



Urinary tract infection in men

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Key words

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Abstract. Objective: To explore the prevalence and microbiology of urinary tract infection (UTI) in symptomatic men in a primary care setting and to determine the appropriateness of patient management of these conditions by the general practitioners. **Methods:** A cross-sectional survey was carried out matching documentation of symptoms and management with urine culture and results of susceptibility tests. All patients presenting with symptoms typical for a UTI in 36 teaching general practices in the area of Göttingen, Germany, were eligible for enrolment in the study. 15% (n = 90) of all patients were adult men. General practitioners (GPs) were instructed to manage patients as usual. Patient characteristics, dipstick tests and treatment were matched with results of urine cultures and susceptibility testing. **Results:** Men presenting with symptoms indicative of UTI were predominantly elderly (median age 61 years) and 41% had additional risk factors. Antibiotics were prescribed for 36%, but these were not well-targeted. Urine culture revealed UTI in 60%, of which half had low colony counts (23% of all patients) or multiple bacterial growth (7%); 40% had sterile urine. Dipstick tests proved unhelpful: leukocytes and nitrite had sensitivities of 54% and 38%, specificities of 55% and 84%, positive predictive values of 65% and 78% and negative predictive values of 44% and 46%, respectively. Resistance levels were 53% for amoxicillin and cefaclor, 28% for cefixim, 22% for ciprofloxacin, 34% for both trimethoprim as individual substance and the combination with sulfamethoxazole (cotrimoxazole) and 25% for nitrofurantoin. **Conclusion:** Men with symptoms indicative of a UTI should not be treated empirically. A urine culture and antibiogram should be obtained before a treatment decision is made. A low-count UTI was common and should not be considered normal.

a much higher incidence, men are also not free of this condition and may present with a more complex disease and a higher risk of complications [Lipsky 1999, Stamm and Hooton 1993]. It is generally recognized that treatment recommendations for women are not usually appropriate for men. However, guidelines or recommendations for the management of men are mostly based on studies in women, children and institutionalized elderly people of both sexes [Prodigy 2002]. To date, very few studies on community-acquired UTI in males have been published. A recent survey deals with a predominantly gay and 33% HIV-infected population of only 2 urban practices in Australia [Russell and Roth 2001] and therefore cannot be extrapolated to other populations. Two studies focus on diagnostic investigations in men referred to specialist care for a diagnostic workup of confirmed UTI [Andrews et al. 2002, Ulleryd et al. 2001].

The aims of our study were:

- to describe the prevalence of culture-confirmed UTI in men with a suspected UTI presenting in general practices,
- to test the predictive values of dipstick tests and the general practitioners' clinical diagnosis in view of prediction guidelines for male UTI,
- to assess the prevalence of antibiotic resistance in male patients with UTI and to determine the appropriateness of the treatment by the general practitioners.

Methods

In the context of a larger cross-sectional survey on UTI in German general practices, all 118 teaching general practices of the Department of General Practice and Family

Introduction

Although research on urinary tract infection (UTI) has focussed on women because of

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Medicine of the University of Göttingen were invited to participate in this study. All practices cooperated with the only medical laboratory in the area (Medical Partnership Wagner, Stibbe, Kast, Bispink and Partner). During the study period of 4 months, practices were monitored by regular telephone calls. General practitioners (GPs) were instructed to include all patients in whom they considered an acute UTI to exist. In order to reflect the actual situation and daily routine in general practices, patients with comorbidity and those who had recently received antibiotic treatment were not excluded. However, patients in whom it was obvious that other explanations for their symptoms were present (i.e. acute prostatitis) were not to be included. Patients were to be managed in a manner considered usual for the practice involved and including the use of dipstick tests if considered appropriate. For purposes of this study, GPs were required to order a urine culture for all patients regardless of dipstick results, even if they would not have done so outside the study context. All cultures were performed in the same laboratory. GPs were instructed to treat patients empirically if they considered it appropriate and wait for culture results only if this would have been their usual procedure. The age of each patient, sex, current symptoms and risk factors, diagnostic procedures used and treatment were documented on a short, structured form identified by a patient code number. The forms were mailed to the Department of General Practice (not to the laboratory) without disclosing the identity of the patient.

