ORIGINAL ARTICLE

FREQUENCY OF INFECTION IN CHOLELITHIASIS

Irfan Sattar, Adnan Aziz, Shahid Rasul, Zahid Mehmood and Asadullah Khan

ABSTRACT

Objective: To determine the frequency of infection in cholelithiasis and find common infecting organisms with their antibiotic sensitivity.

Design: A descriptive study.

Place and Duration: This study was conducted in Surgical Unit - I, Jinnah Postgraduate Medical Centre (JPMC), Karachi, Pakistan, from April 2001 to March 2002.

Patients and Methods: First 100 cases of cholelithiasis, selected and operated by open or laparoscopic cholecystectomy were included in this study. Patients with acute cholecystitis, history of jaundice, stones and / or dilated common bile duct were excluded from the study. Ultrasound was the main tool for pre-operative diagnosis. During cholecystectomy, bile was aspirated and specimens were sent to laboratory for microbiological examination. The results were recorded on a proforma.

Results: Out of 100, 36 patients had positive bile culture. The most common organism was E. coli (17 patients) followed by Klebsiella (9), Pseudomonas (6), Staphylococcus aureus (2), Salmonella (1) and Bacteroids fragalis (1) patient. In this study, most of the biliary organisms were highly sensitive to the 2nd generation cephalosporins and quinolones.

Conclusion: From the bacteriological assessment, it seems that both endogenous and exogenous contamination were the causes of wound sepsis. It was also found that the infection of bile did not increase the risk of postoperative wound infection when prophylactic perioperative antibiotics were used.

KEY WORDS: *Bile. Biliary infection. Cholecystitis. Cholelithiasis.*

INTRODUCTION

Gallbladder disease is the commonest indication for abdominal surgery and is the second most common intra abdominal operation performed in the western countries.[1] Gall stones are responsible for more than 95% of biliary tract disease.[2]

Different factors have been implicated in the causation of gall stones amongst which infection of the bile is also as important factor. In about 30% of the patients with cholelithiasis, bacteria can be cultured either from the bile or from the wall of the gallbladder. The biliary infection can be caused by any type ranging from aerobic gram positive to gram negative to anaerobic organisms. Aerobic organisms cause 94% of biliary tract infections while anaerobic organisms cause the rest. Bacteria are commonly found in inflamed gallbladder and in patients with cholelithiasis, whereas evidence suggests that normal bile is sterile.[3] Inflamed gallbladder has markedly altered permeability, which permits absorption of bile acids and movement of inorganic salts into the gallbladder lumen. The role of excessive cellular debris and increased protein secretion, which occurs in response to inflammation, may be present. Finally, bacterial enzymes effects constituency of bile which may alter its solubility leading to precipitation of bile salts. Most gall stones are composite in nature. Bacteria can be found in most pure stone (i.e, those whose structure consists more than 90% cholesterol). The natural history of gall stones is unknown. It is likely that brown pigment stones can evolve in their chemical composition after termination of the infection process that initiate their formation, and may further develop into either mixed or nearly pure cholesterol stones. It is difficult to ascertain that whether bacterial infection of bile arose from stone formation or vice versa. Although the exact contribution of bacteria in lithogenesis is not known, it is important for the clinician to realize that most gall stones are likely to be colonized by bacterial biofilm, even though the bile may be culture negative.

The purpose of the study was to determine the frequency of infection in cholelithiasis and to find common infecting organisms and their antibiotic sensitivity.

PATIENTS AND METHODS

This discriptive study was carried out at the Surgical Unit-I of Jinnah Postgraduate Medical Centre (JPMC), Karachi, on 100 consecutive cases undergoing open or laparoscopic cholecystectomy from April 2001 to March 2002.

All the cases of symptomatic cholelithiasis operated by open or laparoscopic cholecystectomy were included in this study. Patients of cholelithiasis admitted in the ward with acute cholecystitis, history of jaundice, stones and/or dilated common bile duct were excluded from the study. After admission, a detailed history and clinical examination was done and investigations-complete blood picture, serum urea creatinine and electrolytes, liver function test were carried out. Blood sugar, chest X-ray and ECG were advised in selected patients. Ultrasound was the main tool for the diagnosis of stone disease.

