Prophylactic antibiotic use in transurethral prostatic resection: a meta-analysis

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Authors' objectives
To determine the efficacy of antibiotic prophylaxis in men undergoing transurethral prostatic resection.

Searching
MEDLINE (from 1979 to 2000), EMBASE (from 1984 to 2000) and the Cochrane Library were searched for publications in the English language. The search was conducted using the terms 'antibiotic prophylaxis', 'transurethral resection', 'chemoprophylaxis', 'prostatic transurethral resection' and 'prostatectomy' in combination with the filter 'randomized controlled trial'. The reference lists from identified trials and reviews were examined.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible.

Specific interventions included in the review
Comparisons of an appropriate antibiotic with a placebo or no treatment control were eligible. The classes of antibiotics included were co-trimoxazole, nitrofurantoin, aminoglycosides, quinolone, penicillin, beta-resistant penicillin, and first-, second- and third- generation cephalosporins. The protocols for treatment duration included the following: single-dose regimens in which the dose was predominantly administered pre-operatively; short-course regimens with more than one antibiotic dose administered within 72 hours of surgery or until catheter removal; and extended-course regimens in which multiple antibiotic doses were administered beyond 72 hours from the time of the procedure or beyond catheter withdrawal.

Participants included in the review
Clearly identified patients with pre-operatively sterile urine undergoing transurethral prostatic resection were eligible. The populations were demographically similar with a mean patient age of 70 years (range: 68 to 73).

Outcomes assessed in the review
Studies that assessed bacteriuria and/or clinical septicaemia were eligible. The primary outcome was the post-operative rate of bacteriuria between post-operative days 2 and 5. The secondary outcome was the rate of clinically apparent sepsis, as defined by the following objective markers: persistent temperature greater than 38.5, rigors, and elevated C-reactive protein. Bacteriuria was defined in the individual studies as growth between $1 \times 10^4$ and $1 \times 10^7$ per mL. The definition of septicaemia was based on clinical and/or bacteriological grounds.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the reviewers performed the selection.

Assessment of study quality
Study quality was assessed on the basis of treatment allocation and blinding of investigators (see Other Publications of Related Interest). For treatment allocation, classification was according to whether there was adequate, unclear or inadequate concealment. Blinded groups were classified as either double-blind if the treating investigators, laboratory staff and patients were blinded, or partially blind if the laboratory staff and patients were blinded. The data on methodological quality were extracted independently, and the data from a random sample of 30% of the studies were compared to assess consistency. The authors do not state how many of the reviewers performed the quality assessment.

Data extraction

Database of Abstracts of Reviews of Effects (DARE)
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The data were extracted independently, and the data from a random sample of 30% of the studies were compared to assess consistency. The authors do not state how many of the reviewers performed the data extraction. There were no differences in the data collection. The following data were extracted: study population characteristics; antibiotic therapy and dosing protocol; sample size; drop-out rate; outcome definitions and events; and adverse events.

Methods of synthesis
How were the studies combined?
The pooled relative risk reduction (RRR) and 95% confidence interval (CI) for bacteriuria and septicaemia was estimated using a random-effects model. The data were weighted by the inverse of the variance for each study.

How were differences between studies investigated?
Statistical heterogeneity was assessed using the Q Cochran chi-squared test, with a p-value of less than 0.1 indicating significant heterogeneity. The analyses were repeated after the studies were separated into subgroups according to antibiotic class and treatment duration protocol.

Results of the review
Thirty-two RCTs (4,260 patients) were included.

Less than 10% of the patients were removed from the analysis after treatment allocation. The most common reasons for removal were pre-operative infected urine and non-satisfactory pre-operative and/or post-operative urine culture. Randomisation was adequately concealed in 47% of the trials, and double-blinding with placebo use was present in 30% of the studies.

Bacteriuria.
Antibiotic prophylaxis significantly decreased the rate of post-operative bacteriuria from 26 to 9.1%. The RRR was 65% (95% CI: -55, -72). There was no statistical evidence of heterogeneity (Q=34, d.f.=31, p=0.31).

Septicaemia (8 RCTs, 1,979 patients).
Antibiotic prophylaxis significantly decreased the rate of post-operative septicaemia from 4.4 to 0.7%. The RRR was 77% (95% CI: -55, -88). There was no statistical evidence of heterogeneity (Q=2.7, d.f.=7, p=0.91).

Bacteriuria by antibiotic class.
Aminoglycosides (4 RCTs) significantly decreased the risk of bacteriuria. The RRR was 55% (95% CI: 0, -80, p=0.051).

