

Living FRIendly Summaries of the Body of Evidence using Epistemonikos (FRISBEE)

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Are antibiotics a safe and effective treatment for acute uncomplicated appendicitis?

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Abstract

Acute appendicitis is a common cause of acute abdominal pain and the most frequent cause of emergency abdominal surgery. In the last two decades, growing evidence has been published about the use of antibiotics as the exclusive treatment for acute appendicitis. Searching in Epistemonikos database, which is maintained by screening 30 databases, we identified nine systematic reviews including five pertinent randomized trials overall. We generated a summary of findings following the GRADE approach. We concluded the use of antibiotics to treat acute uncomplicated appendicitis may be less effective than appendectomy and probably increases major complications compared with appendectomy.

Problem

Acute appendicitis is a common cause of acute abdominal pain and the most frequent cause of emergency abdominal surgery, with an estimated lifetime incidence between 7 and 14% [1],[2]. Since the 1890s, when McBurney described early appendectomy as the therapy of choice for acute appendicitis [3],[4], surgery has remained the mainstay of treatment of this disease, drastically reducing its mortality rate [5].

Treatment of acute appendicitis with antibiotics as initial strategy was historically reserved for patients with several days of evolution of the inflammatory process who developed appendicular plastron or abscess, in an attempt to avoid major surgery [2]. In 1953, Harrison reported 42 of 47 cases of acute appendicitis treated successfully with antibiotics. Meanwhile, Coldrey published an article in 1959 with 471 cases of acute appendicitis treated conservatively, with only 1 death, 9 patients who required drainage of

abscess and only 48 cases requiring a subsequent appendectomy [6].

In the past two decades, growing evidence has been published on the use of antibiotics as the sole treatment of acute appendicitis.

Methods

We used Epistemonikos database, which is maintained by screening more than 30 databases, to identify systematic reviews and their included primary studies. With this information, we generated a structured summary using a pre-established format, which includes key messages, a summary of the body of evidence (presented as an evidence matrix in Epistemonikos), meta-analysis of the total of studies, a summary of findings table following the GRADE approach and a table of other considerations for decision-making.

Mensajes clave

- The use of antibiotics to treat acute uncomplicated appendicitis may be less effective than appendectomy.
- The use of antibiotics to treat acute uncomplicated appendicitis probably increases major complications compared with appendectomy.
- The conclusions of this summary are consistent with existing systematic reviews and the recommendations of the main guidelines.

About the body of evidence for this question

<p>What is the evidence. See evidence matrix in Epistemonikos later</p>	<p>We found nine systematic reviews[5],[6],[7],[8],[9],[10],[11],[12],[13] including seven primary studies [14],[15],[16],[17],[18],[19],[20], from which five correspond to randomized controlled trials [14],[15],[18],[19],[20].</p> <p>This table and the summary in general are based on the latter.</p>
<p>What types of patients were included</p>	<p>All studies included adult patients with suspected acute appendicitis. All studies excluded pediatric patients and one study also excluded women [15].</p> <p>One study established the suspected acute appendicitis based on clinical and laboratory parameters [15], one study on clinical criteria and images [20] and three studies on clinical criteria, laboratory parameters and images [14],[18],[19].</p>
<p>What types of interventions were included</p>	<p>Four of the studies used intravenous antibiotics for 48 hours [14],[15],[18],[19]. Of these, two studies used a combination of cefotaxime with tinidazole [14],[15], another study used ciprofloxacin plus metronidazole [18] and one used associated ampicillin with gentamicin and metronidazole [19].</p> <p>The remaining study [20] used a combination of amoxicillin with clavulanic acid intravenously only if the patient had nausea or vomiting and for a time not specified.</p> <p>All studies continued oral antibiotic therapy. One study completed 7 days of treatment [18], another study completed eight days of treatment [20] and three studies completed 10 days [14],[15],[19].</p> <p>To complete oral treatment, two studies used a combination of ofloxacin with tinidazole [14],[15], another a combination of ciprofloxacin with tinidazole [18], one used amoxicillin with clavulanic acid [20] and one study did not specify the antibiotic used orally [19].</p> <p>All of the studies compared antibiotic treatment versus appendectomy.</p>
<p>What types of outcomes were measured</p>	<ol style="list-style-type: none"> 1. Treatment efficacy, defined as absence of symptoms within two weeks, without major complications (including recurrence) within one year. 2. Major complications defined as the need of further invasive treatment or prolonged admission (e.g. abscesses, ileus, deep wound infection, recurrence, re-operation, secondary perforation). 3. Minor complications (e.g. negative appendectomy, diarrhea, and superficial wound infection). 4. Duration of hospital stay. 5. Period of sick leave. 6. Cost effectiveness.

