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Effect of Prophylactic Antibiotics on Post-ERCP Infectious Complications in Patients with Common Bile Duct Stones: An Open-Label, Three-Arm Controlled Clinical Trial.

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ABSTRACT

Background: The role of antibiotic prophylaxis before endoscopic retrograde cholangiopancreatography (ERCP) remains controversial, particularly in patients with common bile duct (CBD) stones. This study aimed to evaluate the effectiveness of prophylactic antibiotics in reducing post-ERCP infectious complications and to determine whether prolonged antibiotic therapy provides additional clinical benefit.

Methods: This prospective, single-center, open-label, controlled interventional study included patients aged ≥18 years with common bile duct stones who were scheduled to undergo ERCP and had an axillary temperature <37.0°C and a white blood cell count of 4–10 × 10^9/L at admission. Patients were allocated according to a prespecified rule into three parallel groups: no antibiotics; a single intravenous dose of amikacin (15 mg/kg), infused over 60 minutes and completed before ERCP; or amikacin combined with cefoperazone for 4–7 days. Patients were followed for 7 days after ERCP. The primary analysis assessed a composite infectious outcome

comprising acute cholangitis, acute cholecystitis, and/or bacteremia in the modified intention-to-treat (mITT) population; a per-protocol (PP) analysis was performed to assess consistency.

Results: Of 506 eligible patients allocated to three study groups, 498 were included in the mITT analysis (no antibiotics, n=173; single-dose prophylaxis, n=161; prolonged antibiotics, n=164). The composite infectious outcome occurred in 20/173 (11.6%), 6/161 (3.7%), and 7/164 (4.3%) patients, respectively. Compared with no antibiotics, single-dose prophylaxis was associated with a lower risk of infectious complications (RR 0.32, 95% CI 0.13–0.78; P=0.008). No statistically significant difference was observed between single-dose prophylaxis and prolonged antibiotic therapy (RR 0.87, 95% CI 0.30–2.54; P=0.80). Findings were generally consistent in the per-protocol analysis. Lower rates of acute cholangitis (3.1% vs. 9.8%; RR 0.32, 95% CI 0.12–0.84; P=0.013) and bacteremia (0.6% vs. 6.4%; RR 0.10, 95% CI 0.01–0.75; P=0.005) were also observed with single-dose prophylaxis compared with no antibiotics.

Conclusions: A single dose of amikacin before ERCP was associated with lower rates of infectious complications, particularly acute cholangitis and bacteremia, in patients with common bile duct stones. Prolonged antibiotic therapy showed no clear additional benefit over single-dose prophylaxis.

TRIAL REGISTRATION: ISRCTN32773697, retrospectively registered on 1 May 2025 (https://www.isrctn.com/ISRCTN32773697)

KEYWORDS: Endoscopic retrograde cholangiopancreatography; common bile duct stones; antibiotic prophylaxis; cholangitis; bacteremia; infectious complications.

BACKGROUND

Gallstone disease is a common condition in clinical practice and poses substantial challenges in both diagnosis and management. In the United States, gallstone disease places a substantial burden on healthcare services, contributing to approximately 2.2 million ambulatory care visits, 1.2 million emergency department visits, 625,000 hospital discharges, and 2,000 deaths annually [1]. Endoscopic retrograde cholangiopancreatography (ERCP) is considered a

first-line therapeutic option for common bile duct stones because of its high efficacy and minimally invasive nature compared with conventional surgery [2]. However, ERCP carries a risk of adverse events, with reported overall complication rates of 9.4%–15.9% and mortality rates of 0.26%–1.0% [3]. Infectious complications are among the most serious adverse events and account for 7.85% of ERCP-related deaths [4]. The reported incidence of post-ERCP infection ranges from 2.4% to 9.7% [3, 5].

The role of antibiotic prophylaxis in ERCP remains controversial. Clinical practice guidelines from the American Society for Gastrointestinal Endoscopy (ASGE) and the European Society of Gastrointestinal Endoscopy (ESGE) recommend against routine antibiotic prophylaxis, while supporting its use in selected high-risk patients, including liver transplant recipients, patients with severe immunosuppression or primary sclerosing cholangitis, and those in whom complete biliary drainage is not expected to be achieved [6, 7]. In contrast, evidence from the Cochrane review [8], previous studies and other meta-analyses [9-12], together with the randomized controlled trial by Leem et al [13] suggested that antibiotic prophylaxis may reduce infectious complications, particularly cholangitis. Notably, a protective effect against infectious complications was also observed among patients in whom successful biliary drainage was achieved [13].