Selection of the patients for the procedure was on clinical ground. Patients undergoing open and laparoscopic

Department of Surgery, Jinnah Postgraduate Medical Centre, Karachi.

Correspondence: Dr. Irfan Sattar, 209, DOHS-1, Malir Cantt., Karachi.
E-mail: irfansattar786@hotmail.com

Received May 19, 2005; accepted December 05, 2006.

cholecystectomy were assessed by the anaesthetist a day prior to surgery. Consent was taken from the patient after explaining the nature of procedure and potential for conversion of the laparoscopic approach to open cholecystectomy.

A dose of prophylactic antibiotic, injection Cefuroxime 1.5 gram (second generation cephalosporin) was administered in all cases at the time of induction and was continued for 24 hours postoperatively. Time lapse between specimen collection and antibiotic administration was 10 -15 minutes.

After opening the abdomen and confirming the diagnosis, bile was aspirated from the gallbladder at fundus in a five milliliter syringe. A pair of artery forceps was applied immediately to close the puncture site. In laparoscopic cases, bile was collected by using long spinal needles through the abdominal wall under direct vision through the telescope. All these specimens were immediately transported in a cooked meat culture medium to the department of microbiology. The specimens were cultured both aerobically and anaerobically.

Database was developed on Epi Info 6. For qualitative data, the chi-square test was used for comparison of various proportions. For the comparison of quantitative data, the mean of the value was tested by either student's t-test or F-test.

RESULTS

There were 100 patients including 73 females and 27 males in the ratio of 3:1. The ages of the patients ranged from 22 years to 72 years with a mean of 48 years. Forty-two (42%) patients were above the age of 50 years, 32% were 41-50 years old, 22% were 31- 40 years old and only 4 % of the patients were 30 years or below.

Abdominal pain was the major presenting feature which was located in the right hypochondrium, left hypochondrium and / or epigastrium in 97 cases. Three cases had no history of abdominal pain. Dyspepsia was the next common presenting symptom reported by 73 cases and 71 cases complained of nausea or vomiting.

Gallbladder was distended in 96 cases while 4 had contracted gallbladder. The wall of gallbladder was thick in 36 cases and normal in 64 cases. Seventy-nine cases had multiple stones and 21 had single stone in the gallbladder. Common bile duct was not dilated in any case, as cases with dilated common bile duct were excluded from the study. Liver parenchyma showed no change in 93 cases, while in 04 cases liver was enlarged and in 03 cases, it was cirrhotic. Out of 100 cases of cholelithiasis, 40 cases were treated by laparoscopic cholecystectomy and 60 cases by open cholecystectomy.

Thirty-six patients had positive bile culture. The frequency of organisms is shown in Table I.

All of these biliary organisms were found sensitive to cephalosporins, quinolones, gentamycin and penicillin group of antibiotics specially checked for 2nd generation cephalosporin (Cefuroxime).

Four patients developed wound infection (4%) on the 3rd postoperative day. Among them, 2 had a positive bile culture and were managed conservatively by regular dressings by pyodine solution and antibiotics.

Table I: Organisms found in positive bile culture and their sensitivity.

Organism	Frequency	Cefradine	Cefuro-xime	Ceftria-one	Ciproflo-xacine	Amoxi-cillin
E.coli	17	R	S	S	S	S
Klebsiella	9	S	S	S	S	S
Pseudomonas	6	R	S	S	R	S
Salmonella typhi	1	S	S	S	S	S
Staphylococcus aureus	2	S	S	S	S	S
Bacteroids fragalis	1	S	S	S	S	R

DISCUSSION

Cholecystitis and cholelithiasis are prevalent in certain regions of the world and quite rare at other places. Hence, these are sometimes called South Western American disease[1] and has been reported in 54% of the adults above 21 years of age.[4]

