Systematic Review and Meta-Analysis of Postoperative Antibiotics for Patients with a Complex Appendicitis

Anne Loes van den Boom  Elisabeth M.L. de Wijkerslooth  Bas P.L. Wijnhoven

Department of Surgery, Erasmus MC, University Medical Centre, Rotterdam, The Netherlands

Keywords
Complex appendicitis · Postoperative antibiotic · Complications · Intra-abdominal abscess

Abstract
Postoperative antibiotics are recommended after appendectomy for complex appendicitis to reduce infectious complications. The duration of this treatment varies considerably between and even within institutions. The aim of this review was to critically appraise studies on duration of antibiotic treatment following appendectomy for complex appendicitis. A systematic literature search according to the PRISMA guidelines was performed. Comparative studies evaluating different durations of postoperative antibiotic therapy. Primary endpoint was intra-abdominal abscess (IAA) after appendectomy. Secondary endpoints were surgical site infection, readmission and length of hospital stay. The quality of evidence was assessed with the Grading of Recommendations Assessment, Development and Evaluation (GRADE) tool. Pooled event rates were calculated using a random-effects model. Nine studies reporting 2006 patients with complex appendicitis were included. The methodological quality of the included articles was poor. IAA was seen in 138 patients (8.6%). Meta-analysis revealed a statistically significant difference in IAA incidence between antibiotic treatment of ≤5 vs. >5 days (risk ratio (OR) 0.36 [95% CI 0.23–0.57] (p < 0.0001)) but not between ≤3 vs. >3 days (OR 0.81 [95% CI 0.38–1.74] (p = 0.59)). Descriptive statistics were used for secondary endpoints. The duration of postoperative antibiotic treatment is not associated with IAA following appendectomy for complex appendicitis.

Introduction
Appendicitis is one of the most common acute gastrointestinal inflammatory disorders in children and adults, often requiring surgery and hospitalization [1–3]. In the Netherlands, approximately 14,000 patients undergo an appendectomy for suspected appendicitis annually [4]. Acute appendicitis is classified into 2 distinct types: simple and complex. A simple appendicitis is a suppurative or phlegmonous appendicitis (transmural inflammation, ulceration, or thrombosis) with or without extramural pus. A complex appendicitis includes a gangrenous (transmural inflammation with necrosis) appendicitis, a perforated appendicitis and/or appendicitis with abscess formation (pelvic/abdominal) [5]. Some 25–30% of all appendicitis is complex [6–12]. A Cochrane Systematic review revealed that antibiotic prophylaxis is effective in the prevention of postoperative complications in patients undergoing appendectomy for simple and complex appendicitis.
pendicitis, whether the administration is given pre, peri- or postoperatively [13]. Complex appendicitis is associated with increased risk of infectious complications after appendectomy [14–17]. Therefore, in addition to preoperative antibiotic prophylaxis, guidelines recommend postoperative antibiotic treatment for complex appendicitis. There is considerable variability in the route of administration (IV or oral), agents, dosage and duration of postoperative antibiotics practiced worldwide [18–21].

According to a nationwide study from the Netherlands in 2014, the majority of patients (65%) with a complex appendicitis are prescribed 5 days of postoperative antibiotic treatment. Ultimately, almost 80% of patients actually receive antibiotics for 5 days or more [22]. Treatment duration varied from 2 to 10 days [22]. In a survey among Dutch surgeons and residents, postoperative antibiotics were given for 3 days (by 58% of surgeons) or 5 days (by 40% of surgeons) [23]. Restricting postoperative antibiotics to <3 days was uncommon in hospital protocols (2.5%), but 31 per cent of surgeons or residents indicated that would be favoured by them [23]. A survey sent to all practicing paediatric surgeons in North America to assess the management of perforated appendicitis (in 2003) also showed a wide variation in the postoperative duration of antibiotic treatment [24]. In a more recent American cohort study among children, 66% of patients with perforated appendicitis received 5 or more days of intravenous antibiotics [25]. And in 92% of these patients, oral antibiotics were prescribed in addition to the intravenous treatment, which led to a median total course of 13 days [25].

A duration of 3–5 days best reflects current common practice in the Netherlands and is generally considered safe and effective internationally as well [8, 12, 22, 23]. An increasing amount of evidence indicates that a shorter duration may suffice, especially if certain discharge criteria are met [6, 8, 10, 22, 23, 26–40].

