Antibiotic Prophylaxis in Urologic Procedures: A Systematic Review

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Abstract

Objective: Antibiotic prophylaxis is used to minimize infectious complications resulting from interventions. Side-effects and development of microbial resistance patterns are risks of the use of antibiotics. Therefore, the use should be well considered and based on high levels of evidence. In this review, all available evidence on the use of antibiotic prophylaxis in urology is gathered, assessed, and presented in order to make choices in the use of antibiotic prophylaxis on the best evidence currently available.

Methods: A systematic literature review was conducted, searching Medline, Embase (1980–2006), the Cochrane Library, and reference lists for relevant studies. All selected articles were reviewed independently by two, and, in case of discordance, three, reviewers.

Results: Only the transurethral resection of prostate (TURP) and prostate biopsy are well studied and have a high and moderate to high level of evidence in favour of using antibiotic prophylaxis. Other urologic interventions are not well studied. The moderate to low evidence suggests no need for antibiotic prophylaxis in cystoscopy, urodynamics investigation, transurethral resection of bladder tumor, and extracorporeal shock-wave lithotripsy, whereas for therapeutic ureteroscopy and percutaneous nephrolithotomy, the low evidence favours the use of antibiotic prophylaxis. Urologic open and laparoscopic interventions were classified according to surgical wound classification, since no studies were identified. Antibiotic prophylaxis is not advised in clean surgery, but is advised in clean-contaminated and prosthetic surgery.

Conclusions: Except for the TURP and prostate biopsy, there is a lack of well-performed studies investigating the need for antibiotic prophylaxis in urologic interventions.

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1. Introduction

Antibiotic prophylaxis is a brief course of antibiotics administered before or at the start of an intervention and used to minimize the infectious complications resulting from diagnostic and therapeutic interventions. While the rationale for the use of antibiotics is well accepted, possible side-effects and development of microbial resistance patterns are potential risks. Therefore, an antibiotic prophylaxis policy should be well considered and, ideally, based on high levels of evidence.

Urology is a surgical speciality which has undergone many changes in the last decade. Surgical procedures have mainly shifted from open to endoscopic and laparoscopic procedures, and nowadays, a greater number of elderly patients or carriers of temporary urinary derivations are being operated on. These developments can influence the choice of antibiotic prophylaxis policy.

Although it is common practice to administer antibiotic prophylaxis in many urologic procedures, there is still little evidence for the use of antibiotic prophylaxis in most of these procedures. This is mainly due to the lack of well-designed studies as well as the lack of clear definitions of favourable outcome parameters.

The question remains to what extent antibiotic prophylaxis is beneficial in the different urologic procedures. Various authors have addressed this issue in reviews in recent years [1–4]. Also, the European Association of Urology (EAU) has recently updated the guideline “Management of urinary and male genital tract infections,” including a chapter on perioperative antibacterial prophylaxis in urology [5]. However, with the exception of the transurethral resection of the prostate [6,7], few of the recommendations in these reviews and guidelines are supported by evidence gathered in a structured systematic review. The aim of this paper is to provide a systematic review on the value of antibiotic prophylaxis during different urologic procedures in order to make choices in the use of antibiotic prophylaxis on the best evidence currently available.

2. Methods

Between June 2006 and March 2007, the electronic databases Medline, Embase (1980–2006), and the Cochrane Library were searched using the terms postoperative complications, infection, bacteriuria, antibiotic prophylaxis, chemoprophylaxis, antibiotics, and premedication plus randomized controlled trial (RCT). Additional search terms were added for the different urologic interventions investigated (Table 1). Reference lists were screened for relevant trials.

RCTs comparing antibiotic prophylaxis during urologic procedures with a placebo or no antibiotic prophylaxis in patients with preoperative sterile urine were selected with language restriction (English, French, Spanish, German). Studies included in a pre-existent systematic review of good quality were not separately included. In the absence of a relevant RCT on the subject, case series and expert opinions were selected. Inclusion criteria were RCT, and, if absent, observational study, of good quality, clear definitions of outcome parameters, and minimal post-intervention follow-up of 30 d. All selected articles were reviewed independently on inclusion criteria and study design by two reviewers (AB, MPL). In case of discordance, a third reviewer was consulted (AG). Each included article was graded on level of evidence according to the level-of-evidence list of the Oxford Centre for Evidence-Based Medicine [8].

The primary outcome parameter was postoperative bacteriuria, in which postoperative was defined as the period of 30 d after the procedure, and bacteriuria as $\geq 10^3$ colony forming units (CFU/ml in symptomatic urinary tract infection and $\geq 10^5$ CFU/ml in asymptomatic bacteriuria [5]. The secondary outcome parameters were postoperative symptomatic urinary tract infection, fever, sepsis, and bacteraemia. Antibiotic prophylaxis was defined as use of antibiotics around an

| Table 1 – Search terms per urologic intervention |
|-----------------|-----------------|
| Intervention | Search terms |
| Cystoscopy | Cystoscopy |
| Prostate biopsy | Prostate biopsy |
| Urodynamic investigation | Urodynamic investigation, urodynamic examination, urodynamic study |
| Transurethral resection of prostate | Transurethral resection, prostatic transurethral resection, prostatectomy, TURP |
| Transurethral resection of bladder tumor | TURT, TURB, transurethral resection bladder tumor, bladder tumor resection |
| Extracorporeal shock wave lithotripsy | Lithotripsy, ESWL, shock wave therapy, shock wave lithotripsy, extracorporeal lithotripsy |
| Ureterorenoscopy | Ureteroscopy, ureterorenoscopy |
| Percutaneous nephrolithotomy | Kidney stone surgery, percutaneous nephrolithotomy, percutaneous nephrostomy lithotripsy |
intervention, preferably for a duration of less than 24 hr, with the first dose given before or at the start of the intervention.

