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Effect of perioperative antibiotics on postoperative infection in laparoscopic cholecystectomy: A retrospective study --Manuscript Draft--

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Abstract:	Objective: The effect of perioperative antibiotics on postoperative infection (PI) in laparoscopic cholecystectomy (LC) remains unclear. This study aimed to assess the effectiveness of prophylactic antibiotics in preventing postoperative infection and to identify related risk factors. Methods: This retrospective study included 464 patients who underwent LC. Patients were divided into the antibiotic group (260 patients, received cephalosporins after anesthesia induction) and the no-antibiotic group (204 patients). Demographic data and infection rates were compared using chi-squared and t-tests, and binary logistic regression was applied to identify risk factors, with results presented as Odds Ratios and Confidence Intervals. Results: The overall PI rate was 2.4% (11 of 464 patients), with no statistically significant difference between the antibiotic group (2.0%, 5 of 260 patients) and the no-antibiotic group (3.0%, 6 of 204 patients; P-value = 0.474). Risk factors significantly associated with PI included advanced age (P = 0.001), low albumin levels (P = 0.010), long hospital stay (P < 0.001), and prolonged operation time (P = 0.002). Logistic regression analysis revealed that advanced age (odds ratios = 1.08, 95% confidence intervals: 1.00–1.16) and extended hospital stay (odds ratios = 1.33, 95% confidence intervals: 1.14–1.56) significantly increased the risk of postoperative infection. Conclusion: Routine prophylactic antibiotics may not be necessary for all patients undergoing LC; however, older patients and those with extended hospitalizations should be carefully evaluated, as they may be at higher infection risk. Further prospective studies are warranted to confirm these findings and optimize antibiotic use in this context.

Effect of perioperative antibiotics on postoperative infection in laparoscopic cholecystectomy: A retrospective study

Runing title: Effect of perioperative antibiotic on postoperative infection

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Conclusion: Routine prophylactic antibiotics may not be necessary for all patients undergoing LC; however, older patients and those with extended hospitalizations should be carefully evaluated, as they may be at higher infection risk. Further prospective studies are warranted to confirm these findings and optimize antibiotic use in this context.

Keywords Laparoscopic cholecystectomy; Perioperative antibiotics; Postoperative infection.

Introduction

Cholecystectomy, classified as a class II (clean-contaminated) surgical procedure, includes two primary methods: laparoscopic cholecystectomy (LC) and open cholecystectomy¹. Before LC became common in the late 1980s, the incidence of surgical site infections (SSIs) in open cholecystectomy was reported to range from 3% to 43%². A meta-analysis of 42 studies indicated that prophylactic antibiotics could reduce postoperative infection (PI) rates by up to 9%³. Given the frequency and severity of PI following open cholecystectomy, these findings strongly supported the use of antimicrobial prophylaxis. However, LC has since largely replaced open

cholecystectomy, offering advantages such as reduced postoperative pain, shorter hospital stays, and lower morbidity and mortality ⁴.

Postoperative infections remain a significant clinical issue and contribute to substantial financial burdens on healthcare systems ⁵. Treating infections requires additional medical interventions, prolonged antibiotic use, and extended hospital stays, further increasing healthcare costs ⁶. In addition to financial impacts, PIs can compromise patient outcomes, heightening readmission rates and posing severe risks in critical cases ^{7,8}. Current research suggests that LC is associated with a lower incidence of PIs (0.4%–6.3%) compared to open surgery ⁹. However, the benefits of perioperative antibiotics in LC appear limited relative to open biliary surgery ¹⁰. Emerging data also highlight the potential for perioperative complications, including allergic reactions, secondary infections, and increased treatment costs ¹¹. Given these considerations, combined with antibiotic stewardship and rising concerns about antibiotic resistance, the necessity of routine antibiotic prophylaxis in LC cases warrants re-evaluation.

While previous studies have examined the prevalence of LC and the effectiveness of prophylactic antibiotics, findings are inconsistent ^{4,12-16}. Therefore, this study aimed to assess the effectiveness of prophylactic antibiotics in preventing PIs after LC and to identify risk factors associated with these infections. These insights could help improve patient outcomes, optimize antibiotic use, and reduce associated healthcare costs.