In 2015, the European Association of Endoscopic Surgery initiated a consensus meeting on the management of acute appendicitis [41]. No recommendation could be made regarding the duration or route of postoperative antibiotics for complex appendicitis due to the lack of studies. To reduce the length of hospital stay (LOS), costs, and the risk of developing antimicrobial resistance, it is important to establish a short but safe and effective antibiotic regimen. The aim of this study was to review the literature regarding duration of postoperative antibiotic treatment for complex appendicitis and its effect on the rate of infectious complications, hospital stay and readmission in both children and adults.

Methods

This study was reported according to the preferred reporting items for systematic reviews and meta-analyses guidelines for reporting systematic reviews and meta-analyses [42].

Search Strategy

A comprehensive literature search was performed on February 27, 2018. Databases from the National Library of Medicine (MEDLINE ovid), the Cochrane Library, Web of Science, Embase, PubMed and Google Scholar were searched from inception. Trial registries www.clinicaltrial.gov and the World Health Organization International Clinical Trials Portal [43] were also searched to identify unpublished trials. Search terms included: “appendicitis”, “appendectomy”, “antibiotics”, “anti-bacterial agents”, “anti-infective agents”, “postoperative period” and “postoperative care”. A librarian performed the search. The supporting information (online suppl. Appendix S1; for all online suppl. material, see www.karger.com/doi/10.1159/000497482) outlines the complete search strategy. Manual reference checks of included papers were performed to check for relevant studies. The literature search was restricted to articles published in the English language.

Eligibility Criteria

Articles were included if they were comparative studies on duration of postoperative antibiotics for complex appendicitis in adults and/or children. Complex appendicitis was defined as a gangrenous and/or perforated appendicitis or appendicitis with a pelvic or intra-abdominal abscess (IAA) [5]. Randomized controlled trials, prospective and retrospective observational studies and case series were eligible for inclusion. Studies were excluded if the abstract revealed no relevance to the subject or if they were one of the following: case reports, letters, editorials, animal studies. For publications without an abstract, the full article was retrieved and assessed for eligibility. If full text was not available, even after contacting the original author to request access to the date, the article was excluded. Studies describing preoperative prophylactic antibiotics or antibiotics as conservative treatment for acute appendicitis were outside the scope of the study. Studies reporting postoperative antibiotic treatment prolonged beyond 5 days in both the intervention and control group were outside the scope of this review as well, based on current practice in the Netherlands and the aim of this review to evaluate evidence for a shorter duration. If the duration of antibiotics was unclear or variable, the author was contacted in order to retrieve exact durations.

Study Selection

Two reviewers independently assessed the articles for inclusion by screening the titles and abstracts. All duplicates were removed. Full-text articles of possibly eligible studies were reviewed for inclusion. Excluded articles were recorded along with the reason for exclusion.

Data Extraction

Data on authors, country of origin, year of publication, study design, study population, definition of complex appendicitis, details on the duration of postoperative antibiotic treatment, route and type of antibiotic used, follow-up period, readmission, hospital stay, postoperative complications, IAA and surgical site infections (SSI) in particular were extracted by the first reviewer. The
second reviewer verified the data extraction. Postoperative antibiotic treatment durations were classified into the following duration categories based on what was reported in the selected studies: up to 5 days versus >5 days, up to 3 days versus >3 days and up to 24 h versus >24 h. This classification was made in such a way that a clear comparison could be made between a short and long course of postoperative antibiotic treatment. If no exact postoperative antibiotic durations could be retrieved – for example, given only a minimum duration and variable prolongation given and overlapping median durations reported for the short and long course groups – then they were excluded from the meta-analysis. We provided only descriptions of these studies.

Quality Assessment

Two reviewers each independently assessed the level of evidence of each paper, using the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) tool by Cochrane [44]. The GRADE approach defines the quality of a body of evidence by consideration of within study risk of bias (methodology quality), directness of evidence, heterogeneity, precision of effect estimates, and risk of publication bias.

Outcomes

The primary outcome was postoperative IAA after appendectomy. Definitions of IAA in the included studies can be found in online supplementary Appendix S2. Secondary endpoints were SSI, LOS and readmission.

