Conventional vs Short Duration of Antibiotics in Patients With Moderate or Severe Cholangitis: Noninferiority Randomized Trial

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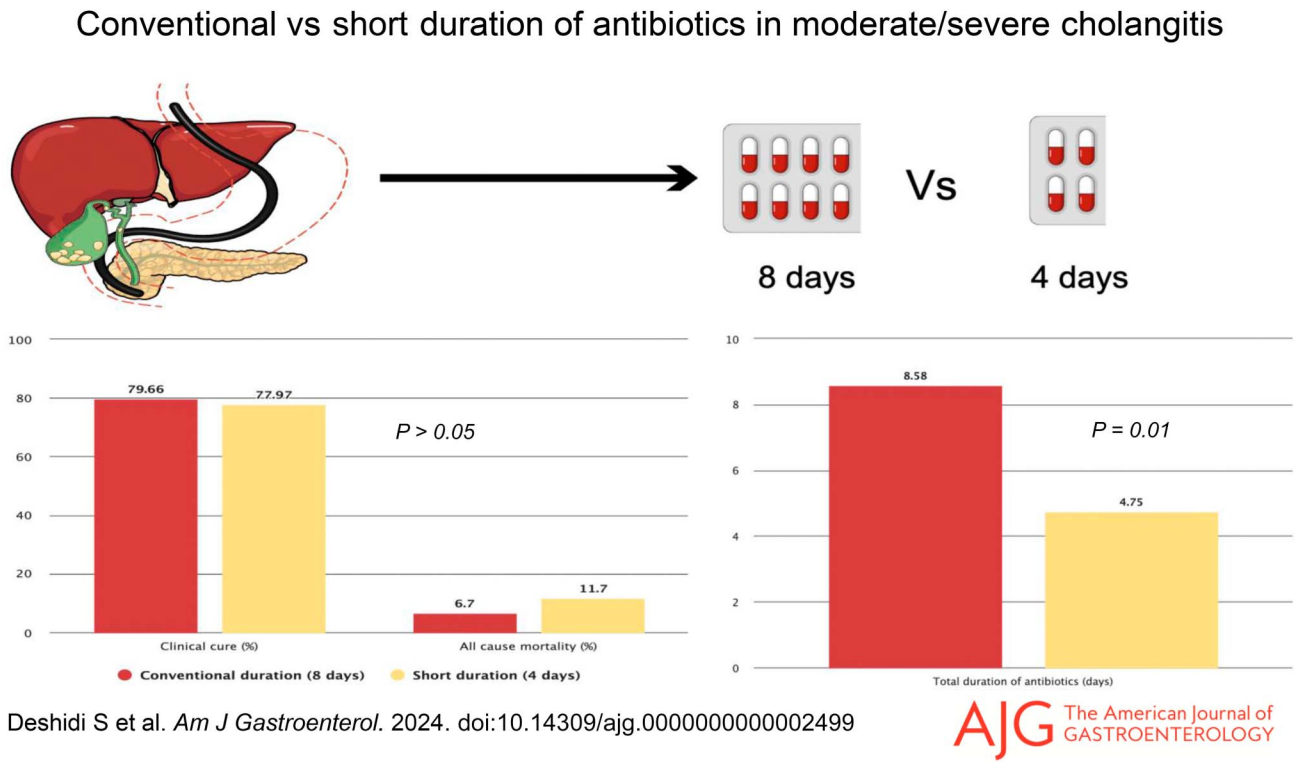
INTRODUCTION: **Successful biliary drainage and antibiotics are the mainstays of therapy in management of patients with acute cholangitis. However, the duration of antibiotic therapy after successful biliary drainage has not been prospectively evaluated. We conducted a single-center, randomized, noninferiority trial to compare short duration of antibiotic therapy with conventional duration of antibiotic therapy in patients with moderate or severe cholangitis.**



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METHODS: **Consecutive patients were screened for the inclusion criteria and randomized into either conventional duration (CD) group (8 days) or short duration (SD) group (4 days) of antibiotic therapy. The primary outcome was clinical cure (absence of recurrence of cholangitis at day 30 and >50% reduction of bilirubin at day 15). Secondary outcomes were total days of antibiotic therapy and hospitalization within 30 days, antibiotic-related adverse events, and all-cause mortality at day 30.**