Although previous studies have evaluated the effectiveness of antibiotic prophylaxis in preventing post-ERCP infectious complications, uncertainty remains regarding whether prolonged antibiotic administration provides additional benefits over single-dose prophylaxis. To address this evidence gap, we conducted a three-arm, open-label, controlled study comparing no antibiotics, single-dose prophylaxis, and prolonged antibiotic administration in patients undergoing ERCP for common bile duct stones.

METHODS

Study design and setting

This was a prospective, single-center, open-label, three-arm, parallel-group, quasi-randomized controlled study with an intended allocation ratio of 1:1:1, conducted at 108 Military Central Hospital from November 2022 to September 2026. The analysis focused on comparing single-dose antibiotic prophylaxis with no antibiotics and prolonged antibiotic therapy to evaluate its effectiveness in preventing post-ERCP infectious complications and the additional benefit of prolonged antibiotic treatment. The study was approved by the Institutional Ethics Committee for Biomedical Research of 108 Military Central Hospital (approval No. 6893/GCN-BV, dated November 25, 2022) and was retrospectively registered with the ISRCTN registry (ISRCTN32773697). Written informed consent was obtained from all participants before enrollment. Patients and the public were not involved in the design, conduct, or reporting of this study.

Study participants

Inclusion criteria: Patients were eligible for inclusion if they were aged ≥18 years; had common bile duct stones documented by abdominal ultrasonography, endoscopic ultrasonography, computed tomography, magnetic resonance imaging, or cholangiography; had an axillary temperature <37.0°C and a white blood cell count of 4–10 × 10^9/L at admission; and were classified as American Society of Anesthesiologists (ASA) physical status I or II.

Exclusion criteria: Patients were excluded if they had severe coagulopathy, defined as an international normalized ratio (INR) >1.5 or a platelet count <50 × 10^9/L; severe systemic disease; an active infection at another site requiring antibiotic therapy; systemic antibiotic use within 48 hours before ERCP; pregnancy; known allergy to the study antibiotics; or refusal to participate in the study.

Group allocation

Eligible patients were allocated to one of three study groups using a quasi-random allocation method based on hospital medical record numbers. Medical record numbers were automatically generated by the hospital information system at the time of admission as part of the routine hospital-wide administrative process and were independent of the study team. Investigators were not involved in generating, selecting, or modifying these numbers. After eligibility was confirmed,

patients were assigned to one of three groups according to a prespecified allocation rule based on their medical record numbers. Patients whose medical record numbers yielded a remainder of 1 or 2 when divided by three were allocated to Group 1 (no antibiotics) or Group 2 (single-dose prophylaxis), respectively, whereas those whose numbers were divisible by three were allocated to Group 3 (prolonged antibiotics).

Antibiotic interventions

Antibiotic selection: Amikacin was selected based on local microbiological data from 108 Military Central Hospital [14], which showed that biliary isolates were predominantly Gram-negative organisms and remained highly susceptible to amikacin, whereas relatively high rates of resistance to third- and fourth-generation cephalosporins and quinolones were observed. In the prolonged-antibiotic group, combination therapy with amikacin and cefoperazone was initiated before ERCP and continued for 4-7 days.

Study interventions: Patients were allocated to three treatment groups:

Group 1 (no antibiotics) received standard supportive care, including isotonic intravenous fluids when clinically indicated, without antibiotic administration.

Group 2 (single-dose prophylaxis) received a single dose of amikacin (15 mg/kg), administered as an intravenous infusion over 60 minutes and completed before the start of ERCP.

Group 3 (prolonged antibiotics) received amikacin 15 mg/kg/day in combination with intravenous cefoperazone 2 g every 12 hours, initiated before ERCP and continued for 4-7 days. The amikacin dose was adjusted according to renal function when necessary.

If an infectious complication occurred during follow-up, therapeutic antibiotics were administered as clinically indicated, regardless of the originally assigned study group.

Interventions were administered by the treating clinical team according to the assigned study group. Deviations from the assigned antibiotic regimen were recorded as protocol deviations and were accounted for in the per-protocol analysis. Apart from the assigned antibiotic strategy, all groups received the same routine supportive and post-ERCP care according to standard clinical practice.