Statistical Analysis

Risk ratios (RR) were calculated using a random-effects meta-analysis model based on the DerSimonian-Liard method for estimating the between-study variance in order to take into account any potential heterogeneity between the studies. The random-effects model accounts for the heterogeneity between the studies while at the same time larger samples with smaller standard errors receive more weight when calculating the overall RR. Forest plots were created for the primary outcome. Each forest plot shows the effect size of the individual studies and an overall pooled event rate with a confidence interval. Statistical analyses were conducted using Review Manager (RevMan) version 5.3 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration) [45]. Descriptive statistics was used for secondary endpoints.

Results

Study Selection

A total of 1,612 articles were identified through the comprehensive electronic search. After reading titles and abstracts, 1,520 articles were excluded mostly reporting preoperative prophylaxis for appendectomy or evaluating different surgical approaches. Two additional articles were identified after manually scrutinizing reference lists.

Fig. 1. PRISMA flow diagram.
Of the 94 full-text articles assessed for eligibility, 9 were included into this review describing outcome for 2,006 patients with complex appendicitis. Figure 1 shows the preferred reporting items for systematic reviews and meta-analyses flow diagram for systematic reviews. Characteristics of the included studies are shown in Table 1.

**Quality of Evidence Assessment**

Quality of the included articles ranged from very low to low. A detailed assessment of the quality of the available evidence using the GRADE tool is presented in Table 2.

**Outcome Assessment**

Intra-Abdominal Abscess

One study did not report IAA as an outcome [36], leaving 8 studies that reported 138 IAAAs in 1,596 patients (8.6%). Two articles compared different antibiotic strategies dependent on clinical criteria without reporting exact durations in the intervention and control groups [10, 30]. We could not retrieve the exact duration data and therefore their data were not suitable for meta-analysis. Data from 5 remaining studies could be incorporated in meta-analysis, including a total of 1,292 patients [8, 22, 30, 35, 38]. The only RCT showed no events and therefore was left out of the analysis [34]. The last remaining study showed only data of ≤24 vs. >24 h of antibiotic duration but included too less number of patients [37]. No funnel plots were provided due to the low number of included studies according to the recommendation of the Cochrane Network [45].

**Up to 5 vs. >5 days of postoperative antibiotic treatment:**

In the ≤5 days group, 49 of 986 patients (5%) had an IAA versus 34 of 261 patients (13%) in the >5 days group. The overall RR estimate was 0.36 (95% CI 0.23–0.57; \( p < 0.0001 \)) in favour of ≤5 days postoperative antibiotics (Fig. 2). There was no heterogeneity between the studies.

**Up to 3 vs. >3 days of postoperative antibiotic treatment:**

In the ≤3 days group, 21 of 424 (5%) patients developed an IAA versus 62 of 823 (7.5%) in the >3 days group. The overall RR estimate was 0.81 (95% CI 0.38–1.74; \( p = 0.59 \)) in favour of ≤3 days of antibiotic treatment (Fig. 3). There was little heterogeneity between the studies.

**Up to 24 vs. >24 h of postoperative antibiotic treatment:**

Two studies reported outcomes after postoperative antibiotic treatment limited to 24 h or no postoperative treatment at all [37, 38]. Due to the small number of patients, a meaningful meta-analysis was not possible. In only one of these studies, antibiotic duration of ≤24 h \(( n = 8 \) was directly compared with >24 h \(( n = 44 \). The authors concluded there was no significant difference in IAA forma-

