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ORIGINAL ARTICLE

ANTIBIOTIC PROPHYLAXIS IN ELECTIVE LAPAROSCOPIC CHOLECYSTECTOMY: A PROSPECTIVE STUDY

By
Sabry A. Mahmoud, Wael W. Khafagy, Waleed Omar, Samir Atia, Nariman M. El-Nashar*
General Surgery Departement, *Microbiology Departement, Mansoura University Hospital, Mansoura, Egypt.

Aim: ***Laparoscopic cholecystectomy gives rise to a very complicated issue concerning the use of antimicrobial prophylaxis. The role of antibiotic prophylaxis in elective laparoscopic cholecystectomy and the relation between post-operative septic complication and bile microbiology will be assessed in this study.***
Patients and methods: ***64 patients were included in the study and divided into two groups; group A: (29 patients) received antibiotic prophylaxis (cefotaxime) and group B (35 patients) received 100ml isotonic saline (placebo). Bile sampling and culture was taken for all cases and the patients were followed up for incidence of sepsis where the wounds were swapped and cultured.***
Results: ***Bile sampling and culture revealed no growth in 41 cases (64.1%) (19 in group A and 22 in group B). Postoperative infection developed in two cases of group A and in three cases of group B. Incidence of wound infection was significantly related to incidence of GB perforation ($p < 0.0001$). Swabbing of infected wounds and collections revealed infecting organisms other than that detected in bile culture except in one case of group B.***
Conclusion: ***There is no relation between bile microbiology and postoperative infection, so, antibiotic prophylaxis is to be used in high-risk patients and in patients suspected to have difficult operation and GB perforation.***
Keyword: *Surgical prophylaxis, Laparoscopy, Biliary microbiology*

INTRODUCTION

Bacterial infection has been considered a primary factor, not only in the pathogenesis of brown stones, but also in the formation of black pigment stones.(1) Although bile is usually sterile, bacteria isolated from intraoperative bile culture was 25%, 66%, 67% and 9% for gall bladder (GB) stones, common bile duct (CBD) stones, intrahepatic duct (IHD) stones and biliary malignancy, respectively.(2)

The bacteria isolated from bile in all disease states of the biliary tract are primarily gram-negative enteric coliforms. Escherichia coli (E.coli) alone or mixed with another organism is present in 50% of the positive cultures.(3) Other coliforms e.g. klebsiella, enterobacter and proteus are less commonly isolated. Streptococcus faecalis (enterococcus) is an aerobic gram-positive coccus that is also frequently isolated. Anaerobic microorganisms are isolated in less than 10% of the cases, clostridium perfrgens being the most common.(2) This profile of biliary bacteria, with predominance of aerobic organisms, is consistent with an ascending rout of infection from the small intestine.(4)

Elective laparoscopic cholecystectomy (LC) has a low risk for infective complications. The incidence of surgical infections after LC is reported to be less than 2%, because of the minimal trauma due to this approach. The umbilicus is the preferred site of infection in obese patients after the laparoscopic procedure.(5) The need to administer antibiotic prophylaxis during LC is still a matter of significant controversy.(6)

The aim of the study is to evaluate the role of antibiotic prophylaxis in elective laparoscopic cholecystectomy and the relation between post-operative septic complication and bile microbiology.

PATIENTS AND METHODS

This study was conducted between May 2002 and April 2004 in General Surgery Departement, Mansoura University Hospital. Sixty-four patients with chronic calcular cholecystitis were included in this study; they were 53 females and 11 males.

The following patients were excluded from the study: patients who administered antibiotics one week before operation, patients with acute cholecystitis within 6 months, diabetic patients, patients on regular corticosteroids, patients with elevated liver enzymes twice the reference level, patients who were treated with ERCP, above 60 years and failed laparoscopy.

Preoperative abdominal ultrasonography stressed on GB regarding wall thickness, stones (size and number), contents (mud, mucocele …etc) and state of biliary tree. Preoperative upper GIT endoscopy was done to exclude peptic ulcer and hiatus hernia. Preoperative informed consent was taken.

The patients were randomly divided into two groups: **Group A:** included 29 patients, they received cefotaxim (2gms) in 100ml saline 30 minutes before induction of anaesthesia. Cefotaxime (3rd generation cephalosporin) was used as it is effective against most of Gram negative organisms, safe in hepatic patients and excreted via the kidney.