3. Results

The included RCTs are presented in Tables 2–8, along with their level of evidence. When no RCT was included, the results and level of evidence of the non-RCTs are described in the corresponding paragraph below, along with the reasons for exclusion of the corresponding RCTs. For uniformity of outcomes, asymptomatic bacteriuria and asymptomatic urinary tract infection are both referred to as bacteriuria and symptomatic urinary tract infection (UTI) and symptomatic bacteriuria is referred to as symptomatic UTI.

3.1. Cystoscopy

A total of nine RCTs was found, of which four were included in this review (Table 2) [9–12]. The other studies were excluded because of lack of description of randomization method and group composition [13,14], investigating the effect of antibiotic treatment instead of prophylaxis [15], and studying more interventions than cystoscopy alone, without possibility of a separate analysis [16,17]. Of the included studies, Wilson et al [12] and Tsugawa et al [11] did not find a decrease in either bacteriuria or in symptomatic UTIs after use of antibiotic prophylaxis. Two studies, Jimenez Cruz et al [9] and MacDermott et al [10], found a significant decrease of symptomatic UTIs and bacteriuria, respectively.

Additionally, two useful case series were identified describing the post-cystoscopy infection incidence without use of antibiotic prophylaxis [18,19] (level of evidence (LOE) 4). Almallah et al [18] found a bacteriuria incidence of 4.9% (n = 103) within 48 hr post-cystoscopy. Although 14% of all patients reported irritative symptoms within 48 hr, only a small portion developed bacteriuria as well, resulting in a symptomatic UTI incidence of 1.9%. Clark et al [19] described a 7.5% incidence of post-cystoscopy bacteriuria. After identifying and excluding patients with risk factors, the incidence dropped to 0.8%. A history of symptomatic UTI and additional procedures performed during cystoscopy were identified as risk factors for developing post-cystoscopy bacteriuria.

In summary, it can be concluded that there is low to moderate evidence for the use of antibiotic prophylaxis in cystoscopy. A low incidence of bacteriuria and symptomatic UTIs is seen after cystoscopy, irrespective of the use of antibiotic prophylaxis. These results suggest that antibiotic prophylaxis is not needed for cystoscopy in the absence of risk factors for developing UTI.

3.2. Prostate biopsy

Thirteen RCTs were identified concerning prostate biopsy. Seven were excluded because they investigated prophylaxis methods other than antibiotic prophylaxis [20,21], used inadequate randomization methods [22–25], or investigated the effect of antibiotic treatment instead of prophylaxis [26]. Six RCTs comparing antibiotic prophylaxis with the use of a placebo or no antibiotic prophylaxis were included [27–32] (Table 3). They show a significant decrease of bacteriuria after prostate biopsy with the use of antibiotic prophylaxis compared with no use of antibiotics. Several RCTs also reported secondary outcome parameters. Fever was not significantly reduced after use of antibiotic prophylaxis in four RCTs [27,28,31,32], but was significantly reduced in another RCT of lower quality [29]. No significant difference in bacteraemia was found between placebo or control and antibiotic prophylaxis in four RCTs [27–29,32]. Two studies with high level of evidence showed opposite results regarding the incidence of post-procedural symptomatic UTI [27,31].

Consequently, there is moderate to high evidence that the use of antibiotic prophylaxis in prostate biopsy reduces the incidence of postprostate biopsy bacteriuria, although no conclusive evidence was found on the effect of antibiotic prophylaxis on symptomatic UTIs and other infectious complications. These results indicate a need for antibiotic prophylaxis in prostate biopsy.