van den Boom/de Wijkerslooth/Wijnhoven

**Discussion**

The present study shows that there is no clear association between duration of postoperative antibiotic treatment and the incidence of IAA after appendectomy for complex appendicitis. While RRs for IAA where in favour of ≤5 days of postoperative antibiotics compared to >5 days, this could not be demonstrated for ≤3 days compared to >3 days. One could argue that antibiotics could be safely stopped after 3 days of intravenous treatment or possibly even earlier. However, all studies included in the meta-analysis were observational studies and 2 out of 4 reported very low IAA rate. Therefore, selection bias may have significantly influenced the present results. Less “fit” patients, for example, with more comorbidities, who were perhaps more at-risk for IAA to begin with, might have been prescribed longer courses compared to the patients.
<table>
<thead>
<tr>
<th>Reference</th>
<th>Study design</th>
<th>Participant</th>
<th>Duration postop AB, n</th>
<th>Follow-up</th>
<th>IAA, n (%)</th>
<th>SSL, n (%)</th>
<th>LOS, days, median (IQR)</th>
<th>Readmission, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basoli et al. [34], 2008 (Italy)</td>
<td>Multicentre randomized trial</td>
<td>Adults (n = 45) with localized secondary peritonitis due to appendicitis, with improvement in temperature, WBC and presence of abdominal sounds at the third postoperative day</td>
<td>3 days (22) ≤5 days (23) AB IV: ertapenem</td>
<td>Not reported</td>
<td>0</td>
<td>2 (9.1)</td>
<td>0</td>
<td>Not reported</td>
</tr>
<tr>
<td>Cho et al. [35], 2016 (South Korea)</td>
<td>Single-centre retrospective observational study</td>
<td>Adults and children (n = 496) with complex appendicitis treated by laparoscopic appendectomy</td>
<td>1–2 days (55) 3 days (128) 4 days (100) 5 days (103) 6 days (54) &gt;6 days (56) AB IV: cefotaxime and metronidazole</td>
<td>30 days</td>
<td>0</td>
<td>1 (0.8)</td>
<td>0</td>
<td>Not reported</td>
</tr>
<tr>
<td>Hughes et al. [38], 2013 (UK)</td>
<td>Single-centre prospective observational study</td>
<td>Adults (n = 78) with complex appendicitis treated by laparoscopic appendectomy</td>
<td>None (2) ≤24 h (9) 2–3 days (6) 4–5 days (18) ≥5 days (43) AB IV: piperacillin/tazobactam AB oral: amoxicillin/clavulanic acid</td>
<td>30 days</td>
<td>0</td>
<td>0</td>
<td>1 (16.7)</td>
<td>Not reported</td>
</tr>
<tr>
<td>Kim et al. [36], 2015 (USA)</td>
<td>Multicentre retrospective observational study</td>
<td>Adults (n = 410) with complex appendicitis treated by laparoscopic appendectomy in n = 343 (84%). Intraoperative drain inserted in n = 48 (12%)</td>
<td>None (136) ≥0 (274) AB: not described</td>
<td>Not reported</td>
<td>Not reported</td>
<td>5 (4%)</td>
<td>4 (2–6)</td>
<td>11 (8)</td>
</tr>
<tr>
<td>Kimbell et al. [37], 2014 (USA)</td>
<td>Single-centre retrospective observational study</td>
<td>Adults (n = 52) with complex appendicitis treated by laparoscopic appendectomy in n = 34 (65%). Intraoperative drain inserted in n = 15 (29%)</td>
<td>≤24 h (8) &gt;24 h (44) AB IV and PO: piperacillin/tazobactam, cefotaxin, moxifloxacin, amoxicillin/clavulanic acid, ciprofloxacin/metronidazole, trimethoprim/sulphamethoxazole, tobramycin and linezolid, cefuroxime and clindamycin, and vancomycin</td>
<td>1 month</td>
<td>2 (25)</td>
<td>9 (20.5)</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td>Van Rossem et al. [8], 2014 (The Netherlands)</td>
<td>Single-centre retrospective observational study</td>
<td>Adults (n = 267) with complex appendicitis treated by laparoscopic appendectomy in n = 87 (33%). Intraoperative drain placement not mentioned</td>
<td>3 days (135) 5 days (116) 6 days (1) 7 days (3) 8 days (1) 10 days (2) Unknown (9) AB IV: cefuroxime and metronidazole</td>
<td>Not reported</td>
<td>13 (9.6)</td>
<td>6 (5.2)</td>
<td>6 (4.4)</td>
<td>Not reported</td>
</tr>
</tbody>
</table>