RESULTS: **The study included 120 patients (the mean age was 55.85 ± 13.52 years, and 50% were male patients). Of them, 51.7% patients had malignant etiology and 76.7% patients had moderate cholangitis. Clinical cure was seen in 79.66% (95% confidence interval, 67.58%–88.12%) patients in the CD group and 77.97% (95% confidence interval, 65.74%–86.78%) patients in the SD group ($P = 0.822$). On multivariate analysis, malignant etiology and hypotension at presentation were associated with lower clinical cure. Total duration of antibiotics required postintervention was lower in the SD group (8.58 ± 1.92 and 4.75 ± 2.32 days; $P < 0.001$). Duration of hospitalization and mortality were similar in both the groups.**

DISCUSSION: **Short duration of antibiotics is noninferior to conventional duration in patients with moderate-to-severe cholangitis in terms of clinical cure, recurrence of cholangitis, and overall mortality.**

KEYWORDS: piperacillin-tazobactam; endoscopic ultrasound; mortality; endoscopic retrograde cholangiopancreatography

SUPPLEMENTARY MATERIAL accompanies this paper at http://links.lww.com/AJG/D37

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INTRODUCTION

Cholangitis is one of the most common gastrointestinal emergencies requiring hospital admission and immediate intervention. It is associated with high morbidity and mortality especially in patients with moderate or severe cholangitis (1,2). Choledocholithiasis (28%–70%), biliary stricture (5%–28%), and various pancreatobiliary malignancies (10%–57%) are frequent causes of biliary obstruction (2–4). Biliary drainage and systemic antibiotics along with supportive care are the mainstay of therapy in the presence of acute cholangitis (5–7). Different methods of biliary drainage include endoscopic retrograde cholangiography (ERC), percutaneous transhepatic biliary drainage (PTBD) or EUS-guided biliary drainage (8,9). Antibiotics play a key role in the management of cholangitis before and after biliary drainage. Choice and route of antibiotics depends on various factors including severity of cholangitis, bacteremia, and associated local complications such as liver abscess, acute cholecystitis, or distant infective complications, e.g., infective endocarditis (5,10). Recent guidelines suggest antibiotic duration of 4–7 days after successful biliary drainage, though the level of evidence is weak in absence of prospective studies (5). Few studies have shown that short duration of antibiotics (<4–14 days) is equal to longer duration. However, these studies are retrospective in nature with small sample size (11–14). Sawyer et al (15) recently performed a multicenter randomized trial of 4 vs 8 days antibiotic therapy in patients with intra-abdominal infection and showed that both groups were equal in terms of surgical site infection, recurrent intra-abdominal infection, or death. However, such prospective well-designed trials are lacking in patients with acute cholangitis.

Duration of antibiotic therapy after effective source control is one of the most important aspects of antibiotic stewardship program. Prolonged antibiotic therapy is associated with an increased risk of emergence of multidrug resistance organisms, antibiotic-associated diarrhea, prolongation of hospitalization, and increased health care–related costs. At the same time, inadequate antibiotic duration is associated with an increased risk of recrudescence or recurrence of infective complication, need for emergency admission, and morbidity (16–18). So, optimum antibiotic duration is of utmost importance for improved outcome in patients with acute cholangitis apart from effective biliary drainage. Hence, we planned a noninferiority trial to compare short-duration antibiotic therapy with conventional duration antibiotic therapy in patients with moderate or severe cholangitis.

METHODS

Setting

Our study was a single-center, randomized, open-label, noninferiority trial conducted at a tertiary care hospital in North India (CTRI/2021/05/033535). The study was conducted as per Helsinki guidelines and Indian Council for Medical Research guidelines.

Patient profile

All consecutive patients presenting to our institute with moderate or severe cholangitis from May 2021 to June 2022 were screened. All patients were included after obtaining an informed consent and approval of the institutional ethics committee. All authors had access to the study data and had reviewed and approved the final manuscript.