Group B: composed of 35 patients who received 100ml isotonic saline before induction of anaesthesia (placebo).

LC was performed under strict aseptic precaution where bile sampling (5 cc) was done before GB retrieval using sterile syringe. The samples were put in a labelled, sterile test tube, secured and sent immediately to the laboratory in Microbiology Department. No transport media was used.

Bile samples were cultured aerobically (on blood agar and MacConky agar and incubated at 37^{o}C for 48 hours) and anaerobically (on prereduced Columbia blood agar supplemented with vit. K). The obtained growth was examined for colonial characters, biochemical reactions, sensitivity test and Gram stain.

Postoperatively, the patients were examined for output of drains, fever and incidence of wound sepsis. After discharge the patients were followed up twice per week for one month and the followings were recorded; fever, wound infection and follow up US for febrile patients. Infection was classified according to the site into superficial (skin and subcutaneous tissue) and deep seated (intraperitoneal) infection.

Swabs were taken from septic wounds and also from any abdominal collection and cultured. The organisms were identified and antibiotic sensitivity was done. Organisms isolated from bile were compared to those causing wound sepsis to identify the exact source of infection (endogenous via bile or exogenous {i.e. hospital acquired}).

Statistical methods: Findings were calculated as numbers, simple percentages and mean ± standard deviation. Statistical analysis was done using Chi-square test and student t test.

RESULTS

Patients' mean age was 39 ± 2.4 years in group A and 40 ± 2.2 years in group B. Female patients represented most of patients in both groups (82.8% in group A and 82.9% in group B). Symptomatic patients represented 86.2% of group A and 85.7% of group B. Body mass index (BMI), Hb% and serum albumin were compatible in both groups. Abdominal ultrasonography discovered asymptomatic cases and also gave data about wall thickness of the gall bladder and number of stones inside; single or multiple Table 1.

Operative time ranged from 25 - 65 minutes in group A and 25 – 75 minutes in group B but mean operation time was compatible in both groups ($p = 0.91$) Table 1.

Operative and post operative complications included GB perforation (3 patients) (10.9%), fever noticed in 5 cases (20.3%) and intraperitoneal collection was detected in 2 patients (6.25%). Frank wound infection occurred in 5 patients (7.8%) (2 in group A [6.9%] and 3 in group B [8.6%]). A patient in group B developed infection on top of collection associated with wound infection Table 2.

Bile microbiology revealed positive culture in 23 patients (35.9%) (10 in group A [34.5%] and 13 in group B [37.1%]). Of these positive cultures, 11 specimens (47.8%) showed E.coli, the rest of specimens showed other coliforms and gram positive cocci Table 3.

No significant difference was observed as regard incidence of infection in both groups ($P= 0.47$ in wound infection and 0.55 in collection) Table 3. Staphylococcus aureus (staph. aureus) was the commonest organism isolated from infected wounds (2 cases). Other organisms include E. coli, proteus and enterococcus Table 4.

Incidence of wound infection (2 patients in group A and 3 patients in group B) was highly significant related to incidence of GB perforation ($p < 0.0001$) as patients with wound infection had intraoperative GB perforation Table 5.

The organisms isolated from infected wound cultures were different from that isolated from bile except for one case where the infecting strain was the same as in bile culture and the infection was on top of collection and in port-site wounds. In this patient, the operation time was long with ruptured GB and lost stones in peritoneal cavity.

Table 1. Clinical, radiological, laboratory and operative data of all patients (n = 64).