According to current recommendations, GPs were asked to sample freshly voided urine only, but midstream sampling was not required [Hummers-Pradier and Kochen 2002, Lipsky et al. 1984]. Urine samples were stored in sterile containers, supplied by the laboratory and kept refrigerated until processing the same day at the laboratory. The laboratory performed a standard urine culture with antibiotic susceptibility testing according to DIN guidelines in case of bacterial growth. Culture results were communicated to the Department of General Practice (labeled with the patients' code numbers) and to the participating GPs (with patients' names). Our laboratory used the traditional definition of 10^5 colony-forming units (CFU)/ml of a single species for a "microbiologically

proven UTI". Cultures with 10^3 or 10^4 CFU/ml or 3 or more species of bacteria which are traditionally considered as "contamination" in voided urine samples [Lipsky et al. 1984] were interpreted as "ambiguous". The presence of 10^2 CFU/ml was labeled as "normal" and no identification of pathogens or susceptibility testing was performed in such cases. Since lower cutoff values are significant in women (10^2 CFU/ml) [Kunin et al. 1993, Stamm and Hooton 1993] and have been discussed in regard to adult males (10^3 CFU/ml) [Lipsky 1999], we evaluated traditionally defined "high-count UTI" (10^5 CFU/ml) separately and "any UTI" (10^2 CFU/ml, including mixed growth) in our analysis.

All data were entered into SAS, Version 8 [SAS Institute 1999]. Patient documentation and laboratory results were linked by means of the patient code number. Descriptive statistics, 2×2 contingency tables and logistic regression models with backward selection were calculated using SAS.

Results

Participants

Of the 118 general practitioners invited, 36 (31%) participated in the study (8 were women and 14 were working in group practices with 2–4 partners); 585 patients of both sexes were recruited within a 4-month period; 15% ($n = 90$) were adult men, recruited by 25 practices (1–12 per practice). In 88% ($n = 79$), symptoms had been recorded on the documentation sheet. Median duration of symptoms was 4 days (interquartile range 2–10 days). In 7%, GPs had documented that the urine culture was ordered in the context of a control or preventive consultation. In some patients it was unclear why the GP had suspected a UTI.

Patient characteristics, symptoms and risk factors (as documented by the GPs) are presented in Table 1.

GPs' diagnostic procedures and diagnoses are presented in Table 2.

In 97% of patients the GP had performed a dipstick test. In 51%, leukocytes were recorded as positive and nitrite was positive in 31%. 32% of patients without leukocyturia

Table 1. Patient characteristics, symptoms and risk factors (as documented by the GPs) (n = 90).

Age (median, range)	61 (19 – 94)	
Recurrent urinary tract infection	18%	
Patient symptoms (multiple answers possible)		
	n	%
Pollakiuria	40	44
Dysuria	38	42
Suprapubic pain	12	13
Kidney/flank pain	12	13
Fever	7	8
Others	7	8
Additional risk factors (multiple answers possible)		
	n	%
Total	37	41
Diabetes	12	13
Indwelling catheter	9	10
History of urinary surgery	6	7
Bladder or prostate cancer	4	4
Renal failure	4	4
Antibiotics in the last 2 weeks	4	4
Chronic prostatitis	3	3
Others	10	11

Table 2. Patient management by general practitioners for men with suspected urinary tract infection (n = 90).

Diagnostic procedures (multiple answers possible)		
	n	%
Dipstick test	88	97
Sediment microscopy	33	37
Physical examination	30	33
Ultrasound of urinary tract	21	23
Referral to urologist	6	7
Control consultation recommended	32	35
Diagnosis by general practitioners		
	n	%
Urinary tract infection	48	53
Healthy/no diagnosis	15	17
Urethral syndrome	12	13
Hematuria	5	6
(Suspected) pyelonephritis	3	3
Uncertain	2	2
Others	5	6

were judged to have UTI by their GP and 10 patients (25%) with leukocyturia were considered not to have UTI. The odds ratio for a 1. GP diagnosing UTI 2. in presence of with a positive leukocyte dipstick was 7.50 (95% CI 2.91 to 19.33).

43% of patients negative for nitrite were considered to have UTI anyway and 5 patients positive for nitrite (13%) were thought 1. for a GP not to have UTI. The odds ratio for

a 1. GP diagnosing UTI 2. in presence of a positive nitrite test was 6.19 (95% CI 2.08 – 18.46).