Inclusion criteria were as follows: (i) 18 years of age or older, (ii) patients with moderate or severe acute cholangitis according to Tokyo guidelines 2018 (19), and (iii) patients who underwent successful biliary drainage through ERC, EUS-guided drainage, or PTBD.

Exclusion criteria were as follows: (i) suspected incomplete biliary drainage: patients with primary sclerosing cholangitis or portal cavernoma cholangiopathy with multiple intrahepatic biliary stricture or Bismuth type III or IV type of hilar stricture, (ii) patients requiring ventilatory support, (iii) patients with Glasgow coma scale of less than 8, (iv) patients with cholangitis-related complications that require longer duration of antibiotics (liver abscess, acute cholecystitis or metastatic complications such as infective endocarditis, pneumonia, or septic arthritis during diagnosis), (v) immunocompromised patients (patients

on chemotherapeutic drugs, prednisolone >10 mg/d, or other immunosuppressive agents), (vi) patients with concomitant acute pancreatitis and other septic foci who might require longer duration of antibiotic therapy, (vii) pregnant women, and (viii) patients not willing to participate in the study.

Intervention

All patients with moderate or severe cholangitis were planned for emergent biliary drainage (within 48 hours of admission) (20). Once successful biliary drainage was achieved, patients were randomized into 2 groups: conventional duration group (CD group): 8 days of intravenous antibiotic therapy; short duration group (SD group): 4 days of intravenous antibiotic therapy (15). The choice of antibiotic was as per guideline and institutes bacteriological profile (5,21). Antibiotics were stopped after prespecified period in both the groups if the following criteria were fulfilled: (i) body temperature less than 37.7°C for 24 hours or more, (ii) the mean arterial blood pressure above 65 mm Hg for 24 hours or more, (iii) respiratory rate below 20 breaths/min, and (iv) maintaining an oxygen saturation above 90% at room air. If a patient did not fulfill those criteria, the antibiotic treatment was continued till the patient fulfilled the same.

Discharge criteria: Patients were discharged from hospital if they remained afebrile for 24 hours along with resolution of systemic inflammatory response syndrome and organ failure if any. Patients were advised to continue antibiotics as day care treatment for prespecified duration as per the allotted group with written advice about warning signs and contact number in case of emergency. All patients had a scheduled outpatient clinic visit at day 4 or 8 to decide regarding stoppage of antibiotics or need for additional antibiotics.

Follow-up: Patients were followed up on day 15 after biliary drainage with liver function test and hemogram to check for clinical success. They were further followed up till 30 days to check for clinical cure and any recurrence of cholangitis. In case of recurrence of cholangitis, patients underwent repeat biliary drainage and antibiotics were added as per the clinical judgment. Randomization was done only for the first presentation of acute cholangitis.

Study outcomes

Primary outcome. The primary outcome was clinical cure at 30 days after randomization. Clinical cure was defined as absence of recurrence of cholangitis at day 30 and >50% reduction of bilirubin compared with initial level after 15 days of successful biliary drainage.

Secondary outcomes. (i) Total days of antibiotics required in both the groups till 30 days after randomization, (ii) total days of hospitalization required in both the groups till 30 days after randomization, (iii) adverse events due to antibiotics, and (iv) all-cause mortality at day 30.

Sample size calculation and randomization

Based on a previous retrospective study comparing the short-term antibiotic with conventional antibiotic, absence of recurrence of cholangitis was assumed in 93% and 88% of patients, respectively (14). We calculated sample size of 120 (60 in each group; 1:1) with one-sided alpha of 0.025, power of 80%, and noninferiority margin of −10%. Randomization was done by a third person not involved in patient enrollment using a computer-generated sequence of random numbers with variable block randomization. Block size of 4 and 6 were chosen. Allocation was concealed by the use of serially numbered opaque sealed envelopes, and they were opened once a decision to include the patient and an informed consent had been obtained.

