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SYSTEMATIC REVIEW AND METANALYSIS ABOUT THE DURATION OF POSTOPERATIVE ANTIBIOTICS AND INFECTIOUS COMPLICATIONS RATE AFTER LAPAROSCOPIC APPENDECTOMY FOR COMPLICATED ACUTE APPENDICITIS

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Abstract

Purpose: The World Health Organization emphasizes the importance of limiting antibiotic treatment in order to reduce antibiotic resistance. The purpose of this systematic review was to look into the relationship between the length of antibiotic treatment and the occurrence of infectious complications after laparoscopic appendectomy.

Methods: Following the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis, a thorough search was conducted in multiple databases, including PubMed, Scopus, Cochrane Library, Google Scholar, and Web of Science. The search was carried out until May 20, 2023, and eligible studies were found. The duration of antibiotics after laparoscopic appendicectomy in complicated cases was extracted. To determine the complication across different durations of antibiotic use, a meta-analysis was performed.

Results: In this systematic review, we searched seven databases and found 1640 articles that were eligible for screening. We included 18 articles in this review after a thorough review. We discovered that the antibiotics used to treat complicated appendicitis vary significantly between institutions. We also discovered that the incidence of complications was nearly the same regardless of antibiotic duration.

Conclusion: While the majority of the included studies recommend the use of postoperative antibiotics after a laparoscopic appendectomy, there is no agreement on the optimal duration or specific antibiotic regimen. Notably, all studies found that prolonged antibiotic use following laparoscopic appendectomy for complicated cases did not result in a reduction in infectious complications, such as superficial or deep wound site infections.

Keywords: Metanalysis, postoperative, antibiotics, infectious, appendectomy, appendicitis

Introduction

Currently, uncomplicated and complicated appendicitis are regarded as distinct conditions requiring distinct treatment approaches [1]. Although the use of antibiotics as an alternative to surgery has been extensively researched in adults and, more recently, in children, uncomplicated or simple acute appendicitis is frequently treated with appendectomy [2, 3]. Acute complicated appendicitis, on the other hand, which involves necrosis or perforation of the appendix, is usually treated with appendectomy followed by additional antibiotic therapy to reduce postoperative infectious complications. To reduce harmful side effects on patients and prevent the development of antibiotic resistance, it is critical to exercise caution and proper antibiotic use.

There has been little research into the importance of the duration of antibiotic administration following an appendectomy, particularly in adults. Following complicated appendicitis, American guidelines recommend a 4- to 7-day course of antibiotics. [4] The majority of previous research in this area has concentrated on children [5, 6]. As a result, due to concerns about potential infectious complications, it is uncommon to limit antibiotic duration to less than 5 days after surgery for

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complicated appendicitis. Nonetheless, a study of adults with complicated appendicitis found that a 3-day course of antibiotics is feasible and safe [7].

The purpose of this systematic review is to investigate the relationship between antibiotic treatment duration and the occurrence of infectious complications following laparoscopic appendectomy for complicated acute appendicitis. The study also aims to identify potential risk factors for postoperative infectious complications.

Methods

To conduct a comprehensive systematic review and meta-analysis, we followed the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [8].

Search strategy

We developed a database search strategy that combines mesh terms and text words to improve the efficacy and precision of our searches. The research domain, as well as key concepts, keywords, and terms related to the use of antibiotics in patients with complicated appendicitis who underwent laparoscopy, were identified. We identified relevant Medical Subject Headings (Mesh) terms and compiled a list of text words that included keywords and synonyms. To capture a wide range of relevant documents, we considered using different variations of terms, alternative spellings, and related phrases. The mesh terms and text words were combined using Boolean operators (e.g., AND, OR). We tested and refined the search strategy using a sample set of relevant documents to determine if they align with our research objectives.

Database search

Two reviewers conducted a thorough literature search with no restrictions on timeframe, geographical location, or language. The search will include popular databases such as PubMed, Scopus, Cochrane Library, Google Scholar, and Web of Science. The search included articles published up until May 20, 2023. The goal of searching these various databases was to include a wide range of relevant studies and to conduct a thorough review of the available literature on the topic. A third author independently reran the database search to ensure the accuracy of the search strategy and the reported number of citations. He also double-checked the number of citations exported to the reference manager.

