ORIGINAL ARTICLE

CONTENTS

Shortening antibiotic duration in the treatment of acute cholangitis due to choledocholitiasis with successful biliary duct drainage

Julia Fuss[1], Anna Voloboyeva[2], Valerij Boiko[3], Viktor Polovyj[4]

[1]ST.PARASKEVA MEDICAL CENTER, LVIV, UKRAINE

[2]COMMUNAL MUNICIPAL CLINICAL HOSPITAL No 8, LVIV, UKRAINE

[3]SURGERY, ZAYCEV V.T. "INSTITUTE OF GENERAL AND EMERGENCY SURGERY OF THE NATIONAL ACADEMY OF MEDICAL SCIENCES OF UKRAINE, KYIV, UKRAINE

[4]BUKOVINIAN STATE MEDICAL UNIVERSITY, CHERNIVTSI, UKRAINE

ABSTRACT

Aim: To evaluate the efficacy and safety of short duration vs 14-day antibiotic therapy in acute cholangitis associated with common bile duct stone.

Materials and Methods: We divided 278 patients with all stages of acute cholangitis who underwent technically successful ERCP from January 2019 to June 2023 and had positive bile cultures into two groups: antibiotic therapy within two days of ERCP (short-course therapy, SCT; n = 48), and for >3 days (long-course therapy, LCT; n = 230).

Results: Three recurrence occurred in STC and one recurrence occurred in LTC (p = 0.19). Clinical outcomes were similar between the two groups. The fever duration was similar between mild and moderate cholangitis within the same group and between the 2 groups. Duration of antibiotic therapy in LTC was 4.22 + 1.37 days with 39 (81.3%) needing treatment for < 5 days.

Conclusions: Short duration antibiotic treatment based on fever resolution of 72 hours was effective and safe in patients with mild to moderate cholangitis due to common bile duct stone.

KEY WORDS: treatment, antibiotic, endoscopic retrograde cholangiopancreatography, acute cholangitis

Wiad Lek. 2025;78(12):2735-2741. doi: 10.36740/WLek/210014 DOI

INTRODUCTION

Acute cholangitis is a severe complication of diseases hepatobiliary system. Despite advances in diagnosis and treatment diseases of the biliary tract, acute cholangitis remains quite complex diagnostic and far unresolved therapeutic and diagnostic problem. The unflagging interest of clinicians of any profile in this. The problem is due to a number of reasons. Acute purulent cholangitis (ACH) is one of the frequent complications of benign diseases of the extrahepatic biliary tract and large papilla of the duodenum.

It is connected not only with high mortality, which is 15-60%, but also, first of all, from it key role in the development of biliary sepsis [1,2]. Obstruction of the biliary tract, which develops in 87.1% of cases with choledocholithiasis [3], in 6-21% with stenosis of the large papilla of the duodenum [4]. Violation of the outflow of bile is facilitated by the attachment and reproduction of microorganisms, and hypertension leads to cholangiovenous reflux with a massive entry into the systemic bloodstream of bacterial endotoxins, which reliably correlates with the progression of endogenous intoxication, the development of systemic inflammation and syndrome of multiple organ failure.

In the complex treatment of AC, certainly the leading role belongs to surgical intervention, aimed at decompression and recovery outflow of bile. Variants of treatment tactics at AC has gradually undergone some changes in recent years. Wide implementation in clinical practice the practice of radiodiagnostic methods, endoscopic and laparoscopic interventions, additional active remediation of the biliary tract allowed reduce mortality, reduce the number of complications, increase the effectiveness of treatment [5,6]. However, the wide implementation of decompression requires minimally invasive surgical technologies clear justification of indications, duration, sequence of application, criteria of their effectiveness, as well as terms of operative interventions. All that determines the expediency of further research aimed at increasing the effectiveness of

Table 1. Clinical characteristics of the patients receiving short- and long-course antibiotics

