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The change in microorganisms reproducing in bile and blood culture and antibiotic susceptibility over the years

BILIARY

Nuretdin Suna[1], Hakan Yıldız[1], Mahmut Yüksel[1], Erkan Parlak[1], Selçuk Dişibeyaz[1], Bülent Ödemiş[1], Onur Aydınlı[1], Zülfükar Bilge[1], Serkan Torun[1], Ayşe Yasemin Tezer Tekçe[2], İsmail Taşkıran[1], Nurgül Şaşmaz[1]

[1]Department of Gastroenterology, Türkiye Yüksek İhtisas Hospital, Ankara, Turkey
[2]Department of Infection, Türkiye Yüksek İhtisas Hospital, Ankara, Turkey

Original Article

ABSTRACT

Background/Aims: Infection in the bile tract is a major cause of bacteremia and is related to high morbidity and mortality. We examined the changes in bacteria types and antibiotic susceptibility in bile cultures and simultaneous blood cultures taken from patients who applied for endoscopic retrograde cholangio pancreatography (ERCP)/ percutaneous transhepatic cholangiography (PTC) for different bile duct diseases in recent years.

Materials and Methods: Bacteria types that reproduce in bile and blood cultures from patients who applied for ERCP/PTC between the years of 2007 and 2012 in our clinic were examined. All patients were evaluated together, and in addition, the periods between 2007 and 2009 (Group 1) and between 2010 and 2012 (Group 2) were compared.

Results: In total, 550 patients applied to this study. There were 266 patients in Group 1 and 284 in Group 2. Reproduction occurred in 77.6% of bile cultures. In the order of frequency, these cultures consisted of Escherichia coli (32.8%), Enterococcus spp. (26.2%), and Pseudomonas aeruginosa (11%). Enterococcus spp. were determined to be higher in Group 2 than Group 1 ($p<0.016$). Resistance to quinolones was found in 74.1% of patients, to ampicillin in 73.2%, and to cephalosporins in an average of 61%. Vancomycin was the most susceptible antibiotic (93.4%) to gram-positives. Resistance to piperacillin-tazobactam and amikacin was higher in Group 2 than Group 1 ($p=0.001$ and $p=0.003$, respectively).

Conclusion: The most frequently reproducing bacteria in the bile cultures evaluated in our hospital were Escherichia coli and Enterococcus spp. Although it was thought that the antibiotics given empirically were effective against these bacteria, there was resistancerate of 75% in our study. We determined that the first- and second-step treatment protocols must be updated.

Keywords: Bile cultures, blood cultures, antibiogram, bacteria types

INTRODUCTION

In a healthy person under normal conditions, the bile tracts are sterile. Although there are 100-1000 bacteria in 1 milliliter in the duodenum, that the bile remains sterile is possible through existence of the biliary sphincter. In addition, bile flow, mucus secreted by the biliary epithelium, and immunoglobulins contribute to keeping the bile sterile. Bile acids and immunoglobulin A (IgA) have antibacterial qualities, and bile acids are bacteriostaticat the same time. These factors contribute to hindering the bacterial growth in the bile except for in the duodenum (1,2).

Because the enteric-biliary barrier disappears in patients who have biliary sphincterotomy and a stent placed in the bile tract, ascending bacterial colonization of the bile tract is absolute. In one of our studies, this colonization was reported in 100% of our patients

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Address for Correspondence: Nuretdin Suna, Department of Gastroenterology, Türkiye Yüksek İhtisas Hospital, Ankara, Turkey
E-mail: nurettinsuna.44@hotmail.com

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and, in another study, in 98% of the patients. It was known that microorganisms were polymicrobial in these cases (3,4).

Because of this high frequency of bacteriobili, even if there is no clinical infection, especially in patients who have hilar stenosis, antibiotic prophylaxis is suggested before percutaneousor endoscopic intervention, which should also take place. In addition, even though the definitive treatment of patients who develop cholangitisis resolving the bile stasis, administering suitable empiric antibiotics is an indispensable part of treatment (5,6).

Beginning immediate suitable antibiotherapy in bile tract infections decreases morbidity and mortality. Therefore, it is important to determine if there are any possible microorganisms or antibiotic susceptibility that could cause cholangitis before choosing the antibiotics to be given. Just as the antibiotic susceptibility of microorganisms in bile ducts changes from society to society, susceptibility changes over time even within the same society (7).

