East and Central African Journal of Surgery Volume 15 Number 2. July/August 2010.

Association between Intraoperative Bactibilia and Postoperative Septic Complications in Biliary Tract Surgery.

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Background: The present study intended to clarify the role of biliary bacteria in the development of postoperative septic complications in patients undergoing biliary operations and need for antibiotic prophylaxis.
Patient and methods: A total of 121 patients with various biliary tract diseases underwent various surgical interventions. The relation between contaminated ductal bile and postoperative septic complications was analyzed prospectively.
Results: 42/121 patients were bile culture positive (B+) while 79/121 patients were bile culture negative (B-).14 patients in B (+) group developed septic complications compared to only 3 patients in B (-) group (P = 0.0001). In B (+) group, bacteria found in ductal bile were also detected in infected sites of 85% of patients with septic complications. In B (+) group postoperative antibiotic modification significantly (p=0.001) reduced infectious complications.
Conclusion: Infected bile plays a critical role in development of post operative septic complications. Hence patients with risk factors for bactibilia should receive prophylactic antibiotics covering endogenous gram negative organisms which should be modified in postoperative phase according to the results of sensitivity. However this issue requires further investigations by studies conducted on similar lines.

Introduction

Benign disease of the biliary tract is one of the most common indications for major abdominal surgery in India, particularly in the northern part of the country. Bactibilia has long been known to be associated with biliary tract diseases and culturable bacteria in bile can represent a state of asymptomatic bactibilia which can disseminate after any intervention causing infective complications [1]. Various risk factors for the presence of bactibilia like age>65 years, recent acute cholecystitis, recent acute pancreatitis, cholangitis, jaundice, and choledocholithiasis have been well established [2,3].Septic complications have been established to play an increasingly important role in the morbidity and mortality of biliary tract diseases and biliary surgery, and despite advances in the antibiotic therapy such complications still continue to be a problem in biliary surgery [2,4,5]. There has been a considerable debate on the use of antibiotics in biliary surgery with some favoring antibiotic prophylaxis in open biliary surgery while others disapproving the need for routine antibiotic prophylaxis in elective cholecystectomy [6,7,8]. But all of these studies included patients undergoing cholecystectomy alone and there is dearth of data regarding the need for antibiotics in open and complex biliary operations . In order to associate high incidence of septic complications in biliary surgery to culturable bacteria in bile, it needs to be proven that same organisms are cultured from the infected source, in case a postoperative septic

complication occurs. So the aim of our study was to find a relation between postoperative septic complications and culturable bacteria in bile and to assess the need for antibiotic prophylaxis. The present study further explored, is it worthwhile to prolong and tailor antibiotic prophylaxis in the postoperative period as per the results of culture sensitivity patterns of organisms present in ductal bile.

Patients and Methods

This prospective study included 121 consecutive patients who underwent various biliary operations in the department of surgery of a tertiary hospital over a period of one year. Following groups of patients were included in the study: Recent acute cholecystitis (21), recent acute pancreatitis (3), obstructive biliopathy due to carcinoma or stones (12), cholelithiasis (71), CBD stones without jaundice (10) and cholangitis (4). Details of age, history, radiology, operation and postoperative course were noted in SPSS version 14 database . Patients were included in the study after obtaining an informed consent. All patients received a single preoperative shot of cefazolin at induction of anesthesia as per the previously established protocols.

Surgical procedures

The surgical procedures performed are shown in Figure 1.