Assessment and follow-up: All patients underwent clinical and laboratory assessments before and after ERCP. Laboratory investigations included complete blood count, aspartate aminotransferase (AST), alanine aminotransferase (ALT), urea, creatinine, total and direct bilirubin, gamma-glutamyl transferase (GGT), alkaline phosphatase (ALP), amylase, lipase, C-reactive protein (CRP), and procalcitonin. These tests were performed before ERCP and repeated within 24–48 hours after the procedure. Additional imaging studies were performed when clinically indicated to evaluate suspected post-procedural complications.

Patients were observed in hospital for at least 48 hours after ERCP. Clinically stable patients were discharged and followed until day 7 after ERCP for assessment of post-procedural complications and other adverse events. Blood cultures were obtained in patients who developed a fever >38.0°C. Post-ERCP complications were managed according to current clinical practice until clinical stabilization and discharge.

ERCP procedure

ERCP for common bile duct stone extraction was performed according to standard clinical practice by an experienced endoscopy team consisting of two physicians and two nurses. After successful biliary cannulation, cholangiography was performed to assess the number, size, and location of stones and the morphology of the common bile duct. Endoscopic sphincterotomy and/or papillary balloon dilation were performed when indicated. Stones were extracted using a retrieval balloon, basket, or a combination of both, depending on stone characteristics and biliary anatomy. Mechanical lithotripsy and biliary stent placement were used in cases of difficult stones, incomplete stone clearance, or when adequate biliary drainage needed to be ensured. After the procedure, patients were transferred to the post-anesthesia care unit and, once clinically stable, were handed over to the attending physician for continued monitoring.

Study outcomes and definitions

Primary outcome: Post-ERCP infectious complications were defined as the occurrence of acute cholangitis, acute cholecystitis, and/or bacteremia within 7 days after ERCP. The occurrence of at least one of these events was considered an infectious complication.

Secondary outcomes:

Post-ERCP cholangitis: Post-ERCP cholangitis was defined as new-onset fever >38.0°C accompanied by evidence of systemic inflammation and cholestasis. Systemic inflammation was defined as a white blood cell count >10 × 10^9/L, a C-reactive protein level >10 mg/L, or a further increase in either marker if already elevated before ERCP. Cholestasis was defined as total bilirubin >2.0 mg/dL, worsening pre-existing hyperbilirubinemia, liver enzyme levels (GGT, ALP, AST, or ALT) >1.5 times the upper limit of normal, or further increases in previously elevated liver enzymes. No alternative source of infection was identified.

Acute cholecystitis: Diagnosed according to the Tokyo Guidelines 2018 [15].

Bacteremia: Defined as a positive blood culture for a bacterial pathogen.

Other outcomes: Bleeding: Bleeding observed during the procedure or clinical signs such as melena, anemia, and a decrease in hemoglobin level exceeding 2 g/dL [16].

Post-ERCP pancreatitis: Diagnosed according to the Revised Atlanta Classification (2012), requiring at least two of the following three criteria: new or worsening abdominal pain consistent with acute pancreatitis, serum amylase or lipase levels ≥3 times the upper limit of normal, or characteristic imaging findings of acute pancreatitis [17]. In patients with elevated pancreatic enzyme levels before ERCP, the diagnosis of PEP was based on the onset or worsening of abdominal pain after the procedure, changes in pancreatic enzyme levels relative to baseline, and abdominal computed tomography findings when clinically indicated.

Acute kidney injury was defined according to KDIGO criteria as an increase in serum creatinine of ≥0.3 mg/dL (≥26.5 μmol/L) within 48 hours [18].

Statistical analysis

Data were analyzed using IBM SPSS Statistics version 22.0. Categorical variables are presented as counts and percentages, whereas continuous variables are summarized as mean ± standard deviation or median (range), as appropriate according to their distribution. Between-group comparisons were performed using the chi-square test or Fisher's exact test for categorical variables and one-way analysis of variance (ANOVA) or the Kruskal–Wallis test for continuous variables.

The primary analysis was performed in the modified intention-to-treat (mITT) population, which included all allocated patients who underwent successful ERCP and were analyzed according to their originally assigned group. A per-protocol (PP) analysis, including patients in the mITT population who completed the study without major protocol deviations and were analyzed according to their originally assigned group, was conducted to assess the consistency of the findings. An exploratory post-hoc analysis was performed to compare the incidence of post-ERCP fever >37.0°C among the study groups. No subgroup analyses were performed. The two pairwise comparisons of primary interest were Group 2 versus Group 1 and Group 2 versus Group 3. To account for multiple testing across these two comparisons, a Bonferroni-adjusted significance threshold of $P < 0.025$ was applied. Effect estimates for binary outcomes are reported as relative risks (RRs) with 95% confidence intervals (CIs). All statistical tests were two-sided.

