

THE INCIDENCE OF BILIARY TRACT INFECTIONS IN BENIGN GALLBLADDER DISEASE

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REZUMAT

Scopul studiului a fost să determine incidența prezenței florei bacteriene în cadrul bolilor benigne ale veziculei biliare, principalii germeni implicați și sensibilitatea lor la antibiotice, pentru a putea aplica un tratament curativ și profilactic corect. Pentru aceasta, s-a recoltat randomizat bilă intraoperator, folosită pentru culturi bacteriene aerobe și anaerobe. Aceste culturi au demonstrat prezența majoritară a bacteriilor Gram-negative, dintre care *Escherichia coli*, *Proteus spp.* și *Klebsiella spp.* au fost cele mai frecvent întâlnite. S-a evaluat profilul de rezistență locală al speciilor microbiene cultivate.

Cuvinte cheie: infecție biliară, cultură bacteriană, tratament antibiotic, antibioticoprofilaxie.

ABSTRACT

The purpose of this study is to establish the incidence of bacterial presence in benign gallbladder diseases, the main germs involved and their sensitivity to antibiotics, in order to perform an appropriate curative and prophylactic therapy. Bile has been randomly harvested during surgery and used for aerobic and anaerobic bacterial cultures. These cultures revealed the prevalent presence of Gram-negative germs, among which *Escherichia Coli*, *Proteus spp.*, and *Klebsiella spp.* were the most frequent ones. The local antibiotic sensitivity profile was assessed for the cultured germs.

Key Words: biliary infection, bacterial culture, antibiotic treatment, antibiotic prophylaxis.

INTRODUCTION

The benign diseases of the biliary tract, especially the cholecystitis, acute or chronic, calculous or acalculous, represent an important percentage in the activity of any general surgery clinic. The indications for surgery, especially for gallstones have expanded during the last decade, due to the various possibilities of evolution, to the appearance of complications, and, nevertheless, due to the unquestionable advantages of the laparoscopic cholecystectomy for the patient.^{1,2}

Even though most of the authors report mortality rates lower than 0.5%, and a relatively low morbidity rate, their causes are still representing a major preoccupation for researchers.

The infection remains one of the most important factors. There are multiple possible sources of infection: external contamination during pre- or intraoperative exploration procedures, the patient's tegument, and last, but not necessarily least, the bile itself. Although only part of the patients develop bile infections, in their cases, even the surgical act may be responsible for releasing bacteria in the tissues, where they can multiply, thus determining complications. Various studies (Scott, Cox, Mason, Reiss etc.), which correlated the development of the infectious complications with the presence of the infected bile, have found an incidence of positive bacterial bile cultures in 28 to 64% of the cases.³ For this reason, we consider the knowledge of the bacterial flora and its antibiotic sensitivity important for many prophylactic or curative therapeutic decisions.

MATERIAL AND METHODS

This is a preliminary study. Its purpose, for now, is to evaluate the incidence of biliary infections only in chronic and simple acute cholecystitis, deliberately excluding the complicated cases: the obstruction of the main biliary ducts, with jaundice, cholangitis, or

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biliary peritonitis etc. We have also tried to determine the type of germs and their incidence, the antibiotic sensitivity for the usual medication, the correlation with the postoperative complications, and, eventually, to determine clinically assessable risk factors for the rational use of antibiotics in biliary surgery.

From January 1st 2002, to September 1st 2003, in the 3rd Surgery Clinic of the Timișoara Clinical Emergency Hospital, a number of 385 patients with benign diseases of the gallbladder underwent surgery. The sex ratio in this group was M/F = 1/3. The mean age was 47.9 years, varying from 17 to 87 years. Approximately a quarter of the cases were emergencies. Among these, a number of 154 randomly selected patients were included in the test, by harvesting during surgery bile and gallbladder fragments. The specimens were used for cultures: aerobic (gelose with blood, AABTL, glucose, and solid Chapman) and anaerobic (5% blood gelose, with a reductive agent). The group was formed by a number of 103 women and 51 men, with a mean age of 53.5 years; 55 (35.71%) were emergencies.