Study selection and data extraction:

We included randomized controlled trials as well as observational studies that reported on the duration of postoperative antibiotics in cases of complicated acute appendicitis treated with laparoscopic appendectomy. Case reports, editorials, reviews, and letters that were not relevant to the research question were excluded. These articles, however, were screened for potential additional references. There was an evaluation of full-text eligibility. Any disagreements about study judgements were settled through discussion and consultation with the principal investigator. Various study characteristics (e.g., study design, sample size), participant characteristics, intervention details, outcomes, and other relevant data points were extracted during the data extraction process. Two authors extracted data independently and cross-checked each other's work. By implementing a system of checks and balances, this approach

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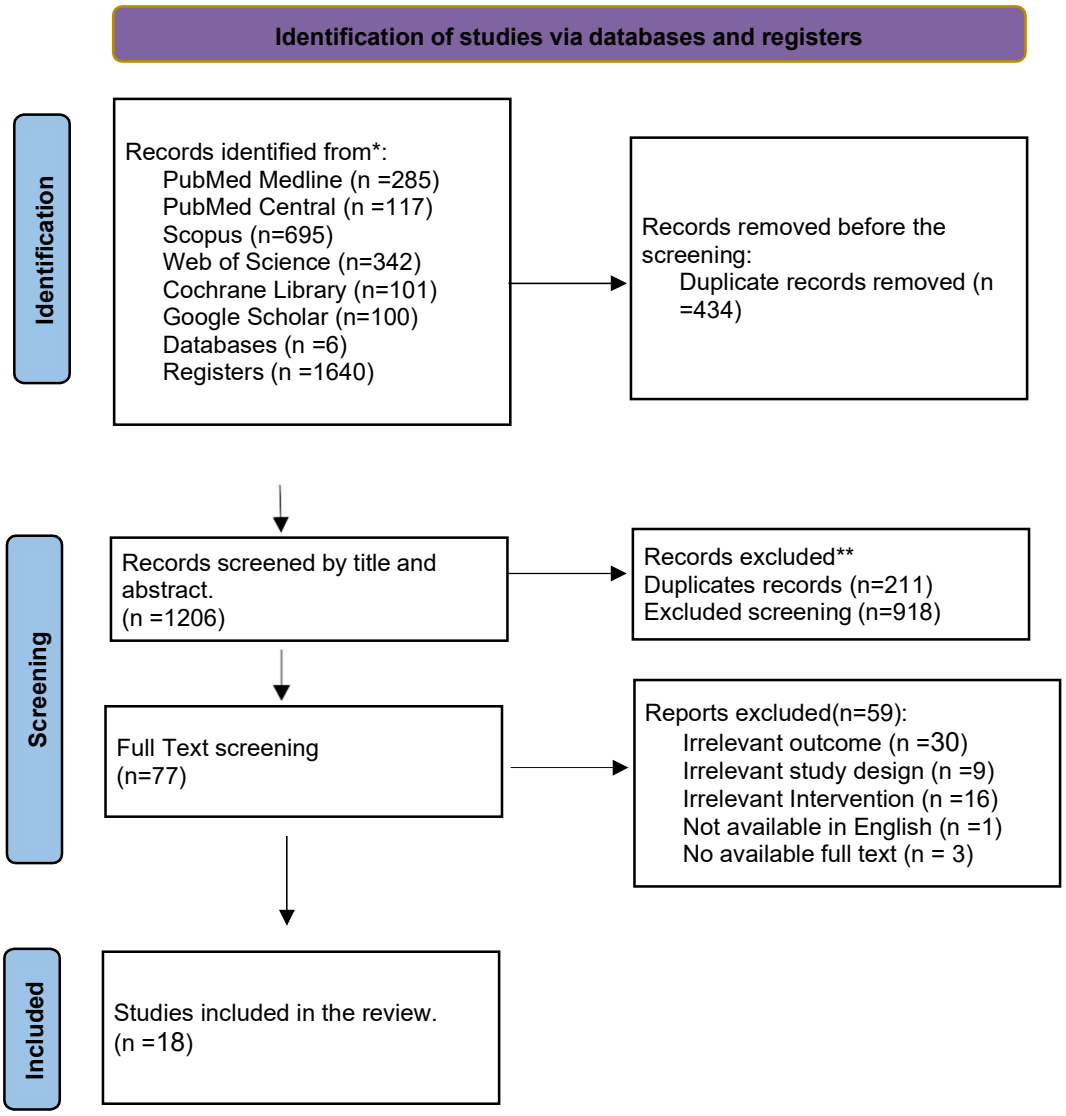
ensured data accuracy and minimized errors. The principal investigator independently verified the data extraction.