Sample size calculation

The initial minimum sample size was estimated using G*Power version 3.1, based on a chi-square test to detect an overall difference among the three study groups, with a two-sided α of 0.05, 80% power, and a medium effect size according to Cohen ($w = 0.30$). Because sufficiently reliable data on the overall rate of post-ERCP infectious complications in a comparable population were unavailable at the time of study design, a standardized effect size was used for sample-size estimation. The minimum required sample size was 108 participants. The recruitment period was subsequently extended through September 2026, resulting in a final sample larger than the minimum required sample size.

Changes from the original protocol

Several modifications were made after study initiation. Although the original protocol identified post-ERCP infectious complications as the primary outcome, its detailed definition was based on fever >38.0°C within 24–48 hours after ERCP. Because fever alone was considered insufficiently specific, the primary outcome was revised before statistical analysis to a composite of acute cholangitis, acute cholecystitis, and/or bacteremia within 7 days after ERCP. These infectious outcomes and the 7-day follow-up period were already included in the original protocol.

The final analysis prioritized Group 2 versus Group 1 and Group 2 versus Group 3, with mITT and PP analyses and an additional exploratory analysis of fever >37.0°C. The planned study period was extended beyond December 2025 to allow additional recruitment and improve the precision of effect estimates.

RESULTS

Study population

Patients were recruited from November 2022 to September 2026. A total of 506 eligible patients with common bile duct stones were allocated to three study groups using a prespecified quasi-random method: 175 to the no-antibiotic group, 165 to the single-dose prophylaxis group, and 166 to the prolonged-antibiotic group. Eight patients did not undergo successful ERCP and were excluded from the modified intention-to-treat (mITT) analysis. The mITT population therefore comprised 498 patients: 173, 161, and 164 patients in Groups 1, 2, and 3, respectively. After the additional exclusion of 36 patients who did not meet the per-protocol (PP) criteria, the PP population comprised 462 patients: 164, 151, and 147 patients in Groups 1, 2, and 3, respectively (**Figure 1**).