3.3. Urodynamic investigation

A total of five RCTs evaluated the effect of antibiotic prophylaxis on bacteriuria after urodynamic investigation. However, none were included in this review because no “true” antibiotic prophylaxis was used, but rather administration of antibiotics after the intervention, use of incorrect randomisation methods, or use of outdated investigation techniques [33–37]. Cundiff et al investigated the effect of prophylaxis on combined cystoscopy and urodynamics in a well-designed study in women with stress incontinence (LOE 1B) [16]. No significant differences were found between the frequency of bacteriuria after use of prophylaxis (7.1%) and placebo (4.7%) at 1 wk follow up. However, since no separate analyses of both interventions were given, the study was excluded.
<table>
<thead>
<tr>
<th>Author</th>
<th>Level of evidence</th>
<th>Study type*</th>
<th>Population control/ intervention</th>
<th>Inclusion criteria</th>
<th>Intervention/ Control</th>
<th>Outcome parameter</th>
<th>Outcome</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wilson et al, 2005 [12]</td>
<td>1B</td>
<td>RCT, double blind</td>
<td>$N = 234$ (122/112)</td>
<td>- No AB prior</td>
<td>- Single dose norfloxacin 400 mg p.o.</td>
<td>- Symptomatic UTI: bacteriuria $&gt; 10^5$ CFU/ml + symptoms 7 d post-cystoscopy</td>
<td>- Post-cystoscopy incidence symptomatic UTI: placebo 0.82%, ABP 0.89%</td>
<td>- Trial discontinued at interim analysis (low infection rate + no differences between 2 groups)</td>
</tr>
<tr>
<td>Tsugawa et al, 1998 [11]</td>
<td>2B</td>
<td>RCT</td>
<td>$N = 45$ (24/21)</td>
<td>- No bacteriuria ($&gt; 10^4$, no pyuria ($&gt; 5$ white blood cells/HPF)</td>
<td>- Single dose ofloxacin 200 mg p.o.</td>
<td>- Pyuria, bacteriuria, fever 1 mo post-cystoscopy</td>
<td>- None of patients in control or intervention group developed pyuria, bacteriuria, or fever</td>
<td></td>
</tr>
<tr>
<td>Jimenez Cruz et al, 1993 [9]</td>
<td>2B</td>
<td>RCT</td>
<td>$N = 2172$ (1057/1115)</td>
<td>- Pre-cystoscopy sterile urine</td>
<td>- Single dose ceftriaxon 1 gram i.m.</td>
<td>- ASB, symptomatic UTI 2–3 d + 1 mo post-cystoscopy</td>
<td>- Incidence control/intervention group: ASB: 3.02%/1.52% (not significant)</td>
<td>- No definition of bacteriuria (count) - Most cultured organism: E. coli</td>
</tr>
<tr>
<td>MacDermott et al, 1988 [10]</td>
<td>2B</td>
<td>RCT</td>
<td>$N = 98$ (51/47)</td>
<td>- Pre-cystoscopy sterile urine</td>
<td>- 3 doses cephradine 1 g $&lt; 24$ h around cystoscopy</td>
<td>- Bacteriuria $&gt; 10^5$ CFU/ml 5 d post-cystoscopy</td>
<td>- Post-cystoscopy incidence bacteriuria no ABP 15.7% $\rightarrow$ ABP 2% (significant)</td>
<td></td>
</tr>
</tbody>
</table>

*RCT = Randomized Controlled Trial, AB = antibiotics, p.o. = per os (orally), UTI = urinary tract infection, CFU = colony forming units, ABP = antibiotic prophylaxis, HPF = high power field, ASB = asymptomatic bacteriuria, i.m. = intramuscular.

* It is mentioned if the study was performed in a double-blind, investigator-blinded, or patient-blinded manner. When no blinding took place, nothing is mentioned.
<table>
<thead>
<tr>
<th>Author</th>
<th>Level of evidence</th>
<th>Study type</th>
<th>Population control/intervention</th>
<th>Inclusion criteria</th>
<th>Intervention/Control</th>
<th>Outcome parameter</th>
<th>Outcome</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kapoor et al, 1998 [31]</td>
<td>1B</td>
<td>RCT, double blind</td>
<td>N = 457 (230/227)</td>
<td>- No bacteriuria</td>
<td>- Single dose ciprofloxacin 500 mg p.o.</td>
<td>- Bacteriuria &gt; 10⁴ CFU/ml 15 d postprostate biopsy</td>
<td>Incidence postprostate biopsy bacteriuria placebo 8% → ABP 3% (significant difference)</td>
<td>- Incidence postprostate biopsy symptomatic UTI placebo 5% → ABP 3% (not significant)</td>
</tr>
<tr>
<td>Aron et al, 2000 [27]</td>
<td>1B</td>
<td>RCT, patient blinded</td>
<td>N = 231 (75/79/77)</td>
<td>- No UTI</td>
<td>- Single dose ciprofloxacin 500 mg + tinidazole 600 mg p.o. + placebo until 3 d</td>
<td>- Bacteriuria (48 h post-biopsy) - Fever (&gt; 38 °C) - Bacteraemia</td>
<td>Incidence postprostate biopsy bacteriuria placebo 18.6% → ABP 5%–7.8% (significant difference)</td>
<td>Incidence postprostate biopsy fever placebo 6.7% → ABP 2.5%–2.6%</td>
</tr>
<tr>
<td>Crawford et al, 1982 [29]</td>
<td>2B</td>
<td>RCT, patient blinded</td>
<td>N = 48 (25/23)</td>
<td>- No UTI</td>
<td>- Carbenicillin 1 d prior + 1 d post biopsy - Placebo</td>
<td>- Bacteriuria (&gt; 10⁵ CFU/ml) 2 + 14 d post biopsy - Bacteraemia - Fever (&gt; 38.5 °C)</td>
<td>Incidence postprostate biopsy bacteriuria day 2 placebo 36% → ABP 8.6%, day 14 placebo 20% → ABP 8.6%</td>
<td>Incidence postprostate biopsy bacteraemia placebo 16% → ABP 22%</td>
</tr>
</tbody>
</table>