Methods

Study design and participants

We retrospectively reviewed medical records of 541 patients who underwent LC at our hospital between January 2015 and October 2019. Patients were eligible if they had been diagnosed with gallstones, chronic cholecystitis, cystic polyps, or adenomyomatosis. Exclusion criteria included: (1) diagnoses of acute cholecystitis or cholangitis, obstructive jaundice, biliary pancreatitis, or gallbladder pyothorax; (2) antibiotic intake within seven days preoperatively; (3) a history of acute cholecystitis in the previous six months; (4) routine corticosteroid therapy; (5) pregnancy or lactation; and (6) previous biliary surgery or endoscopic retrograde cholangiopancreatography. Based on these criteria, 77 cases were excluded, and 464 patients were evaluated and divided into two groups: the antibiotic group (260 patients receiving first- or second-generation cephalosporins post-anesthesia induction) and the no-antibiotic group (204 patients receiving no prophylactic antibiotics).

Parameters Studied

Demographic data, including age, sex, diabetes mellitus status, hypertension, immune-compromised status, length of hospital stay, and surgical duration, were collected for all patients. Preoperative laboratory results were recorded, including albumin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and creatinine levels. Clinical characteristics and perioperative results were compared between the antibiotic and no-antibiotic groups.

Operative procedure

Patients were positioned supine and underwent general anesthesia via endotracheal intubation. The skin was prepped with iodine, and LC was performed using a three-port placement. A 1.2-cm incision was made in the lower umbilical region to introduce a laparoscope via a trocar. Additional 0.5-cm incisions were created at 1 cm below the right xiphoid and 2 cm below the midclavicular costal margin.

Postoperative complications

Complications, including SSIs, urinary infections, and pneumonia, were monitored until hospital discharge. SSI diagnoses followed Centers for Disease Control criteria, with symptoms of superficial wound infections involving pain, tenderness, swelling, and redness at the incision site¹⁷. Deep wound infections were indicated by pus effusion from the incision. All complications were diagnosed by physicians based on the clinical presentation.

Statistical analysis

Data were analyzed using SPSS software version 22.0. Descriptive statistics are presented as means and standard deviations for continuous variables and as frequencies and percentages for categorical variables. The Pearson chi-squared test and Student's t-test were used to compare categorical and continuous variables, respectively. Multivariable logistic regression analysis identified independent risk factors for PIs. Variables with a P-value < 0.05 in univariate analysis were included in the multivariable model, with results expressed as Odds Ratios (OR) and 95% Confidence Intervals (CI). Statistical significance was defined as $P < 0.05$.

Ethical Considerations

This study adhered to the Declaration of Helsinki guidelines. Ethical approval was obtained from the Medical Ethics Committee of the Affiliated Hospital of Jinggangshan University. Due to the retrospective nature of the study, the need for informed consent was waived.

Results

This study initially included 541 patients who underwent LC, from which 77 cases were excluded due to acute cholecystitis (45 cases), pancreatitis (24 cases), and suppurative cholecystitis (eight cases). The final analysis included 464 patients, divided into an antibiotic group (260 patients) and a no-antibiotic group (204 patients). No significant differences were found between the groups regarding age, sex, hypertension, diabetes, immune-compromised status, length of hospital stay, drainage tube use, or preoperative laboratory values, including albumin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and creatinine levels (Table 1).

The overall PIs rate was 2.4% (95% CI: 1.2–4.2%; 11 out of 464 patients), with five PIs in the antibiotic group and six in the no-antibiotic group. Among those in the antibiotic group, infections included three cases of SSIs—one superficial and two

deep—one urinary infection, and one pneumonia case. In the no-antibiotic group, infections included four SSIs (two superficial and two deep), one urinary infection, and one pneumonia case. There was no statistically significant difference in overall infection rates between the antibiotic (2.0%; 95% CI: 0.6–4.4%) and no-antibiotic groups (3.0%; 95% CI: 1.0–6.2%; $P = 0.474$) (Table 2). However, hospital expenses ($P = 0.034$) and length of hospital stay ($P = 0.0001$) were significantly different between the two groups (Table 2).

Patients who developed PIs tended to be of advanced age (66.45 ± 9.77 vs. 52.32 ± 13.25 years, $P = 0.001$), have lower albumin levels (39.94 ± 3.98 vs. 40.51 ± 3.93 , $P = 0.010$), experience longer hospital stays (8.30 ± 3.60 vs. 6.60 ± 3.40 days, $P < 0.001$), and have longer surgical durations (70.88 ± 29.00 vs. 63.26 ± 21.47 minutes, $P = 0.002$) (Table 3). In the binary logistic regression model (adjusted for age, albumin levels, surgery duration, and length of hospital stay), both age (OR = 1.08; 95% CI: 1.00–1.16; $P = 0.049$) and hospital stay length (OR = 1.33; 95% CI: 1.14–1.56; $P < 0.001$) were significantly associated with the risk of PIs (Table 4).