The aim of this study is to investigate the changes in the types of bacteria that reproduced in the bile cultures and blood cultures of patients in our hospital who applied for endoscopic retrograde cholangiopancreatography (ERCP)/percutaneous transhepatic cholangiography (PTC) for different bile duct diseases. Additionally, the changes in their antibiotic susceptibility in recent years to determine the choice of antibiotics to be given for the purpose of both empiricaland non-empirical treatment.

MATERIALS AND METHODS

In our clinic, bile cultures and simultaneous blood cultures of patients who applied for ERCP/PTK for various reasons between June 2007 and September 2012 were examined retrospectively. Patient data were taken from the AviCenna Hospital Information Management System (Datasel Information Systems, Ankara,Turkey), which has been used since 2007. AviCenna Hospital Information Management System has a technical infrastructure that can operate in both single and multiple layers, suitable to J2EEstandards, and it supports the international medically accepted standards (ICD-10, SNOMED, ATC, GMDN, etc.) as well.

Bile cultures were taken from nasobiliary or percutaneous-biliary drains. For the patients who applied for PTC, bile samples were taken from external catheters, compatible with sterility rules. New bile was sent for culture. Blood cultures were taken, paying attention to asepsis and antisepsis, in accordance with suitable procedures.

The samples that were taken into the injector, which was deflated and closed with sterilized caps or an anaerobe-carrying broth medium, were taken to the microbiology laboratory immediately. Macroscopic and microscopic examinations of the materials were made. Materials that were examined by gram and Giemsa stain were inoculated to aerobic and anaerobic environments. For aerobic bacteria, inoculations were made in 5% agar with sheep blood and EMB agar, and they were incubated for 48 hours at 37°C. For anaerobic bacteria, inoculations were made in an anaerobic jar system by Gaspak method, and they were incubated for 48 hours in the incubatorat 37°C. In addition, for fungi isolation, inoculation was made in Sabouraud dextrose agar, and it was controlled after 48-72 hours at 37°C; incubation was extended to 5-7 days in the cultures in which there was no reproduction.

The reproducing aerobic bacteria and antibiotic susceptibility were identified usinga VITEK2 (bio Merieux, Lyon, France) automized system, a VITEK2 GN 21341 for gram-negative bacteria and a VITEK2 21342 with an identification card for gram-positive bacteria.

AST-N261 for enteric bacteria, AST-N262 for non-fermentative bacteria, and AST-P592 and AST-P619 for gram-positive bacteria antibiotic susceptibility panels were used. For antifungal susceptibility, panel AST-YS06 was used.

Patients who were thought to have contamination were excluded from the study. Blood cultures that were not sent simultaneously with bile cultures were not included. In addition, patients with infections outside of the biliary tract were not included in the study.

The types of bacteria that reproduced in bile and blood cultures and antibiotic susceptibility were evaluated in all patients. In addition, the study period was divided into two to determine the arbitrary changes in these parameters over time; specifically, the periods June 2007-December 2009 (Group 1) and January 2010-September 2012 (Group 2) were compared.

Considering the laboratory reference intervals used in our hospital, if alanine aminotransferase (ALT) was >41 U/L, aspartate aminotransferase (AST) >40 U/L, gamma-glutamyl transferase (GGT) >61 U/L, alkaline phosphatase (ALP) >130 U/L, total bilirubin (T. bilirubin) >1.2 mg/dL, the international normalized ratio (INR) >1.25 (ISI:1.02), creatinine >1.2 mg/dL, white blood cell count (WBC) >9.7 10'3/uL, C-reactive protein (CRP) >7 mg/dL, anderythrocyte sedimentation speed (ESR) >15 mm/hour, the levels were accepted as high. The study was confirmed by the hospital's ethics council.

Statistical analysis

To evaluate the data obtained from the study, SPSS version 18 (SPSS Inc., Chicago, IL, USA) was used. To compare the variables between the groups, chi-square and crosstab statistical analyses were used.

RESULTS

In total, 338 (61.5%) of the 550 patients who were included in study were male, and 212 (38.5%) were women. The average

Table 1. The distribution of patients with indications for ERCP/PTC

Diagnosis	Choledocholithiasis, n (%)	Malign biliary stricture, n (%)	Benign biliary stricture, n (%)	Others, n (%)	Total, n (%)	p value
Group 1	46 (17.3)	123 (46.3)	79 (29.7)	18 (6.7)	266 (48)	
Group 2	53 (18.7)	126 (44.4)	80 (28.2)	25 (8.8)	284 (52)	0.346
Total	99 (18)	249 (45.3)	159 (28.9)	43 (7.8)	550 (100)	

Others: Bile leakage, sphincter of Oddi dysfunction, anastomosis stricture, etc.