	SCT, n = 48 (17.3%)	LCT, n = 230 (82.7%)	P-value
Age	78.3±8.32	85.4 ± 7.91	0.33
Sex			
male	29	125	0.63
female	19	105	0.58
severity			
Mild	15	92	
Moderate	25	104	
severe	8	34	
Morbidity, n			
Diabetes mellitus, n (%)	9	43	0.48
Heart disease, n (%)	26	147	0.69
Chronic renal failure , n (%)	5	21	0.73
Hepato-pancreato-biliary cancers	8	19	0.63
Laboratory parameters			
WBC at diagnosis, /mm3 (mean)	10936	11127	0.86
Temperature >38°C, n (%)	37.6	37.9	0.38
Bilirubin at diagnosis mg/dl	2.71	3.04	0.51
ALT, mean (SD), U/L	206	142	0.317
ALP, mean (SD), U/L	314	332	0.817
AST, mean (SD), U/L	371	208	0.269

WBC – white blood cells, ALT- alanine transaminase, ALP - alkaline phosphatase, AST - aspartate aminotransferase
Source: compiled by the authors of this study

traditional, as well as the development of new methods of treatment patients with AC [7].

AIM

To evaluate the efficacy and safety of short duration vs 14-day antibiotic therapy in acute cholangitis associated with common bile duct stone.

MATERIALS AND METHODS

Patients with acute cholangitis diagnosed by specialists based on findings such as fever, abdominal pain, liver function test abnormality, or imaging studies will be eligible for trial entry. Approval of the Ethics Committee of the institute was obtained before commencing the study (IEC no. 2020/SPL-1645). The study participants are enrolled in this trial if they meet all of the inclusion criteria and none of the exclusion criteria.

INCLUSION CRITERIA

1. Patients are 18 years or older. 2. Diagnosed as having acute cholangitis by treating. 3. Biliary duct obstruction was removed by endoscopic retrograde cholangiopancreatography (ERCP).

EXCLUSION CRITERIA

1. Antibiotic hypersensitivity. 2. Inadequate drainage due to remaining biliary strictures. 3. Biliary stent occlusion. 4. Sclerosing cholangitis. 5. Previous choledochojejunostomy. 6. Previous heart valve replacement.

In the SCT group, intravenous antibiotics will be continued at least for 4 days, and can be discontinued if all of the following criteria are fulfilled: 1) maintenance of body temperature under 37.5 °C for more than 48 h, 2) systolic blood pressure above 90 mmHg, 3) heart rate below 100 beats/min. In the LCT group, intravenous antibiotics will be given for the duration of usual care, at least for 7 days, at the discretion of both the treating doctors.

STATISTICAL ANALYSIS

To analyse categorical variables, we used Fisher's exact test when appropriate. For continuous variables, we usedthe Shapiro-Wilk normality test to check whether the parametric model was appropriate. We then used the Student's test when appropriate. For the sensitivity analysis, we useded a propensity score for SCT using variables likely to influence the outcomes, for both the

Table 2. Time from admission to ERCP

	SCT, n = 48 (17.3%)	LCT, n = 230 (82.7%)	p-value
Duration from admission to ERCP (hours), mean	17.5	21.9	0.387
ERCP within 24 h	36	127	
ERCP within 36 h	10	71	
ERCP within 48 h	2	32	0.159

STC- short-course therapy, LTC - long-course therapy, ERCP - endoscopic retrograde cholangiopancreatography
Source: compiled by the authors of this study

