Antibiotics versus placebo in the treatment of women with uncomplicated cystitis: a meta-analysis of randomized controlled trials
Falagas ME, Kotsantis IK, Vouloumanou EK, Rafailidis PI

CRD summary
The authors concluded that clinical and microbiological success was more likely to occur in women with acute uncomplicated cystitis when treated with antibiotics compared to placebo. This was a generally well-conducted review. The authors’ conclusion is likely to be reliable.

Authors’ objectives
To evaluate the effectiveness and safety of antibiotics in the treatment of acute uncomplicated cystitis.

Searching
PubMed, Scopus and Cochrane Central Register of Controlled Trials (CENTRAL) were searched to November 2008. Search terms were reported. Bibliographies of relevant articles were hand-searched for additional material. Conference abstracts, commentaries, editorials, letters, or studies published in languages other than English, Spanish, French, German, Italian and Greek were excluded from the review.

Study selection
Randomised controlled trials (RCTs) that involved women (not pregnant or immunocompromised) with acute uncomplicated cystitis (with symptoms suggestive of urinary tract infection and confirmed by positive dipstick test and/or a positive urine culture) were eligible for inclusion in the review. Eligible comparators were antibiotics versus placebo.

Outcomes of interest were: clinical success defined as complete (cure) or non-complete (improved) at the first evaluation after the end of treatment (symptoms that remained after at least one day of treatment were defined as persistent); bacteriological success (eradication) confirmed by a negative urine culture at the end of treatment and at first follow-up assessment after the end of treatment; microbiological reinfection confirmed by a positive urine culture (with a different micro-organism to the initial culture) at the long-term follow-up assessment (regardless of a sterile urine culture at a previous time point); microbiological relapse confirmed by a positive urine culture with the same micro-organism as the initial culture; development of pyelonephritis defined as a complication indicated by fever and flank pain; and adverse events.

All studies were performed in Europe. Participants were women aged between 15 and 84 years, largely with mild to moderate symptoms of cystitis. Included antibiotics were pivmecillinam, nitrofurantoin, cefixime, co-trimoxazole and amoxicillin. Dosing schedules varied. Follow-up ranged from three days from commencement to three months after end of treatment.

Two reviewers independently selected studies for inclusion in the review.

Assessment of study quality
Trial quality assessment was conducted using the Jadad scale in relation to randomisation, blinding and the description of withdrawals. The maximum achievable score was 5. Trials graded higher than 2 were considered to be of adequate methodological quality.

Two reviewers independently performed the quality assessment.

Data extraction
Where possible, intention-to-treat data were extracted to calculate odds ratios (ORs) and 95% confidence intervals (CI).
Two reviewers independently extracted the data.

**Methods of synthesis**

Where dichotomous data were available, a random-effects meta-analysis was used to synthesis odds ratios and 95% CIs. Heterogeneity was assessed using the $X^2$ test; a p value less than 0.1 indicated statistically significant heterogeneity.

**Results of the review**

Five RCTs (n=1,407) were included in the meta-analysis. Two trials received a Jadad score of 2, two scored 3 and one scored four. All RCTs were double-blinded.

Clinical success was significantly higher in patients treated with antibiotics than placebo (OR 4.81, 95% CI 2.51 to 9.21; four trials, n=1,062). This was particularly noted for cure (OR 4.67, 95% CI 2.34 to 9.35, p<0.0001).

Microbiological success at the end of treatment was significantly higher in the treatment group (OR 10.67, 95% CI 2.96 to 38.43, p=0.0003; three trials, n=967). The direction of effect remained after the end of treatment (OR 5.38, 95% CI 1.63 to 17.77, p=0.006; three trials, n=738). There was significant heterogeneity in both analyses ($I^2=82\%$, p=0.004 and $I^2=76\%$, p=0.01).

Re-infection or relapse after the end of treatment was significantly more likely in the placebo group after the end of treatment (OR 0.27, 95% CI 0.13 to 0.55; five trials, n=843). There was no significant difference in the incidence of pyelonephritis (two trials, n=962) or in emergence of resistance (three trials, n=173) between treatment and placebo groups.

Adverse events were more likely to occur in women treated with antibiotics compared with placebo (OR 1.64, 95% CI: 1.10 to 2.44, p=0.01; four trials, n=1,069). There was no significant heterogeneity. There was no significant difference between groups in terms of withdrawals due to adverse events.

**Authors' conclusions**

Clinical and microbiological success was more likely to occur in women with acute uncomplicated cystitis when treated with antibiotics compared to placebo.

**CRD commentary**

This review addressed a clear research question supported by inclusion criteria that were potentially reproducible. The search strategy appeared to include some relevant sources and attempts were made to minimise language bias. There was no apparent search for unpublished material, so relevant trials may have been missed and publication bias could not be ruled out. An appropriate validity assessment tool was used to evaluate the included study designs; the quality of trials was deemed adequate. Adequate steps were taken throughout the review process to minimise errors and bias. Sufficient study details were provided. The chosen method of synthesis appeared to be appropriate, although clinical heterogeneity was noted among the trials. This was a generally well-conducted review, and the authors' conclusion is likely to be reliable.

**Implications of the review for practice and research**

**Practice:** The authors stated that physicians should continue prescribing antibiotic treatment to women with symptoms of cystitis, although some discretion should be considered in terms of postponing treatment for those with minimal symptoms.

**Research:** The authors stated that further RCTs should focus on correlations between the severity of symptoms and clinical and bacteriological outcomes, using an accepted symptom score to help decide on the cost-effective treatment option.

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Record Status
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.