Figure (1): Flow chart of included studies



Results

The systematic review and meta-analysis retrieved a total of 1640 articles using specific search strategies. Using Endnote software, 434 duplicate studies were removed, yielding 1206 unique citations for further review based on titles and abstracts. Following this screening phase, 211 duplicates and 918 citations were removed, leaving 77 articles eligible for full-text review. Following the full-text screening phase, the 77 articles were meticulously evaluated, resulting in the exclusion of 59 studies.

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The presence of irrelevant intervention (16 studies), incompatible study design (9 studies), incongruous outcomes (30 studies), lack of full text (3 studies), and one study written in German were all reasons for exclusion. Ultimately, 18 studies met the predetermined eligibility criteria and were included in the systematic review and meta-analysis for subsequent analysis and synthesis (Figure 1).

All the included studies were cohort s design except fonnes, 2020, [9] it was Quasi-randomized controlled trial, Liu, 2020, [10] it was Multi-center, parallel group, randomized study, Lee, 2021, [11] it was RCT. Studies were conducted in USA [11, 12,13,14,15], three studies in Netherlands [6,16,17] and two studies in China. 10,18 The sample size ranged from 13 [9] to 716 [10]. The duration of antibiotic use was different 4 or 14 days [12], below or more than 7 days [13], 5-7 days [19], below 5 days or 7 days [6,14], 3 or 5 days 7,10,16, 5 days 20, 3 days or 5 days or more 17, metronidazole with broad spectrum antibiotics or broad antibiotics alone [18], IV antibiotics or Iv and oral Antibiotics [21], 9 days (7-11)[22]. Outcomes include: hospital stay duration [7,10,12,19,23], readmission [7,12,15,18], duration of the drain until removal [12], pneumonia 18 in hospital complications, intrabdominal infection (including abscess formation) [6,11,18,20,23,24], postoperative abscess [7,14,19,21] wound infection ileus [18,20,21, 24], reoperation [7], and ileus [7,18] (Table 1).

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Table (1): Data extraction of the included studies

Author, Year	**Study design**	**study setting, country**	**Study Period**	**Sample size, female (%)**	**Age mean (SD)**	**Antibiotic type, Duration**	**Outcome**
David, 2019 [12]	Retrospective cohort	Froedtert Lutheran Memorial Hospital in Milwaukee, Wisconsin, USA	August 2011 to December 2017	109 58 long duration 51 short duration	Long duration 44 years short duration 52 years	short duration is 4 days long duration is 14 days	Duration of hospital stay 6.3,4.7 vs 6.0,7.8, p =0.8) Duration of Ab 5.5,2.9 vs 4.1, 1,7 p = 0.005 readmission in 30 days 16% vs 2% p =0.017, rate of hospital infection 23% vs 25% p =0.788, duration of the drain 6.2, 4,7 vs 6.0, 7.9 p = 0.88 in hospital complication 13% vs 13% p = 0.82
Desai et al.,2015 [13]	Retrospective cohort	Children's Mercy Hospital and Clinics, USA	August 2011 to January 2014	G1: 270, **77%** G2: 270, **44%**	G1: 9.6 ± 3.8 G2: 10 ± 3.9	IV: received 50 mg/kg (max 2 g) IV ceftriaxone and 30 mg/kg (max 1 g) IV metronidazole every 24 hours for 2 days Oral: oral amoxicillin clavulanate	post operative abscess: 7.9% in G1 vs 4.4% in G2 , p =0.3