Table 3. The laboratory findings of microbial cultures

	SCT, n = 48 (17.3%)	LCT, n = 230 (82.7%)	p-value
Blood culture			
Positive rate	15/28 (53.6%)	93/175 (53.2%)	0.134
Escherichia coli	5 (10.4%)	43 (18.7%)	0.351
Klebsiella sp	4 (8.4%)	31 (13.5%)	0.129
Enterococcus sp.	0	10 (4.4%)	0.228
Enterobacter sp.	1 (2%)	9 (3.9%)	>0.99
Citrobacter sp.	0	2 (0.9%)	0.483
Staphylococcus sp.	1 (2%)	9 (3.9%)	>0.99
Streptococcus sp.	1 (2%)	5 (2.2%)	0.478
Pseudomonas sp.	1 (2%)	2 (0.9%)	0.344
Aeromonas sp.	1 (2%)	15 (6.5%)	0.619
Others	1 (2%)	6 (2.6%)	>0.99
Negative	13 (27%)	101 (43.9%)	0.059
No culture	20 (41.6%)	55 (23.9%)	<0.001
Bile culture			
Positive rate	46/48 (95.9%)	230/230 (100%)	>0.99
Escherichia coli	22 (45.8%)	103 (44.8%)	0.287
Klebsiella sp	18 (37.5%)	98 (42.6%)	0.258
Enterococcus sp.	24 (50%)	101 (43.9%)	0.103
Enterobacter sp.	4 (8.3%)	35 (15.2%)	>0.99
Citrobacter sp.	6 (12.5%)	18 (7.8%)	0.108
Staphylococcus sp.	0	6 (2.6%)	0.401
Streptococcus sp.	5 (10.4%)	33 (14.3%)	>0.99
Pseudomonas sp.	1 (2%)	30 (13%)	0.598
Aeromonas sp.	2 (4.2%)	24 (10.5%)	0.798
Others	5 (10.4%)	19 (8.3%)	0.287
Negative	1 (2%)	2 (0.9%)	>0.99
No culture	1 (2%)	3 (1.3%)	>0.99

Source: compiled by the authors of this study

primary outcomes and the composite outcomes. A p-value of <0,05 was considered to indicate statistical significance.

ETHICS

This work complies with the principles of the Declaration of Helsinki.

RESULTS

During the study period 278 patients with acute cholangitis due to choledocholithiasis who had undergone ERCP were identified. Among the analyzed patients, 48 (17.3%) received SCT, while 230 (82.7%) received LCT. Acute cholangitis was mild in 107 patients, moderate in 129 patients and severe in 42 patients. The characteristics of all patients included herein are summarized in Table 1.

Table 4. Empiric antibiotic therapy

	SCT, n = 48 (17.3%)	LCT, n = 230 (82.7%)	p-value
Ampicillin/sulbactam	6 (12.4%)	51 (22.2%)	0.461
Piperacillin/tazobactam	5 (10.4%)	41 (17.8%)	>0.99
Ceftriaxone	4 (8.4%)	23 (10%)	>0.99
Cefuroxime	33 (68.8%)	81 (35.2%)	0.319
Meropenem	0 (0.0%)	12 (5.2%)	0.613
Ciprofloxacin	0 (0.0%)	15 (6.6%)	0.366
Levofloxacin	0 (0.0%)	3 (1.2%)	>0.99
Vancomycin	0 (0.0%)	2 (0.9%)	>0.99
Others	0 (0.0%)	2 (0.9%)	>0.99

Source: compiled by the authors of this study

Table 5. Primary and secondary outcomes of patients receiving short- and long-course antibiotics

	SCT, n = 48 (17.3%)	LCT, n = 230 (82.7%)	p-value
30-days mortality, n (%)	0	3 (1.3%)	1
Reccurence cholangitis within 3 month, n (%)	3 (6.3%)	1 (0.5%)	0.19
Bacteremia, n(%)	5 (10.5%)	89 (39%)	0.08
Duration of hospitalization	7 days (3-30)	7 days (3-120)	0.09

Source: compiled by the authors of this study

In both groups, we examined the time from the patient's admission to the hospital to ERCP. We also conducted a study of the state after ERCP (Table 2).

The laboratory findings of microbial cultures from the patients are summarized in table 3. The positive rates of blood and bile cultures were 53.6% (15/28) and 95.9% (46/48) in the SCT group, and 53.2% (93/175) and 100% 230/230) in the LCT group, respectively. There were no significant differences in the positive rates of blood or bile cultures. A total of 198 patients (71.2%) had polimicrobial infections, for E.coli, Klebsiella sp., Enterococcus sp., and Enterobacter sp. were most common pathogens (Table 3).

Table 4 summarizes the findings related to antibiotics in the present study. Cefuroxime, ampicillin/sulbactam, and piperacillin/tazobactam were the most commonly used antibiotics. There were no significant differences in the rate of use of each antibiotic. Four patients in the SCT group (8.3 %) did not receive any antibiotics.