Summary of findings

Information on the effects of antibiotic treatment versus appendectomy is based on five randomized trials[14],[15],[18],[19],[20] including 901 patients, of whom 415 were initially treated with antibiotic and 486 with appendectomy.

All studies reported the outcomes effectiveness of treatment and major complications.

- The use of antibiotics to treat acute uncomplicated appendicitis may be less effective than appendectomy. The certainty of the evidence is low.
- The use of antibiotics to treat acute uncomplicated appendicitis probably increases major complications compared with appendectomy. The certainty of the evidence is moderate.

Antibiotic treatment versus appendectomy for acute uncomplicated appendicitis				
Patients	Acute uncomplicated appendicitis			
Intervention	Antibiotic treatment			
Comparison	Appendectomy			
Outcomes	Absolute effect*		Relative effect (95% CI)	Certainty of the evidence (GRADE)
	WITH APPENDECTOMY	WITH ANTIBIOTICS		
	Difference: patients per 1000			
Treatment efficacy	965 per 1000	762 per 1000	RR 0.79 (0.70 to 0.88)	⊕⊕○○ ^{1,2} Low
	Difference: 203 patients less per 1000 (Margin of error: 116 to 290 less)			
Major complications	21 per 1000	128 per 1000	RR 6.22 (2.59 to 14.93)	⊕⊕⊕○ ¹ Moderate
	Difference: 107 patients more per 1000 (Margin of error: 33 to 287 more)			
Margin of error = 95% confidence interval (CI) RR: Risk ratio GRADE: evidence grades of the GRADE Working Group (see later in this article). * The risk WITH APPENDECTOMY is based on the control group of the trials. The risk WITH ANTIBIOTIC TREATMENT (and its margin of error) is calculated from relative effect (and its margin of error). ¹ The certainty of the evidence was downgraded because of risk of bias. Randomization methods (sequence generation and allocation concealment) were not well reported. Only two studies had an adequate method for randomization [15], [20]. The remaining articles did not fully describe their methods of randomization. ² The certainty of the evidence was downgraded for inconsistency, since some studies showed benefit and others did not (I ² =67%).				

About the certainty of the evidence (GRADE)*

⊕⊕⊕⊕

High: This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different† is low.

⊕⊕⊕○

Moderate: This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different† is moderate

⊕⊕○○

Low: This research provides some indication of the likely effect. However, the likelihood that it will be substantially different† is high.

⊕○○○

Very low: This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different† is very high.

*This concept is also called 'quality of the evidence' or 'confidence in effect estimates'.

† Substantially different = a large enough difference that it might affect a decision.

Other considerations for decision-making

To whom this evidence does and does not apply

- The evidence included in this summary is applicable to adult patients with acute uncomplicated appendicitis, independent of sex and age.
 - It does not apply to patients presenting complications of acute appendicitis (such as drilling, appendicular mass, peritonitis, gangrene or other), since they have a clinical course and treatment indication different than acute uncomplicated appendicitis.
 - Studies in pediatric patients were not included in this summary, so this evidence cannot be extrapolated to that population.
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About the outcomes included in this summary

- Effectiveness of treatment and presence of major complications were selected as critical outcomes for decision-making.
 - Other outcomes such as length of hospital stay or time to return to work, were considered less important when choosing a treatment over the other.
-

Balance between benefits and risks, and certainty of the evidence

- While the certainty of the evidence is low or moderate for major outcomes, it is an intervention which benefits are likely to outweigh the low risk associated with appendectomy.
 - In patients with a high surgical risk, this balance could eventually favor antibiotic treatment [2],[21].
-