Discussion

Our findings indicate that routine prophylactic antibiotic use in LC does not significantly reduce PIs rates, with an overall infection rate of 2.4% and no significant difference between the antibiotic group (2.0%) and the no-antibiotic group (3.0%). Furthermore, this study identified advanced age, low albumin levels, prolonged hospital stays, and extended surgery duration as key risk factors for PIs.

While Chinese clinical guidelines recommend prophylactic antibiotics for class II surgeries, such as LC, to prevent infections, our results diverge from these guidelines, as the PIs rate in LC was not associated with perioperative antibiotic use¹⁸. This lack of difference between groups suggests that routine antibiotic use may be unnecessary, which is significant given the increasing global emphasis on antibiotic stewardship and the need to curb antibiotic resistance. A targeted approach, reserving antibiotics for high-risk patients, could minimize resistance while safeguarding vulnerable patients.

Our findings align with previous studies indicating that prophylactic antibiotics may not be essential for all LC patients. Studies^{15,19} also found no reduction in PIs with antibiotic prophylaxis in low-risk patients. However, our study adds specificity by identifying particular risk factors, which could be used to tailor antibiotic use more effectively to high-risk patients. Similar to our findings, previous studies have reported PIs rates in LC ranging from 0.4% to 6.3%⁹. On the other hand, several trials suggest that omitting prophylactic antibiotics could reduce hospital costs²⁰⁻²². A meta-analysis of 14 randomized controlled trials (RCTs) also showed a reduction in SSIs in low-risk LC patients who received prophylactic antibiotics (RR 0.66; 95% CI 0.45–0.98)²³. Discrepancies between our findings and the meta-analysis could be attributed to differences in study design, patient population, and clinical settings. While RCTs typically minimize bias, our retrospective study may have been affected by selection and data biases. Additionally, variations in antibiotic protocols, surgical techniques, and patient demographics likely contribute to the differing results, underscoring the importance of a patient-specific approach to antibiotic prophylaxis.

Current guidelines in China recommend prophylactic antibiotics for high-risk patients, including those with advanced age, diabetes, implants, immune-compromised status, extensive surgical areas, operation times longer than 3 hours, or blood loss exceeding 1500 ml¹⁸. In our study, univariate analysis identified advanced age, low albumin levels, prolonged hospital stays, and extended surgery times as associated with PIs. In multivariate analysis, advanced age and prolonged hospital stays emerged as independent risk factors for PIs. Advanced age likely increases susceptibility to infection due to immune system decline and the presence of comorbidities²⁴⁻²⁶. Similarly, extended hospital stays can expose patients to hospital-acquired infections and may indicate underlying complications that predispose patients to infection^{27,28}. These results suggest that a more targeted antibiotic prophylaxis approach could benefit older patients and those with extended hospital stays.

Our study has the following limitations. First, as a retrospective study, it relies on existing patient data, introducing potential biases. Second, data were collected from multiple departments, which may have led to variability in infection assessment. Third, our sample size was relatively small, and the study focused on low-risk patients, limiting the generalizability of findings to high-risk populations. Future research with larger sample sizes and diverse patient populations is needed to validate these results and evaluate specific risk factors more comprehensively.

Conclusion

In conclusion, our findings suggest that routine prophylactic antibiotics may not be necessary for all patients undergoing LC. Instead, an individualized approach, targeting high-risk patients based on age and hospital stay length, could improve antibiotic use and patient outcomes. Further studies are essential to confirm these findings and refine prophylactic antibiotic guidelines in this surgical context.

Authors' Contribution: Study concept and design, S. Y and G. L.; statistical analysis and interpretation of data, S. Y., X. H., and C. H.; drafting of the manuscript, S. Y., G. L. and D. P.; critical revision of the manuscript for important intellectual content, G. L. and D. P.; study supervision, G. L.

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Availability of data and material: The data that support the findings of this study are available from Affiliated Hospital of Jinggangshan University but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of Jinggangshan University.

Ethical Approval: This study was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained from the Medical Ethics Committee of the Affiliated Hospital of Jinggangshan University.

Human Ethics and Consent to Participate: not applicable due to retrospective nature of the study.

Consent for publication: Not applicable

Competing Interests: The authors have declared that no competing interests exist.