Remarks:
- No significant differences between single dose and 3 d of antibiotics.
<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>N</th>
<th>Procedure</th>
<th>Infections Post Prostate Biopsy</th>
<th>Result</th>
</tr>
</thead>
</table>
| Isen et al, 1999 | 1B RCT | N = 110 (23/42/45) | - No AB 3 d prior  
- No VHD, indwelling catheter, DM, steroid use, prostatitis  
- Single dose ofloxacin  
400 mg p.o.  
- Single dose TMP/SMX  
160/800 mg p.o.  
- No AB  
- Bacteriuria 7–10 d post biopsy  
- Incidence postprostate biopsy bacteriuria no AB 26.1% → ABP ofloxacin 4.8%, ABP TMP/SMX 6.7% | - Difference significant between no-AB group and ABP-group. No significant difference between 2 antibiotic schemes. |
| Melekos et al, 1990 | 2B RCT | N = 38 (16/22) | - Negative urine and blood cultures prior  
- No AB or endoscopic manipulation 24 h prior  
- No VHD  
- Piperacillin  
2 g i.v. 2 h prior + 2 h post biopsy  
- No AB  
- Bacteriuria 1 d post biopsy  
- Bacteraemia 1 d post biopsy  
- Incidence postprostate biopsy bacteriuria no AB 31% → ABP 9%  
- Incidence postprostate biopsy bacteraemia no AB 37.5% → ABP 14%  
- No significant differences.  
- In the same study, effect of povidone-iodine enema on post biopsy infectious complications was studied. | |
| Brown et al, 1981 | 2B RCT | N = 19 (9/10) | - Negative urine and blood cultures prior  
- No AB or endoscopic manipulation 24 h prior  
- No VHD  
- Gentamicin  
80 mg i.v. 30 min before biopsy  
- No AB  
- Bacteriuria  
(> 10^5 CFU/ml) 1 d post biopsy  
- Bacteraemia  
- Fever (> 101°F)  
- Incidence postprostate biopsy bacteriuria no AB 44% → ABP 20%  
- Incidence postprostate biopsy bacteraemia no AB 33% → ABP 40%  
- Incidence postprostate biopsy fever no AB 22% → ABP 50%  
- No significant differences.  
- In the same study, effect of povidone-iodine enema on post biopsy infectious complications was studied. | |

**RCT** = Randomized controlled trial, **AB** = antibiotics, **p.o.** = per os (orally), **UTI** = urinary tract infection, **CFU** = colony forming units, **ABP** = antibiotic prophylaxis **TMP/SMX** = trimethoprim/sulfamethoxazole, **i.v.** = intravenously, **DM** = diabetes mellitus, **VHD** = valvular heart disease.

*It is mentioned if the study was performed in a double-blind, investigator-blinded, or patient-blinded manner. When no blinding took place, nothing is mentioned.*
<table>
<thead>
<tr>
<th>Author</th>
<th>Level of evidence</th>
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<th>Outcome parameters</th>
<th>Outcome</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Berry et al, 2002 [6]</td>
<td>1A</td>
<td>Meta-analysis</td>
<td>- Bacteriuria: 32 RCTs N = 4260 (1914/2346) - Sepsis: 8 RCTs N = 1979</td>
<td>- Pre-TURP sterile urine RCT</td>
<td>- Different ABP schemes</td>
<td>- Postoperative bacteriuria (10⁴–10⁷ CFU/ml) 2-5 d after surgery - Postoperative sepsis (&gt; 38.5 °C, rigors, elevated CRP)</td>
<td>ABP gives: - Postoperative bacteriuria significant decrease 26% → 9.1% - Postoperative sepsis significant decrease 4.4% → 0.7% - All treatment duration protocols significant decrease bacteriuria: - Single dose: 57% decrease, short course (&lt; 72 h) 68% decrease, extended course (&gt; 72 h) 72% decrease - Most common organisms cultured: E. coli, Staphylococcus, enterococcus, Streptococcus. - Single dose seems less effective than short-term dose prophylaxis</td>
<td></td>
</tr>
<tr>
<td>Qiang et al, 2005 [7]</td>
<td>1A</td>
<td>Systematic review</td>
<td>- 28 RCTs N = 4694</td>
<td>- Pre-TURP sterile urine (&lt; 10⁸ CFU/ml) RCT</td>
<td>- Different ABP schemes</td>
<td>- Postoperative bacteriuria 1 wk post-TURP - Postoperative fever, bacteraemia, sepsis, additional antibiotic treatment needed, urethral stricture, catheterization, hospital duration</td>
<td>ABP gives significant reduction in postoperative complications: - Postoperative bacteriuria incidence decrease 26% → 9%; - Postoperative fever RD –0.11; - bacteraemia RD –0.02; - use additional antibiotics RD –0.20; - No significant reduction in post-TURP catheterization or hospitalization</td>
<td>- Significant decrease by different AB: aminoglycosides, TMP/SMX, 1st/2nd/3rd generation cephalosporin, quinolone - No significant decrease: nitrofurantoin, penicillin, β-penicillin</td>
</tr>
<tr>
<td>Author</td>
<td>Level of evidence</td>
<td>Study type</td>
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<tr>
<td>Delavierre et al, 1993 [53]</td>
<td>2B RCT</td>
<td>N = 61 (29/32)</td>
<td>Pre-TURT sterile urine (&lt; 10^9 CFU/ml)</td>
<td>- No AB &lt; 14 d prior</td>
<td>- Single dose levofoxacin 500 mg p.o. (A)</td>
<td>- Bacteriuria &gt; 10^4 CFU/ml 2 wk post-TURT</td>
<td>Incidence bacteriuria 3-5 d post-TURT decrease 29.7% (C) → 21.2% (A)/19.9% (B)</td>
<td>Post-TURT incidence bacteriuria placebo 24.1% → ABP 9.4% (not significant)</td>
</tr>
<tr>
<td>MacDermott et al, 1988 [10]</td>
<td>1B RCT</td>
<td>N = 91 (47/44)</td>
<td>Pre-TURT sterile urine (&lt; 10^9 CFU/ml)</td>
<td>- No AB &lt; 7 d prior</td>
<td>- 3 doses cephradine 1 g &lt; 24 h around TURT</td>
<td>- Bacteriuria &gt; 10^5 CFU/ml 5 d post-TURT</td>
<td>Incidence bacteriuria 3-5 wk post-TURT decrease 36.3% (C) → 25.9% (A)/26.1% (B)</td>
<td>Higher additional AB consumption no-ABP group, significance 5.0 (A+B) → 6.9 doses/patient (C)</td>
</tr>
</tbody>
</table>

TURT = Transurethral resection of bladder tumor, RCT = Randomized controlled trial, AB = antibiotics, CFU = colony forming units, i.v. = intravenously, UTI = urinary tract infection, ABP = antibiotic prophylaxis.