Statistical analysis

Statistical analysis was conducted using IBM SPSS v23.0 statistics software. The Shapiro-Wilk test was applied to check the normal distribution of continuous data. The mean value with SD was calculated for normally distributed continuous data, otherwise median and interquartile range were calculated. Categorical variables were presented as frequency and percentages. Independent t test was used to compare normally distributed quantitative variables between 2 study groups. For skewed data, the Mann-Whitney U test was applied. The χ^2 test or Fisher exact test was used to compare the categorical variables. Univariate analysis was performed to find the significant variable for clinical cure. Using all the significant variables (P value < 0.05) on univariate analysis, multivariate analysis was performed using logistic regression method to identify the independent predictors of clinical cure. The results were presented as odds ratios with 95% confidence intervals (CI). P value ≤ 0.05 was taken as statistically significant.

RESULTS

Baseline characteristics

A total of 197 consecutive patients with acute moderate or severe cholangitis were screened during the study period. Of them,, 120 met the inclusion criteria and were randomized to the CD or SD group (Figure 1).

The mean age of included patients was 55.85 ± 13.52 years and 50% were male. In the study cohort, 92 (76.7%) patients had moderate cholangitis and 28 (23.3%) patients had severe cholangitis (Table 1). Most of the patients (51.7%) had malignant etiology of cholangitis, while remaining patients (48.3%) had benign etiology of cholangitis. Choledocholithiasis (n = 48; 40%), followed by gall bladder carcinoma (n = 22; 18.3%) and pancreatic carcinoma (n = 14; 11.7%) were the most common etiologies of cholangitis in the study cohort (Table 2). For biliary drainage, ERC (n = 101; 84.2%) was the most commonly used procedure followed by PTBD (n = 18; 15%) (see Supplementary Table 1, http://links.lww.com/AJG/D37). One hundred eleven (92.5%) patients underwent drainage within 48 hours of admission (81 patients within 24 hours and 30 patients between 24 and 48 hours of admission); however, 9 (7.5%) patients underwent drainage after 48 hours because of logistic reasons. All 9 patients had moderate cholangitis.

Predrainage intravenous antibiotics were given to all included patients. One hundred fourteen patients received intravenous piperacillin-tazobactam, and 6 patients received carbapenems. Of 120 patients, bile culture was sent in 74 (65.8%) patients. Positive bile cultures were seen in 37 (50.0%) patients (18 [42.9%] patients in the CD group and 19 [59.4%] patients in the SD group B; P = 0.1). *Escherichia coli* (16.2%) and *Pseudomonas* sp. (9.5%) were the most common organisms grown in bile culture (see Supplementary Table 2, http://links.lww.com/AJG/D37). None of the patients had Gram-positive cocci growth in bile culture. Of 37 growths in bile culture, 20 (54%) organism growth was pansensitive to antibiotics and 17 (46%) organism growth was with multidrug resistance organism. Of 120 patients, blood cultures were taken in 65 (54%) patients at admission. Fifty-six patients