The primary and secondary outcomes are presented in Table 5.

Accordingly, no significant differences in 30-day mortality rates (0%, 0/22 and 2.7%, 2/74 for the SCT and LCT group, respectively) and 3-month recurrence rates were observed between both groups. Although the LCT group were hospitalized longer than the SCT group, no significant difference was found (p = 0.75). Moreover, the LCT group had a higher acute bacteremic cholangitis rate than the SCT group, albeit not significantly (p = 0.08).

DISCUSSION

There is limited information regarding the duration of treatment for acute cholangitis. In the observation by Van Lent et al., it was suggested that a short treatment duration (≤3 days) appeared to be sufficient after appropriate drainage was performed [8]. However, their study was a descriptive case series without proper statistical analysis, and only 26.7% of patients had concomitant bacteremia. Dooley et al. recommended 7-10 days of treatment, although their recommendation was also not based on clinical evidence [9]. Kogure et al. proposed a temperature-based approach, where antimicrobial use was discontinued two days after fever resolution following successful endoscopic drainage [10]. However, this relatively small study was a case series consisting of only 18 patients, without a control group for comparison. Another study compared shorter versus longer antibiotic treatment for acute cholangitis with gram-negative bacteremia [11].

After studying the duration of antibiotic therapy for acute cholangitis with gram-negative bacteremia, Uno et al. (2016) concluded that a treatment duration of less than 2 weeks may be sufficient [11]. However, the mortality rate (11%) and the recurrence rate (24%) in patients were higher than in other studies. Doi et al. (2018) showed that a shortened (six days) duration of antibiotic therapy for acute cholangitis with successful drainage of bile ducts might be a reasonable option, although the duration of antibiotic therapy was defined as the 'total' duration, rather than the duration conducted

after the successful drainage of the bile ducts. By studying the outcomes of antibiotic therapy duration after successful bile duct drainage, this study allowed for a better comparison of 30-day mortality and 3-month recurrence rates. Thus, we believe that this study was the first to report that SCT (≤3 days) is not inferior to LCT (≥4 days) among patients with mild to moderate acute cholangitis caused by choledocholitiasis [12].

Gomi et al. recommended in the Tokyo Guideline a duration of 4e7 days after source control for non-bacteraemic cholangitis, and recommended a minimum of 2 weeks duration in association with bacteraemia, especially when caused by Gram-positive cocci, provided that anatomical problems were resolved upon the presence of residual stones or obstructions of the bile duct. In fact, infectious diseases specialists tend to recommend a relatively long duration of antimicrobial therapy for bacteraemic cholangitis, reflected in the statistically significant tendency for those patients on LCT to have an infectious diseases consultation found in our study. However, this recommendation was based on the guideline for the management of complicated intra-abdominal infection, which does not specifically recommend treatment for acute cholangitis [13]. In addition, the recommen dations were not based on relevant clinical evidence.

Recently, a randomized controlled trial studying treatment duration for appropriately drained intra-abdominal infections compared outcomes 4e5 days after drainage with a conventional duration of up to 10 days [14]. The short treatment duration did not have worse outcomes such as the occurrence of recurrent intraabdominal infection or mortality. However, only 10.8% of the participants had acute cholangitis and only a few had concurrent bacteraemia [14]. Likewise, short courses of antimicrobial therapy of 6e10 days had similar outcomes compared with longer courses for Enterobacteriaceae bacteraemia [15]. Our findings were more specific to those who have acute bacteraemic cholangitis, for which many experts have considered longer treatment necessary. There fore, our findings are quite novel.

Treatment of acute cholangitis consisted primarily of decompression of the bile ducts and elimination of the cause obstruction of the bile ducts [16, 17]. At the same time, depending on the general condition of the patients, the severity of the manifestation of cholangiogenic infection, endotoxemia and hyperbilirubinemia were produced one- and two-stage treatment methods using modern technologies and traditional surgical interventions. Typically, after completing two-stage and one-stage endoscopic interventions, external removal of toxic bile was carried out through external drainage [18, 19].