What would patients and their doctors think about this intervention

- It is highly likely that patients and their carers would be inclined to surgery, since it is the established treatment for both clinicians and patients, which is reinforced by the evidence.
-

Resource considerations

- Although surgery has a higher cost, it is likely that the costs of complications and low effectiveness of antibiotic treatment make surgery the most cost-effective intervention
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Differences between this summary and other sources

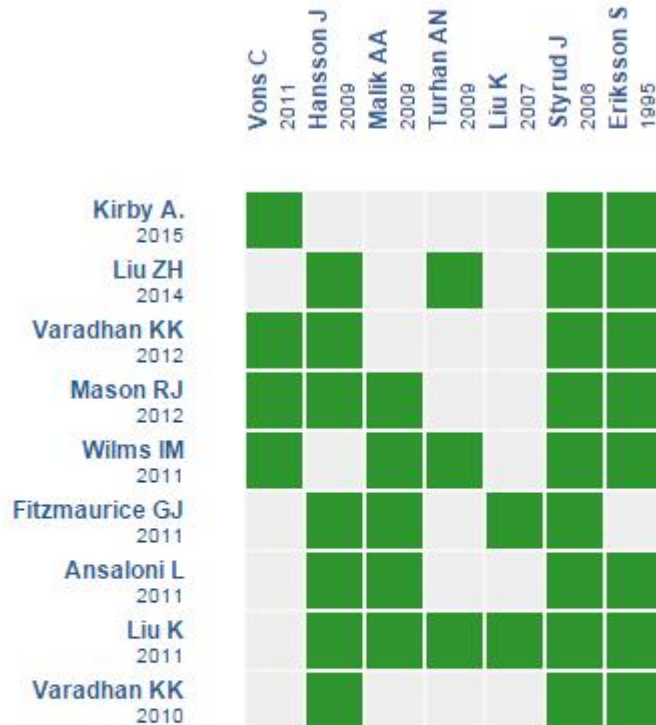
- The conclusions of this summary are consistent with those of the systematic reviews identified and existing overviews of reviews [1],[21].
 - The main guideline on the subject [22] recommends appendectomy as the treatment of choice for acute appendicitis. It states antibiotic therapy as primary treatment is safe for patients with acute uncomplicated appendicitis, but less effective in the long-term because of higher rate of recurrence.
-

Could this evidence change in the future?

- The probability that future studies change what we know is low, because of the certainty of the evidence.
 - However, there is at least one randomized controlled trial that is not included in any of the identified systematic reviews [23] and at least one ongoing study, which will provide new evidence in this regard [24].
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How we conducted this summary

Using automated and collaborative means, we compiled all the relevant evidence for the question of interest and we present it as a matrix of evidence.



Starting from any systematic review, Epistemonikos builds a matrix based on existing connections in the database.

The author of the matrix can select relevant information for a specific health question (typically in PICO format) in order to display the information set for the question.

The *rows* represent systematic reviews that share at least one primary study, and *columns* display the studies.

The boxes in green correspond to studies included in the respective reviews.

Follow the link to access the **interactive version**: [Antibiotics versus appendectomy for acute uncomplicated appendicitis](#)

Notes

The upper portion of the matrix of evidence will display a warning of “new evidence” if new systematic reviews are published after the publication of this summary. Even though the project considers the periodical update of these summaries, users are invited to comment in *Medwave* or to contact the authors through email if they find new evidence and the summary should be updated earlier. After creating an account in Epistemonikos, users will be able to save the matrixes and to receive automated notifications any time new evidence potentially relevant for the question appears.

The details about the methods used to produce these summaries are described here <http://dx.doi.org/10.5867/medwave.2014.06.5997>.

Epistemonikos foundation is a non-for-profit organization aiming to bring information closer to health decision-makers with technology. Its main development is Epistemonikos database (www.epistemonikos.org).

These summaries follow a rigorous process of internal peer review.

Conflicts of interest

The authors do not have relevant interests to declare.

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