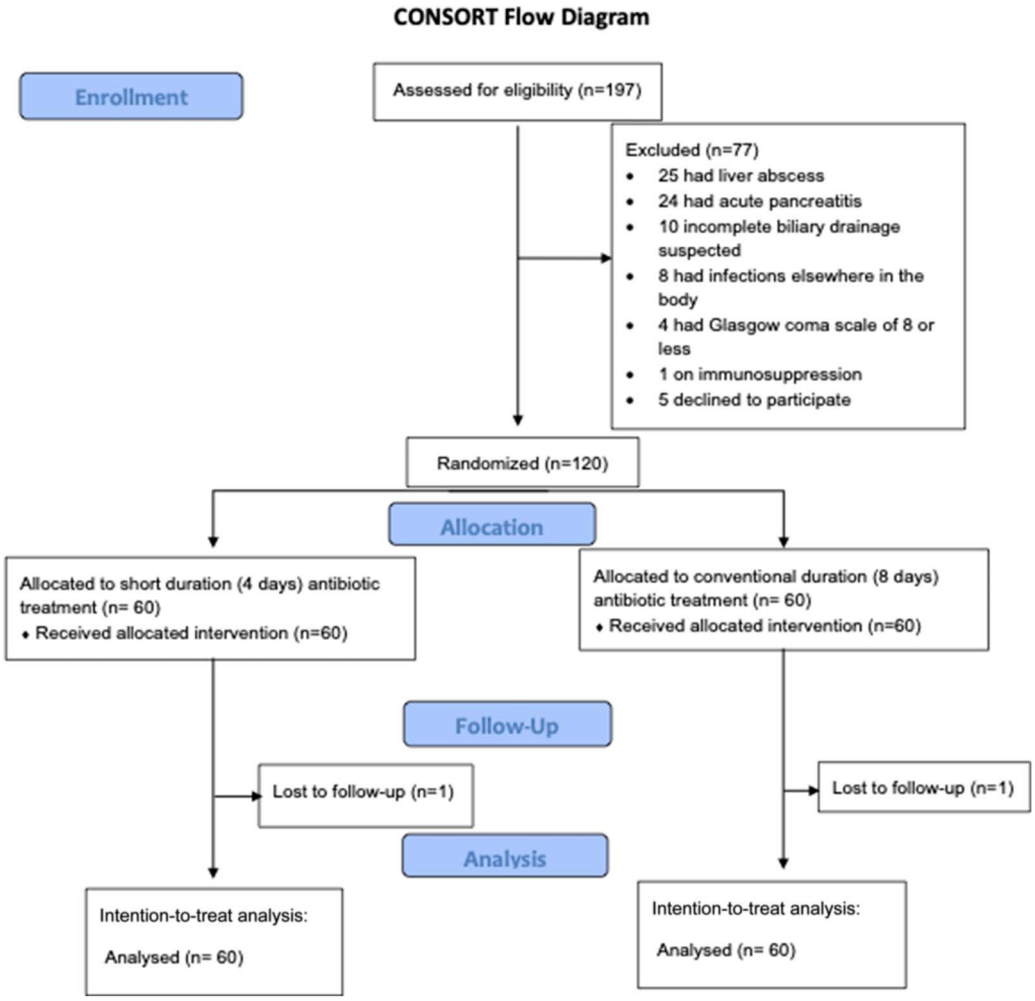

Figure 1. Consort diagram of study cohort.

(86.2%) had sterile culture, and 9 cultures (13.8%) were positive for organism. *E. coli* (n = 4) was the most common organism, and 3 patients had gram-positive cocci (*Enterococcus* sp. in 1 and *Staphylococcus hominis* in 2). Patient with growth of *Enterococcus* sp. was in the CD group, and after 8 days of therapy with clinical improvement, the antibiotic was stopped. Two patients with *S. hominis* were in the SD group, and of which 1 patient required extension of antibiotic due to persistence of fever. After successful biliary drainage, patients were randomized and started on antibiotics. Most of the patients continued on piperacillin-tazobactam (106; 88.3%). Nine patients were changed to carbapenem or aminoglycoside or vancomycin as per culture report (see Supplementary Table 3, http://links.lww.com/AJG/D37).

Primary outcome

Overall, 79.66% (95% CI, 67.58%–88.12%) patients in the CD group and 77.97% (95% CI, 65.74%–86.78%) patients in the SD group had clinical cure ($P = 0.822$) (Table 3). Noninferiority in clinical cure was shown in short-duration antibiotic group when compared with the conventional duration antibiotic group. On multivariate regression analysis, malignant etiology and hypotension requiring inotropic support at admission were associated with lower clinical cure (Table 4).