		Group A (n = 29)	Group B (n = 35)	X2*, t**	P
Age:	Mean ± SD	39 ± 2.4	40 ± 2.2	-1.43 (**)	0.32
	Range	23 – 60	24 – 60		
Gender:	Males	5 (17.2%)	6 (17.1%)	0.00 (*)	0.99
	Females	24 (82.8%)	29 (82.9%)		
BMI:	Mean ± SD	26.3 ± 1.6	26.1 ± 1.8	-0.106 (**)	0.99
	Range	23.9 – 28.2	24.6 – 28.1		
C/O:	Symptomatic	25 (86.2%)	30 (85.7%)	0.003 (*)	0.96
	Asymptomatic	4 (13.8%)	5 (14.3%)		
U/S:	Single stone	6 (20.7%)	8 (22.9%)		
	Multiple stones	23 (79.3%)	27 (77.1%)	0.044 (*)	0.84
	Thick walled	25 (86.2%)	30 (85.7%)		
Hb (gm%)	Mean ± SD	11.4 ± 1.08	11.4 ± 1.10	-0.731 (**)	0.47
	Range	10.5 – 13.5	10.6 – 13.9		
Albumin (gm%)	Mean ± SD	3.8 ± 0.466	3.71 ± 0.38	-0.112 (**)	0.97
	Range	3.3 – 4.70	3.2 – 4.20		
Op. time (min)	Mean ± SD	40 ± 5	41 ± 8	-1.14 (**)	0.91
	Range	25 – 65	25 – 75		

(*) Chi-square test (**) Student t test

Table 2. Operative & postoperative complications in both groups (all patients).

	Group A (n = 29)		Group B (n = 35)		Total (n = 64)		Chi-square	
	No	%	No	%	No	%	X2	p
GB perforation	3	10.3	4	11.45	7	10.9	0.019	0.61
Fever	5	17.2	8	22.9	13	20.3	0.309	0.41
Collection	2	6.9	2	5.7	4	6.25	0.038	0.62
Wound infection	2	6.9	3	8.6	5	7.8	0.60	0.44
Infected collection	0	00	1	2.9	1	1.6	0.842	0.55

Chi-square test

Table 3. Isolated organisms from positive bile culture of both groups (23 patients).

	Group A (n = 10)		Group B (n = 13)		Total (n = 23)		Chi-square	
	No	**%**	**No**	**%**	**No**	**%**	**X2**	**p**
E. coli	5	50.0	6	46.2	11	47.8	0.034	0.59
Enterococci	2	20.0	2	15.4	4	17.4	0.084	0.6
Proteus	1	10.0	2	15.4	3	13.0	0.144	0.6
Enterobacter	1	10.0	2	15.4	3	13.0	0.144	0.6
Klebsiella	1	10.0	1	7.7	2	8.7	0.005	0.74
Total	10	100.0	13	100.0	23	100.0	0.049	0.52

Chi-square test

Table 4. Relation between bile culture and wound infection.

Organisms	Group A (n = 29)		Group B (n = 35)		Total (n = 64)	
	Bile	**Wound**	**Bile**	**Wounds & Collection**	**Bile**	**Wounds & collections**
E. coli	5	---	6	1	11	1
Enterococci	2	---	2	1	4	1
Proteus	1	1	2	--	3	1
Enterobacter	1	--	2	---	3	0
Klebsiella	1	---	1	---	2	0
Staph. Aureus	---	1	---	1	0	2
Total	10	2	13	3	23	5

Table 5. Gall bladder perforation and its relation to incidence of infection.

	Perforation (n = 64)		Chi-square	
	Yes	NO	X2	P
Infection	5	0	31.42	< 0.0001
No infection	2	57		
Total	7	57		

Chi-square test

DISCUSSION

The use of prophylactic antibiotics for LC is inconsistent and varies widely among surgeons.[7]

Asymptomatic gall stones represented 14% of all patients. In literatures, 10-15% of all gallstone patients develop complications so that a prophylactic cholecystectomy is advisable as acute cholecystitis as well as common bile duct stones occur significantly more often with increasing duration of the gallstone disease.[8]

LC was done for all patients. Mean operative time was matched in both groups (P = 0.91), but the range was higher in group B (25 – 75 min) as there was difficulty in dissection and GB retrieval with spill over of bile and stones in two cases. Iatrogenic GB perforation and spillage of bile and gall stones is not uncommon during LC. In a literature, there was statistical difference in mean time of operation with GB perforation.[9] GB perforation occurred in 10.9% of all cases which is an accepted rate where it ranged from 11.6%[9] to 14%.[10] Mean operative time and incidence of GB perforation tend to diminish as the surgeon gains experience.[9]

Postoperative wound infection occurred in both groups (6.9% in group A and 8.6% in group B). The results are matched with many reports (7.9%,[11] 5.3%[12]) but higher than that of others [2% in group A and 2.5% in group B](7)). The cumulative infection rate was 2.8% in prophylaxis group and 4.4% in placebo group.[6] Every effort should be made to find and remove gall stones lost in the abdominal cavity to prevent complications.[13]

Bile culture revealed no significant difference between both groups (P = 0.6). The overall positive rate of bile culture matched with published data (31%[14] and 36%[3]).