Figure 1. Participant flow through the study

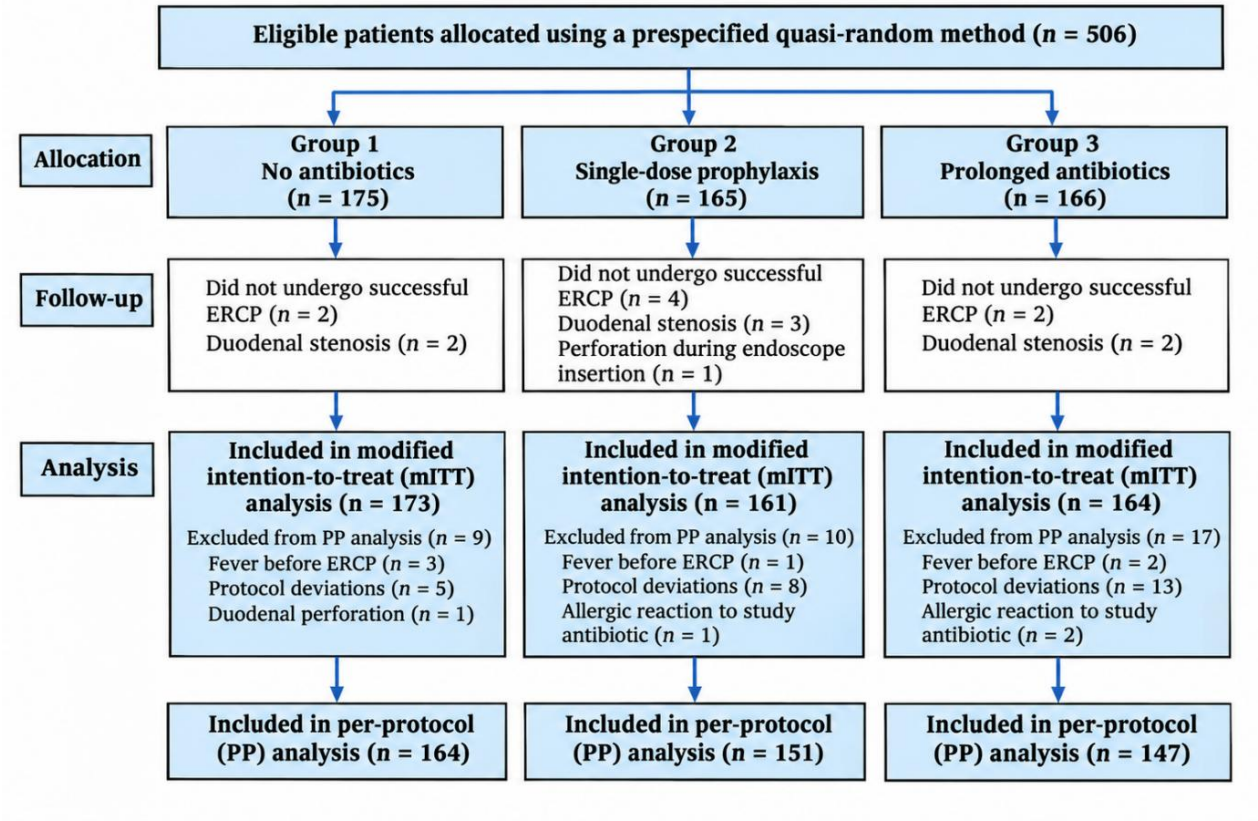


Figure legend. The flow diagram begins with 506 eligible patients allocated to three treatment groups using a prespecified quasi-random method. Eight patients did not undergo successful ERCP and were excluded from the mITT analysis. After additional exclusions according to the PP criteria, 462 patients were included in the PP analysis.

Baseline characteristics: The baseline characteristics of the three groups are presented in Table 1 and were generally comparable across groups. No statistically significant differences were observed in age, sex, abdominal pain, ASA classification, white blood cell count, CRP, procalcitonin, AST, ALT, GGT, or stone-related characteristics. However, the prevalence of jaundice, total bilirubin levels, and ALP levels differed among the three groups, with P values of 0.026, 0.003, and 0.037, respectively (**Table 1**).

Table 1: Baseline characteristics

Characteristic	Group 1 (n=173)	Group 2 (n=161)	Group 3 (n=164)	p-value

A. Clinical characteristics				
Age, years, mean ± SD	62.4±15.18	61.55±15.01	62.98±16.23	0.71
Male sex, n (%)	81(46.8)	79(49.1)	82(50)	0.84
Abdominal pain, n (%)	120(69.4)	106(65.8)	112(68.3)	0.78
Jaundice, n (%)	49(28.3)	53(32.9)	69(42.1)	0.026
ASA class II, n (%)	67(38.7)	62(38.5)	69(42.1)	0.78
B. Laboratory characteristics				
WBC, G/L	7.20±1.53	7.11±1.59	7.32±1.43	0.45
CRP, mg/L	2.9(0.2-81.2)	2.8(0.2-130.6)	4(0.2-159.2)	0.17
Procalcitonin, ng/mL	0.07(0.02-7)	0.08(0.02-7)	0.09(0.02-33.4)	0.09
AST, U/L	36(13-2255.9)	39.2(15.2-2748.6)	49.6(4-1756.2)	0.37
ALT, U/L	48.5(4-1838.7)	58.2(6-1025.5)	75.35(6.6-1132.6)	0.41
Total bilirubin, μmol/L	14.3(2.9-278)	16.4(1.5-416.9)	18.95(4.7-556)	0.003
ALP, U/L	103(14-595.6)	107.9(33-1002)	129.25(38.4-796.3)	0.037
GGT, U/L	168.8(11.7-4441)	222(9-1978)	259.9(10.4-2866.8)	0.41
C. Stone-related characteristics				
CBD diameter, mm	12.4±4.66	12.5±4.42	12.69±4.52	0.83
Number of stones ≥3, n (%)	47(27.2)	42(26.1)	43(26.2)	0.97
Stone ≥15 mm, n (%)	40(23.1)	47(29.2)	35(21.3)	0.23
Concomitant biliary stones, n (%)	63(36.4)	65(40.4)	71(43.3)	0.43

Continuous variables were presented as mean ± standard deviation (SD) for normally distributed data and median (range) for non-normally distributed data.Concomitant biliary stones were defined as gallbladder stones and/or intrahepatic bile duct stones.

