

Systematic Review

Single-dose versus multiple-dose antibiotic prophylaxis in elective laparoscopic cholecystectomy

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ABSTRACT

The benefit of continuing prophylactic antibiotics beyond the perioperative period in elective laparoscopic cholecystectomy remains uncertain. Prolonged antibiotic exposure may increase healthcare costs, adverse drug events, and antimicrobial resistance without providing additional clinical benefit. This systematic review was conducted between May and July 2026 and followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) framework. Adults aged 18 years or older undergoing elective laparoscopic cholecystectomy were eligible. Studies directly comparing single-dose perioperative antibiotic prophylaxis with multiple-dose or prolonged prophylaxis were included. The primary outcome was postoperative surgical-site infection or a clinically equivalent infectious complication. Randomized studies were assessed using the Cochrane Risk of Bias 2 (RoB 2) tool, while non-randomized studies were assessed using ROBINS-I. A narrative synthesis was performed because of clinical and methodological heterogeneity. Eighteen eligible studies involving 3,448 participants were included. Of these, 1,723 participants received single-dose prophylaxis and 1,725 received multiple-dose or prolonged prophylaxis. Most studies reported no statistically significant difference in postoperative infectious outcomes between the two strategies. Haider et al. reported significantly fewer postoperative infections in the single-dose group, whereas the remaining evidence generally showed comparable outcomes. Secondary outcomes, including hospital length of stay and healthcare resource utilization, were inconsistently reported. In adults undergoing uncomplicated elective laparoscopic cholecystectomy, single-dose perioperative antibiotic prophylaxis appears to provide postoperative infectious outcomes comparable to multiple-dose or prolonged regimens. The available evidence does not demonstrate a consistent clinical benefit from extending prophylaxis beyond the perioperative period. These findings should be interpreted in light of the methodological heterogeneity, limitations in study quality, and inconsistent outcome reporting across the included studies.

Keywords: Antibiotic prophylaxis, Laparoscopic cholecystectomy, Surgical site infection, Antimicrobial stewardship, Systematic review

INTRODUCTION

Elective laparoscopic cholecystectomy is one of the most frequently performed abdominal surgical procedures. The minimally invasive approach is associated with a relatively low incidence of postoperative infectious complications, particularly among patients undergoing uncomplicated elective surgery. Despite the relatively low baseline risk of infection, perioperative antibiotic prophylaxis remains widely used.^{1,2} An important unresolved question is whether prophylaxis should be restricted to a single perioperative administration or continued through multiple postoperative doses.

Multiple-dose and prolonged antibiotic regimens increase antimicrobial exposure and may increase medication costs, adverse drug events, and selection pressure for antimicrobial resistance. Conversely, clinicians may continue prophylaxis because of concerns regarding postoperative surgical-site infection. Previous studies comparing single-dose and multiple-dose prophylaxis have reported heterogeneous findings.¹⁻³ Differences have been observed in antibiotic selection, dose, timing, duration of therapy, definitions of infection, follow-up periods, and study methodology.

The objective of this systematic review was therefore to synthesize the available evidence comparing single-dose perioperative antibiotic prophylaxis with multiple-dose or prolonged postoperative prophylaxis in adults undergoing elective laparoscopic cholecystectomy, with particular attention to postoperative infectious outcomes and healthcare resource utilization.

METHODS

Study Design, Reporting, and Setting

This systematic review was conducted between May and July 2026 at the Hospital General Presidente Lázaro Cárdenas del Río, Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado (ISSSTE), Chihuahua, Chihuahua, Mexico. The review was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) framework. The review question was formulated using the Population, Intervention, Comparator, and Outcomes (PICO) framework. No patients were prospectively recruited, as this review was based on previously published studies.

Eligibility criteria

The eligibility criteria were defined according to the PICO framework.

Population

Adults aged 18 years or older undergoing elective laparoscopic cholecystectomy.

Intervention

Single-dose perioperative antibiotic prophylaxis administered around the time of surgery.

Comparator

Multiple-dose or prolonged antibiotic prophylaxis extending beyond the perioperative period.

Primary outcome

Postoperative surgical-site infection (SSI) or a clinically equivalent postoperative infectious complication, as defined by the individual study.