Although there is still no clear timing of ERCP in patients with acute cholangitis [20], a study showed that ERCP performed >72 hours after hospitalization had higher rates of organ failure and mortality than those performed before <72 hours. [21]. In another study, patients who underwent ERCP >48 hours after hospitalization had a higher incidence of liver failure than patients who underwent ERCP before 48 hours [22,23]. Many studies have observed a recommendation for ERCP within 24 hours of hospitalization; since mortality as a result of organ failure practically does not occur. Therefore, we recommend ERCP within 24 hours of hospitalization in patients with acute cholangitis.

CONCLUSIONS

Our study shows that short-term ATB therapy using 48-hour relief of inflammatory symptoms as a safe time to stop ATB therapy for acute cholangitis with or without bacteremia after successful endoscopic biliary drainage is safe and effective. By reducing the duration of ATB use, the cost of treatment, the risk of developing microbial resistance, as well as the risk of complications associated with antibiotics and multiple organ failure will be reduced.

PROSPECTS FOR FURTHER RESEARCH

Prospects for further research are to study reducing the duration of antibiotic therapy for acute cholangitis, with the aim of clarify methods of possible therapeutic correction.

REFERENCES

1. Kramer A, Schwebke I, Kampf G. How long do nosocomial pathogens persist on inanimate surfaces? A systematic review. BMC Infect Dis. 2006,6:130. doi:10.1186/1471-2334-6-130 DOI
2. Esposito AL, Gleckman RA, Cram S et al. Community-Acquired Bacteremia in the Elderly: Analysis of One Hundred Consecutive Episodes. J Am Geriatr Soc. 1980;28(7):315–319. doi: 10.1111/j.1532-5415.1980.tb00622.x. DOI
3. Erbay A, Idil A, Gözel MG et al. Impact of early appropriate antimicrobial therapy on survival in Acinetobacter baumannii bloodstream infections. Int J Antimicrob Agents. 2009;34:575-9. doi:10.1016/j.ijantimicag.2009.07.006. DOI
4. Harbarth S, Garbino J, Pugin J et al. Inappropriate initial antimicrobial therapy and its effect on survival in a clinical trial of immunomodulating therapy for severe sepsis. Am J Med. 2003;115:529-35. doi:10.1016/j.amjmed.2003.07.005. DOI