ERCP procedural characteristics: No statistically significant differences were observed among the three groups in the rates of precut sphincterotomy, difficult biliary cannulation, or

pancreatic cannulation. Therapeutic ERCP techniques, including interventions on the sphincter of Oddi, balloon stone extraction, mechanical lithotripsy, and biliary stent placement, were also comparable across groups. Complete stone clearance was achieved in 71.7%, 80.1%, and 73.2% of patients in Groups 1, 2, and 3, respectively, with no statistically significant difference among the groups (P = 0.17) (**Table 2**)

Table 2: ERCP procedural characteristics

Characteristic	Group 1 (n=173)	Group 2 (n=161)	Group 3 (n=164)	p-value
A. Papillary and cannulation characteristics				
Precut sphincterotomy, n (%)	6(3.5)	3(1.9)	5(3.0)	0.71*
Difficult biliary cannulation, n (%)	31(17.9)	29(18.0)	30(18.3)	0.99
Pancreatic cannulation, n (%)	25(14.5)	21(13.0)	30(18.3)	0.39
B. Therapeutic procedures				
EST alone, n (%)	40(23.1)	30(18.6)	30(18.3)	0.29
EPBD alone, n (%)	38(22)	45(28)	37(22.6)	
EST and EPBD, n (%)	74(42.8)	70(43.5)	86(52.4)	
No EST/EPBD, n (%)	21(12.1)	16(9.9)	11(6.7)	
Balloon stone extraction, n (%)	159(91.9)	152(94.4)	149(90.9)	0.34
Mechanical lithotripsy, n (%)	62(35.8)	53(32.9)	42(25.6)	0.18
Biliary stent placement, n (%)	50(28.9)	36(22.4)	47(28.7)	0.31
Complete stone clearance, n (%)	124(71.7)	129(80.1)	120(73.2)	0.17

** Fisher's Exact Test; EST, Endoscopic sphincterotomy; EPBD, Endoscopic papillary balloon dilation*

Primary outcome

In the mITT analysis, the composite infectious outcome occurred in 20/173 (11.6%) patients in the no-antibiotic group, 6/161 (3.7%) in the single-dose prophylaxis group, and 7/164 (4.3%) in the prolonged-antibiotic group. Compared with no antibiotics, prophylactic antibiotics were

associated with a lower risk of infectious complications (RR 0.32, 95% CI 0.13–0.78; P = 0.008). No significant difference was observed between the single-dose prophylaxis and prolonged-antibiotic groups (RR 0.87, 95% CI 0.30–2.54; P = 0.80).

The PP analysis yielded findings consistent with the mITT analysis. The composite infectious outcome occurred in 19/164 (11.6%), 6/151 (4.0%), and 7/147 (4.8%) patients in the three groups, respectively. Compared with no antibiotics, prophylactic antibiotics were associated with a lower risk of infectious complications (RR 0.34, 95% CI 0.14–0.84; P = 0.013), whereas no significant difference was observed between the single-dose prophylaxis and prolonged-antibiotic groups (RR 0.83, 95% CI 0.29–2.42; P = 0.74) **(Table 3).** After adjustment for potential confounders, the difference between single-dose prophylaxis and no antibiotics remained significant, whereas prolonged therapy showed no significant additional benefit **(Supplementary Table S4).**

Table 3. Primary composite infectious outcome in the mITT and PP populations

Analysis	**No antibiotic n/N (%)**	**Prophylaxis antibiotics n/N (%)**	**Prolonged antibiotics n/N (%)**
mITT	20/173 (11.6)	6/161 (3.7)	7/164 (4.3)
PP	19/164 (11.6)	6/151 (4.0)	7/147 (4.8)
Comparison		**mITT RR (95% CI); P**	**PP RR (95% CI); P**
Prophylaxis vs no antibiotics		0.32 (0.13–0.78); 0.008	0.34 (0.14–0.84); 0.013
Prophylaxis vs prolonged antibiotics		0.87 (0.3–2.54); 0.80	0.83 (0.29–2.42); 0.74

RR, risk ratio; CI, confidence interval

Secondary outcomes

In the mITT analysis, acute cholangitis occurred in 17/173 (9.8%) patients in the no-antibiotic group and 5/161 (3.1%) in the single-dose prophylaxis group (RR 0.32, 95% CI 0.12–0.84; P = 0.013). Bacteremia occurred in 11/173 (6.4%) and 1/161 (0.6%) patients, respectively (RR 0.10, 95% CI 0.01–0.75; P = 0.005). No significant differences were observed between the

single-dose prophylaxis and prolonged-antibiotic groups for the individual infectious outcomes. The PP analysis showed a similar pattern of results **(Table 4).**