Secondary outcomes

Port-site infection, wound infection, hospital length of stay, antibiotic exposure, healthcare costs or resource utilization, and adverse events.

Studies were excluded if they included pediatric patients without separately extractable adult data; evaluated open cholecystectomy; included mixed surgical populations without separately extractable data for laparoscopic cholecystectomy; compared single-dose prophylaxis with no antibiotic prophylaxis rather than with a multiple-dose or prolonged regimen; or did not provide a direct comparison relevant to the review question.

Study selection

The original literature search and screening process were retained without retrospective modification. Records were assessed according to the predefined eligibility criteria. Duplicate publications representing the same patient cohort were treated as a single study to avoid double-counting participants. Yadav et al was excluded because the study included patients younger than 18 years without separately extractable adult outcome data. A separate 180-patient publication identified as a duplicate cohort of Sutariya and Thekdi was also excluded from the study count.

Search strategy and PRISMA reporting

The original search strategy and screening process were retained. Complete database-level counts for records identified, duplicates removed, records screened, and full-text reports assessed were not preserved in the available review records. Consequently, these intermediate values were not retrospectively estimated or fabricated. The final audited evidence base comprised 18 eligible studies involving 3,448 participants.

Data extraction

The following information was extracted from the included publications: first author, year of publication,

study design, total sample size, number of participants receiving single-dose prophylaxis, number receiving multiple-dose or prolonged prophylaxis, antibiotic regimen, duration of prophylaxis, postoperative infectious outcomes, hospital length of stay, healthcare costs or resource utilization, statistical comparisons, and relevant methodological characteristics.

AI-assisted tools were used to support literature-screening and data-extraction workflows but were not considered independent sources of evidence. The authors checked study eligibility decisions and extracted values against the underlying publications.

Risk of bias assessment

Randomized studies were assessed using the Cochrane Risk of Bias 2 (RoB 2) tool. Non-randomized comparative studies, prospective observational studies, and quasi-experimental studies were assessed using the Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) tool. Risk-of-bias judgments were based on the methods reported in the original publications rather than solely on the authors' designation of a study as randomized.

Data synthesis

A narrative synthesis was performed to summarize the findings across the included studies. Quantitative meta-analysis was not undertaken because of substantial heterogeneity in antibiotic regimens, definitions of postoperative infection, follow-up periods, study designs, allocation methods, reporting completeness, and outcome measurement.

RESULTS

Study selection and characteristics

The final audited evidence base comprised 18 eligible studies involving 3,448 participants. Of these, 1,723 participants received single-dose prophylaxis and 1,725 received multiple-dose or prolonged prophylaxis. The studies were published between 2016 and 2026 and included randomized trials, prospective comparative studies, observational cohorts, and quasi-experimental studies.

Table 1: Characteristics of included studies.

Study	Year	Design	N	SD	MD	Primary outcome
Sutariya and Thekdi ¹	2016	Prospective randomized	180	90	90	SSI
Thapa et al ²	2017	RCT	240	118	122	SSI
Chauhan et al ³	2018	Randomized	210	112	98	SSI
Naser et al ⁴	2019	Comparative	60	30	30	Port-site infection
Gupta & Singh ⁵	2020	Comparative	70	35	35	SSI
Phadnis et al ⁶	2020	Prospective comparative	152	74	78	SSI
Chand et al ⁷	2021	Prospective	100	50	50	SSI
Husein et al ⁸	2022	Randomized comparative	200	100	100	SSI
Haider et al ⁹	2022	Prospective comparative	374	187	187	SSI
Thareja et al ¹⁰	2023	Prospective cohort	160	80	80	SSI
Mistry and Chandnani ¹¹	2024	Comparative	50	25	25	Wound infection
Zafar et al ¹²	2024	Quasi-experimental	798	399	399	SSI
Patel et al ¹³	2024	Prospective non-randomized	200	100	100	SSI
Shrestha et al ¹⁴	2024	Prospective comparative	238	119	119	SSI
Islam et al ¹⁵	2024	Comparative	100	50	50	SSI
Mishra et al ¹⁶	2025	Prospective	126	59	67	SSI
Patowary et al ¹⁷	2026	RCT	100	50	50	SSI
Reddy et al ¹⁸	2026	RCT	90	45	45	SSI
TOTAL			3,448	1,723	1,725	