Postoperative Antibiotic Complex Appendixitis

Dig Surg
DOI: 10.1159/000497482
who showed swift postoperative recovery. Beside this potential selection bias, the type of antibiotics differed between the studies and no separate analysis for children and adults could be performed. One study included patients who underwent open appendectomy as well as patients that underwent laparoscopic appendectomy. Stratification was not possible due to the low number of studies, patients and events. Hence, the efficacy of antibiotics for subgroups could not be investigated, which may have introduced bias. Due to a lack of high-level studies, no final conclusions can be drawn concerning the optimum duration, let alone the safety and efficacy of <3 days of antibiotics. Reducing the duration from 5 to 3 days could already have major implications, as the majority of patients in the Netherlands and worldwide still receive antibiotics for 5 days after appendectomy for a complex appendicitis [22, 23, 46]. This is instigated by the current guidelines of the Dutch Surgical Association (NVvH), the Surgical Infection Society and Infectious Diseases Society of America and the Dutch Working Party on Antibiotic Policy (SWAB) that recommend 3–7, 4–7 and 5–14 days of postoperative antibiotics respectively [18, 19, 21]. This review shows little evidence in support of the current guidelines. At a time when antimicrobial resistance is an increasingly urgent global health threat, the use of antibiotics should be minimized where possible. Resistance is a natural biological outcome of antibiotic use. Antibiotic overtreatment, however, increases the speed of emergence and selection of resistant bacteria [47, 48]. It is plausible that reducing the duration of antibiotic treatment may not increase the rate of IAA, as the development of infectious complications following appendectomy is a multifactorial process. Many risk factors have been identified including preoperative C-reactive protein level, timing of appendectomy, technique of appendiceal stump closure, operation approach (laparoscopic versus open), the presence of a faecolith, longer operation time, simple versus complex appendicitis, body temperature, American Society of Anesthesiology classification, age, body mass index and gender [6, 14–17, 26, 49]. Recent studies provide support for the concept that beneficial effect of systemic antibiotic therapy after adequate source control during surgery is limited [33, 50]. A randomized controlled trial (“STOP-IT”) published in 2015 showed that after adequate source control for complicated intra-abdominal infections, outcomes after a short course of antibiotics (median 4 days, n = 257) were similar after long course therapy (me-

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study design</th>
<th>Participant</th>
<th>Duration postop AB, n</th>
<th>Follow-up</th>
<th>IAA, n (%)</th>
<th>SSL, n (%)</th>
<th>LOS, days, median (IQR)</th>
<th>Readmission, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Van Rossem et al.</td>
<td>Multicentre prospective observational study</td>
<td>Adults and children (n = 415) with complex appendicitis treated by laparoscopic appendectomy Intraoperative drain placement not mentioned</td>
<td>2–3 days (89) 4–5 days (225) 5+ days (101)</td>
<td>30 days</td>
<td>6 (6.7)</td>
<td>1 (1)</td>
<td>4</td>
<td>1 (1)</td>
</tr>
<tr>
<td>(The Netherlands)</td>
<td>2016</td>
<td>AB: usually a combination of cephalosporin and metronidazole</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Van Wijck et al.</td>
<td>Multicentre retrospective observational study</td>
<td>Children: (n = 149) with perforated appendix treated by laparoscopic appendectomy in n = 72 (48%) Intraoperative drain placement not mentioned</td>
<td>Median 5 days (68) Variable duration based on clinical grounds, minimum 5 days Median 7 days (81) Variable duration based on CRP level, minimum 5 days AB IV: amoxicillin/clavulanic acid and gentamycin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(The Netherlands)</td>
<td>2010</td>
<td>Not reported</td>
<td>Not reported</td>
<td>13 (19.1)</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td></td>
</tr>
<tr>
<td>Yu et al.</td>
<td>Single-centre prospective propensity-score matched study</td>
<td>Children: (n = 94) years with complex appendix Operation technique and intraoperative drain placement not mentioned</td>
<td>Median 3 days IV (47) Variable duration based on clinical criteria, unclear duration additional PO antibiotics Median 5 days IV (47) Variable duration based on clinical criteria, minimum 5 days IV, unclear duration additional PO antibiotics AB IV: amoxicillin, metronidazole and gentamycin</td>
<td>30 days</td>
<td>6 (12.8)</td>
<td>1 (2)</td>
<td>4 (2)</td>
<td>6 (13)</td>
</tr>
<tr>
<td>(New Zealand)</td>
<td>2014</td>
<td>AB: usually a combination of cephalosporin and metronidazole</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Postop AB, postoperative antibiotics; IAA, intra-abdominal abscess; SSL, surgical site infection; LOS, length of hospital stay; readm, hospital readmission; IV, intravenous; PO, per os; CRP, C-reactive protein.
Table 2. GRADE evidence profile of the included studies