Post-ERCP fever >37.0°C was less frequent in the single-dose prophylaxis group than in the no-antibiotic group (6.2% vs 15.6%; RR 0.40, 95% CI 0.20–0.80; P = 0.006), whereas no significant difference was observed compared with the prolonged-antibiotic group. Noninfectious adverse events, including post-ERCP pancreatitis, bleeding, perforation, acute kidney injury, and allergic reactions, did not differ significantly among the groups. No deaths occurred **(Supplementary Table).**

Table 4. Individual infectious outcomes in the modified intention-to-treat population

Outcome	Group 1 n/N (%)	Group 2 n/N (%)	Group 3 n/N (%)	Group 2 vs Group 1 RR (95% CI); P	Group 2 vs Group 3 RR (95% CI); P
Acute cholangitis	17/173 (9.8)	5/161 (3.1)	3/164 (1.8)	0.32(0.12-0.84);0.013	1.7(0.41-7);0.46
Bacteremia	11/173 (6.4)	1/161 (0.6)	2/164 (1.2)	0.1(0.01-0.75);0.005	0.51(0.05-5.56);1*
Acute cholecystitis	2/173 (1.2)	0/161 (0)	3/164 (1.8)	NE;0.50*	NE;0.25*

*RR, risk ratio; CI, confidence interval; NE, not estimable; * Fisher's Exact Test.*

DISCUSSION

This prospective, single-center, three-arm controlled study found that single-dose amikacin prophylaxis before ERCP was associated with a significantly lower incidence of infectious complications compared with no antibiotic administration in patients with common bile duct stones. The findings were generally consistent across the mITT and PP analyses, with the observed difference mainly attributable to lower rates of acute cholangitis and bacteremia. In contrast, prolonged antibiotic administration did not demonstrate a clear additional benefit over single-dose prophylaxis.

These findings are broadly consistent with those reported by Leem et al [13] in patients with biliary obstruction. In that trial, post-ERCP infectious complications occurred in 2.8% of patients receiving prophylactic cefoxitin compared with 9.8% in the placebo group, and the incidence of cholangitis was also lower with antibiotic prophylaxis. Notably, complete biliary drainage was achieved in more than 90% of patients, and subgroup analysis among those with successful biliary drainage suggested a benefit of prophylactic antibiotics over placebo. These findings suggest that the potential benefit of antibiotic prophylaxis may not be limited to patients in whom incomplete biliary drainage is anticipated.

Previous evidence regarding the role of antibiotic prophylaxis in ERCP has been inconsistent. Several prospective trials, including those by Llach et al [19] and Finkelstein et al [20], failed to demonstrate a clear benefit of routine antibiotic prophylaxis in reducing post-ERCP bacteremia or cholangitis. Similar findings were reported in the meta-analysis by Harris et al [21], in which antibiotic prophylaxis showed a trend toward reducing bacteremia but did not significantly reduce sepsis or cholangitis, and therefore did not support routine use. A subsequent meta-analysis by Bai et al [22] likewise found no clear benefit in preventing post-ERCP cholangitis, including in analyses restricted to patients with suspected biliary obstruction. More recently, Merchan et al [9] reported that antibiotic prophylaxis reduced bacteremia but did not significantly reduce cholangitis, pancreatitis, or mortality.

In contrast, several studies have reported a benefit of antibiotic prophylaxis in reducing infectious complications after ERCP. In the trial by Byl et al [23], prophylactic piperacillin reduced infectious complications following therapeutic ERCP in patients with cholestasis due to biliary obstruction, whereas Lorenz et al [24] observed a trend toward a lower incidence of bacteremia that did not reach statistical significance. A subsequent Cochrane review by Brand et al [8] showed that antibiotic prophylaxis reduced bacteremia and suggested a possible reduction in cholangitis. More recent meta-analyses have provided further support for the role of antibiotic prophylaxis. Habib et al [11] reported reduced risks of cholangitis, bacteremia, and overall

infectious complications in patients with suspected biliary obstruction, whereas Smith et al [10] found reductions in overall infectious complications and bacteremia but no significant differences in cholangitis, sepsis, pancreatitis, or mortality. Overall, the available evidence increasingly suggests that antibiotic prophylaxis may reduce post-ERCP infectious complications, particularly in patients with biliary obstruction.

Unlike most previous studies that included patients with biliary obstruction of heterogeneous etiologies, our study focused specifically on patients with common bile duct stones who met predefined admission criteria for body temperature and white blood cell count. These findings provide more specific evidence regarding the potential role of antibiotic prophylaxis in this selected population.