Secondary outcomes

Total duration of antibiotics required postintervention till day 30 was 8.58 ± 1.92 and 4.75 ± 2.32 days in the CD and SD groups, respectively ($P < 0.001$). The mean total duration of hospitalization in the CD and SD groups was 2.81 ± 1.48 days and 3.0 ± 1.76 days, respectively ($P = 0.53$). Six patients developed post-ERC pancreatitis (5 had mild pancreatitis and 1 had moderately severe pancreatitis). One patient had a liver abscess during recurrent cholangitis episode, which was treated with antibiotic and stent exchange with ERC. None of the patients in the study population reported any antibiotic-associated adverse effects. Overall, during the study period, 4 (6.78%) patients in the CD group died compared with 7 (11.86%) patients in the SD group ($P = 0.342$) (Table 4 and see Supplementary Table 4, http://links.lww.com/AJG/D37). Of 11 mortality cases, 7 patients succumbed to illness during initial admission before antibiotic stoppage criteria. Three patients succumbed to illness during episode of recurrent cholangitis. All 3 patients had malignant etiology of disease and severe disease with cardiovascular failure during recurrent cholangitis episode. One patient died because of unrelated event (acute cardiac event) after improvement and discharge from cholangitis episode. On multivariate logistic regression analysis, malignant etiology and hypotension requiring inotropic support were associated with higher all-cause mortality.

Table 1. Comparison of baseline characteristics between study groups (n = 120)

Variables	Study group (Mean ± SD)		*P* value
	CD group (n = 60)	SD group (n = 60)	
Age (yr)	55.85 ± 13.52	55.33 ± 13.7	0.836
Gender (M)	31	29	0.715
Fever at admission (%)	49 (81.7%)	51 (85%)	0.624
Fever duration (d)	5.2 ± 3.54	6.37 ± 4.45	0.150
Hemogram (Hb) gm/dL	10.36 ± 2.42	10.42 ± 1.97	0.885
Total leukocyte count ($\times 10^9$/L)	14,533.33 ± 8,664.98	13,576.67 ± 5,968	0.483
Platelet count ($\times 10^9$/L)	257.65 ± 138.19	252.6 ± 139	0.8
Creatinine (mg/dL)	1.05 ± 0.79	1.02 ± 0.79	0.819
Total bilirubin (mg/dL)	14.07 ± 7.7	13.21 ± 8.8	0.571
Albumin (gm/L)	28 ± 6.8	29 ± 9.7	0.685
INR	1.53 ± 0.89	1.58 ± 1.09	0.756
Duration between hospitalization and biliary drainage	1.47 ± 0.89	1.45 ± 0.72	0.911
Predrainage antibiotic duration (mean ± SD, d)	2.35 ± 1.43	2.37 ± 1.49	0.95
Prior ERC	6 (10%)	8 (13.33%)	0.570
Severity of cholangitis			0.95
Moderate	46 (76.7%)	46 (76.7%)	
Severe	14 (23.3%)	14 (23.3%)	
Current drainage procedure			0.540
ERC	51 (85%)	50 (83.33%)	
PTBD	8 (13.3%)	10 (16.67%)	
EUS-BD	1 (1.67%)	0 (0%)	

CD group, conventional duration group; ERC, endoscopic retrograde cholangiography; EUS-BD, endoscopic ultrasound–guided biliary drainage; INR, international normalized ration; PTBD, percutaneous transhepatic biliary drainage; SD group, short duration group.

Per-protocol analysis

During initial admission, 3 patients (5%) in the CD group and 4 patients (6.67%) in the SD group succumbed to their illness before the antibiotic stoppage criteria. Two patients (3.33%) in the CD group and 6 patients (10%) in the SD group required extension of the antibiotics ($P = 0.304$). Five patients required extension of antibiotic due to persistence of fever, 2 patients required due to persistence of organ failure, and 1 patient required due to development of post-ERC pancreatitis with local complication. All patients required antibiotic extension during ongoing hospitalization. One patient in each group was lost to follow-up after initial admission. In the per-protocol analysis, 46 patients (85.2%; 95% CI, 78.9%–91.3%) in the CD group and 44 patients (89.8%; 95% CI, 84.2%–95.3%) in the SD group achieved clinical cure ($P = 0.482$).

Table 2. Comparison of etiology of obstruction between study groups (N = 120)

Etiology	CD group (n = 60)	SD group (n = 60)
Choledocholithiasis	26 (43.3%)	22 (36.7%)
Gall bladder carcinoma	11 (18.3%)	11 (18.3%)
Pancreatic carcinoma	6 (10%)	8 (13.3%)
Distal cholangiocarcinoma	6 (10%)	5 (8.3%)
Benign biliary stricture	2 (3.3%)	5 (8.3%)
Hilar cholangiocarcinoma	1 (1.7%)	4 (6.7%)
Periampullary carcinoma	4 (6.6%)	3 (5%)
Others	4 (6.6%)	2 (3.3%)

CD group, conventional duration group; SD group, short duration group.

