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Antibiotics-first strategy for uncomplicated acute appendicitis in adults is associated with increased rates of peritonitis at surgery. A systematic review with meta-analysis of randomized controlled trials comparing appendectomy and non-operative management with antibiotics☆

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ABSTRACT

Background: Acute appendicitis is the most common surgical diagnosis in young patients, with lifetime prevalence of about 7%. Debate remains on whether uncomplicated AA should be operated or not. Aim of this meta-analysis of randomized controlled trials was to assess current evidence on antibiotic treatment for uncomplicated AA compared to standard surgical treatment.

Methods: Systematic literature search was performed using PubMed, EMBASE, Medline, Google Scholar and Cochrane Central Register of Controlled Trials databases for randomized controlled trials comparing antibiotic therapy (AT) and surgical therapy-appendectomy (ST) for uncomplicated AA. Trials were reviewed for primary outcome measures: treatment efficacy based on 1 year follow-up, recurrence at 1 year follow-up, complicated appendicitis with peritonitis identified at the time of surgical operation and

List of abbreviations: AA, acute appendicitis; NOM, non-operative management; RCT, randomized controlled trial; AT, antibiotic therapy; ST, surgical therapy; ED, emergency department; US, ultrasonography; CT, computed tomography; WBC, white blood cells; CRP, C-reactive protein; LA, laparoscopic appendectomy; SILS, single-incision laparoscopic surgery.

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post-intervention complications. Secondary outcomes were length of hospital stay and period of sick leave.

Results: Five RCTs comparing AT and ST qualified for inclusion in meta-analysis, with 1.351 patients included: 632 in AT group and 719 in ST group. Higher rate of treatment efficacy based on 1 year follow-up was found in ST group (98.3% vs 75.9%, $P < 0.0001$), recurrence at 1 year was reported in 22.5% of patients treated with antibiotics. Rate of complicated appendicitis with peritonitis identified at time of surgical operation was higher in AT group (19.9% vs 8.5%, $P = 0.02$). No statistically significant differences were found when comparing AT and ST groups for the outcomes of overall post-intervention complications (4.3% vs 10.9%, $P = 0.32$), post-intervention complications based on the number of patients who underwent appendectomy (15.8% vs 10.9%, $P = 0.35$), length of hospital stay (3.24 ± 0.40 vs 2.88 ± 0.39, $P = 0.13$) and period of sick leave (8.91 ± 1.28 vs 10.27 ± 0.24, $P = 0.06$).

Conclusions: With significantly higher efficacy and low complication rates, appendectomy remains the most effective treatment for patients with uncomplicated AA. The subgroups of patients with uncomplicated AA where antibiotics can be more effective, should be accurately identified.

Introduction

Acute appendicitis (AA) is among the most common causes of lower abdominal pain leading patients to emergency department (ED) and the most common diagnosis made in young patients admitted to hospital for acute abdominal pain, with a lifetime prevalence of about 7%, and highest incidence in the second decade of life.[1,2]

Significant debate remains on whether uncomplicated (non-perforated) AA should be operated or not.

In 1886, Fitz reported that many autopsy specimens were showing pathologic signs consistent with AA, therefore hypothesizing that in some patients the disease could resolve without any surgery.[3] In 1953, Harrison reported 42 of 47 cases of AA being successfully treated using antibiotics and Coldrey in 1956 published the data on 471 patients with AA treated conservatively, with low morbidity, mortality (0.2%), and recurrence rates (14.4%).[4,5]

The renewed interest in the non-operative management (NOM) of uncomplicated AA has been highlighted by the latest guidelines for diagnosis and treatment of acute appendicitis, published in 2016. Within the discussion on this topic, the "Jerusalem guidelines" stated that the antibiotic therapy can be successful in selected patients with uncomplicated appendicitis who wish to avoid surgery, and accept the risk up to 38% recurrence.[6]

Therefore the main question is whether it is possible to treat patients having uncomplicated AA with antibiotic therapy and how to distinguish during the patients' assessment those who might respond well to antibiotic treatment alone from those who would require surgery. Moreover the comparison of conservative management and surgical treatment needs to take into consideration the widespread use of laparoscopic appendectomy (LA) which is considered, in most cases, the gold standard surgical treatment.[7,8]

The aim of this systematic review and meta-analysis of randomized controlled trials (RCTs) was the up-to-date reassessment of the current available evidence on the antibiotic approach to uncomplicated AA when compared to the standard surgical treatment, with particular focus on safety and efficacy, and to discuss the limitations of published randomized trials, potentially limiting a more widespread diffusion of the antibiotic-first treatment.

Materials and methods

Search methods for identification of randomized controlled trials

A systematic literature search was performed using PubMed, EMBASE, Medline, Google Scholar and The Cochrane Central Register of Controlled Trials databases for studies comparing *Antibiotic Therapy* (AT) and *Surgical Therapy – Appendectomy* (ST). We combined database-specific search terms for AT (*acute, appendicitis, antibiotic, nonoperative treatment, conservative management, nonoperative management, medical treatment*), and ST (*acute, appendicitis, appendectomy, appendicectomy, laparoscopy*). The search was then extended to related articles suggested by the databases and supplemented with manual searches for reference lists of all relevant articles. Literature search was completed in May 2016.

Selection of studies

RCTs comparing AT and ST as primary treatment for uncomplicated AA in adults were included in the systematic review and meta-analysis, irrespective of language or publication status. Studies meeting the inclusion criteria had to describe well-defined treatment protocols.