Table 2. Laboratory values

Parameters	Group 1, n (%)	Gruop 2, n (%)	Total, n (%)	p value
ALT >41 U/L	170 (63.9)	173 (60.9)	343 (62.4)	0.558
AST >40 UL	170 (63.9)	166 (58.5)	336 (61)	0.192
GGT >61 UL	231 (86.8)	240 (84.5)	471 (85.6)	0.503
ALP >130 UL	234 (87.9)	237 (83.4)	471 (85.6)	0.158
T. bilirubin >1.2 mg/dL	189 (71)	164 (57.7)	353 (64.2)	0.001
INR >1.25 (ISI:1.02)	126 (47.3)	80 (28.1)	206 (37.4)	0.001
Creatinine >1.2mg/dL	76 (28.6)	56 (19.7)	132 (24)	0.01
WBC >9700/mm^3	147 (55.2)	148 (52.1)	295 (53.6)	0.506
CRP >7 mg/dL	185 (69.5)	225 (79.2)	410 (74.5)	0.004
ESR >15 mm/hour	199 (74.8)	219 (77.1)	418 (76)	0.433

ALT: aminotransferase; AST: aspartate aminotransferase; GGT: gamma-glutamyltransferase; ALP: alkaline phosphatase; T. Bilirubin: total bilirubin; INR: international normalized ratio; WBC: white blood cell; CRP: C-reactive protein; ESR: erythrocyte sedimentation speed

age of patients was 61.8 (16-93) years.Bile samples were taken from a nasobiliary drain (NBD) in 314 (57.1%) patients and from a PTC drain in 236 (42.9) patients. There were 266 (48%) patients in Group 1 and 284 (52%) patients in Group 2; 249 (45.3%) patients had malignant biliary strictures, 159 (28.9%) had benign biliary strictures, 99 (18%) had choledocholithiasis, and 43 (7.8%) had otheretiologies (Table 1).

Among the others were bile leakage, sphincter of Oddi dysfunction, anastomosis strictures, etc. The average age, sex, NBD and PTC distribution, and ERCP/PTC indications were similar in both groups. High levels of ALT were identified in343 (62.4%) patients, of AST in 336 (61%), of GGT in 471 (85.6%), of ALP in 471 (85.6%), of T. bilirubinin 353 (64.2%), of INR in 206 (37.4%), of creatinine in 132 (24%), of WBC in 295 (53.6%), of CRP in 410 (74.5%), and of ESR in 418 (76%) (Table 2). T. bilirubin, INR, and creatinine were higher in Group 1 than in Group 2 (p=0.001, p=0.001, and p=0.01, respectively). CRP was higher in Group 2 than in Group 1 (p=0.004).

When all patients were evaluated together,reproduction occurred in 427 (77.6%) bile cultures. When looked at over the years, reproduction occurred in 212 patients (79.7%) in Group 1 and 215 patients in Group 2 (75.7%). Reproduction rates were similar in both groups.

The microorganisms that reproduced in the bile cultures and their distribution over the years are shown in Table 3; the most frequently reproducing bacteria in all bile cultures were, in order: Escherichiacoli in 140 (32.8%) patients, Enterococcus spp. in 112 (26.2%), Pseudomonas aeruginosain 47 (11%), and Klebsiellapneumoniae in 34 (8%) patients. When looked by years, the rate of Enterococcus spp. reproduction in the bile cultures was determined to be meaningfully high in Group 2 (34%) in comparison with Group 1 (18.4%) (p<0.016). The rate of Pseudomonas aeruginosa was higher in Group 2 (12%) than in Group 1 (9.9%), but it was not meaningful statistically. Escherichia coli, Klebsiella pneumoniae, Enterobacter spp., Staphylococcus aureus, Candida albicans, and Acinetobacterbaumannii reproduction rates were higher in Group 1 (35.4%, 8.9%, 6.1%, 4.7%, 3.8%,and 3.3%, respectively) than in Group 2 (30.2%, 6.5%, 3.2%, 1.9%, 3.2%, and 1.9 %, respectively) but were not meaningful statistically.