Postoperative infectious outcomes

Overall, postoperative infectious outcomes were generally comparable between single-dose and multiple-

dose/prolonged prophylaxis. Most studies reported no statistically significant difference in postoperative infectious outcomes. Sutariya and Thekdi reported infection rates of approximately 4.4% versus 3.3% in the

single-dose and multiple-dose groups, respectively.¹ Thapa et al reported 4.2% versus 3.3%.² Phadnis et al reported 2.43% versus 2.57% ($p=0.693$).⁶ Chand et al. reported 6% versus 4% ($p=0.65$).⁷ Husein et al. reported 1% versus 1%.⁸ Mishra et al reported 3.4% versus 3.0% ($p=0.897$).¹⁶ Patowary et al. reported 5% versus 4%, without a statistically significant difference.¹⁷ Reddy et al reported 6.7% versus 4.4% ($p=0.900$).¹⁸

Zafar et al reported SSI in 1.6% versus 1.7% of participants receiving single-dose and multiple-dose prophylaxis, respectively, without a significant difference.¹² Haider et al reported significantly fewer postoperative infections in the single-dose group (4.28% vs. 9.63%, $p=0.042$).⁹ This isolated finding was not consistently reproduced across the remaining studies and therefore does not establish superiority of single-dose prophylaxis.

Port-site infection

Naser et al specifically evaluated port-site infection.⁴ Zafar et al also reported port-site infections, occurring in 5 of 399 participants in the single-dose group and 8 of 399 in the multiple-dose group.¹² These findings do not suggest a consistent advantage from prolonged prophylaxis. Because definitions and ascertainment differed among studies, port-site infection was not pooled with all SSI outcomes.

Hospital length of stay and resource utilization

Hospital length of stay was inconsistently reported. Shrestha et al. reported 2.60 ± 0.81 days with single-dose prophylaxis compared with 3.06 ± 0.72 days with multiple-dose prophylaxis.¹⁴ Islam et al reported 1.44 versus 1.50 days, respectively.¹⁵

Thareja et al specifically evaluated healthcare expenditure and reported lower treatment cost with the single-dose

strategy.¹⁰ Mistry and Chandnani compared a short preoperative regimen with five days of postoperative coverage.¹¹ Other studies also reported reduced antibiotic exposure or lower costs with shorter prophylaxis.¹¹ These secondary outcomes were inconsistently reported and were not quantitatively synthesized. Chauhan et al was included in the final qualitative synthesis.³

Risk of bias

Gupta and Singh were judged as having some concerns under RoB 2 because randomization was reported, but sequence generation and allocation concealment were insufficiently described.⁵ Reddy et al was also classified as having some concerns because, despite reporting computer-generated randomization and concealed allocation, the study was open-label and some outcome-assessment concerns remained.¹⁸

Among randomized studies, most were judged to have some concerns, primarily because of incomplete reporting of sequence generation, allocation concealment, or blinding. Reddy et al described randomization and allocation concealment more clearly than several other studies, although the trial was open-label.¹⁸

Non-randomized studies generally showed serious or critical concerns, particularly related to confounding, non-random allocation, and incomplete control of baseline differences. Thareja et al was a prospective observational cohort in which treatment allocation was influenced by the treating surgeon.¹⁰ Zafar et al was quasi-experimental and was therefore assessed using ROBINS-I.¹² Shrestha et al used roll-based allocation and was not treated as a conventional randomized controlled trial.¹⁴

Gupta and Singh described the allocation as randomized but reported insufficient detail to establish conventional sequence generation and allocation concealment.⁵

Table 2: Risk-of-bias assessment of included studies.

Study	Tool	Overall judgment
Sutariya and Thekdi ¹	RoB 2	Some concerns
Thapa et al ²	RoB 2	Some concerns
Chauhan et al ³	RoB 2	Some concerns
Naser et al ⁴	ROBINS-I	Serious concerns
Gupta and Singh ⁵	RoB 2	Some concerns
Phadnis et al ⁶	ROBINS-I	Serious concerns
Chand et al ⁷	ROBINS-I	Serious concerns
Husein et al ⁸	RoB 2	Some concerns
Haider et al ⁹	ROBINS-I	Serious concerns
Thareja et al ¹⁰	ROBINS-I	Critical
Mistry and Chandnani ¹¹	ROBINS-I	Serious concerns
Zafar et al ¹²	ROBINS-I	Critical
Patel et al ¹³	ROBINS-I	Critical
Shrestha et al ¹⁴	ROBINS-I	Critical
Islam et al ¹⁵	RoB 2	Some concerns

Continued.

