CHOLELITHIASIS AND ACUTE CHOLECYSTITIS IN PATIENTS WITH CHRONIC LIVER DISEASE

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SUMMARY

Some studies show an approximately two to threefold increased incidence of cholelithiasis in cirrhotic patients as compared to the non-cirrhotic population. In this study, the incidence of gallstones, acute cholecystitis and cholelithiasis related mortality have been investigated in patients with chronic liver disease. Seventy two patients with liver cirrhosis were included in the study. Nineteen of the patients (26%) had cholelithiasis and 12 of these had acute cholecystitis (63.1%).

Seven patients underwent surgery of whom three requiring emergency cholecystectomy died of sepsis and hepatic failure in the early postoperative period. There was only one death amongst the four patients who underwent elective cholecystectomy. Overall mortality in patients with acute cholecystitis and liver cirrhosis was 41%. The mortality in patients classified as belonging to CHILD A, B or C groups was 0%, 40% and 57% respectively.

Emergency cholecystectomy carries greater risk in patients with advanced liver disease and those patients with symptomatic stones may better benefit from elective operations at an early stage in their liver disease.

Key Words: Liver cirrhosis, cholelithiasis, acute cholecystitis, cholecystectomy.

INTRODUCTION

Large autopsy series have shown that the incidence of cholelithiasis in patients with cirrhosis is higher than that in the normal population (1-4). Two thirds of patients in these series had bilirubinate stones as compared with a 15-20 % incidence in the non cirrhotic population. According to Sheen et al., the increased prevalence of cholelithiasis in HBV induced liver cirrhosis is related to the severity and duration of chronic liver disease and portal hypertension and is 4.5 to 5.5 times higher than that of the non cirrhotic population (5). More recent sonographic studies have shown an even higher incidence of gallstones in this group (59%), and similar findings have been reported in patients with alcoholic cirrhosis (6-9).

The long-term effects of gallstones on the survival of cirrhotic patients are unknown. In the study of Finucci et al. survival curves were no different in patients with or without gallstones (10). Although less frequent in patients with cirrhosis, acute cholecystitis is known to be associated with a less favourable course, particularly following emergency operations. In this study, the prevalence of cholelithiasis and acute cholecystitis in patients with cirrhosis has been retrospectively investigated and the results of various treatment modalities have been evaluated.

MATERIALS AND METHODS

Seventy two patients with cirrhosis followed-up between 1987 and 1989 in the Gastroenterology Department of Marmara University Hospital were included in the study. The diagnosis of cirrhosis as established by liver biopsy, laparoscopy or laparotomy in 62 patients, and by clinical, biochemical assessment, and endoscopic demonstration of esophagogastric varices in 10. Patients were considered to have symptomatic gallstones if they had a history of biliary colic (pain in the epigastrium or right upper quadrant of at least 15 to 20 minutes of duration) and/or a clinical picture of acute cholecystitis. All other patients were assigned to the asymptomatic group. Patients were also classified according to CHILD-PUGH criteria. Patient follow-up varied from 1-3 years duration. Cholelithiasis was demonstrated by ultrasonography (US) using real time machines with a 3.5 MHz and/or 5.0 MHz transducer in all cases. Patients fasted for at least 8 h before US and following the identification of the gallbladder images were taken in longitudinal, transverse, left lateral or erect positions and by the intercostal approach to show gallstones. The presence of mobile echogenic structures with posterior acustic shadows within the gallbladder

lumen was considered diagnostic of stone (s). The management and outcome of patients with acute cholecystitis was evaluated retrospectively.

RESULTS

Ultrasound examination revealed cholelithiasis in 19 of 72 patients (26.6%). No patient had prior cholecystectomy. There were 7 females and 12 males with cirrhosis and gallstones and their age ranged from 38 to 75 years (mean age 56.6 ± 12.2 years). The etiology of cirrhosis was HBV or HCV related in 10 patients, alcohol induced in 6 patients, primary biliary cirrhosis in 2 patients and cryptogenic in one patient. Seven of 19 patients were asymptomatic whilst 12 patients were admitted with acute cholecystitis. The incidence of acute cholecystitis amongst our cirrhotic patients with gallstones was 63.2 %, whilst overall incidence amongst cirrhotic patients with and without gallstones was 16.6% (Table I). When Child classification was applied to patients with gallstones 7 patients were in Child A, 5 patients in Child B and 7 patients in Child C group.