The antibiotic susceptibility of the reproducing microorganisms and their distribution by years are shown in Table 4; the most frequently resisted antibiotics were, in order: quinolones (74.1%), ampicillin (73.2%), and cephalosporins (average 61%). The most sensitive antibiotics were amikacin (78.5%) and carbapenems (75.8%). The most sensitive (93.4%) antibiotic to gram-positives was vancomycin. According to the distribution by years, resistance to a mikacin and piperacillin-tazobactam were determined to be higher in Group 2 (29, 2%, 56, 1%) than in Group 1 (14.4%, 40.1%), (respectively, p=0.03 and p=0.03). ESBL was found in 36.9% of gram-negative bacteria, and there was no meaningful difference between the two groups.

Table 3. The microorganisms that reproduced in the bile cultures and theirdistribution by years

Microorganisms	Group 1, n (%)	Gruop 2, n (%)	Total, n (%)
Escherichia coli	75 (35.4)	65 (30.2)	140 (32.8)
Enterococcus spp*	39 (18.4)	73 (34)	112 (26.2)
Pseudomonas aeruginosa	21 (9.9)	26 (12)	47 (11)
Klebsiella pneumonia	19 (8.9)	14 (6.5)	34 (8)
Enterobacter spp.	13 (6.1)	7 (3.2)	20 (4.7)
Candida albicans	8 (3.8)	7 (3.2	15 (3.5)
Staphylococcus aureus	10 (4.7)	4 (1.9)	14 (3.3)
Acinetobacter baumannii	7 (3.3)	4 (1.9)	11 (2.6)
Others	20 (9.4)	15 (7)	35 (8)
Total	212 (79.7)	215 (75.7)	427 (77.6)

Others: Streptococci and other enteric bacteria, other non-fermentatives, anaerobes, etc.
*p<0.05

Table 4. Antibioticresistance of the reproducing microorganisms and their distribution by years

Antibiotics	Group 1 (%)	Gruop 2 (%)	Total (%)	p value
Amikacin	14.4	29.2	21.5	0.03
Ampicillin	70.3	76	73.2	0.245
Cefazolin	67.9	72.6	70	0.491
Cefepime	53.9	55.4	54.6	0.815
Ceftazidime	61.5	54.3	58.1	0.268
Ceftriaxone	64.8	55.7	61.6	0.197
Gentamicin	36.6	35.7	36.1	0.93
Carbapenems	19.9	29.1	24.2	0.78
Quinolones	71.5	77	74.1	0.269
Piperacillin-tazobactam	40.1	56.1	47	0.03

Table 5. The microorganisms that reproduced in the blood cultures and their distribution by years

Bacteria	Group 1 n (%)	Group 2 n (%)	Total n (%)
Escherichia coli	17 (54.8)	15 (53.5)	32 (54.2)
Pseudomonas aeruginosa	4 (12.9)	6 (21.4)	10 (16.9)
Enterococcusspp.	4 (12.9)	3 (10.7)	7 (11.9)
Klebsiella pneumonia	3 (9.6)	2 (7.1)	5 (8.5)
Staphylococcus aureus	3 (9.6)	2 (7.1)	5 (8.5)
Total	31 (21.3)	28 (18)	59 (19.6)

In 301 (54.7%) of the 550 patients whose bile cultures were evaluated, blood cultures were also taken at the same time, from145 (48.2%) patients in Group 1 and 156 (51.8) in Group 2. In 59 (19.6%) of the 301 patients, reproduction occurred.

The microorganisms that reproduced in the blood cultures and their distribution by years are shown in Table 5. As understood here, the most frequently reproducing bacteria were, in order: Escherichia coliin 32 (54.2%) patients, Pseudomonas aeruginosain 10 (16.9 %), and Enterococcusspp. in 7 (11.9%). The distributions of thebacteriathat reproduced in the blood cultures, including Enterococcus, that also had meaningful differences in the bile cultures was similar over the years.

There was reproduction in the bile cultures of 55 (93.2) of the 59 patients whose blood cultures also had reproduction. Similar microorganisms were determined in the bile and blood cultures of these 55 patients at similar frequencies (Table 6). The antibiotic resistance of the microorganisms that reproduced in the blood cultures and their distribution by years are shown in Table 7; the most frequent resistance was seen, in order, to: ampicillin (80%), quinolones(70%),and cephalosporins (average 65,8%). The most susceptible antibiotics were determined to be, in order, carbapenems (81.6) and amikacin (80%). The susceptibility of vancomycin to gram-positives was determined to be 84.6%. Resistance to quinolones was determined to be meaningfully higherin Group 2 (87.5 %) than in Group 1 (56%) (p=0.011). Extended Spectrum Beta Lactamase (ESBL) was

Table 6. The distribution of microorganisms in patients with both bile and blood culture both

Bacteria	Blood cultures, n (%)	Bile cultures, n (%)
Escherichia coli	29 (52.7)	30 (54.5)
Pseudomonas aeruginosa	10 (18.2)	9 (16.3)
Enterococcus spp.	7 (12.7)	7 (12.7)
Klebsiella pneumonia	5 (9)	4 (7.3)
Staphylococcus aureus	4 (7.8)	4 (7.3)
Total	55 (100)	55 (100)

found in 62% of the gram-negative bacteria, and there was no meaningful difference between the two groups.