A bacterial cause of cholecystitis has been proposed and positive bile cultures have been noted in 46% of patients with acute cholecystitis. In one study from Germany, using molecular genetic methods, bacteria could be found in most pure cholesterol stones (i.e. those whose structure consists of more than 90% cholesterol).[5] It is suggested that bile infection by E. coli, in addition to bile stasis, plays a crucial role in the pathogenesis of brown pigment stones.[6] Bacterial DNA sequences are usually present in mixed cholesterol, brown pigment, and common bile duct, but rarely in pure cholesterol gallstones.[7] Interest has continued to abound in the role of infection in cholelithiasis. Two fallacies, however, exist in this regard. Firstly, the culture of the organism from the bile at the time of the operation does not necessarily indicate a cause-effect relationship between the infective microorganism and lithogenesis, as infection may be secondary to calculus formation. Secondly, the failure to isolate organism from bile also does not indicate that the etiology is unrelated to the infection as it is well-known that organisms which have initiated the stone precipitation may not persist in the viable form in the bile till surgery.

This study shows that this disease is much more common in females as compared to the males. The mean age incidence in this series is 48 years in females and 44 years in males. Iqbal et al. in 2001 reported maximum number of patients with cholelithiasis between the age of 20 – 30 years with the highest incidence of choledocholithiasis accompanying cholelithiasis in 61 – 75 years of age.[8]

In this series, the positive bile culture was 36%, which is considerably higher than that reported by Yaqin and Sultan.[9] However, more recently Sabir[12] has reported an incidence of 16%. Harbi[10] in 2001 reported 25% and Csendes reported 46%.[11] Van Leeuwen from Kuwait showed positive bile cultures in 16.4% and 19 different bacterial species were identified.[13] Guo from China showed the incidence of bacteria to be very high, ranging from 20 to 96%, with an average of 66.7% depending on the kind of gallstone present.[14] Therefore, infection is likely to range from 16 to 96 % which corroborates with the present finding.

Escheria coli was found to be the commonest organism in this study as has already been reported by previous studies. However, Klebsiella pneumonae is repoted by Sabir.[12] In one of the Saudi study, the most common organism isolated were E.coli (28.1%), Enterococcus faecalis (15.6%) and Pseudomonas aeruginosa (9.4%).[10] An Indian study showed E. coli (45.07%) and Klebsiella (25.35%) as predominant among the aerobes and Bacteroids fragilis (58.82%) among the anaerobes.[15] Another study from Ghana found that the commonest organisms were E.coli (28.2%), Klebsiella (17.9%), Pseudomonas (10.2%) and Salmonella typhi in (7.7%).[16]

The importance of the predominance of E. coli is seen by the fact that older studies have shown glucuronidase enzymatic activity of E. coli to have a role to play in calcium bilirubinate gall stone formation.The other organisms found in our study were Klebsiella pneumonae, Pseudomonas, Salmonella typhi, Staphylococcus aureus and Bacteroids fragalis. These are quite consistent with other series as Ohdan et al. showed E.coli, Klebsiella and Enterococcus.[17]

The frequency of postoperative wound infection in this series of 4% was considerably lower than that reported in a similar study by Durani et al. (8.75 %).[18] Van Leeuwen reported wound wound infection rate in 9% of the patients.[13] The patients in this series who developed wound infection had negative bile cultures in 2 and positive in 2 patients. However, the infection could have been due to bile or exogenous organisms.

The low frequency of wound infection in this series may be due to the fact that all the patients were operated electively and had perioperative prophylactic course of antibiotics. According to Gondret, a single injection of antibiotic given one hour before incision is as effective as multiple dose regimens.[19]

All the isolated organisms in this series were highly sensitive to the cephalosporins, quinolones and gentamycin, specially the 2nd generation cephalosporins. For gallstone diseases, ampicillin in combination with sulbactam and amino-glycoside is still a suggestive empirical therapy.[20]

In case of cholecystitis and cholelithiasis, antibiotics can be started subsequently if the clinical situation or the culture reports warrant. Routine culture of all bile samples is, however, desirable.

The limitations of this study were that antibiotic was injected intravenously, about 10 – 15 minutes before the bile sample was collected, therefore, it may be argued that the bile sample could have some quantity of the antibiotic. The pus from the wound was minimal, therefore, role of bile bacteria in wound infection cannot be concluded.