Co-trimoxazole (3 RCTs) significantly decreased the risk of bacteriuria. The RRR was 64% (95% CI: -4, -87, p=0.041).

First-generation cephalosporins (3 RCTs) significantly decreased the risk of bacteriuria. The RRR was 66% (95% CI: -36, -82, p<0.01).

Second-generation cephalosporins (4 RCTs) significantly decreased the risk of bacteriuria. The RRR was 63% (95% CI: -28, -81, p<0.01).

Third-generation cephalosporins (13 RCTs) significantly decreased the risk of bacteriuria. The RRR was 67% (95% CI: -55, -76, p<0.01).

Quinolones (4 RCTs) significantly decreased the risk of bacteriuria. The RRR was 92% (95% CI: -75, -98, p<0.01).

Nitrofurantoin (1 RCT), penicillin (1 RCT) and beta-penicillin (1 RCT) did not significantly decrease the risk of bacteriuria.
Statistical heterogeneity within subgroups was not detected but there was significantly heterogeneous among subgroups (chi-squared test = 14, d.f.=8, p=0.09).

All cephalosporins combined (20 RCTs, 2,874 patients) significantly decreased the risk of bacteriuria. The RRR was 66% (95% CI: -57, -73, p<0.01). Statistical heterogeneity was not detected (Q=5, d.f.=7, p=0.64).

Bacteriuria by treatment duration. Bacteriuria was significantly decreased by all treatment duration protocols and there was no statistical heterogeneity among subgroups (chi-squared test = 2.3, d.f.=2, p=0.31).

The RRR was 72% (95% CI: -42, -87) for extended-course protocols (4 RCTs), 68% (95% CI: -56, -77) for short-course protocols (17 RCTs), and 57% (95% CI: -41, -68) for single-dose protocols (12 RCTs).

Cephalosporins significantly decreased rates of bacteriuria in all treatment duration protocols, and statistical heterogeneity between subgroups was detected (chi-squared test = 9.4, d.f.=2, p<0.01). The RRR was 82% (95% CI: -37, -95, p<0.01) for extended-course protocols (1 RCT), 71% (95% CI: -63, -77, p<0.01) for short-course protocols (12 RCTs), and 52% (95% CI: -38, -62, p<0.01) for single-dose protocols (7 RCTs).

Bacteriuria rates by methodological characteristics.

No significant differences in bacteriuria rates were found between studies in which allocation concealment was adequate and those with unclear or inadequate concealment. No differences were found between double-blind and partially-blind placebo-controlled trials.

Adverse effects.

Overall, nineteen adverse effects of antibiotics were reported. Two severe responses required antibiotic withdrawal. The adverse effects included rashes, gastrointestinal upsets, nausea and confusion.

Authors' conclusions
Antibiotic prophylaxis significantly deceased the incidence of bacteriuria and clinical septicaemia in men with pre-operative sterile urine undergoing transurethral prostatic resection. A significant decrease in bacteriuria incidence can be achieved with a range of antibiotic agents, including quinolones, cephalosporins and co-trimoxazole. Short-course antibiotics may be more effective than single-dose regimens.

CRD commentary
The aims were stated and the inclusion criteria were defined in terms of the study design, intervention, participants and outcomes. Three relevant literature sources were searched, but the methods used to select the studies were not described. The authors acknowledged that the restriction of eligible studies to those published in the English language might have resulted in the omission of other relevant studies. The lack of an attempt to locate unpublished material raises the possibility of publication bias. The included studies were restricted to RCTs and a formal quality assessment was conducted. Relevant data were tabulated and some details of the methods used to extract the data were given, although not the number of reviewers involved. In view of the absence of statistical heterogeneity between the studies for the outcomes assessed and the demographic similarity of the sample populations, the data were appropriately combined in a meta-analysis. Subgroup analyses were used to explore the influence of methodological quality, duration of treatment, and antibiotic class on the results.

This is a clearly presented review and the evidence presented supports the authors' conclusions.

Implications of the review for practice and research
Practice: The authors state that while many common classes of antibiotics are effective in reducing bacteriuria and clinical septicaemia after transurethral prostatic resection, therapeutic agents of the quinolone group and short-dosing protocols appear to provide the greatest decrease in bacteriuria rates. They advise that the appropriate choice of antibiotic agent depends on local bacteria sensitivity and patterns of resistance with time.
Research: The authors did not state any implications for further research.

**Bibliographic details**

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**Other publications of related interest**

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Subject indexing assigned by NLM

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.