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Table 1. Clinical Characteristics of Study Participants by Treatment Group

Characteristics	Antibiotic group (N = 260)	No-antibiotic group (N = 204)	Total (N = 464)	P-Value
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Age; mean year (SD)	52.7 (13.9)	52.6 (12.5)	52.63 (13.32)	0.944
Sex n (%)				
Male	111 (42.7)	79 (38.7)	190 (40.9)	0.388
Female	149 (57.3)	125 (61.3)	274 (59.1)	
Diabetes mellitus n (%)	16 (6.2)	16 (7.8)	32 (6.9)	0.476
Hypertension n (%)	24 (9.2)	28 (13.7)	52 (11.2)	0.128
Immune-compromised status n (%)	4 (1.5)	6 (2.9)	10 (2.2)	0.302
Albumin (g/L)	39.94SD 4.0	40.5 SD 3.9	40.2 SD 4.0	0.124
Aspartate Aminotransferase (U/L)	38.5 SD 88.4	35.6 SD 64.6	37.2 SD 78.8	0.692
Alanine Aminotransferase (U/L)	41.7 SD 73.0	43.2 SD 85.7	42.4 SD 78.8	0.836
Creatinine (μmol/L)	91.4 SD 48.3	88.5 SD 28.0	90.1 SD 40.6	0.440
Drainage tube n (%)	107 (41.2)	104 (51.0)	211 (45.5)	0.544
Duration of operation, minutes (mean SD)	70.9 SD 29.0	63.3 SD 21.5	67.5 SD 26.2	0.002

Abbreviations: N, Number

Table 2. Postoperative Outcomes by Treatment Group

Postoperative results	Antibiotic group (N = 260)	No-antibiotic group (N = 204)	Total (N = 464)	P-Value
Hospital Expenses (mean SD)	16168.9 SD 4896.4	15179.9 SD 5058.2	15734.1 SD 4987.1	0.034
Length of hospital stay, day (mean SD)	8.30 SD 3.60	6.60 ± 3.40	9.00 SD 4.0	0.0001
Surgical site infections n (%)	3 (1.2)	4 (2.0)	7 (1.5)	0.479
Superficial wound infections	1 (0.4)	2 (1.0)	3 (0.7)	0.427
Deep wound infection	2 (0.8)	2 (1.0)	4 (0.9)	0.807
Distant infections n (%)	2 (0.8)	2 (1.0)	3 (0.7)	0.427
Urinary infections	1 (0.4)	1 (0.5)	2 (0.4)	0.863
Pneumonia	1 (0.4)	1 (0.5)	1 (0.2)	0.258
Overall infections n (%)	5 (2.0)	6 (3.0)	11 (2.4)	0.474

Table 3. The risk factors associated with postoperative infection

Risk factors	Infected group (N = 11)	Uninfected group (N = 453)	P-Value
Age, mean year (SD)	66.4 (9.8)	52.32 (13.2)	0.001
Sex n (%)			
Male	7 (63.6)	183 (40.4)	0.121
Female	4 (36.4)	270 (59.6)	

Diabetes mellitus n (%)	2 (18.2)	30 (6.6)	0.135
Hypertension n (%)	2 (18.2)	50 (11.0)	0.458
Immune-compromised status n (%)	0	10 (2.2)	0.618
Albumin (g/L) (mean SD)	36.2 SD 4.6	40.3 SD 3.9	0.010
Aspartate Aminotransferase (U/L) (mean SD)	33.8 SD 28.3	37.3 SD 79.6	0.885
Alanine Aminotransferase (U/L) (mean SD)	58.4 SD 109.2	42.0 SD 78.0	0.494
Creatinine (μ mol/L) (mean SD)	100.8 SD 48.3	89.9 SD 40.4	0.379
Drainage tube n (%)	4 (36.4)	207 (45.7)	0.539
Duration of operation, min (mean SD)	83.9 SD 29.3	67.1 SD 26.0	0.036
Length of hospital stay, day (mean SD)	15.0 SD 3.8	8.4 SD 3.4	0.000

Table 4. inary Logistic Regression Analysis of Risk Factors for Postoperative Infection

	B	S.E.	Wals	P-Value	Odds ratio	95% CI
Age	0.076	0.039	3.87	0.049	1.08	1.00–1.16
Albumin	−0.016	0.089	0.034	0.854	0.98	0.83–1.17
Duration of operation	0.017	0.011	2.36	0.125	1.02	0.99–1.04
Length of hospital stay	0.29	0.08	13.43	0.000	1.33	1.14–1.56