The commonest organism isolated from bile culture was E. coli (47.8% of positive cultures) which is similar to other study (4) where they reported that E. coli alone or mixed with another organism is present in 50% of the positive cultures. In another study, E. coli was the commonest pathogen (36%), followed by Klebsiella (15%), Enterococcus (6%), Staphylococcus (3%), Streptococcus (2%). Bacteroides (5%) and Clostridium (3%). Polymicrobial infection was encountered in 19% and 31% of patients with GB and CBD stones.[3]

Intraperitoneal collection occurred in 4 cases (6.25%) (2 in group A and 2 in group B). Infected collection occurred in only one case in placebo group representing 2.9% (1.6% of both groups). Our results are similar to a published report (2-3%)[15] but higher than another report where intraabdominal purulent complication after LC was 0.71%.[16]

The commonest pathogen detected in infected wound swabs was staph. aureus and represented 40% of all infected cases (3.2% of all patients). Colliza et al[5] found staph. aureus wound infection to be 0.92% following LC in spite of antibiotic therapy. In a literature, surgical site infection rate was 3.03% in clean surgeries; the most common isolate was staph. aureus (35.3%), infection rate increased with longer preoperative hospital stay and with increase in duration of surgery.[17] This fact denotes that patients acquire infection from an external source (theatre, instruments, ward or staff) inside the hospital rather than an endogenous focus.

E. coli was detected in only one case on top of intraperitoneal collection. This is the only case showing the same organism in bile culture and infected wounds. This patient had long operation time, difficult dissection, perforation of GB and spill over of bile and numerous stones, some of them were not retrieved. This event does not cause complications if adequate prophylactic antibiotic therapy is administered; spilled stones are retrieved whenever possible, and the abdominal cavity is abundantly irrigated.[9] Published data revealed no correlation between positive bile culture and surgical wound infection after LC[5,18] also there was no correlation between the presence of bacteria in GB wall and postoperative infection.[18]

Septic sequelae of uncomplicated laparoscopic cholecystectomy are uncommon.[11] In our study, postoperative infection was significantly related to GB perforation ($p < 0.0001$); also, organisms isolated from infected wounds were not the same as in bile culture. In a literature, all infected cases were associated with skin commensals.[11] GB perforation during LC carries no morbidity, provided a total and complete recuperation of gallstones spilled and local treatment of bile contamination with local irrigation and antibiotics.[19]

Postoperative wound infection was limited and was associated with GB perforation and contamination of wounds and peritoneal cavity with spilled bile and missed and crushed stones which are considered to be good media for organism proliferation and colonization raising the incidence of infection. Also, there was no relation, in most of cases between bile organisms and wound infection pathogens. On testing bile bacteriology, a published data stated that bactibilia is the most important predictor of wound infection in low-risk patients undergoing elective LC. As it may not be possible to diagnose which patients have bactibilia by routine investigation, it is advisable to use prophylactic antibiotics to reduce the incidence of wound infection.[20] Our results deny this and consider bile as a good media for colonization, not as a source of infection.

Our results cope with that mentioned in many literatures,[5,7,21-23] where they reported that prophylactic use of antibiotics may not be necessary for low risk LC patients as it does not affect the incidence and severity of infection and degree of bile contamination, while others[24,25] reported that neither LC, nor open cholecystectomy should be performed without per operative antimicrobial prophylaxis since such measure reduces hospital stay and cost. Meanwhile, another author mentioned that in low risk patients, eliminating the unnecessary use of prophylactic antibiotic would result in cost reduction, low the risk of adverse reaction and reduce microbial resistance.[7]

In conclusion, there was no relation between postoperative wound infection and bile microbiology, also prophylactic use of antibiotics did not lower incidence of postoperative infection. Eliminating external sources of wound infection, use of antibiotic prophylaxis is preferred to be restricted to high risk patients as those with long operative time and in patients who are suspected to have difficult dissection and GB retrieval where GB is more liable to perforate.

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