Study	Tool	Overall judgment
Mishra et al ¹⁶	ROBINS-I	Serious concerns
Patowary et al ¹⁷	RoB 2	Some concerns
Reddy et al ¹⁸	RoB 2	Some concerns

DISCUSSION

The principal finding of this systematic review is that extending antibiotic prophylaxis beyond the perioperative period did not demonstrate a consistent reduction in postoperative infectious complications after uncomplicated elective laparoscopic cholecystectomy.

Across 18 studies involving 3,448 participants, most comparisons showed no statistically significant difference between single-dose and multiple-dose/prolonged regimens. One study reported significantly fewer infections with single-dose prophylaxis, but this finding was not consistently reproduced.

The relatively low incidence of postoperative infection in uncomplicated elective laparoscopic cholecystectomy is clinically important. When baseline infectious risk is low, the absolute benefit achievable through prolonged antibiotic exposure is likely to be small. This potential benefit must be balanced against additional antimicrobial exposure and its associated costs and adverse effects.

The included studies demonstrated considerable variation in antibiotic choice, dose, duration, and timing. Therefore, the term multiple-dose encompasses clinically heterogeneous interventions. The overall evidence supports the interpretation that extending prophylactic antibiotic exposure beyond the perioperative period does not consistently improve infectious outcomes in this population.

The findings also have implications for antimicrobial stewardship. When no consistent clinical benefit is demonstrated, extending prophylactic antibiotics increases antimicrobial exposure without a clearly established corresponding benefit. Potential consequences include increased drug exposure, medication costs, adverse drug reactions, healthcare utilization, and selection pressure favoring antimicrobial resistance.

This conclusion should not be extrapolated indiscriminately to patients with complicated biliary disease, active infection, acute cholecystitis requiring therapeutic antibiotics, immunocompromising conditions, or other circumstances in which antibiotics are being administered for treatment rather than prophylaxis.

Strengths

Focused review question addressing elective laparoscopic cholecystectomy. Final evidence base subjected to study-

level eligibility and bibliographic auditing. Duplicate patient cohorts were not counted as independent studies. Randomized and non-randomized evidence were assessed using design-appropriate risk-of-bias frameworks. Infectious outcomes were not automatically treated as equivalent when individual studies used different definitions. No inappropriate pooled analysis was performed in the presence of substantial clinical and methodological heterogeneity.

Limitations

The principal limitation is methodological heterogeneity among the included studies. The evidence ranged from randomized trials to prospective observational and quasi-experimental methodologies. Several studies provided incomplete information regarding allocation, concealment, or blinding. Outcome definitions and follow-up periods differed substantially, and many studies reported relatively few infectious events. Economic and resource-utilization outcomes were inconsistently reported. Finally, although the original search strategy was retained, the historical record available for the current manuscript did not preserve exact database-level counts for records identified, duplicates removed, records screened, and full-text reports assessed. These values were therefore not retrospectively imputed.

CONCLUSION

In adults undergoing uncomplicated elective laparoscopic cholecystectomy, single-dose perioperative antibiotic prophylaxis appears to provide postoperative infectious outcomes comparable to multiple-dose or prolonged antibiotic regimens. Across studies involving 3,448 participants, most studies found no statistically significant difference in postoperative infectious outcomes. Although isolated studies favored one regimen, no consistent evidence demonstrated that extending prophylactic antibiotics beyond the perioperative period provides additional clinical benefit. The evidence is limited by methodological heterogeneity, non-randomized study designs, inconsistent outcome definitions, incomplete reporting, and low infection event rates. Routine continuation of prophylactic antibiotics beyond the perioperative period therefore does not appear to provide a consistent clinical benefit in uncomplicated elective laparoscopic cholecystectomy.

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