A multivariate logistic regression was performed including the presence of typical symptoms (dysuria, frequent/urgent voiding, suprapubic pain, fever, flank/kidney pain), risk factors, leukocytes, nitrite and age (above 60 or younger). Leukocytes (odds ratio (OR) 6.78, 95% confidence interval (CI) 2.54 – 18.14) and dysuria (OR 2.79, 95% CI 1.02 – 7.68) were the only significant predictors for the diagnosis of UTI by the GPs.

Pathogens

Urine culture results were available in 81 patients (90%); 30% of the patients (n = 24) had UTI with 10⁵ CFU/ml, 2% (n = 2) presented with 10⁴ CFU/ml (low-count UTI, interpreted as ambiguous by the laboratory) and 21% (n = 17) had 10² CFU/ml (low-count UTI, interpreted as normal by the laboratory). In 7% (n = 6), cultures were interpreted as ambiguous since 3 or more species of bacteria were present; 40% of patients (n = 32) had sterile urine. Of 24 patients with 10⁵ CFU/ml, 75% carried *Escherichia coli*, (21%) enterococci and (13%) *Proteus* sp., *Klebsiella* sp., *Pseudomonas* sp. and several types of staphylococci and *Citrobacter* sp. were found in 1 or 2 urine samples. In the small group of patients with 10⁵ CFU/ml (n = 24) the presence of naturally unsusceptible pathogens as well as resistant strains resulted in low antibiotic susceptibility: 53% of all pathogens were resistant to amoxicillin and cefaclor, 41% to amoxiclav, 34% to both cotrimoxazole and trimethoprim, 28% to cefixim, 25% to nitrofurantoin and 22% to ciprofloxacin.

Table 3 illustrates the diagnostic value of dipsticks with regard to “high-count” UTI with 10⁵ as well as any UTI” with 10² CFU/ml, including mixed growth (prevalence 60%).

Presence of typical symptoms (dysuria, frequent/urgent voiding, suprapubic pain, fever, flank/kidney pain), risk factors, leukocytes, nitrite and age (above 60 or younger), were used as predictive variables in logistic regression models predicting high-count UTI or any UTI.

Table 3. Diagnostic value of dipstick tests with regard to both definitions of male UTI (n = 79*).

Dipstick tests vs. "high-count" urinary tract infection (10^5 CFU/ml), prevalence 30%					
	Total	Nitrite +	Nitrite –	Leukocytes +	Leukocytes –
"High-count" UTI	24	12	12	16	8
Negative or ambiguous culture	55	11	44	24	31
Total*	79	23	56	40	39
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Sensitivity		50%		67%	
Specificity		80%		56%	
Positive predictive value		52%		40%	
Negative predictive value		79%		80%	
Positive likelihood ratio		2.5		1.5	
Post-test probability		52%		39%	
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Dipstick tests vs. any UTI (10^2 CFU/ml, including mixed growth), prevalence 60%					
	Total	Nitrite +	Nitrite –	Leukocytes +	Leukocytes –
UTI	48	18	30	26	22
Sterile urine	31	5	26	14	17
Total*	79	23	56	40	39
<hr/>					
Sensitivity		38%		54%	
Specificity		84%		55%	
Positive predictive value		78%		65%	
Negative predictive value		46%		44%	
Positive likelihood ratio		2.4		1.2	
Post-test probability		78%		64%	
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* = in 2 patients, no dipstick test and in 9 patients no urine culture had been performed.					

Age greater than 60 predicted UTI according to both criteria (high-count UTI: OR 7.09, 95% CI 2.05 – 24.45 and any UTI: OR 3.32, 95% CI 1.29 – 8.52, respectively). Nitrite was a predictor of a high-count UTI only (OR 3.68, 95% CI 1.18 – 11.44) and all other variables did not contribute significantly to either model.

Adequacy of GPs' management with regard to culture results

Using a culture result of 10^5 CFU/ml as a gold standard and interpreting all other results as "negative", the GPs' diagnosis had a sensitivity of 71% and a specificity of 58%. Due to the relatively low likelihood ratio for a GP diagnosis of UTI (1.7), the positive predictive value (PPV) was only 42% and the negative predictive value (NPV) 83%. With regard to "any UTI" (10^2 CFU/ml, includ-

ing mixed growth), the diagnosis by the GP had a slightly higher PPV of 63%, but sensitivity (53%), specificity (53%) and NPV (43%) were lower.

