Antimicrobial prophylaxis prior to shock wave lithotripsy in patients with sterile urine before treatment: a meta-analysis and cost-effectiveness analysis

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Authors' objectives
To determine the efficacy and cost-effectiveness of routine antimicrobial prophylaxis prior to shock wave lithotripsy (SWL) in patients with sterile pre-treatment urine culture.

Searching
MEDLINE was searched from 1980 to the 'present' day using the following keywords: 'shock wave lithotripsy', 'antibiotics', 'bacteruria' and 'randomised controlled trials'. Reference lists of retrieved articles were reviewed. Non-English language articles were translated by medically-trained employees fluent in the respective language.

Study selection
Study designs of evaluations included in the review
Articles addressing the use of antimicrobial prophylaxis prior to, during and after SWL were studied. Randomised controlled trials (RCTs) and clinical series were included. Articles were excluded if raw data were not provided or subgroup analysis was not complete.

Specific interventions included in the review
Prophylactic antimicrobial therapy with the following drugs: oral quinolone, sulphamethoxazole and trimethoprim, and intravenous amoxycillin, clavulanate, azlocillin and cephalosporin. Combinations of these drugs were also included.

Participants included in the review
Patients undergoing SWL were studied. Of the patients in the individual trials, 50-100% were treated for renal calculi and the remainder for ureteral calculi. The most commonly-used anaesthetics were epidural and general.

Outcomes assessed in the review
The main outcome was the diagnosis of urinary tract infection (UTI) post-lithotripsy. The definition of a positive urine culture varied from 1E4 to 1E5 cfu/mL.

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 authors performed the selection.

Assessment of study quality
The authors do not state that they assessed validity.

Data extraction
Two authors independently extracted the following data onto a data abstraction sheet: number of patients in treatment and non-treatment arms, stone location (kidney versus ureter), mean stone size, endoscopic manipulation prior to lithotripsy, type of lithoscope, type of anaesthetic, prophylactic antimicrobial regime, timing of urine culture after lithotripsy, definition of positive urine culture, and number of patients in each group with a positive urine culture. If required, differences in interpretation were reconciled. The relative risk (RR) of UTI post-lithotripsy and their 95% confidence intervals (CIs) were calculated for the individual studies.

Methods of synthesis
How were the studies combined?
The overall percentage of patients in each treatment group who developed a UTI post-lithotripsy was calculated. Meta-analysis was performed on the 8 RCTs, using the FAST*PRO Confidence Profile Method and a Bayesian approach to give the median probability of a UTI and the 95% CI of patients in the two treatment groups. RRs were calculated using True Epistat (version 5.0).

How were differences between studies investigated?
A chi-squared test was used to assess heterogeneity among RCTs in the incidence of UTI.

Results of the review
Eight RCTs of prophylaxis versus placebo (N=885) and 5 (6 stated in the abstract) clinical series (N=597) were included.

Development of UTI: overall, 2% of treated patients and 7% of untreated patients developed a UTI after SWL. RR of UTI for prophylaxis versus no prophylaxis was 0.45 (95% CI: 0.22, 0.93, P=0.0005). The chi-squared test for heterogeneity showed no significant heterogeneity (P=0.33). Median probabilities of UTI for patients receiving and not receiving prophylaxis were 2.1% (95% CI: 0.9, 3.6) and 5.7% (95% CI: 3.8, 8.4), respectively.

The development rate of UTI for patients without antimicrobial therapy in clinical series was 4%.

Cost information
Cost-effectiveness analysis was performed using the median estimates for UTI post-lithotripsy, based on Bayesian meta-analysis. The cost of antibiotic treatment for documented UTI was graphed against the cost of prophylactic treatment plus treatment of UTI for various values of per-patient prophylaxis costs, to determine the cost-effectiveness according to per-patient prophylaxis costs. It was found that the use of an inexpensive prophylactic regime was critical if the prophylaxis-for-all approach was to be cost-effective.

For a full discussion of the economic aspects of this study see NHS EED record 21997000689.

Authors' conclusions
A policy of antibiotic prophylaxis prior to SWL in patients with sterile pre-treatment urine culture is efficacious in reducing the rate of post-SWL UTI. Discounting in-patient episodes for sepsis and acute pyelonephritis, the strategy is not cost-effective. Using literature-derived incidence estimates for post-SWL urosepsis or pyelonephritis necessitating in-patient treatment, prophylaxis becomes both efficacious and cost-effective and thus constitutes a dominant strategy.

CRD commentary
Retrieved articles were not limited to those written in the English language. Details are given of the methods of data extraction. The efficacy of prophylactic antimicrobial therapy in preventing post-SWL UTI was analysed using RR estimates and the median probability from a Bayesian approach. Various scenarios were investigated in the cost-effectiveness analysis. By limiting the literature search to one database some relevant articles may have been omitted. No details are given of the methods used to select studies for inclusion, or of any evaluation of the validity of the primary studies. More comprehensive details of the primary studies would have been helpful, and may have been obtainable from the original author if not included in the study report. Many differences appear to exist among the trials and some investigation of the influence of these variables on the outcomes would have been welcome, though any investigation of the relative efficacy of different therapeutic regimes was, as the authors state, precluded by eight different regimes in the eight RCTs. No information on the incidence of adverse reactions to antimicrobial therapy, or details of the clinical series, are included.

Without an evaluation of the validity of the included studies, fuller information on the characteristics of the patients and consideration of adverse reactions, it is not possible to support the authors' conclusions.
Implications of the review for practice and research
Studies to compare the efficacy of various prophylactic regimes are required to identify an inexpensive and effective regime.

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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.