

Routine bile collection for microbiological analysis during cholangiography and its impact on the management of cholangitis CME

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Background: Antibiotic treatment of cholangitis is often insufficient because of inappropriate antibiotic use or bacterial resistance.

Objective: To evaluate the role of routine bile collection during endoscopic retrograde cholangiography or percutaneous transhepatic cholangiography for microbiological analysis in the antibiotic management of cholangitis and to identify risk factors of bacteriobilia.

Design: Prospective, observational, diagnostic study.

Setting: Hannover Medical School, Hannover, Germany.

Patients and Intervention: This study involved 243 consecutive patients undergoing endoscopic retrograde cholangiography/percutaneous transhepatic cholangiography for biliary complications after orthotopic liver transplantation (27%), malignancy (27%), primary sclerosing cholangitis (15%), benign strictures (11%), and choledocholithiasis (8%).

Main Outcome Measurements: Microbiological examination of bile samples.

Results: Patients with biliary stents or who were receiving repeated interventions after orthotopic liver transplantation were at increased risk of bacteriobilia ($P < .05$). The rate of gram-positive monomicrobial infection was higher in patients with primary sclerosing cholangitis ($P < .01$). In 40 examinations, patients presented with preprocedural cholangitis although they were receiving antibiotics. According to bile culture results, the antibiotic treatment was modified to a more specific therapy in 72.5% of patients. In patients who developed cholangitis after endoscopic retrograde cholangiography (27 examinations), specific antibiotic treatment was started or refined in 67% of cases, based on bile culture results.

Limitations: Contamination of samples during intervention cannot be totally excluded.

Conclusion: Orthotopic liver transplantation, biliary stenting, and repeated interventions are risk factors of bacteriobilia. In our patients with primary sclerosing cholangitis, gram-positive monomicrobial infections were more common. A bile sample collected during cholangiography for microbiological analysis is a simple, potentially valuable, diagnostic tool in patients with cholangitis. Each center should recognize its own patterns of infection to ensure ideal targeted therapy. (*Gastrointest Endosc* 2010;72:284-91.)

Abbreviations: ERC, endoscopic retrograde cholangiography; OLT, orthotopic liver transplantation; PSC, primary sclerosing cholangitis; PTC, percutaneous transhepatic cholangiography.

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See CME section; p. 392

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Cholangitis is a frequent and potentially life-threatening complication in patients with biliary obstruction.^{1,2} Even recent studies have reported mortality rates of up to 10%.³⁻⁵ The acute inflammation of the bile ducts is mainly a result of microbial infection caused by bacteria or fungi.⁶ Blood cultures give an opportunity to detect the causative organism, but, even in febrile patients with cholangitis, blood cultures remain negative in more than half of the cases.^{1,7,8}

Bile aspiration for microbiological analysis during endoscopic retrograde cholangiography (ERC) or percutaneous transhepatic cholangiography (PTC) is an approach to establish antibiotic susceptibility testing and bacterial resistance profiling in a fluid in which the infection takes place. However, this method is rarely performed because it is not generally recommended by gastroenterology societies because it appears to be technically demanding, time consuming, or unnecessary in the presence of blood cultures.

Based on prior findings from bile cultures obtained at surgery or during endoscopic biliary procedures, it is recommended to include a broad spectrum penicillin derivative (possibly in combination with β -lactamase inhibitors) or a cephalosporin with metronidazole in the empiric antibiotic treatment of cholangitis.⁹ However, as a result of widespread use of such broad spectrum antibiotics, bacterial isolates from some groups of patients who often receive multiple antimicrobial substances (eg, after orthotopic liver transplantation [OLT]), may show resistance toward empirically chosen antibiotics. Hence, bacterial selection needs to be taken into account for the choice of drug in order to avoid insufficient treatment.

Our aim was to evaluate the effectiveness of routine bile collection for microbiological analysis in a large cohort study in order to choose the most appropriate antibiotic management in patients with cholangitis. Furthermore, we investigated risk factors of microbiological colonization of the bile in patients with different diseases.

PATIENTS AND METHODS

Patients

This prospective study was conducted between January 2008 and February 2009 at the endoscopic unit of the Hannover Medical School. Patients with various biliary disorders were included, and some patients participated more than once when repetitive cholangiography was performed. Informed, written consent was obtained from all patients, and the trial was approved by the Ethical Committee of Hannover Medical School. Exclusion criteria were age under 18 years or absence of written, informed consent before examination.

Methods

All duodenoscopes (Olympus, Hamburg, Germany) were disinfected according to the guidelines of the Robert Koch Institute, and contamination was excluded by regular smear tests.¹⁰ Bile was aspirated by placing a single-

Take-home Message

- Bile sample collection during cholangiography for microbiological analysis may be a valuable diagnostic tool in patients with cholangitis because it can lead to a more adequate therapy and may help to reduce the mortality rate.

use, 5F, standard ERC catheter (without flushing or guide-wire cannulation) into the bile duct before contrast material injection. Approximately 0.5 to 6 mL of bile (mean 2 mL) was collected and transferred in a sterile tube. Bile aspiration during PTC was performed directly after sonographic-guided percutaneous puncture of the bile ducts and before contrast material injection.

Samples were cultured under aerobic conditions on 5% Columbia sheep blood agar (Becton Dickinson GmbH, Heidelberg, Germany) and MacConkey agar (Oxoid GmbH, Wesel, Germany), with a first reading after 24 hours. Anaerobic growth was observed by the use of Schaedler agar (Becton Dickinson GmbH). Species differentiation was then performed according to German laboratory practice guideline DIN EN ISO 15189. Species identification and antibiotic susceptibility testing were performed using the VITEK-2-XL system (bioMérieux, Nuertingen, Germany) and Merlin Micronaut Sprint Dispenser automated broth micro-titer system (Genzyme Virotech, Ruesselsheim, Germany). Micro-titer plates of 384 wells (No. EG-009) were used as recommended by the German Network for the Antimicrobial Resistance Surveillance (GENARS).¹¹ Microorganisms in concentrations of >10,000 per mL were considered as infection; lower concentrations were judged as contamination or colonization.

Statistical analysis

Statistical analyses were conducted by using the 2-tailed Fisher exact test or chi-square test. Statistical analyses were carried out by using Epicalc (version 5.0/2000 for Windows; Brixton Health, www.brixtonhealth.com/epicalc.html).

RESULTS

Patients and general microbiological characteristics

In the period between January 2008 and February 2009, 243 patients (56% male, median age 57 years, range 22-86 years) were included in the study and received a total of 400 interventions at our endoscopy unit (366 ERCs, 34 PTCs). PTC was advocated whenever ERC was not possible (16 patients with malignant strictures, 12 patients with benign strictures, 4 patients with bilio-digestive anastomosis, 2 patients after OLT). Main indications for cholangiographic interventions (Table 1) were benign biliary

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