RESULTS

We obtained positive cultures in 59 cases (38.31%) out of a total of 154. The incidence of germ presence was considerably higher in patients with acute cholecystitis: 55 cases with 47 positive cultures, representing 85.45%, as compared to 99 non-acute cases with 12 positive cultures, representing 12.12%.

After sorting the patients with positive cultures by age decades, we noticed that the incidence of germ presence increases with age, tending towards 100% in the seventh and eighth decades, remark that lead us to the conclusion that the susceptibility for developing a biliary infection increases with age. In patients over 50 years, the rate of positive bile cultures is higher than 70%.

The bile cultures revealed most frequently the presence of Gram-negative germs, such as *Escherichia coli*, in 29 cases (49.15%), *Proteus* spp. in 14 cases (23.72%), and *Klebsiella* spp. in 9 cases (15.25%). In a small number of cases, we have also found Gram-positive germs: *Staphylococcus* spp. in four cases (6.78%), and *Streptococcus viridans* in one case (1.69%). Germ associations were discovered in two cases (3.39%). The associations were: *E. coli* with *Staphylococcus* and *E. coli* with *Proteus*. Considering the germ associations, we can consider that *E. coli* is responsible for more than 50% of the biliary infections. No anaerobic germ was isolated.

Our results regarding the sensitivity of germs

to antibiotics are as follows: cephalosporins 82.5%: cefazolin, cefepime, cefotetan, ceftazidime, ceftriaxone, cefoperazone, gentamycin (74%), and ampicillin 3.7%. Even if we take into consideration that the sensitivity of the germs to antibiotics may vary from one to another, and that knowing the local conditions is essential, we have to point out that Ampicillin is not included in the recommendations found in some contemporary works, and that the aminoglycosides are not used in prophylaxis. A special attention must be given to the use of penicillins associated with beta-lactamase inhibitors. Even though the carbapenems are effective in these cases, they are a reserve for the more severe cases.

The aim of this study is to point out the effectiveness of the use of third generation cephalosporins in the prophylaxis of any uncomplicated cases of benign gallbladder disease.

The mortality rate was of 0.51%; two patients were lost, one with pulmonary embolism, and one with myocardial infarction. None of the two cases can be related in any way to the basic biliary disease or to the infection.

DISCUSSIONS

This study allowed us to assess that more than one third of the patients (38.31%) suffering from acute or chronic cholecystitis, with or without calculi, also present bile infection, fact proven by positive bile cultures.

The incidence of biliary germ presence rises in cases of acute cholecystitis. In our study, we found it in 85.45% of the cases, as compared to a 70-75%, as the specific literature mentions it (Keighley, Suzuki, DuPriest etc.).³⁻⁷

Because of the fact that the calculous asymptomatic cholecystitis has a relative indication for surgery, this point of view must be revised, due to the presence of germs within the walls of the calculous gallbladder.²

Seemingly, patients with proven presence of bacteria within the bile are peculiarly prone to developing infectious complications, especially with a high rate of wound infections. This risk is much smaller when laparoscopic surgery is used; hence, no such complication occurred in these cases.

The most frequently isolated germs in bile cultures were the Gram-negative ones, *E. coli* being by far the most frequent, closely followed by *Proteus* spp. and *Klebsiella* spp.; the Gram-positive germs, like *Streptococcus viridans* and *Staphylococcus* spp. were not so frequently met. The data we have obtained

related to the germ identification is similar to that found in the literature, where *Klebsiella* spp. is placed second.^{4,6,7-10}

Anaerobic bacteria can also be present (*Bacteroides* spp., *Clostridium* spp.). Even *Candida* spp. was isolated, but all our fungus cultures were negative and no patient required antifungal prophylaxis.^{3,7} It is important to mention that, even though fungi can be present in up to 25% of all the abdominal infections, the treatment is not necessary, unless obvious clinical signs appear.