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						G1: 7-day G2: 7 days	
Ong C et al., [19]	Retrospective cohort	Singapore	January 1, 2005 to December 31, 2005.	G1: 62 patients followed pathway antibiotics. G2: 20 patients deviated from the pathway by receiving additional empiric gentamycin, **35%**	G1: 10.0 ± 3.2, G2: 9.5 ± 3.4	IV ceftriaxone (50 mg/kg daily) and metronidazole (7.5 mg/kg q8H) for at least 24 hours then oral antibiotics for 5-7 days	day till afebrile 2.3 ± 1.1 vs 2.7 ±1.0 p = 0.28, no of wound infection 0% vs 5% , p =0.24, no of postoperative abscess 6% vs 5%, p =1, length of hospital stay 6.4 ± 3.4 vs 6.3 ± 2.4 p =0.9
Fraser, 2010 [14]	Prospective, randomized trial	The Children's Mercy Hospital, Kansas City, USA	March 2007 to October 2008	IV (n = 52) IV/PO (n = 50) **40%**	10.1 ± 4.6	G1 once daily ceftriaxone and metronidazole IV G2 oral amoxicillin/clavulanate **G1 5 days G2 7 days**	There was no difference in the postoperative abscess rate between the two treatment groups.
Bae et al., 2016 [21]	Retrospective cohort	Kaiser Permanente Fontana Hospital	August 2010 to August 2013	G1: 52 received antibiotic, G2: 91 DID NOT RECIVE Ab	G1: 32 years, G2: 32 years	one or two postoperative doses of IV antibiotics	Intra-abdominal abscess G1:1.9% vs G2: 1.0%, p = 1.0, Wound infection G1: 1.9% vs G2 1.1%, p = 1.0

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Van Rossem et al., 2016 [7]	Retrospective cohort	Holland	June 1, 2014, to July 31, 2014,	G1: 75, **53.7%** G2: 191, **51.3%**	G1: Median = 44years, G2: Media =43 years	Dutch guideline for appendicitis **G1: 3 days, G2: 5 days**	median hospital stay 4 vs 5 days, p < 0.001, complications 16% vs 18.8 p = 0.72, surgical site infection 1.3% vs 1.6%, p =0.89, intraabdominal abcess 8% vs 8.9%, p = 0.81, reintervention 6.7% vs 4.2% p = 0.53, ileus 1.3% vs 3.7% p = 0.45, readmission 8% vs 11.5% p = 0.51)
Hughes et al. 2013 [20]	Retrospective analysis	England	September 1, 2009 to August 31, 2010	78 complicated, **35%**	29.00	The Surgical Infection Society Guidelines **5 days**	Intra-abdominal infection (12.8%), Incisional infection (2.5%)
van Rossem et al., 2014 [17]	Retrospective cohort	Tergooi Hospital, Netherlands	January 2004 to December 2010	G1: 126, **44.4%** G2: 141, **48.9%**	G1: 51 years, G2:46 years	Cefuroxime (750 mg 3 times daily) and metronidazole (500 mg 3 times daily) **G1: 3 days, G2: 5 days or more**	No significant difference between both groups

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Park et al., 2017 [24]	Cohort	Korea	January 2009 to December 2014	non standardized protocol (G1)= 730, **47.5%** standardized protocol (G2) n=613, **45.5%**	G1= 37.8 +/- 12.4, G2: 37.1 +/- 12.4	G1: IV Ab during the immediate post-operative period and then continued treatment with oral Ab after hospital discharge for 10 d. G2: (cefuroxime with metronidazole) for a total of 5 days	Total infection 20.8% vs 17.3% p = 0.241, superficial infection 17.1% vs 14.2% p = 0.298, intrabdominal infection 3.7% vs 3.1% p = 0.651)
Shang et al., 2017 [18]	Retrospective Cohort.	Chongqing Medical University, Chongqing, China	August 2013 to August 2016	G1: 98 G2: 98 **46%**	G1: 2.0±0.8 G2: 2.1±0.7	G1: metronidazole combined with broad-spectrum antibiotics G2: Only with broad spectrum antibiotics. piperacillin/tazobactam (100–150mg/kg/d in 2 divided doses), ceftriaxone (100–150mg/ kg/dose in 2 divided doses), or cefoperazone sodium and sulbactam (100–150mg/kg/dose in 2 divided doses). Metronidazole (30mg/ kg/dose in 2 divided doses)	Total complications 53.1% vs 50.0% , p=0.39, surgical wound infection 14.3% vs 15.3% p = 0.50 peritonitis 7.1% vs 9.2% p = 0.40, sepsis 2% vs 2% p = 0.69, pneumonia 8.2% vs 10.2% p =0.4, late ileus 19.4% vs 17.3% p = 0.43, readmission 9.2% vs 12.2% p =0.32