* It is mentioned if the study was performed in a double-blind, investigator-blinded, or patient-blinded manner. When no blinding took place, nothing is mentioned.
### Table 6 – Included studies on ESWL

<table>
<thead>
<tr>
<th>Author</th>
<th>Level of evidence</th>
<th>Study type</th>
<th>Population control/intervention</th>
<th>Inclusion criteria</th>
<th>Intervention/Control</th>
<th>Outcome parameter</th>
<th>Outcome</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bierkens et al, 1997</td>
<td>1B</td>
<td>RCT, patient blinded</td>
<td>N = 177 (30/41/39/29/38)</td>
<td>- Pre-ESWL sterile urine (&lt; 10⁴ CFU/ml)</td>
<td>- Single dose ciprofloxacin 200 mg iv (A)</td>
<td>Bacteriuria (&lt; 10⁴ CFU/ml)</td>
<td>Incidence 2 wk post-ESWL: Bacteriuria overall 20% Symptomatic UTI placebo 3% — ABP 2% Incidence 6 wk post-ESWL: Bacteriuria placebo 18.9% — ABP 24.3% Symptomatic UTI placebo 2.7% — ABP 1.4% Presence of indwelling catheter no different outcome</td>
<td>Study ended after interim analysis because of no differences between placebo-ABP groups</td>
</tr>
<tr>
<td>Ilker et al, 1995</td>
<td>1B</td>
<td>RCT</td>
<td>N = 311 (148/163)</td>
<td>- Pre-ESWL sterile urine - No risk factors (manipulation pre-ESWL, staghorn stone)</td>
<td>- Single dose ofloxacin 200 mg p.o.</td>
<td>Bacteriuria (&gt; 10⁵ CFU/ml)</td>
<td>Incidence bacteriuria: Control 0.68% — ABP 1.2% 7 d post-ESWL 0% bacteriuria 1 d + 4 wk follow-up No symptomatic UTI in both groups 0% bacteriuria, bacteremia and fever in both groups</td>
<td></td>
</tr>
<tr>
<td>Gattegno et al, 1988</td>
<td>2B</td>
<td>RCT, patient blinded</td>
<td>N = 50 (25/25)</td>
<td>- Pre-ESWL sterile urine - No AB 7 d prior</td>
<td>- Single dose ceftriaxon 1 g iv</td>
<td>Bacteriuria (&gt; 10⁵ CFU/ml) 1 + 7 d post-ESWL  4 wk post-ESWL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Claes et al, 1989</td>
<td>2B</td>
<td>RCT</td>
<td>N = 181 (92/89)</td>
<td>- Pre-ESWL sterile urine - No risk factors (staghorn stone, JJ, UTI)</td>
<td>- Single dose amoxycillin/ clavulanate 2 g/0.2 g iv</td>
<td>Bacteriuria</td>
<td>Incidence symptomatic UTI 7.6% in no AB-group, 0% in ABP group 1 d post-ESWL (significant)</td>
<td></td>
</tr>
</tbody>
</table>

ESWL = Extracorporeal shock-wave lithotripsy, RCT = Randomized controlled trial, CFU = colony forming units, iv = intravenously, UTI = urinary tract infection, ABP = antibiotic prophylaxis, p.o. = per os (orally), AB = antibiotic.

* It is mentioned if the study was performed in a double-blind, investigator-blinded, or patient-blinded manner. When no blinding took place, nothing is mentioned.
### Table 7 – Included studies on therapeutic URS

<table>
<thead>
<tr>
<th>Author</th>
<th>Level of evidence</th>
<th>Study type</th>
<th>Population control/intervention</th>
<th>Inclusion criteria</th>
<th>Intervention/Control</th>
<th>Outcome parameter</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Knopf et al, 2003 [69]</td>
<td>2B</td>
<td>RCT</td>
<td>N = 113 (56/57)</td>
<td>- No clinical/laboratory signs of infection</td>
<td>- Single dose levofloxacin 250 mg p.o.</td>
<td>- Bacteriuria (&gt; 10^5 CFU/ml)</td>
<td>Bacteriuria: control 12.5% → ABP 1.8% (significant difference)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- No AB for 1 wk prior</td>
<td></td>
<td></td>
<td>Symptomatic UTI 1 wk post-URS</td>
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<td></td>
<td>- Bacteriuria: placebo 12.5% → ABP 1.8% (significant difference)</td>
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<td></td>
<td>Symptomatic UTI 0% both groups</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>- Symptomatic UTI 0% both groups</td>
<td></td>
<td></td>
<td>Study reports on both URS and PNL</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- No AB 1 mo prior</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>- Placebo</td>
<td></td>
<td></td>
<td>Group numbers of interventions separate too small for significance.</td>
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</tbody>
</table>