The results of this study also allow recommendations for an adequate antibiotic therapy, as well as for the prophylaxis of complications in high-risk patients. By biliary high-risk patient, one should understand: age over 70 years, acute cholecystitis, non-functioning gallbladder, obstructive jaundice, or common duct stones.^{9,11} The patients with no risk factors do not necessitate any prophylaxis, because of the very low percentage of positive bile cultures, but those with two or more risk factors need a complete prophylaxis. Several studies recommend various methods of antibiotic prophylaxis in patients with benign diseases of the gallbladder, but a consensus does not exist yet.¹²⁻¹⁴

When choosing the antibiotic, one must not overlook the fact that the Minimal Inhibitory Concentration of antibiotic must not be reached within the bile, but, more importantly, within the blood, gallbladder bed, peritoneum, and the surgical wound. Given the local conditions of antibiotic sensitivity, the cephalosporins and gentamycin were proven the most effective ones. Ampicillin, although still recommended by many practitioners, was proven ineffective.

CONCLUSIONS

1. The presence of bacteria in cases of benign diseases of the gallbladder is found in 38.31%, as confirmed by positive cultures; the incidence considerably increases (85.45%) in the acute conditions.

2. The Gram-negative bacilli determine most of the bile infections; *Escherichia coli* is, by far, the most frequent one.

3. The results of the study allow the recommendation for an adequate antibiotic prophylaxis. In the local conditions of antibiotic sensitivity, the

cephalosporins and gentamycin are the most effective drugs.

4. Even though effective, the aminoglycosides are not recommended in prophylaxis.

5. Because of the presence of bacteria within the wall of a gallbladder, also affected by a chronic inflammatory infiltration, the calculous gallbladder, with thick walls, should be removed, in order to avoid the episodes of relapsing cholecystitis.

6. The incidence of bacterial positive bile cultures increases with age.

7. The patients with acute or chronic cholecystitis may benefit from antibiotic prophylaxis.

8. A good prophylaxis is obtained by using ceftriaxone or cefoperazone in all uncomplicated cases of benign gallbladder diseases, in a non-high-risk patient.

REFERENCES

1. Carpenter HA. Bacterial and parasitic cholangitis. *Mayo Clin Proc* 1998;73(5):473-8.
2. Hancke E, Nusche A, Marklein G. Bacteria in the gallbladder wall and gallstones – Indications for cholecystectomy. *Langenbeck's Arch Chir* 1986;368(4):249-54.
3. Keighley MRB, Blenkham FI. Infection and the biliary tree: Surgery of the liver and biliary tract. New York, Churchill-Livingstone, 1998.
4. Fox MS, Wilk DJ, Weissmann HS, et al. Acute acalculous cholecystitis. *Surg Gynecol Obstet* 1984;159:13.
5. Dietrick NA, Cacioppo JC, Davis RP. The vanishing elective cholecystectomy. *Arch Surg* 1988;123:810.
6. DuPriest RW, Khaneja SC, Cowley RA. Acute cholecystitis complicating trauma. *Ann Surg* 1979;189:84.
7. Keighley MRB. Microorganisms in the bile. *Ann R Coll Surg Engl* 1977;59:329.
8. Werbel GB, Nahrwold DL, Joehl RJ, et al. Percutaneous cholecystostomy in the diagnosis and treatment of acute cholecystitis in the high-risk patient. *Arch Surg* 1989;124:782.
9. Gilbert DN, Moellering RC, Sande MA. The Sanford guide to antimicrobial therapy, 33rd edition, 2003, p. 123.
10. Petakovic G, Korica M, Gavrilovic S. Bacteriologic examination of gallbladder contents *Med Precl* 2002;55(5-6):225-8.
11. Landau O, Kott J, Deutsch AA, et al. Multifactorial analysis of septic bile and septic complications in biliary surgery *World J Surg* 1992;16(5):962-4.
12. Krajden S, Yaman M, Fuksa M, et al. Piperacillin vs. cefazolin given preoperatively to high risk patients who undergo open cholecystectomy: a double blind, randomised trial. *Can J Surg* 1993;36(3):245-50.
13. Angio LG, Pacile V, Versaci A, et al. Switch prophylaxis once a day with levofloxacin in laparoscopic cholecystectomy. *Minerva Chir* 2003;58(3):335-40.
14. Colizza S, Rossi S, Picardi B, et al. Surgical infections after laparoscopic cholecystectomy: ceftriaxone vs. ceftazidime prophylaxis. A prospective study. *Chir Ital* 2004;56(3):397-402.