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Taleba, 2018 [23]	Cohort	Rennes University Hospital, France	April 2011 to March 2015	Group 1 (n = 80) Group 2 (n = 91), **44%**	9 [5–13] 10 [7–13]	metronidazole gr1 gentamicin and piperacillin/tazobactam gr2 **Intravenous + oral antibiotic duration (days) 15 [12–16] 5 [5–8]**	Infectious complication 15 (19) 23 (25) Surgical site infection 7 (9) 5 (5) Intra-abdominal abscess 12 (15) 20 (22) Hospital stay (days) 6 [5–8] 6 [5–7]
Ferguson, 2020 [15]	Retrospective cohort	Children's Memorial Hermann Hospital (CMHH), USA	August 1, 2012 to April 30, 2019	617 total G2 409, **35.1%**	10 (3.9)	Amoxacillin-clavulanate G1 4.8 (2.3) G2 11.3 (1.7)	Readmission: gr1 28 (13.1)/ gr2 26 (6.4) 0.005 Any complications: gr1 34 (16.0)/ gr2 34 (8.4) 0.004
fonnes, 2020 [9]	Quasi-randomized controlled trial	Department of Surgery, Herlev Hospital, Denmark	14th February 2018 to 17th June 2018	Intervention group (n = 7), **57%** Control group (n = 6), **17%**	Age, years 52 [21–73] 28 [18–55]	intervention group: 4 g fosfomycin, 1 g metronidazole, and 50 µg recombinant human granulocyte-macrophage intraperitoneally Control: standard intravenous antibiotic **3 days for both**	LOS in the intervention group median 13 h/ in control group median 84 h

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Liu, 2020 [10]	Multi-center, parallel group, randomized study	Qingdao Maternity and Child Care Hospital, Jinan Maternity and Child Care Hospital, and Chongqing Children's Hospital, China	July 1, 2017 to June 30, 2019	Standard 366, **50%** Restrictive 350, **54%**		standard **72-hour short-term course (Restrictive)** **5 days standard**	less antibiotic administration offers equivalent outcomes to the five-day standard treatment in terms of the infectious complications or hospital re-admission
Kwok, 2021 [22]	Retrospective cohort	Clinical Management System (CMS) platform in Hong Kong, Japan	December 2014 to November 2019	126, **35.7%**	10 (6.25–14)	empirical triple antibiotics **9 (7–11)**	Early escalation of antibiotics failed to reduce postoperative complications and antibiotics duration
Lee, 2021 [11]	RCT	USA	May 2017 to May 2020	162 total, **37.5%** PT group (82) and CM group (80).	9.1	CM (control group) Once daily ceftriaxone (50 mg/kg) and metronidazole (30 mg/kg). PT (interventional group) broad spectrum, single-drug regimen (<40 kg: 100 mg/kg Q8HR, >40 kg: 3000 mg Q6HR). **intravenous**	Intra-abdominal abscess: PT: 6.1% CM: 23.8%

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						antibiotic administration 5.2	
Boom, 2023 [16]	Multicenter retrospective cohort	Netherlands	May 2014 to January 2015	112, **40%**	36 (22; 55.75)	cefazolin and metronidazole were given **5 (3; 5)**	Infectious complications occurred in 12% and did not differ between patients reaching discharge criteria before or after 2 postoperative days.

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Wijck, 2010 [6]	Retrospective cohort	Netherlands	January 1992 to December 2006	(A)21, **38%** (b)51, **52%**	A 11 (1–17) -- B 9 (0–17)	Augmentin (amoxicillin clavulanate) **A 5 (1–16) -- B 7 (2–32) , continued until serum C-reactive protein (CRP) was \20 mg/l**	Twenty-nine (19.5%) of all children operated on for perforated appendicitis developed an intra-abdominal abscess: 13 (18.8%) in group A, and 16 (19.8%) in group B

Discussion

Minimal access surgery, which is distinguished by the use of small incisions, has made significant advances in recent years. This method seeks to achieve optimal surgical outcomes while minimizing patient trauma. Laparoscopy is now widely used in general surgery, including in emergency situations. Its adaptability and benefits have led to its increased use in a variety of surgical procedures, including complicated appendectomy. Antibiotics are usually given after this to prevent complications. The approach to antibiotic therapy for perforated appendicitis has changed and advanced significantly over the last several decades. The purpose of this review was to look at the impact of antibiotic administration duration on the occurrence of infectious complications after intervention.