DISCUSSION

The most frequently reproducing bacteria in the bile cultures in this study were Escherichia coli, Enterococcus spp., and Pseudomonas aeruginosa, as in other studies. However, by years, whereas Escherichiacoli incidence decreased, the incidence ofEnterococcus spp. and Pseudomonas aeruginosaincreased. High resistance was established to antibiotics such asquinolones (74.1%), ampicillin (73.2%), and cephalosporins (average 61%), which had been mostly used as the first-line treatments in our study.

In our study, there was 77% reproduction in the bile cultures. This reproduction rate was not surprising because contamination of the biliary system is well-known in patients who have sphincterotomy or a placed stent. In past studies, 16%-85% reproduction was determined (4,8-14). In older studies, 30%-90%polymicrobial reproduction in bile cultures was determined, especially in patients whose bile ducts had previous interference (15-19).

It was reported that microorganisms reproducing in bile cultures stemmed from enteric in previous studies. Aerobic bacteria, such as Escherichia coli, Klebsiellapneumoniae, Enterococcus spp., and Enterobacter, are most frequently isolated (8,13,15,20-22). The results of our study support this finding. The microorganisms that reproduced in the bile cultures were, in order of frequency: Escherichia coli (32.8%), Enterococcus spp. (26.2%), and Pseudomonas aeruginosa (11%) (Table 3). Enterococcus spp. is the most commongram-positive bacteria that causes cholangitis (10%-20%). In our study, Enterococcus spp. was the most frequent gram-positive bacteria that reproduced in the bile cultures. In addition, the rate of Enterococcus spp. that reproduced in the bile cultures was determined to be statistically meaningfully higher in Group 2 in comparison with Group 1 (p=0.016). The gradually increasing frequency of Enterococcus mightbe because the dominant flora becomes gram-positiveas a result of the recent preference for antibiotics that treat the negative bacterium spectrum in general..

Table 7. Antibioticresistance of the microorganisms in the blood cultures and their distribution by years

Antibiotics	Group 1 (%)	Group 2 (%)	Total (%)	p value
Amikacin	22	18	20	0.80
Ampicillin	70.4	91.4	80	0.66
Cefazolin	62.5	79	70	0.324
Cefepime	48.2	60.9	54	0.470
Ceftazidime	52.2	66.7	59.1	0.373
Ceftriaxone	62.5	87.5	68.8	0.380
Gentamicin	38	20	29	0.104
Carbapenems	22	14.3	18.4	0.70
Quinolones	56	87.5	60	0.011
Piperacillin-tazobactam	57.2	67	61.2	0.70

In our study, there was reproduction in 19.6% of the blood cultures that were taken simultaneously with the bile cultures. Blood cultures provide an opportunity to determine effective organisms. In past studies, in patients with cholangitis, reproduction in blood cultures was reported as 20%-80% (14,15,23-27). The low reproduction rates in our blood cultures could have been because cases that did not have cholangitis were included in the study. The bacteria that reproduced in the blood cultures were frequently microorganisms, such as Escherichia coli (54.2%), Pseudomona saeruginosa(16.9%),and Enterococcus spp. (11.9%). This profile was compatible with the literature (7,23,24,28,29).Normally, bile ducts are sterile as a result of various anatomic and physiological mechanisms (1,30,31). A competent sphincter of Oddi prevents intestinal contents from refluxing into the bile duct, and anterograde bile flow periodically flushes the biliary system, keeping it free of organisms. In addition, bile components including bile salts and immunoglobulin A (IgA) have antibacterial characteristics. Bile salts are bacteriostatic, which directly promotes thesterility of the biliary tree and also limits the growth of bacteria within the duodenum (1,2). Tight junctions between hepatocytes separate the bile canaliculi from hepatic sinusoids, thereby protecting the biliary tree from bacteremia. In addition, Kupffer cells within the hepatic sinusoids maintain the sterility of the biliary system by phagocytosing organisms (30).