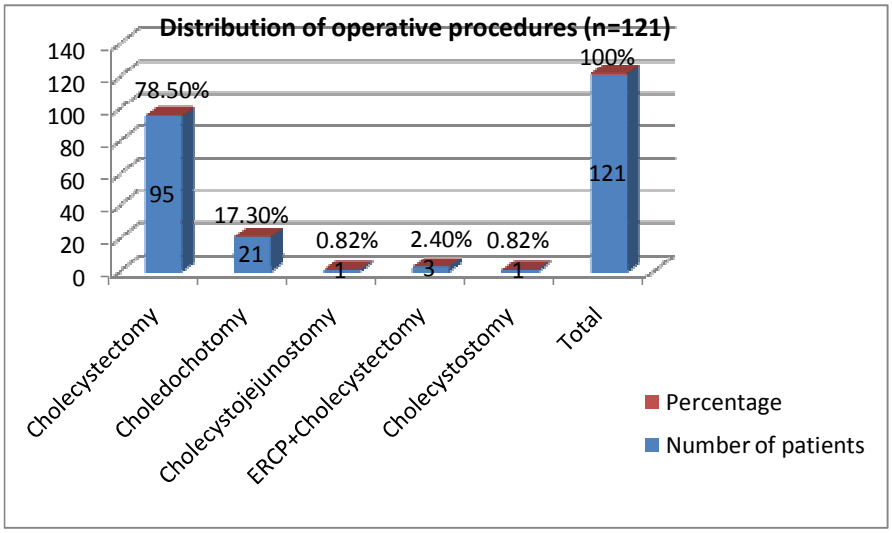

Figure 4. Operative Procedures Performed

Bile cultures

At operation about 3-5ml of bile was harvested and transported immediately to lab for testing. Patients were were stratified in to bile culture positive (B+) and bile culture negative (B -) groups according to the presence and absence of culturable bacteria in bile. Both groups were analyzed for the absence or presence of risk factors for bactibilia including age>65 years, recent acute cholecystitis, recent acute pancreatitis, jaundice, CBD stones without jaundice and cholangitis. B (+) patients were randomly selected to receive or not to receive postoperative therapeutic antibiotics as dictated by the results of culture sensitivity.

Postoperative complications
Infectious complications were demonstrated by positive site specific cultures and need for antibiotic therapy. Samples were taken for culture in each complication and compared to intraoperative culture sensitivity of bile. Postoperative complications in B+ group were compared with B- group and inferences were drawn.

Statistical analysis:
Statistical analysis of qualitative variables was performed using the $\chi 2$ test and analysis of quantitative variables was performed using unpaired t test and statistical significance was taken at 5% level.

Results

There were121 biliary operations performed. 42 patients were B(+) while 79 patients were (B-). The characteristics of these two groups are shown in the following table (Table I). Greater number of patients in B+ group had acute presentations. The analysis of prevalence of the risk factors for bactibilia is shown in Table 2. B+ group had 14(33.3%) infective complications with wound infection being the most common complication while B- group had 3(3.7%) wound infections only ($p<0.0001$) as summarized in the following Table 3.

As per the study protocol patients in B+ group were randomly selected to receive or not to receive postoperative antibiotics. Hence antibiotics in 17 patients in B (+) group were modified as dictated by culture sensitivity, where as in 25 patients they were not modified.

Table 1. Patient Characteristics (n=121).

Patient characteristic	Bile culture(+)	Bile culture (-)	P value
Age(Mean±SD)	65±3.6	55.5±10.2	0.0001*
Sex(M/F)	28/14	30/49	0.003*
Diagnosis			
Chronic cholecystitis	14	57	0.0001*
Recent acute Cholecystitis	10	11	0.20
Recent acute pancreatitis	1	2	1.00
Jaundice	8	4	0.02*
CBD stones, no jaundice	6	4	0.09
Cholangitis	3	1	0.11
Operative procedures			
Cholecystectomy	24	71	0.0001*
Choledochotomy	14	7	0.27
Cholecystojejunostomy	1	0	0.34
ERCP+Cholecystectomy	3	0	0.03*
Cholecystostomy	0	1	1.00

*$p<0.05$ by unpaired t test

Table 2. Prevalence of risk factors for bactibilia

Parameter	Bile culture+(n =42)	Bile culture-(n=79)	P value
Age>65 years	7(16.6%)	4(5.0%)	0.04*
Recent acute cholecystitis	10(23.8%)	11(13.9%)	0.20
Recent acute pancreatitis	1(2.3%)	2(2.5%)	1.00
Jaundice	8(19.0%)	4(5.0%)	0.02*
CBD stones, no jaundice	6(14.2%)	4(5.0%)	0.09
Cholangitis	3(7.1%)	1(1.2%)	0.11
Total proportion with risk factors for bactibilia	35(83.3%)	26(32.9%)	0.0001*

*p≤0.05 statistically significant by $\chi 2$ test

Table 3. Septic complications as per bile cultures

Parameter	Bile culture +(n=42)	Bile culture – (n=79)	P value
Wound infection	9	3	0.001*
Intra-abdominal abscess	1	0	0.34
Bacteremia	1	0	0.34
Septicemia	2	0	0.11
UTI	1	0	0.34
Total	14(33.3%)	3(3.7%)	0.0001*

P=0.0001 by $\chi 2$ test

Table 4. Antibiotic versus no antibiotic modification arms in B (+) group

Parameter	Antibiotic modification	No antibiotic modification
No. of patients	17(40.4%)	25(59.6%)
Wound infection	1	8
Intra-abdominal abscess	0	1
Septicemia	0	2
Bacteremia	0	1
UTI	0	1
Total	1(2.3%)	13(30.9%)*

*p=0.001 by $\chi 2$ test

In the antibiotic modification arm only one wound infection was seen, where as in no antibiotic modification arm, 13 septic complications (p=0.001) occurred as shown in Table 4.