The observed benefit may also be biologically plausible. During ERCP, biliary cannulation, contrast injection, sphincterotomy, papillary balloon dilation, and stone extraction may facilitate bacterial translocation into the biliary tract or bloodstream, particularly when bile flow is impaired. Administration of antibiotics before the procedure may provide antimicrobial coverage during the period of greatest risk of bacterial translocation.

Another important finding was that infectious complications did not differ significantly between the single-dose prophylaxis and prolonged-antibiotic groups. This suggests that, in the selected study population, continuation of antibiotics after ERCP may not provide a clear additional clinical benefit. In the context of antimicrobial stewardship, avoiding unnecessary prolonged antibiotic therapy may reduce overall antibiotic exposure and the selective pressure for antimicrobial resistance.

No significant differences were observed among the groups in noninfectious adverse events, including post-ERCP pancreatitis, bleeding, and perforation. This finding is consistent with previous meta-analyses, which have generally shown little or no effect of antibiotic prophylaxis on noninfectious ERCP-related adverse events. It is also biologically plausible, as antibiotic

prophylaxis is primarily intended to prevent infectious complications rather than mechanical or inflammatory adverse events directly related to the procedure.

This study has several limitations. First, it was conducted at a single center, which may limit the generalizability of the findings because local antimicrobial susceptibility patterns and clinical practice may differ across institutions. Second, group allocation was based on a prespecified rule derived from hospital medical record numbers rather than a computer-generated random sequence with allocation concealment; therefore, the possibility of selection bias cannot be excluded. Third, the open-label design may have influenced some post-procedural monitoring decisions and the use of additional diagnostic investigations. Fourth, although most baseline characteristics were comparable across groups, imbalances in the prevalence of jaundice and in total bilirubin and alkaline phosphatase levels were observed. Finally, blood cultures were obtained only in patients who developed fever >38.0°C; consequently, transient or asymptomatic bacteremia may have been missed.

Conclusions

A single dose of prophylactic amikacin administered before ERCP was associated with fewer infectious complications in patients with common bile duct stones, particularly acute cholangitis and bacteremia. Prolonged antibiotic therapy did not provide a clear additional benefit over single-dose prophylaxis. These findings support further consideration of a pre-procedural prophylactic strategy in this patient population.

Abbreviations

ALP Alkaline phosphatase

ALT Alanine aminotransferase

ANOVA Analysis of variance

ASA American Society of Anesthesiologists

ASGE American Society for Gastrointestinal Endoscopy

AST Aspartate aminotransferase

CBD Common bile duct

CI Confidence interval

CRP C-reactive protein

EPBD Endoscopic papillary balloon dilation

ERCP Endoscopic retrograde cholangiopancreatography

ESGE European Society of Gastrointestinal Endoscopy

EST Endoscopic sphincterotomy

GGT Gamma-glutamyl transferase

INR International normalized ratio

mITT Modified intention-to-treat

PP Per-protocol

RR Relative risk

SD Standard deviation

ULN Upper limit of normal

WBC White blood cell count

Declarations

Ethics approval and consent to participate: This study was approved by the Biomedical Research Ethics Committee of 108 Military Central Hospital (approval No. 6893/GCN-BV). The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and applicable institutional regulations. Written informed consent was obtained from all participants prior to enrollment in the study.

Consent for publication: Not applicable.

Availability of data and materials: The datasets generated and/or analyzed during the current study are not publicly available due to participant privacy and institutional restrictions but are available from the corresponding author on reasonable request and subject to applicable ethical and institutional requirements.

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Authors' contributions: Thanh Tran Van conceived the study, contributed to the study design and methodology, performed the data analysis, interpreted the findings, and drafted the manuscript. Tung Nguyen Lam and Binh Nguyen Canh contributed to the study design and methodology, supervised the study, participated in interpretation of the findings, and critically revised the manuscript for important intellectual content. Ky Thai Doan and Hoai Ngo Thi performed ERCP procedures, participated in study supervision, and critically revised the manuscript. Hoan Pham Van, Cuong Nguyen Manh, and Tuan Nguyen Anh participated in patient recruitment, performed ERCP procedures, contributed to clinical management and post-procedural follow-up, and assisted with data collection. Quang Pham Minh Ngoc contributed to data collection and data verification and assisted with English-language editing and proofreading. All authors read and approved the final manuscript.

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