<table>
<thead>
<tr>
<th>Reference</th>
<th>Quality assessment</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basoli et al. [34]</td>
<td>Serious(^a)</td>
<td>☮️ ☯️ ☯️ ☯️ Low</td>
</tr>
<tr>
<td>Cho et al. [35]</td>
<td>Serious(^d), e</td>
<td>☮️ ☯️ ☯️ ☯️ Very low</td>
</tr>
<tr>
<td>Hughes et al. [38]</td>
<td>Not serious</td>
<td>☮️ ☯️ ☯️ ☯️ Very low</td>
</tr>
<tr>
<td>Kim et al. [36]</td>
<td>Serious(^d)</td>
<td>☮️ ☯️ ☯️ ☯️ Very low</td>
</tr>
<tr>
<td>Kimbrell et al. [37]</td>
<td>Serious(^e)</td>
<td>☮️ ☯️ ☯️ ☯️ Very low</td>
</tr>
<tr>
<td>Van Rossem et al. [8]</td>
<td>Not serious</td>
<td>☮️ ☯️ ☯️ ☯️ Low</td>
</tr>
<tr>
<td>Van Rossem et al. [22]</td>
<td>Not serious</td>
<td>☮️ ☯️ ☯️ ☯️ Low</td>
</tr>
<tr>
<td>Van Wijck et al. [10]</td>
<td>Serious(^e)</td>
<td>☮️ ☯️ ☯️ ☯️ Very low</td>
</tr>
<tr>
<td>Yu et al. [30]</td>
<td>Not serious</td>
<td>☮️ ☯️ ☯️ ☯️ Low</td>
</tr>
</tbody>
</table>

\(^a\) No information provided on sequence generation or allocation concealment; loss to follow-up and protocol violations not further clarified.
\(^b\) No report of power analysis for sample size calculation; small sample size.
\(^c\) Risk of underreported outcome (low number of events).
\(^d\) Exposure and outcome measurement not described, therefore not reproducible.
\(^e\) No analysis on possible confounders (with detected inequalities at baseline).
\(^f\) Unclear what determined the duration of antibiotic treatment per patient (either surgeons’ preference or not described).

GRADE, Grades of Recommendation, Assessment, Development and Evaluation.

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>≤5 days</th>
<th>&gt;5 days</th>
<th>Weight</th>
<th>RR M-H, random (95% CI)</th>
<th>RR M-H, random (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>van Rossem, 2016 [22]</td>
<td>26 314 24 101</td>
<td>78.3%</td>
<td>0.35 [0.21, 0.58]</td>
<td>0.36 [0.23, 0.57]</td>
<td></td>
</tr>
<tr>
<td>Hughes, 2013 [38]</td>
<td>3 35 7 43</td>
<td>12.4%</td>
<td>0.53 [0.15, 1.89]</td>
<td>0.14 [0.01, 1.56]</td>
<td></td>
</tr>
<tr>
<td>van Rossem, 2014 [8]</td>
<td>19 251 1 7</td>
<td>5.8%</td>
<td>0.53 [0.08, 3.42]</td>
<td>0.35 [0.21, 0.58]</td>
<td></td>
</tr>
<tr>
<td>Cho, 2016 [35]</td>
<td>1 386 2 110</td>
<td>3.5%</td>
<td>0.14 [0.01, 1.56]</td>
<td>0.35 [0.21, 0.58]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>986 261</td>
<td>100.0%</td>
<td>0.36 [0.23, 0.57]</td>
<td>0.36 [0.23, 0.57]</td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>49 34</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: \(\tau^2 = 0.00; \text{chi}^2 = 1.10, \text{df} = 3 (p = 0.78); I^2 = 0\%

Test for overall effect \(z = 4.41 (p < 0.0001)\)

Fig. 2. Meta-analysis of the RR of IAA development between patients with until 5 days of postoperative antibiotics treatment and patients with >5 days of postoperative antibiotics treatment. RR, risk ratio.
In conclusion, there is no clear evidence in favour of an optimal duration of postoperative antibiotic treatment for complex appendicitis. However, the present results...
may suggest that treatment for longer than 3 days is not significant more beneficial. Adequately powered, randomized studies with clear definitions of the study population and the endpoints are needed to define the optimal postoperative antibiotic regimen for complicated appendicitis in children and adults.

Acknowledgements

The authors thank Wichor Bramer of the Medical Library of the Erasmus MC – University Medical Centre for developing search strategies.

References


Statement of Ethics

The authors have no ethical conflicts to disclose.

Disclosure Statement

The authors have no conflicts of interest to disclose.

Funding Sources

Not applicable.


43 Available from https://www.who.int/ictrp/search/en/.

44 GRADEpro GDT: GRADEpro Guideline Development Tool/ McMaster University. 2015 (developed by Evidence Prime, Inc.). Available from: gradepro.org.