A total of 33 (36%) patients were treated empirically with antibiotics before culture results were available. These patients had been diagnosed with UTI (n = 29, 63% of all patients with this diagnosis) or pyelonephritis (n = 2; 1 patient was not treated), 1 patient was labeled as "uncertain diagnosis" and in another, no diagnosis was specified. Cotrimoxazole (42%) and fluoroquinolones (38%) were the most frequently prescribed antibiotic. In some cases, amoxicillin (6%), trimethoprim (6%) or several other antibiotics (12%) were used. Aspirin, a spasmolytic drug (trospium chloride) and a herbal drug were prescribed in single cases.

Figure 1 details the treatment of all patients with regard to presence of culture-confirmed UTI and susceptibility to the antibiotic prescribed.

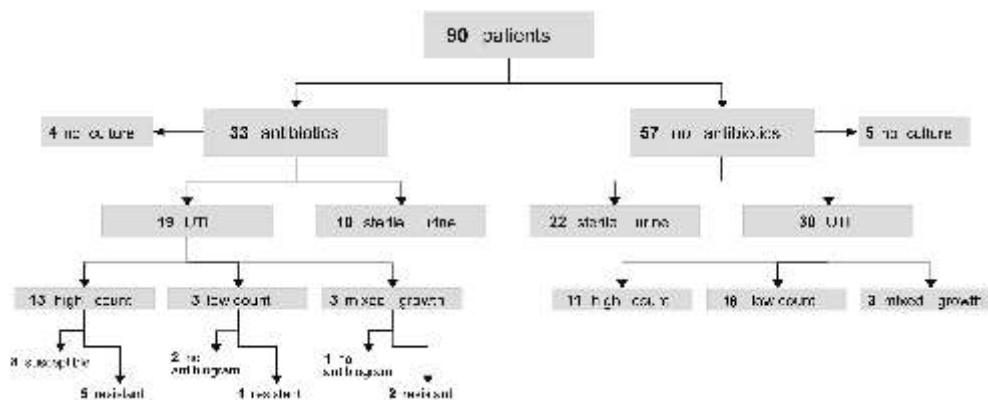


Figure 1. Adequacy of treatment in all patients with regard to presence of culture-confirmed UTI and susceptibility to the individual antibiotic prescription.

Discussion

Men in whom their GP suspected UTI were a heterogeneous group. They were predominantly elderly and many had additional complicating factors as observed previously by other investigators [Lipsky 1999]. Only 60% of men presenting with symptoms indicative of UTI had bacteriuria confirmed by culture and half of these patients had low colony counts which would traditionally be interpreted as contamination rather than “significant” UTI. In our primary care population, male UTI was difficult to diagnose with clinical information and dipsticks alone, both of which were not reliable. GPs had difficulty in distinguishing who should be treated with antibiotics, and resistance levels appear to be high.

Our study has some limitations due to the research setting and cross-sectional study design: GPs participating in our survey practice in both rural and urban settings and were not routinely involved in research. Although there may be selection bias concerning GPs, their patients are not likely to differ from patients in nonparticipating practices. As is typical for general practice studies in countries without practice lists (such as Germany), the catchment rate of our study is uncertain and it was necessary to rely on the participating GPs to include all their eligible patients [Bell-Syer and Moffett 2000, Wilson et al. 2000]. We attempted to ensure active participation through regular telephone monitoring. In order to ensure a valid representation of the daily practice, we made the inclusion criteria relatively

broad and purposefully avoided restrictive exclusion criteria. The number of included patients (of both sexes) corresponds to the prevalence reported in other German studies on UTI in general practice [Egidi and Gebhardt 2003, Gulich et al. 2001, Hummers-Pradier et al. 2001]. The prevalence of men presenting with symptoms of UTI is similar to that reported in an earlier Swedish survey but more recent data are not available [Ferry et al. 1987]. Nevertheless, the total numbers of male patients and outcome events are relatively small, resulting in large confidence intervals and imprecise predictive models. Cross-sectional data collection did not allow for a stepwise analysis of the diagnostic approach of the GPs. However, dipstick tests were performed in almost all patients. The diagnosis by GPs was therefore based on both dipstick results and additional clinical information.