### Table 8 – Included studies on PNL

<table>
<thead>
<tr>
<th>Author</th>
<th>Level of evidence</th>
<th>Study type</th>
<th>Population control/intervention</th>
<th>Inclusion criteria</th>
<th>Intervention/Control</th>
<th>Outcome parameter</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fourcade et al, 1990 [68]</td>
<td>2B</td>
<td>RCT, double blind</td>
<td>N = 71 (38/33)</td>
<td>- Pre-intervention sterile urine</td>
<td>- Single dose cefotaxim 1 gram iv</td>
<td>- Bacteriuria (&gt; 10^5 CFU/ml)</td>
<td>Bacteriuria: placebo 13% → ABP 3.5% 3 d post-PNL (not significant)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- No AB 1 mo prior</td>
<td></td>
<td></td>
<td>Fever not separately reported</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Placebo</td>
<td></td>
<td></td>
<td>Study reports on both URS and PNL</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Fever (&gt; 38 °C) 3 + 30 d post-PNL</td>
<td></td>
<td></td>
<td>Group numbers of interventions separate too small for significance.</td>
</tr>
</tbody>
</table>

**URS** = Ureterorenoscopy, **RCT** = Randomized controlled trial, **AB** = antibiotics, **p.o.** = per os (orally), **CFU** = colony forming units, **UTI** = urinary tract infection, **ABP** = antibiotic prophylaxis, **iv** = intravenously, **PNL** = Percutaneous nephrolithotomy.

* It is mentioned if the study was performed in a double-blind, investigator-blinded, or patient-blinded manner. When no blinding took place, nothing is mentioned.

**PNL** = Percutaneous nephrolithotomy, **RCT** = Randomized controlled trial, **AB** = antibiotics, **iv** = intravenously, **CFU** = colony forming units, **ABP** = antibiotic prophylaxis, **URS** = Ureterorenoscopy.

* It is mentioned if the study was performed in a double-blind, investigator-blinded, or patient-blinded manner. When no blinding took place, nothing is mentioned.
Case series (LOE 4) report a pre-urodynamics bacteriuria incidence of 1.9%–10.3% [38–41]. Without use of antibiotic prophylaxis, the post-urodynamics bacteriuria frequency was 1.1%–19.6% after 2–3 d follow-up and 4.1%–13.9% after 1 wk followup [38,39,41–46], whereas with use of antibiotics, the reported incidence was 1.8%–4.0% for women and 3.6%–6.2% for men [47,48]. Additionally, increasing age was identified as a risk factor for developing posturodynamics bacteriuria [41,43,45]. Consequently, the evidence for use of antibiotic prophylaxis in urodynamic investigation is low and can only be gained from case series. Furthermore, a relatively low incidence of posturodynamics bacteriuria is seen, with a small increase in bacteriuria when no antibiotic prophylaxis is given, whereas no information on posturodynamics symptomatic UTI is available. These results suggest there is no need for antibiotic prophylaxis in urodynamic investigations.

However, the same low level of evidence may support the use of antibiotic prophylaxis in those patients with known increased risk for infections (eg, neurogenic bladder, transplant patients, immunodepressed patients, or carriers of vesicoureteral reflux).

3.4. Transurethral resection of the prostate

Transurethral resection of the prostate (TURP) is the most extensively studied subject in urology regarding the use of antibiotic prophylaxis. A good number of RCTs published before 2005 was identified, but since those RCTs were already included in the high-quality systematic reviews of Berry and Qiang, they were not included separately in this review. Next to the systematic reviews of Berry [6] and Qiang [7], one study was included [49]; and another was excluded [50] because no univocal antibiotics regimen was followed.

The systematic reviews by Berry et al [6] and Qiang et al [7] included 32 and 28 RCTs, respectively, with 21 RCTs reviewed in both studies. The average enrollment was 4474 patients (Table 4). Both reviews used postoperative bacteriuria as their main outcome parameter, complemented by several additional outcome parameters. Their conclusions were similar, favouring the use of antibiotic prophylaxis in TURP. They concluded that antibiotic prophylaxis gives a significant decrease in post-TURP bacteriuria, post-TURP fever, sepsis, and the need for additional antibiotics post-TURP. There was a trend suggesting higher efficacy for a short course (< 72 hours) of antibiotic prophylaxis than for a single-dose regimen [6]. The findings of Wagenlehner et al [49] are comparable, although the findings did not reach statistical significance.

In summary, it can be concluded that there is high evidence that the use of prophylactic antibiotics in TURP decreases bacteriuria and clinical infectious complications.

3.5. Transurethral resection of bladder tumor

Four studies of transurethral resection of bladder tumor (TURT) met the inclusion criteria. Two were excluded from the present review due to a lack of proper randomisation [51] and questionable statistical analysis [52]. The two included studies of Delavierre et al [53] and MacDermott et al [10] are relatively outdated and included small numbers of subjects (Table 5). Both studies found a nonsignificant decrease in incidence of post-TURT bacteriuria with the use of antibiotic prophylaxis, and the 0% incidence of symptomatic UTIs in both groups precludes any conclusion in the study of Delavierre et al [53].

In conclusion, there is moderate to low-grade evidence suggesting that antibiotic prophylaxis is not necessary in TURT.

