Meta-analysis of randomized trials comparing antibiotic therapy with appendectomy for acute uncomplicated (no abscess or phlegmon) appendicitis

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CRD summary
Authors concluded that management of appendicitis with antibiotics was associated with fewer complications, better pain control and shorter sick leave. However, antibiotics were generally less effective due to a higher rate of recurrence compared to appendectomy. Overall, the reliability of the authors’ conclusions is uncertain given the poor quality and variability of studies and small number of participants.

Authors' objectives
To evaluate the efficacy of antibiotics versus appendectomy in the management of acute uncomplicated (no abscess or phlegmon) appendicitis.

Searching
MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL) were searched for eligible studies. Search terms were reported. Meeting abstracts published between January 1950 and May 2011 were screened for additional studies. The date of the search was not reported and it is unknown whether a language restriction was applied to the search.

Study selection
Randomised controlled trials (RCTs) that compared any antibiotic regimen to appendectomy for the management of appendicitis were eligible for inclusion. Trials had to include patients (any age, either sex) with suspected acute uncomplicated appendicitis as determined by clinical presentation. Trials both with and without radiologic confirmation of the diagnosis were eligible for inclusion. Any type and duration of antibiotic treatment as well as any appendectomy technique (open or laparoscopic) were considered. Studies that included patients with known complicated appendicitis at the time of randomisation were excluded.

All but one study were conducted in Europe. All studies used a clinical diagnosis as well as some kind of imaging technique to establish the presence of appendicitis. All studies excluded children, one study also excluded women. Patient age ranged from 17 to 94 years. In two studies that reported surgical technique, both laparoscopic and open approaches were used. Antibiotic treatments varied in drug, dose and duration.

Two reviewers selected studies for inclusion. Any disagreements were resolved in discussion with a third reviewer.

Assessment of study quality
The Jadad scale was used to assess study quality. Studies were awarded scores between zero (worst) and five (best) based on reporting of randomisation, blinding, and loss to follow-up.

The number of reviewers conducting the quality assessment was not reported.

Data extraction
Data were extracted on initial treatment failure rate, overall treatment failure rate, duration of pain, utilisation of pain medication, length of hospital stay and duration of sick leave from work. Data were used to calculate odds ratios (ORs) for dichotomous and standardised mean differences (SMDs) for continuous outcomes, with 95% confidence intervals (CIs). Data on overall complication rate were used to calculate Peto Odds Ratios and 95% confidence intervals.

Two reviewers extracted data. Disagreements were resolved through discussion with a third reviewer.

Methods of synthesis
Data were synthesised using a random-effects meta-analysis to calculate odds ratios and standardised mean differences with 95% confidence intervals as appropriate. Complication rates were summarised using Peto Odds Ratios with 95%
confidence intervals. \( \bar{I}^2 \) and \( \chi^2 \) statistics were used to assess heterogeneity between studies. \( \bar{I}^2 \) values were interpreted as follows: zero to 40% unimportant, 30 to 60% moderate, 50 to 90% substantial, 75 to 100% considerable heterogeneity. Funnel plots were used to assess publication bias.

A post-hoc sensitivity analysis was conducted to investigate the impact of one trial in which the minority of patients received the treatment they had been randomly assigned to.

**Results of the review**

Five RCTs (980 participants) were included in the review. Sample sizes ranged from 40 to 369. Across studies, mean Jadad score was 1.8 out of 5 with scores ranging from 1 to 3. Three trials reported adequate randomisation procedures and one described loss to follow-up. Due to the nature of the treatments being compared, none of the studies was blinded. Follow-up ranged from seven months to one year.

Compared to appendectomy, participants who received antibiotics had significant reductions in complications (OR 0.54, 95% CI 0.37 to 0.78; five trials), duration of sick leave (SMD -0.19, 95% CI -0.33 to -0.06 unit of measurement not reported; three trials) and in the use of pain medication (SMD -1.55, 95% CI -1.96 to -1.14 unit of measurement not reported; two trials). Appendectomy significantly reduced overall treatment failure compared to antibiotics treatment (OR 6.72, 95% CI 3.48 to 12.99; five trials). For complications and overall treatment failure, an \( \bar{I}^2 \) value of 52% suggested the presence of moderate to substantial heterogeneity. There were no significant differences between antibiotic and appendectomy groups for initial treatment failure, length of stay, and duration of pain. The authors suggested evidence of publication bias for initial and overall treatment failure. The sensitivity analysis when one trial was removed did not alter the results.

**Authors’ conclusions**

Management of non-complicated appendicitis with antibiotics was associated with fewer complications, better pain control and shorter sick leave. Overall, antibiotics were less effective due to a higher rate of recurrence compared to appendectomy.

**CRD commentary**

The review question and inclusion criteria were clear. Some relevant sources were searched. Potential for language and publication bias was unclear. The authors’ assessment of funnel plots indicated that publication bias was present for some outcomes. The use of independent and duplicate processes for study selection and data extraction reduced risk of reviewer error and bias in these domains. However, it was unclear if the same processes were in place for quality assessment.

The methods of synthesis were appropriate and suitable measures were used to assess heterogeneity between studies. Despite specifying different levels of heterogeneity, the authors did not take the considerable heterogeneity observed in some analyses into account when interpreting the results. This made it difficult to assess the comparability of studies included in the analyses. While details of the quality assessment were reported, the generally low quality of the studies was not taken into consideration in the interpretation of findings. Authors recognised some variability between treatment regimes and the small overall number of participants in some trials to be potential limitations of the review.

Overall, the reliability of the authors’ conclusions is uncertain given the poor quality and variability of studies and small number of participants.

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

The authors did not report any implications for practice or research.

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Not reported.

**Bibliographic details**

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Record Status
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