DISCUSSION

In this single-center, prospective, randomized trial, we compared conventional with short duration of antibiotics in patients with moderate or severe cholangitis after successful biliary drainage. Overall, both the groups had similar rates of clinical cure, recurrence of cholangitis, and mortality. Only a minority of patients required extension of antibiotics beyond stipulated duration in either group, and requirement of extension of antibiotics was mainly due to persistence of fever after successful biliary drainage.

Recently, Uno et al performed a single-center retrospective study on duration of antibiotics in patients with acute cholangitis with bacteremia secondary to Gram-negative bacilli. They showed that patients who received short term (<14 days) vs long term (>14 days) of antibiotics had similar mortality rates ($P = 0.179$) and rather higher recurrence rates with long-term antibiotic therapy ($P = 0.036$) (11). Haal et al also conducted a multicenter retrospective study of 426 patients of acute cholangitis due to bile duct stones who

Table 3. Primary and Secondary outcomes

Outcomes	CD group (n = 60)	SD group (n = 60)	*P* value
Clinical cure	47 (79.66%) (95% CI = 67.58–88.12)	46 (77.97%) (95% CI = 65.74–86.78)	0.822
Causes of absence of clinical cure			0.822
• Recurrence of cholangitis	5	5	
• <50% reduction of bilirubin after 2 wk of initial admission	5	5	
• Mortality	4	7	
Total duration of antibiotics	8.58 ± 1.92	4.75 ± 2.32	0.001
Total days of hospitalization	2.81 ± 1.48	3 ± 1.76	0.535
All-cause mortality	4 (6.7%)	7 (11.7%)	0.342

CD group, conventional duration group; CI, confidence interval; SD group, short duration group.

underwent successful ERC. In that study, 11% of patients with longer duration of antibiotics (>4 days) developed recurrence of cholangitis compared with 7% of patients in short duration of antibiotics ($P = 0.32$) with similar mortality between the 2 groups ($P = 0.13$) (14). Kogure et al conducted a prospective study on 18 patients with acute moderate or severe cholangitis. Antibiotics were stopped once patients became afebrile for 24 hours. In that study, patients became afebrile 2 days after endoscopic biliary drainage (range 1–6) with a median duration of antibiotic for 3 days (range 2–7 days). None of the patients developed recurrence of cholangitis within 3 days of stoppage of antibiotics (22). The findings of our study are concurrent with those of the previous studies. In our study, 9% of patients developed recurrent cholangitis within 30 days of follow-up period (4.5% in each group), which is similar to previously reported studies (14,23). However, in our study, duration of hospitalization was equal in both groups due to predefined discharge criteria, and patients were advised to complete remaining antibiotic course as day care treatment.

In this study, overall mortality was similar in both the groups. On multivariate logistic regression analysis, we found that malignant etiology and hypotension at presentation were associated with higher mortality rate. Van Lent et al (12) also reported 11.3% overall mortality in their retrospective study. The overall high mortality rate (9.2%) in our study and in the study by Van Lent et al was likely due to higher number of patients of acute cholangitis with malignancy (52% and 45% respectively) as an etiological factor and inclusion of only patients with moderate or severe cholangitis in this study.

Table 4. Multivariate logistic regression of factors affecting on clinical cure

Parameter	Odds ratio	95% CI for OR		*P* value
		Lower	Upper	
Malignant etiology	0.101	0.017	0.590	0.011
Hypoalbuminemia	0.362	0.074	1.787	0.212
Inotropic support	0.044	0.005	0.422	0.007
AMS	0.00	0.00	—	0.999
ALI P/F <300	0.00	0.00	—	0.999
INR >1.5	1.27	0.065	24.587	0.876
PTBD	0.00	0.00	—	1.00

ALI, acute lung injury; AMS, altered mental status; CI, confidence interval; INR, international normalized ration; OR, odds ratio; P/F, Po2/Fio2 ratio; PTBD, percutaneous transhepatic biliary drainage.