3.6. Extracorporeal shock-wave lithotripsy

Extracorporeal shock-wave lithotripsy (ESWL) originated in the 1980s as a treatment for renal and ureter stones. Since then, several studies have been performed questioning the need for antibiotic prophylaxis in this intervention. Pearle et al [54] concluded in a meta-analysis of eight RCTs that the use of antibiotic prophylaxis in patients with pre-ESWL sterile urine is beneficial and reduces the post-ESWL complication rate. However, since several of the evaluated studies in their review did not meet the selected inclusion criteria of the present systematic review; ie, evaluation of the effect of antibiotic prophylaxis instead of treatment [55,56], this review was excluded. Reference lists were screened and RCTs meeting our inclusion criteria were added to the already identified ones and assessed. Four RCTs met the inclusion criteria and were included in this review [57–60] (Table 6). Two RCTs were excluded because of incomplete description of methodology and results [61] and inconsistency between results and conclusions [62]. Only one of the included studies showed a significant decrease in the incidence of post-ESWL symptomatic UTIs after use of antibiotic prophylaxis [58]. None of the other included RCTs with a higher level of evidence reproduced those data. The overall incidence of post-ESWL
symptomatic UTIs was low both with and without use of antibiotics. In a number of case series, the reported incidence of post-ESWL bacteriuria is 0%–5.1% in patients with pre-ESWL sterile urine (LOE 4) [63–67]. This finding is consistent with the results from the RCTs. Presence of a struvite stone was identified as a risk factor for developing post-ESWL bacteriuria [65].

Altogether, there is a fair amount of evidence available for this intervention showing that the post-ESWL rate of bacteriuria and symptomatic UTIs is low and use of antibiotic prophylaxis does not decrease this incidence. This implies there is no need for antibiotic prophylaxis in uncomplicated patients undergoing ESWL when preoperative cultures are negative.

3.7. Ureterorenoscopy

Ureterorenoscopy (URS) can be used for diagnostic and therapeutic measures. No studies were found examining the diagnostic option. Two small RCTs concerning the use of antibiotic prophylaxis in endoscopic stone removal were identified and included [68,69] (Table 7). They both describe a positive effect of antibiotic prophylaxis on post-URS bacteriuria. Post-URS symptomatic UTI was 0% in both groups in a study by Knopf et al [69]. Only moderate to low-level evidence advocates the use of antibiotic prophylaxis in therapeutic URS with respect to postoperative bacteriuria. Low evidence supports the nonbeneficial effect of prophylactic antibiotics regarding post-URS symptomatic UTI.

For diagnostic URS, no studies were found and reference to expert opinion may be advocated, with consequent low evidence (LOE 5). The results suggest no need for prophylaxis in diagnostic URS in uncomplicated patients and moderate to low evidence for prophylaxis in therapeutic URS [2,5].

3.8. Percutaneous nephrolithotomy

Only one RCT was found comparing placebo with antibiotic prophylaxis in both percutaneous nephrolithotomy (PNL) and URS, with separate analyses possible for both interventions [68] (Table 8). Unfortunately, the individual group size was too small to reach statistically significant differences in both PNL and therapeutic URS. Several case studies were identified [70,71]. Following 107 patients with preoperative sterile urine, Charton et al found a post-PNL bacteriuria of 35% while using no antibiotic prophylaxis and 10% of patients presenting with post-PNL fever without sepsis or bacteraemia [70] (LOE 4). Whereas Osman et al describe a post-PNL transient fever and symptomatic UTI in 32.1% and 3.5% of 315 patients, needing treatment with antibiotics [71] (LOE 4). When comparing different antibiotic prophylaxis regimens in a RCT, it showed that a single dose was as effective in preventing postoperative infections as multiple doses when using ofloxacin or cefuroxim in combination with norfloxacin [72,73].

Therefore, when the preoperative urine culture is negative, there is low evidence suggesting a more favourable outcome after PNL when using prophylactic antibiotics, without an evident advantage for any specific antimicrobial regimen.

3.9. Open/laparoscopic urologic interventions

An extensive search was performed addressing urologic open and laparoscopic interventions, but no relevant urologic studies could be identified. Subsequently, the relevant surgical literature was screened. Surgical wound classification in the categories clean, clean-contaminated, contaminated, and dirty seems just as relevant for urologic surgery as for general surgery [74]. In this way, by assessing the pre-intervention surgical wound class, an estimate can be made of the need for antibiotic prophylaxis during surgery.

Clean surgery involves uninfected tissues without opening of the urinary tract and with primary closure of the wound. In clean-contaminated surgery, the urinary tract is entered under controlled conditions, without the presence of infected tissues or bacteriuria. Surgery with use of bowel tissue is also classified as clean-contaminated. The presence of a nontreated infection, including UTI, should be considered as contaminated urologic surgery. When pus is present, the surgery is labelled dirty [74].

Implantation of prosthesis material is not classified as above. Since infectious complications are potentially serious when involving prosthesis material, antibiotic coverage is advocated irrespective of surgical class [74].

Derived from the surgical literature and not supported by urologic evidence, there is no indication for antibiotic prophylaxis in clean surgery, whereas there is an indication in clean-contaminated and prosthetic surgery. Contaminated and dirty surgery should be covered by therapeutic antibiotics instead of prophylactic dosages.

4. Discussion

In this systematic review, all currently available RCTs addressing the use of antibiotic prophylaxis in
urologic interventions were identified and assessed and the results grouped and presented. For most urologic interventions, there is only moderate to low evidence for the use of antibiotic prophylaxis, with the exception of TURP and prostate biopsy. Strong evidence supports the use of short-term prophylaxis for TURP, and this evidence is moderate to high for prostate biopsy.

