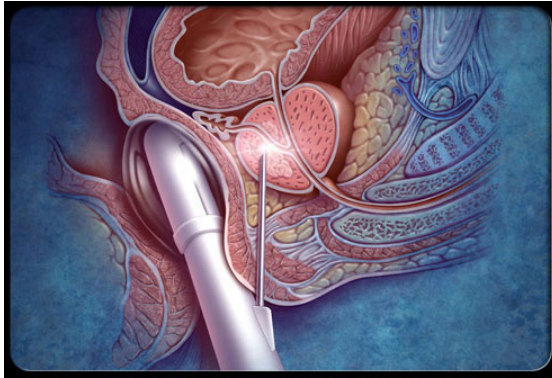
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1) Department of Urology, Naestved Hospital
2) Department of Pathology, Naestved Hospital

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 **FIGURE 1**

Transrectal ultrasound-guided biopsy.



In this study, sepsis as a complication to TRUS was defined as hospitalisation with systemic inflammatory response syndrome and suspicion of bacteraemia within 14 days after the biopsy procedure.

All the patients with sepsis were admitted to the Department of Urology at Naestved Hospital as we recommend that patients are admitted following the procedure. The records were all electronic, and any hospital admissions in the same region would be registered in the patient's record. Any admissions in another region would not be registered, and although no patients had mentioned any problems at a later visit, we cannot establish with certainty if one or more patients had a septic incidence following the procedure, which has not been registered with us.

Trial registration: not relevant.

RESULTS

A total number of 438 patients had TRUS with multiple needle biopsies performed. In all, 53 patients were biopsied twice and ten patients were biopsied three times, resulting in a total of 511 biopsy procedures. At the clinical examination, 314 patients had a T1 tumour, 98 patients had a T2 tumour and 26 patients had a T3-4 tumour (**Table 1**). The median volume of the prostate was 49 ml (interquartile range (IQR): 36-67 ml), and the median value of serum PSA was 9.25 ng/ml (IQR: 6.22-19.25 ng/ml). Prostate cancer was diagnosed in 243 patients (53%). Four patients developed sepsis, corresponding to an incidence of 0.91% of the biopsied patients. Two of these four patients had sepsis after re-biopsy (second biopsy procedure).

Three of the patients were hospitalised the day after the biopsy procedure due to illness, high fever and increased infection parameters; and *Escherichia coli* was cultured from blood samples and urine samples in these

three patients. The bacteria were resistant to ampicillin and ciprofloxacin. The patients were initially treated with intravenous ampicillin, gentamicin and metronidazole. The fourth patient was hospitalised four days after biopsy procedure with fever and illness. The day before the hospitalisation, the general practitioner had started antibiotic treatment with pivampicillin. At the hospital, the patient continued this treatment, and no bacteria were cultured from blood sample or urine sample.

All four patients were discharged from the hospital after few days of hospitalisation and continued their treatment with oral antibiotics. There were no adverse effects. All four patients had lower urinary tract symptoms (LUTS) before biopsy procedures, and two of the patients had known diabetes mellitus. None of the remaining 434 patients were hospitalised.

DISCUSSION

At the Urology Department, Naestved Hospital, the incidence of sepsis after prostate biopsies was found to be 0.91% when prophylactic procedures with ciprofloxacin and metronidazole were used. The Urology Department and the Microbiology Department at the hospital agree that this was best practice in 2009, but the decision has not been revised since. Two of the patients had known diabetes mellitus, and the two other patients had sepsis after the second biopsy series. Diabetes mellitus is well known as a significant risk factor for sepsis after prostate biopsy [7], while there is no correlation between the number of biopsies and sepsis [5, 11]. Among other risk factors are indwelling urinary catheter, previous urinary tract infection or prostatitis, large prostate and bacteriuria [12].

More studies [3, 5, 6] show that ciprofloxacin is an effective prophylactic antibiotic for prostate biopsies, but a Cochrane study [9] demonstrated that many classes of antibiotics are effective as prophylaxis. The Cochrane study could not show if long-term treatment was better than short-term treatment, and it could also not be established if multiple drug treatment was better than single drug treatment. A drawback of the Cochrane study is that it was based on non-randomised studies.

In the three hospitalised and documented cases in our study where *E. coli* was cultured, the bacteria were resistant to ciprofloxacin (**Table 2**). There is an increased frequency of resistance to ciprofloxacin [7, 13-15], and there is a connection between the use of antibiotics and resistance [13, 16]. This means that the effect of ciprofloxacin could lessen over time. Because of the increasing demand for swift diagnosis and treatment, there is rarely enough time to culture the patients prior to the procedure, for instance via rectal swabs.

It is also worth noting that in two of the patients, we found bacteria resistant for cefuroxim which is often



TABLE 1

Findings.

	Outcome
Age, median (IQR), yrs	67 (63-73)
<i>Referral reason, n</i>	
Suspected cancer	385
Lower urinary tract symptoms	37
Other	16
PSA-concentration, median (IQR), ng/ml	9.25 (6.2-19.3)
Prostate volume, median (IQR), ml	49 (36-67)
<i>Patients, n (%)</i>	
CT-stage:	
T1	314
T2	98
T3	26
Procedures, n:	
1	375
2	53
3	10
With sepsis	4 (0.9)
With diabetes	21 (4.8)

IQR = interquartile range; PSA = prostate-specific antigen.



TABLE 2

Culture and sensitivity.

Patient no.	Blood culturing	Sensitivity	Resistance
I	<i>E. coli</i>	Gentamicin, meropenem	Ampicillin, ciprofloxacin, cefuroxime
II	<i>E. coli</i>	Gentamicin, meropenem	Ampicillin, ciprofloxacin, cefuroxime
III	<i>E. coli</i>	Cefuroxime, mecillinam, gentamicin	Ampicillin, ciprofloxacin
IV	No growth	–	–

the first choice in the treatment of sepsis with suspicion of focus in the urinary tract.

CONCLUSION

From the investigation at the Urology Department, Naestved Hospital, we can conclude that using the prophylactic regime of ciprofloxacin and metronidazol, the rate of serious infectious complications is comparable to that reported internationally. Severe infectious complications seem to be correlated with bacteria resistant to ciprofloxacin. There is a great demand for proper randomised trials regarding prophylactic antibiotic treatment for patients undergoing TRUS with biopsies from the prostate because of the increasing problem with resistant bacteria.

CORRESPONDENCE: Khalilullah Hayatzaki, Urologisk Afdeling, Næstved Sygehus, Ringstedgade 61, 4700 Næstved, Denmark.

E-mail: khah@regionsjaelland.dk

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