In this systematic review, we searched seven databases and found 1640 articles that were eligible for screening. We included 19 articles in this review after careful consideration. However, due to a variety of factors, we were unable to conduct a meta-analysis. For starters, the duration of antibiotic use varied across studies, making it difficult to pool data. Second, the studies focused on different outcomes, which made the results difficult to compare. Finally, many studies did not separate the outcomes based on whether the surgery was open or laparoscopic.

We discovered significant variation in the selection of antibiotics for complicated appendicitis across institutions in this review. Local guidelines, institutional protocols, surgeon preferences, and patient-specific considerations may all influence antibiotic selection. This wide variation highlights thelack of standardized antibiotic selection guidelines in the management of complicated appendicitis, emphasizing the need for additional research and consensus in this area.

We also discovered that the incidence of infectious complications was nearly the same regardless of antibiotic duration. Other factors, rather than antibiotic duration, were identified as predictors of complications. The perforation of the appendix was identified as a risk factor for developing an

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infectious complication by Van Rossem et al., [7]. Interestingly, Bae et al., [21] discovered that postoperative antibiotics have no effect on the rate of intra-abdominal abscess formation in cases of suppurative appendicitis. As a result, routine postoperative antibiotics may not be required in this patient population.

Historically, practitioners treated infections with antibiotics for 7 to 10 days based on systemic inflammatory response syndrome criteria. Numerous studies, however, have looked into whether a shorter duration of postoperative antibiotic treatment with source control is the best approach for complicated appendicitis. Other infections, such as pneumonia, have shown that a shorter course of antibiotics can be equally effective.[25,26] The World Health organization has identified antibiotic misuse and overuse as a contributing factor to antibiotic resistance. A shorter course of antibiotics could help to mitigate this risk. Furthermore, it would result in a shorter hospital stay, potentially resulting in cost savings, though our study did not include a cost analysis. In many cases, the antibiotic regimen was quickly switched from intravenous to oral administration, contributing to a shorter hospital stay and, theoretically, lower costs. [12]

Strengths and limitations

There are several advantages to this systematic review. First, we conducted a thorough search across multiple databases to ensure that all relevant published papers on our topic were included. Second, while our study is unique in that it examines the impact of antibiotic duration on postoperative complications following laparoscopic appendectomy for complicated acute appendicitis, it is important to recognise the limitations we encountered during our research. To begin, not all of the included studies examined complications associated with laparoscopic appendectomy separately from open appendectomy. This lack of distinction may have influenced the overall findings and their relevance to laparoscopic procedures. Second, there were differences in the duration and types of antibiotics given following laparoscopy across the included studies, which could introduce heterogeneity and limit the generalizability of our findings. Despite these limitations, our systematic review adds to the existing literature by providing valuable insights into the relationship between antibiotic duration and postoperative complications in laparoscopic appendectomy for complicated acute appendicitis.

Conclusions

Our systematic review shows that postoperative antibiotics are widely recommended in the majority of included studies; however, it is important to note that there is currently no consensus regarding the optimal duration and specific antibiotic regimen for this procedure. Significantly, all of the studies we looked at consistently showed that prolonged antibiotic use after laparoscopic appendectomy for complicated cases did not result in a reduction in infectious complications, particularly superficial or deep wound site infections. This finding calls into question the efficacy of long antibiotic courses in preventing such complications in this setting. The lack of agreement on postoperative antibiotic duration and regimen highlights the need for additional research and guidelines to provide clearer recommendations for postoperative antibiotic use in laparoscopic appendectomy. Future research should focus on determining the optimal duration and specific antibiotic choices to improve patient outcomes and reduce the risk of complications.

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: all shared in designing the study, wrote the protocol and planed the study and helped in data extraction. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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