The main point of consideration when assessing the benefit of antibiotic prophylaxis is what to consider as a favourable outcome. Is it decrease of postintervention bacteriuria, or the decrease of symptomatic UTIs or other infectious complications? While the aim of preventing symptomatic UTIs and other serious infectious complications seems evident, the need to prevent asymptomatic bacteriuria remains questionable. Asymptomatic bacteriuria is often of no clinical importance and resolves spontaneously in many cases. While all the studies included in our review had bacteriuria as primary parameters, few of them [6,7,9,11,12,27,31,53,57,58,60,69] contemplated UTI, fever, or symptoms as an outcome. Since “postoperative bacteriuria” is the best-assessed outcome parameter, we chose it as the primary outcome parameter for our review purposes. Because we were aware of the possible lack of clinical significance of bacteriuria, our secondary outcome parameters were symptomatic UTI, fever, sepsis, and bacteraemia. In our review, we could not find high evidence supporting the use of antibiotic prophylaxis in urologic interventions to prevent UTI except for TURP [6]. The evidence was moderate to high for prostate biopsy [27,31], and low to moderate for cystoscopy [9,11,12]. Currently, not enough evidence supports the systematic use of antibiotic prophylaxis to prevent UTIs in the rest of the procedures.

However, when performing the present systematic review, we realized not only that variations in duration, antibiotic agent, or dose of what was considered “antibiotic prophylaxis” existed, but also that variables of importance in some complicated conditions as can be the presence of indwelling upper urinary tract drainages (eg, lithiasic obstruction, simple interventions in immunodepressed patients) were insufficiently explored. In fact, the presence of risk factors for infection was an exclusion criterion in all the RCTs analyzed. The presence of general risk factors (eg, comorbidity), risk factors related to the type of intervention (eg, oncologic) or urologic risk factors (eg, high irrigation pressure during endoscopy or infected stone) [5,74] increases the risk of a postoperative infectious complication and, therefore, the need for an adequate antibiotic prophylaxis even in cases of low evidence for benefit. Still, good clinical practice should drive the decision in those circumstances.

The inclusion of laparoscopic intervention under the same classification as for open surgery is justified by the lack of RCTs examining antibiotic prophylaxis. Some observational series illustrate the direct correlation between complication rate and complexity of the laparoscopic surgery. It is possible that infective outcomes increase with laparoscopic complexity, but the urologic case series report an extremely low rate, between 0.1% and 0.8% of infective complications. However, neither UTI as such nor the relation between infection rate and type of laparoscopic procedure were described in any of those series [75–77].

Finally, the reader should keep in mind that antibiotic prophylaxis is only one of the various measures to prevent post-intervention infectious complications. Antibiotic prophylaxis cannot compensate for inadequate operative care, and, therefore, general recommendations for prevention of surgical site infections should be followed [74]. Altogether, the evidence presented in this review can be used to establish local antibiotic prophylaxis guidelines. Such guidelines will increase the quality of care and at the same time reduce both costs and the development of microbial resistance [78,79].

5. Conclusions

Ideally, antibiotic prophylaxis in urologic procedures should only be administered when well-performed studies demonstrate its beneficial effect on post-intervention infectious complications. Because of the current lack of evidence, those patients with increased risk for infectious complications should receive antibiotic prophylaxis. Further research is needed because, except for TURP and prostate biopsy, there is a lack of well-performed studies.

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Study concept and design: Goossens, Laguna.
Acquisition of data: Bootsma, Laguna, Goossens.
Analysis and interpretation of data: Laguna, Geerlings.
Drafting of the manuscript: Bootsma.
Critical revision of the manuscript for important intellectual content: Laguna, Geerlings, Goossens.
Statistical analysis: Goossens, Bootsma, Laguna.
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Supervision: Goossens, Geerlings.
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References


Editorial Comment on: Antibiotic Prophylaxis in Urologic Procedures: A Systematic Review

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Antimicrobial prophylaxis for urologic procedures is a major issue, as potential advantages of antibiotic administration should be carefully weighed against potential side effects, microbial resistance, and health care costs.

The present systematic literature review [1] adds further information to available European Association of Urology (EAU) recommendations for antibiotic prophylaxis in urologic surgery, which currently exist in the form of a nonstructured review [2]. Both reviews recommend no prophylaxis for cystoscopy, transurethral resection of bladder tumours, urodynamics, simple ureteroscopy (diagnostic or for distal uncomplicated stones), extracorporeal shock wave lithotripsy (ESWL), and clean (urinary tract not opened) open or laparoscopic surgery, providing absence of risk factors. Both recommend prophylaxis for transurethral resection of the prostate (TURP); but while EAU guidelines suggest it can be omitted for low-risk patients with small prostates, the present review outlines the higher efficacy of short-course (<72 h) over single-shot prophylaxis found in randomised controlled trials (RCTs). Both reviews recommend prophylaxis for prostate biopsy, complicated (proximal or impacted stone) ureteroscopy, percutaneous nephrolithotomy, and clean-contaminated (urinary tract opened) surgery (either open or laparoscopic), but EAU guidelines favour short-course prophylaxis over single-shot prophylaxis. Again, the present review outlines no advantage of short-course over single-shot prophylaxis for prostate biopsy in RCTs, and that issue is far from having been solved or even adequately addressed for the other procedures. While for endourologic procedures such lack of information may be justified by the great number of clinical
variables (infection, obstruction, surgical technique, patient conditions, and comorbidities) to be taken into account, quite impressive is the absence of RCTs testing antibiotic prophylaxis in open and laparoscopic urological procedures. It is noteworthy that EAU recommendations on open procedures are based on general surgery, whereas laparoscopic procedures are just assumed to require the same prophylactic regimen used for the corresponding open procedures.

Well-designed RCTs are therefore eagerly awaited, as in the era of evidence-based medicine rational use of antibiotics should be a marker of quality in a urologic centre.

References


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