5. Sokal A, Sauvanet A, Fantin B et al. Acute cholangitis: diagnosis and management. J Visc Surg. 2019;156:515-25. doi:10.1016/j.jviscsurg.2019.05.007. DOI
6. Kristich CJ, Rice LB, Arias CA. Enterococcal infection—treatment and antibiotic resistance. Enterococci: From Commensals to Leading Causes of Drug Resistant Infection. Massachusetts Eye and Ear Infirmary, Boston. 2014.
7. Lai EC, Mok FP, Tan ES et al. Endoscopic Biliary Drainage for Severe Acute Cholangitis. N Engl J Med. 1992;326:1582–1586. doi: 10.1056/NEJM199206113262401. DOI
8. Van Lent AU, Bartelsman JF, Tytgat GN et al. Duration of antibiotic therapy for cholangitis after successful endoscopic drainage of the biliary tract. Gastrointest Endosc 2002;55:518e22. doi: 10.1067/mge.2002.122334. DOI
9. Dooley JS, Hamilton-Miller JM, Brumfitt W, Sherlock S. Antibiotics in the treatment of biliary infection. Gut. 1984;25:988e98. doi: 10.1136/gut.25.9.988. DOI
10. Kogure H, Tsujino T, Yamamoto K et al. Fever-based antibiotic therapy for acute cholangitis following successful endoscopic biliary drainage. J Gastroenterol. 2011;46:1411e7. doi: 10.1007/s00535-011-0451-5. DOI
11. Uno S, Hase R, Kobayashi M et al. Short-course antimicrobial treatment for acute cholangitis with Gram-negative bacillary bacteremia. Int J Infect Dis. 2017;55:81e5. doi: 10.1016/j.ijid.2016.12.018. DOI
12. Loozen CS, Kortram K, Kornmann VNN et al. Randomized Clinical Trial of Extended Versus Single-Dose Perioperative Antibiotic Prophylaxis for Acute Calculous Cholecystitis. Br J Surg. 2017;104:e151–e157. doi: 10.1002/bjs.10406. DOI
13. Solomkin JS, Mazuski JE, Bradley JS et al. Diagnosis and management of complicated intra-abdominal infection in adults and children: guidelines by the surgical infection society and the in fectious diseases society of America. Surg Infect (Larchmt). 2010;11(1):79-109. doi: 10.1089/sur.2009.9930. DOI
14. Sawyer RG, Claridge JA, Nathens AB et al. Trial of short-courseantimicrobial therapy for intraabdominal infection. N Engl J Med. 2015;372:1996e2005. doi: 10.1056/NEJMoa1411162. DOI
15. Chotiprasitsakul D, Han JH, Cosgrove SE et al. Comparing the outcomes of adults with Enterobacteriaceae bacteremia receiving short-course versus prolonged-course antibiotic therapy in a multicenter, propensity score-matched cohort. Clin Infect Dis. 2018;66:172e7. doi: 10.1093/cid/cix767. DOI
16. Johnson MT, Reichley R, Hoppe-Bauer J. Impact of previous antibiotic therapy on outcome of Gram-negative severe sepsis. Crit Care Med. 2011;39:1859–65. doi: 10.1097/CCM.0b013e31821b85f4. DOI
17. Stevens V, Dumyati G, Fine LS et al. Cumulative antibiotic exposures over time and the risk of Clostridium difficile infection. Clin Infect Dis. 2011;53:42–8. doi: 10.1093/cid/cir301. DOI
18. Piaggio G, Elbourne DR, Pocock SJ et al. Reporting of noninferiority and equivalence randomized trial: extension of the CONSORT 2010 statement. JAMA. 2012;308:2594–604. doi: 10.1001/jama.2012.87802. DOI
19. Chow S-C, Shao J, Wang H, Lokhnygina Y. Sample size calculations in clinical research. 3rd ed. Boca Raton: Chapman & Hall/CRC. 2017. doi:10.1201/9781315183084. DOI
20. Spellberg B, Talbot GH, Boucher HW et al. Antimicrobial agents for complicated skin and skin-structure infections: justification of noninferiority margins in the absence of placebo-controlled trials. Clin Infect Dis. 2009;49(3):383–91. doi: 10.1086/600296. DOI
21. Sawyer RG, Claridge JA, Nathens AB et al. Trial of short-course antimicrobial therapy for intraabdominal infection. N Engl J Med. 2015;372:1996–2005. doi: 10.1056/NEJMoa1411162. DOI
22. Hygienemaßnahmen bei Infektionen oder Besiedlung mit multiresistenten gramnegativen Stäbchen. [Hygiene measures in case of infections or colonization with multi-resistant gram-negative rods]. Bundesgesundheitsblatt. 2012;55:1311–54. doi: 10.1007/s00103-012-1549-5. (German) DOI
23. Negm AA, Schott A, Vonberg RP et al. Routine bile collection for microbiological analysis during cholangiography and its impact on the management of cholangitis. Gastrointest Endosc. 2010;72(2):284–91. doi: 10.1016/j.gie.2010.02.043. DOI

CONFLICT OF INTEREST

The Authors declare no conflict of interest

CORRESPONDING AUTHOR

Julia Fuss
St.Paraskeva medical center
64 Brochure Chervono Kalini, 79000 Lviv, Ukraine
e-mail: juliafuss78@gmail.com

ORCID AND CONTRIBUTIONSHIP
Julia Fuss: 0000-0003-0114-9475 A B C E
Anna Voloboyeva: 0000-0001-6599-8308 A B D
Valerij Boiko: 0000-0002-0527-0451 A D E
Viktor Polovyj: 0000-0002-4345-9802 A C F

A – Work concept and design, B – Data collection and analysis, C – Responsibility for statistical analysis, D – Writing the article, E – Critical review, F – Final approval of the article

RECEIVED: 01.01.2025
ACCEPTED: 28.08.2025