All urine cultures and susceptibility tests were performed in a single laboratory, but dipsticks were assessed by the individual GPs who reported their reading. There are various possible sources of error which limit the reliability of dipstick testing, i.e. dilution by increased diuresis, discoloring due to excretion of glucose or protein and contamination. This may be reflected in the low predictive values of dipsticks in our sample, indicating their limited use as a guide to decision-making by GPs in male patients. However, a detailed analysis of each reading, including sources of error, was neither feasible nor the focus of our study. Although the readings made by GPs using urinary dipsticks are known to vary, our approach reflects the real situation more ac-

curately than would be the case if a "standardized" reading technique in a study center had been used and such a method would have been difficult to implement anyway due to reasons of feasibility [Christiaens et al. 1998, Winkens et al. 1995].

Our results suggest that male UTI cannot be diagnosed reliably without a culture, which is in line with international recommendations [Prodigy 2002, Hummers-Pradier and Kochen 2002, Orenstein and Wong 1999]. Age was the only factor predicting bacteriuria and only nitrite was associated with "high-count" UTI but had poor predictive values. The only factors that could be identified as (significantly) contributive to the decision-making by the GP (presence of dysuria and a dipstick test positive for leukocytes) proved inappropriate for prediction of culture results. It must be noted, however, that apparently irrational and essentially intuitive diagnosis by GPs had a similar (low) precision than an approach based on dipstick tests only (with a somewhat higher sensitivity but lower specificity). GPs were better at identifying patients with high-count UTI than patients with low bacteria counts. Presumably, these patients had more pronounced symptoms (severity of symptoms was not recorded).

More research is required on cutoff values for diagnosing UTI in men. Although the traditional definition of male UTI requires presence of 10^5 colony-forming units, the high prevalence of low-count bacteriuria in symptomatic male patients is notable. Further research on the correlation of urinary symptoms and low-count bacteriuria in men is needed. A prospective study of men with symptomatic low-count UTI should determine whether these patients will benefit from antibiotic treatment. If this should prove to be the case, cutoff values ought to be set at 10^2 CFU/ml for both men and women. Lipsky [1999] already proposed a cutoff at 10^3 CFU/ml in his review article, however, no original evidence was presented.

Based on our data, there is room for improvement in the empirical treatment of men with UTI. Relatively few men were asked to return for further investigations or referred to an urologist. The need for a diagnostic workup in men with UTI is discussed somewhat controversially [Andrews et al. 2002,

Prodigy 2002 is missing in the References, Lipsky 1999, Orenstein and Wong 1999], and in some cases of recurrent UTI, investigations may have taken place before our survey was carried out. Antibiotic treatment was poorly targeted: one third of patients with sterile urine received antibiotics, the majority of patients with UTI, even high-count UTI, were not treated. Due to the cross-sectional survey design, neither clinical outcomes nor prescriptions issued after the GPs received the culture results were recorded. Our sample is probably too small to be fully representative with regard to antibiotic susceptibility, and the laboratory failed to do susceptibility testing in cases with low-count bacteriuria. However, resistance levels for all common antibiotics including fluoroquinolones were very high in our sample [Christiaens et al. 2002, Gupta et al. 2001, Magee et al. 1999, McIsaac et al. 2002, Schaeffer 2002]. Almost half of the antibiotics prescribed to patients with culture-confirmed UTI can be expected to be ineffective, although sometimes clinical results have proved to be better than in vitro susceptibility tests predict [Gupta et al. 2001]. Due to the difficulties in diagnosing male UTI with clinical information and dipstick tests alone, deferring antibiotic treatment until culture results are available (unless there is a medical emergency) may be a more rational approach, which, however, must be evaluated for safety.

Conclusion

In symptomatic men, UTI cannot be reliably diagnosed with dipstick tests and clinical information. Therefore, GPs cannot easily identify patients who should be treated empirically with antibiotics and current treatment strategies carried out in general practices are often not appropriate. Low-count UTI seems to be common among symptomatic males attending general practices.

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