Table 5. Septic Complication Related to Type of Operation

Operation	Number of patients/Bile culture(+)	Septic complication/no. of pts.
Cholecystectomy(open)	35 / (8)	Wound infection 4
Cholecystectomy(Laparos)	60/ (12)	UTI 1,
Choledochotomy	21/ (18)	Wound infection 4, Intra-abdominal abscess 1, septicemia 1
Cholecystojejunostomy	1/ (1)	Septicemia 1
Cholecystostomy	1/ (1)	Bacteremia 1
ERCP+Open cholecystectomy	3/(2)	Wound infection 1

Table 6. Correlation between intraoperative bile culture and organism recovered in case of infective complication

		Bile culture + (n=42)		
Complications	**No. of patients**	**Intraoperative bile cultures/no. of patients**	**Postoperative culture source**	**Complicating organism/no. of patients**
Wound infection	9	E coli/7 Proteus/2	Wound swab	Ecoli/6 Staphylococcus/1 Proteus/1 Staphylococcus/1
Intra-abdominal abscess	1	E coli/1	Pus	Ecoli/1
Septicemia	2	Ecoli/1	Blood	Ecoli/1
		Klebsiella/1		Klebsiella/1
Bacteremia	1	Ecoli/1	Blood	Ecoli/1
UTI	1	Ecoli/1	Urine	Ecoli/1
		Bile culture – (n=79)		
Wound infection	3	Negative	Wound swab	Staphylococcus/3

In order to find the influence of severity of operative trauma on septic complication in wake of positive bile culture, a note was taken of different septic complications in different operative procedures in presence of bactibilia. In laparoscopic cholecystectomy group (n=60), 12 patients were bile culture positive and only 1 patient developed urinary tract infection. While patients who underwent open cholecystectomy (n=35), 8 were bile culture positive and 4 developed infective complications. Similarly in all other operative groups the severity of operative trauma correlated with occurrence of postoperative infective complications. These observations are tabulated in Table 5.

The organism obtained on culture in case of a postoperative septic complication was compared with the organism obtained during intraoperative bile culture. Overall in B (+) group 9 wound infections occurred. 6/9 were caused Ecoli, 1 by Proteus and remaining 2 by staphylococcus. In 7/9wound infections the complicating organism from wound swab culture and organism grown on bile culture displayed same colony, sensitivity and resistance

patterns. In all other infective complications specimen culture grew the organisms similar to that grown on intraoperative bile culture. Thus the organism grown from septic source correlated with the organisms grown on intraoperative bile culture in 85% of cases. These results are shown in Table 6.

Discussion

In the present study the bile of 121 consecutive patients undergoing various biliary procedures was examined for the presence of bactibilia and the patients were followed for the development of septic complications in the postoperative course. Certain preoperative risk factors were identified to be associated with the possibility of having positive bile cultures viz: age>65 years, recent acute cholecystitis, recent acute pancreatitis, jaundice, choledocholithiasis and cholangitis. Similar risk factors have been confirmed by previous studies [3,9,15]. In the present study the preoperative risk factors predictive of bactibilia were present in 35/42(83.3%) (B+) patients, whereas only 26/79 (32.9%) B- patients had presence of such risk factors. This difference could be explained by the greater proportion of patients with complicated gall bladder disease in B (+) group compared to B (-) group. Moreover the absence of culturable bacteria in bile in many patients in B (-) group who otherwise had risk factors predictive of bactibilia could be explained by frequent antibiotic courses which these patients had received during the course of their illness. As the presence of these risk factors correlates with the incidence of positive bile cultures, it would be worthwhile to categorize the patients with such risk factors as high risk, and subject such patients to routine bile cultures. This finding is in accordance with published study by Morris et al[9], who found one of the risk factor to be present in 19 out of 20 patients with bactibilia. Though it has been established through various studies that bile is colonized in biliary diseases and high incidence of septic morbidity has been identified in such patients[2,10]. On the other hand patients with out biliary disease have been found to have sterile bile. A study by Csendes et al[11] compared the prevalence of bactibilia in normal controls (gastric ulcer surgery) to patients undergoing cholecystectomy for acute and chronic cholecystitis. They found that all controls had sterile bile while those with acute and chronic cholecystitis had positive cultures in 47% and 30% of cases, respectively.

In the present study antibiotics were administered following induction of anaesthesia in all cases, in accordance with published recommendations [12]. It may be argued that administration of antibiotics may have adversely biased the positive culture rates of the bile. A study by the Pitt et al showed that antibiotic therapy does not sterilize bile, but merely altered biliary bacteriology [13]. So it seems highly unlikely that a single dose of an antibiotic would have rendered bile sterile. Another consideration is that the antibiotics may have influenced the incidence of postoperative infections. As Cephazolin was used which has good activity against gram positive organisms and extremely poor gram negative spectrum, it is conceivable that the effect would have been comparable for the two groups. So in present study effect of Cephazolin on endogenous biliary organisms was considered to be minimal based on predominant gram positive spectrum of this antibiotic. A further support for inability of preoperative antibiotics to completely prevent septic complications of biliary surgery comes from the study of Harling et al, where the authors found that septic sequelae of uncomplicated laparoscopic cholecystectomy were not entirely prevented by antibiotic or mechanical prophylaxis[14].