Complete biliary obstruction creates a state of immune dysfunction (32). Studies indicate that the absence of bile salts and IgA in the intestine leads to changes in the bacterial flora that colonize the small intestine. Under normal circumstances, colonization of the duodenum and jejunum with coliforms is limited (33,34), but this has been shown to change in studies of bile-duct-ligated rats, indicating a shift in the small bowel flora with Escherichia coli predominating (35). In addition to the change in the bacterial flora of the duodenum, intestinal bacteria are more likely to translocate in rodents with ligated bile ducts (36). The increased translocation may be in part caused

by the absence of bile salts. Bile salts have a detergent effect on bacterial endotoxins, and therefore, their absence may be responsible for increased endotoxin translocation (37). A number of changes in neutrophil function have also been noted in patients with obstructive jaundice, such as reduced phagocytosis, impaired adhesion, and abnormal response to cytokines. All these changes may diminish the neutrophil response to infection (15,32). Inaddition, some studies have shown impaired phagocytic function of the Kupffer cells in animal models of biliary obstruction, with recovery when the obstruction is relieved (38).

The basis of the treatment of bile duct infection is biliary decompression, together with antibiotics. Early diagnosis and beginning suitable antibiotherapy decrease morbidity and mortality. The combination of ampicillin and aminoglycoside was accepted as the standard regimen for cholangitis in the 1980s (5). In most studies, the efficiency of newly developed antimicrobial drugs and their usefulness were similar to those of ampicillin and aminoglycoside (39,40).Therefore, in accordance with available clinical experiments, piperacillin, ampicillin, aminoglycoside, and a number of cephalosporins are advised for acute cholangitis treatment (5). Despite this, there is no published valid guide for antibiotic treatment in bile duct infections. Therefore, it is very important to determine responsible pathogenesis and antibiotic susceptibility for successful treatment of bile duct infections. In our study, the highest resistance was determined to be to quinolones at 74.1%, ampicillin at 73.2%, and cephalosporins (61% on average) (Table 4). ESBL was determined in 36.9% of thegram-negative bacteria. In blood cultures, the most frequent resistance was seen, in order, to: ampicillin (80%), quinolones (70%), and cephalosporins (65.8%) (Table 7). Resistance to quinolones in the blood cultures was meaningfully higher in Group 2 (87.5%) than it was in Group 1 (56%) (p=0.011). A possible reason for the increased antibiotic resistance is the inappropriate use of antibiotics (41).

Shivaprakasha et al. (28) reported high resistance to antibiotics such as ampicillin (92.4%), cephalexin (82.4%), ciprofloxacin (68.4%), and piperacillin (64.3%) in thegram-negative bacillusthat reproducedin bile cultures. There was high resistance against ciprofloxacin, ampicillin, and third-generation cephalosporins, which arefrequently used in our clinic empirically. In our study, resistance to quinolones was found to be 74.1%; thus, we showed that bile duct infections could not be treated by quinolones. In the patients who carrieda risk factor for bile duct infections caused by resistant pathogens, resistance to piperacillin-tazobactam,which was preferred as the second-line antibiotic, was meaningfully higher in Group 2 than in Group 1 (p=0.03).Resistance toamikacin, which is used rarely in our clinics, was meaningfully higher in Group 2 in comparison with Group 1 (p=0.03). The increased resistanceto amikacin over time was surprising and, we believe, caused bycross-passingbetween it andthe genes that caused resistance to other antibiotics.

There were some limitations to our study. First, our study was retrospective. However, in our hospital, culture-taking techniques have been standardized for years, and data have been kept well in a computer environment. Second, our cases were not separated into community-acquired vs. hospital-acquired infections. Third, it could not be determined whether the cases that were included in the study had cholangitis.

Consequently, the most frequent bacteria observed in the bile cultures that were evaluated in our hospital were Escherichia coli and Enterococcus spp. Although the antibiotics that are given empirically are thought to be effectiveagainst these bacteria, we determined a resistance of nearly 75% tofrequently preferred antibiotics. Therefore,we believethat first- and second-step treatment protocols must be updated. Comprehensive prospective studies are needed to determine whether certain factors -such as the antibiotics that patients used before their bile cultures were taken,the degree of cholangitis, any underlying diseases, the process used, and whether it was administered inpatient or outpatient-affect bacteria types and their susceptibility to antibiotics.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethic Council of the hospital.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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