In our study, approximately half of bile cultures grew microorganisms and all were gram-negative organisms. This was lower when compared with those observed in previous studies, which were 70%–90% (13,14). This could be due to antibiotics administration before biliary drainage, as shown in our previous prospective study as well (21). None of the patients developed antibiotics-associated diarrhea or *Clostridium difficile*–associated diarrhea. In a study by Haal et al (14) also, none of the included patients developed *C. difficile*–associated diarrhea. It could be due to relatively shorter duration of antibiotic and hospitalization in both the groups.

In this study, we prospectively showed that even patients with moderate or severe acute cholangitis improve rapidly after successful biliary drainage and most of the patients require only short duration of antibiotic therapy. Most of the patients presenting with acute cholangitis with obstructive jaundice have mild cholangitis. However, this group of patients usually have better prognosis with lesser morbidity and results cannot be extrapolated to patients with moderate or severe cholangitis. To obviate that, we only enrolled patients with moderate or severe cholangitis for better generalization of results.

We had discharged patients before completion of intravenous antibiotic therapy, which is one of the important limitations of this study. Our hospital is one of the largest tertiary care academic referral centers in North India, with bed constraints. We discharged patient on predetermined criteria with day care–based intravenous antibiotic course with written advice regarding warning signs and contact number in case of emergency for effective bed utilization. We had also scheduled an outpatient clinic visit at the end of antibiotic duration for all patients to decide regarding need of additional antibiotic or not. However, we do acknowledge that it is not a routine practice in many hospitals and it is one of the important limitations of the study. Moreover, because we performed the first randomized study on impact of short duration of antibiotic therapy, we used 4 vs 8 days cutoff based on a previous study (15). Future studies should explore the role of even shorter duration of stopping antibiotic therapy within 48 hours of successful drainage. We decided to continue intravenous antibiotic throughout the study period to increase homogeneity in the study; however, the role of oral antibiotic should also be explored in subsequent studies. Moreover, wide inferiority

margins and open-label study design are also important limitations of the study. We have not used laboratory parameters such as C-reactive protein, procalcitonin, or other inflammatory parameters to guide the therapy because we wanted to make the study as much clinically applicable as possible for wider generalizability. We have not performed routine postprocedure transabdominal ultrasound to check for development of liver abscess or transthoracic echocardiography to look for infective endocarditis in all patients, rather used such investigation as on-demand basis.

To conclude, short duration of antibiotics is noninferior to conventional duration of antibiotics in patients with moderate to severe cholangitis in terms of clinical cure, recurrence of cholangitis, and overall mortality.

CONFLICTS OF INTEREST

Guarantor of the article: Jimil Shah, MD.

Specific author contributions: D.S., J.S.: concept of study, data acquisition, drafting manuscript, critically revising the manuscript. A.J.: interpretation of data, drafting manuscript, critically revising the manuscript. V.J., A.K.S.: interpretation of data, critically revising the manuscript. H.S.M., V.S.: data acquisition, critically revising the manuscript. S.I., Y.R.S.: data acquisition, interpretation of data, critically revising the manuscript. V.G., R.G., S.R., U.D.: data acquisition, interpretation of data, critically revising the manuscript. Final approval of manuscript: all authors.

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Data transparency statement: Deidentified data are available on a reasonable request from the corresponding author.

Study Highlights

WHAT IS KNOWN

- ✓ Biliary drainage with systemic antibiotics are the mainstay of the therapy in the presence of acute cholangitis.
- ✓ Current guideline suggests antibiotic duration of 4–7 days after successful biliary drainage; however, level of evidence is weak in the absence of prospective studies.

WHAT IS NEW HERE

- ✓ Short duration of antibiotics with clinical improvement is noninferior to conventional duration of antibiotics in terms of clinical response, recurrence of cholangitis, or mortality in patients with moderate or severe cholangitis.

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