In the present study septic morbidity occurred in 14/42 (33.3%) B +ve patients with wound infection dominating (9/14) the group. Whereas only 3/79 (3.7%) B -ve patients got wound infections. These findings are in close agreement to the host of previous studies. Nomura T et al in their series found septic complications in 42% patients, with higher number of complications in patients with contaminated bile[4]. Cainzos et al had septic complications in 42% of patients in their series[5]. Dellikaris et al in their study during 174 operations on extrabiliary tree found 26% patients to be bile culture positive and septic complications occurred in 33.3% patients. Wells GR in their series had septic complications in 22% patients with positive bile culture while the incidence was only 2% in culture negative patients.

In order to find the need for therapeutic antibiotics in bile culture positive patients, as per the study protocol, antibiotic modification as dictated by the result of culture sensitivity was done in 17 B+ patients, while no antibiotics were given in rest of the B+ patients (n=25). Only 1 infection was observed in the former group whereas 13 infections occurred in the latter group. In B (-) group 3 wound infection occurred, 1in cholecystectomy and 2 in choledochotomy patients. Furthermore in B+ve group, the organisms causing the postoperative septic complications were the similar to the organisms grown from the bile culture in 85% of patients. The similarity was known from their colony characteristic and sensitivity patterns. Only 2 wound infections in this group were caused by staphylococcus which was presumably an exogenous organism, as E coli and Proteus were grown on bile culture. In B -ve patients all the three infections were caused by Staphylococcus. Based on this observation it could be argued that septic morbidity in biliary surgery is due to endogenous organisms. Our observation is supported by several previous studies[16,17,18].

Wound infections in culture negative group could be explained on the basis of expected range of operating room contamination or colonization by skin commensals. A further proof in support of this observation comes from a study by Hambraeus et al where patients with and without bactibilia developed wound infections at the rate of at 12.8% versus 3.2%, respectively. In bile culture negative patients S. aureus was the predominant bacteria responsible for causing wound infections[19]. On the contrary occurrence of large number of septic complications in culture positive group could be explained by the spillage occurring during the procedures or dissemination of bacteria occurring through the blood stream secondary to manipulation of biliary tract which is already harboring bacteria[4,16]. In choledochotomy bile invariably spills in peritoneal cavity. Thus it seems likely that direct spread is an important factor in septic complications.

Despite prophylactic antibiotics, bile colonization remains the major factor associated with postoperative sepsis. Scottish Intercollegiate Guidelines Network (SIGN) recommended that antibiotics should not be prescribed, still most patients undergoing laparoscopic cholecystectomy receive a single dose of prophylactic antibiotics on induction of anesthesia [20].This advice is contrary to that given by Meijer and colleagues in a meta-analysis of trials of antibiotic prophylaxis in open biliary tract surgery. From the results of 42 trials looking at the effects of antibiotic prophylaxis in the prevention of wound infection, they suggested that there was an overall 9% benefit in favor of antibiotic prophylaxis. When high-risk patients were analyzed as a subgroup, the benefit of prophylaxis was greater. This paper concluded that antibiotic prophylaxis should be administered[8]. As all of these studies concentrated on cholecystectomy, the present study further explored the role of antibiotics in patients undergoing complex biliary operations.

The findings of the present study support the use of postoperative antibiotics in B+ve patients till the results of culture become available, as it helped to remarkably reduce the incidence of septic complications, as only 1 septic complication occurred B+ve patients who received postoperative antibiotics. The present study had some limitations which could have had an impact on the results. The number of patients included in the study was small. Secondly it involved a biliary case mix. Thirdly both laparoscopic and open biliary operations were included while computing results. Fourthly it did not look at the optimal duration for which antibiotics should be continued in postoperative period. And lastly preoperative antibiotics were routinely given in all the patients. So a study which takes in to account all these limiting factors needs to be designed to explore this topic further.

Taken all evidence together it could be argued that infected ductal bile plays a critical role in postoperative septic complications in biliary surgery. Routine intraoperative bile cultures should be done only in patients with high risk for bactibilia and preoperative antibiotics covering endogenous organisms should be given in such patients which should be modified postoperatively according to the results of culture sensitivity. While patients in absence of these risk factors justify a single preoperative dose of antibiotic covering exogenous gram positive organisms only.

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