There was no control group to compare the exact effect of antibiotic prophylaxis on postoperative infection, which could have been achieved with a no antibiotic group.

Conclusion

The frequency of bile infection in this series was 36%, commonest organisms being E. coli. and Klebsiella. Wound infection, 4%, could have been due to endo or exogenous contamination. Most of the organisms were sensitive to 2nd generation cephalosporins. Bile infection did not increase the risk of infection when prophylactic antibiotics were given.

References

1. Biliary tract. In: Kirk RM. General surgical operations. 3rd ed. London: Churchrill Livingstone, 1994: 319.
2. Crawford JM. The liver and biliary tract. In: Robbins pathological basis of disease. 5th ed. Philadelphia: W.B. Saunders 1994; 831-96.
3. Cuschieri A, Bouchier IAD. The biliary tract. In: Cuschieri A, Giles GR, Moosa AR, (edi). Essential surgical practice. 2nd ed. Edinburgh: Butterworth-Heienemann, 1988: 1020-75.
4. Ananth K, Kapur BML. Chronic cholecystitis and biliary infection. Ind J Surg 1983.
5. Swidsinski A, Lee SP. The role of bacteria in gallstone pathogenesis. Front Biosci 2001; **6** : E93 – 103.
6. Cetta FM. Bile infection documented as initial event in the pathogenesis of brown pigment biliary stones. Hepatology 1986; **6**: 482 – 9.
7. Lee DK, Tarr PI, Lee SP. Bacterial DNA in mixed cholesterol gallstones. Am J Gastroenterol 1999; **94**: 3502-6.
8. Iqbal P, Sial K, Sial E. Gallstone diseases: an experience at Civil Hospital, Karachi. Med Channel 2001; **7(2):** 17 – 20.
9. Yaqin H, Sultan G. Results of culture of gallbladder, bile and gall-stones. J Pak Med Assoc 1978; **28**: 31-2.
10. Al Harbi M, Osoba AO, Mowallid A, Al-Ahmadi K.Tract microflora in Saudi patients with cholelithiasis. Trop Med Int Health 2001; **6**: 570-4.
11. Csendes A, Burdiles P, Maluenda F, Diaz JC, Cseudes P, Mitru N. Simultaneous bacteriological assessment of bile from gallbladder and common bile duct in control subjects and patients with gallstones and common duct stones. Arch Surg 1996; **131**: 389-94.
12. Sabir O. Infected bile in gallbladder in cholelithiasis (dissertation). Karachi: College of Physicians and Surgeon Pakistan 1998.
13. van Leeuwen PA, Keeman JN, Butzelaar RM, Van den Bogaard AE. Correlation between a positive gallbladder culture and subsequent wound infection after biliary surgery: a retrospective study of 840 patients. Neth J Surg 1985; **37**: 179-82.
14. Guo RX, He SG, Shen K. The bacteriology of cholelithiasis – China versus Japan. Japan J Surg 1991; **21**: 606-12.
15. Ballal M. Bacteriological spectrum of cholecystitis and its antibiogram. Indian J Med Microbiol 2001; **19**: 212 -4.
16. Darko R, Archampong EQ. The microflora of bile in Ghanians. West Afr J Med 1994; **13**: 113-5.
17. Ohdan H, Oshiro H, Yamamoto Y, Tanaka I, Inagaki K, Sumimoto K, et al. Bacteriological investigation of bile in patients with cholelithiasis. Japan: Surg Today 1993; **23**: 390-5.
18. Durani MAK. Biliary infection and gall stone diseases (dissertation). Karachi: College of Physicains and Surgeons Pakistan, 1996.
19. Gondret R,Viallard ML, Huguier M. Antibiotic prophylaxis in biliary surgery. Paris: Ann Chir 1995; **49**: 493-9.
20. Chang WT, Lee KT, Wang SR, Chuang SC, Kuo KK, Chen JS, et al. Bacteriology and antimicrobial susceptibility in biliary tract diseases: an audit of 10 years experience. Kaohsiung: J Med Sci 2002: **18**: 221-8.