Presenting symptoms of patients with acute cholecystitis were severe right upper quadrant pain and/or epigastric pain and fever, and prominent laboratory findings were leucocytosis, high levels of bilirubin, alkaline phosphatase and moderately elevated transaminases. Ultrasound examination revealed a thickening of the gallbladder wall of more than 4 mm in patients with acute cholecystitis. One patient in whom US showed common bile duct dilatation had a common bile duct stone on ERCP and was further managed by endoscopic sphincterotomy and duct clearence. Five patients with acute cholecystitis were managed medically whilst 7 patients underwent surgery. Four patients in the medical treatment group who were classified as being either Child A and B class improved with medical treatment whilst one patient with Child C cirrhosis who was unfit for surgery died in septic shock. Although the numbers are small, overall mortality in the medical treatment group was 20%. There were 7 patients in the group treated surgically. Four patients underwent elective cholecystectomy after the acute attack had subsided. Three of these who were Child class A were still alive and symptom free at the time of follow-up, whilst one patient died of mesenteric vein thrombosis during the early post-operative period. The remaining 3 patients -one Child B and two Child C- underwent emergency cholecystectomy. In this group, one patient had flegmoneous cholecystitis and variceal bleeding and the other two had ascites with peritonitis. All 3 patients died with hepatic encephalopathy and sepsis in the early post-operative period. Operative mortality rate in cirrhotic patients with acute cholecystitis was 57.1 % whilst it was 100% when the operation was carried out as an emergency (Table II). The overall mortality rate in patients with acute cholecystitis regardless of the treatment given was 42%. When patients were evaluated with respect to prothrombin times and albumin levels, there were significant differences between patients who died and those who survived ($p< 0.001$ and $p< 0.05$ respectively, Table III). Survival of patients classified according to Child criteria were 100% in Child class A, 60% in Child class B and 43% in Child class C.

Table I- Incidence of gallstones and acute cholecystitis in patients with cirrhosis

	Number of patients	%
With gallstones	19/72	26.4
Acute cholecystitis		
In pts with cirrhosis	12/72	16.6
In pts with cirrhosis & gallstones	12/19	63.2
Choledocholithiasis		
In pts with cirrhosis	1/72	1.4
In pts with cirrhosis & gallstones	1/19	5.5

Table II- Outcome of the patients with cirrhosis and acute cholecystitis

	Number of Patients	Mortality
Medical treatment	5	1 (20 %)
Elective cholecystectomy	4	1 (25 %)
Emergency cholecystectomy	3	3 (100 %)
Overall surgical mortality	4/7	57.1 %

Table III- Albumin and prothrombin time values of patients with cirrhosis and gallstones in regard to survival.

	Survivors	Non-survivors	
Prothrombin time (seconds)	14.4 ± 2.2	15.3 ± 2.0	p< 0.001
Albumin (g/dl)	3.40 ± 0.83	2.83 ± 0.39	p<0.05

DISCUSSION

Cirrhosis of the liver represents a risk factor for gallstones. There is however a much lower incidence of acute cholecystitis and choledocholithiasis in this group of patients as compared to the normal population (11). Schwartz and Castaing have noted a prevalence of cholecystitis of 10% and 6% in their cirrhotic patients (12, 13). The prevalence of cholelithiasis and acute cholecystitis in our cirrhotic patients were 26% and 16.6% respectively and are similar to the findings of Samuel et al. and Okten et al (2, 14). The frequency of acute cholecystitis among our patients with gallstones was however slightly higher than reported (63.1 %).

The management of patients with cirrhosis and symptomatic gallstones is a great challenge. Grassi et al suggested that biliary calculosis does not aggravate the course of liver cirrhosis (15). However in the study of Acalovschi et al. although complications of gallstones occurred less frequently in cirrhotic than in non-cirrhotic patients, complications of cholecystectomy were the cause of death in 27.2% as compared to 14% of non-cirrhotic patients (p< 0.02) (1). Biliary tract operations in this group carry a high mortality rate and the major determinants in this regard are the functional state of the liver, patient age, and/or the presence of concomitant diseases. Most common causes of post-operative death include bleeding from the hypervascular biliary bed, hepatic failure and sepsis.

Cryer et al. found an operative mortality and morbidity rate of 21% and 35% in a series of 39 patients with cirrhosis and gallstones. Preoperative risk factors which were predictive of this high mortality were listed as the presence of ascites, prolonged prothrombin time and a serum albumin level of less than 3.5 g/dl (16). Arranha et al. reported a mortality rate of 83% in the presence of ascites and a prothrombin time greater than 2.5 seconds (17). Blosch et al. observed mortality of 10.2 % in 49 patients with cirrhosis after cholecystectomy or cholecystostomy. The authors concluded that elective surgical intervention for Child A and B patients with symptomatic cholelithiasis is a reasonable approach in cirrhotic patients (18).

In addition to the aforementioned parameters, the outcome of patients undergoing emergency cholecystectomy is greatly influenced by the presence of sepsis and shock on admission to the operating theater (19). In one study, in-hospital mortality of cholecystectomy in patients with cirrhosis was 7%, the main cause of death being acute and chronic liver failure. Emergency cholecystectomy had a mortality of 50% in contrast to elective cholecystectomy which carried a mortality of 5-10% (20). In our study 12 out of 19 patients had acute cholecystitis and 7 of them required surgical management. While the mortality was 100% in cases who underwent emergency operation, it was low in the medically treated group (20%) and in those patients who had an elective cholecystectomy (25%) after the acute attack. The main cause of death in our cases were sepsis, upper GI bleeding and liver failure. Mortality increased in correlation with the Child state. Prothrombin time was significantly prolonged and albumin levels were lower in patients who died as compared to survivors (p<0.001 and p<0.05 respectively).

Alternative treatmet modalities such as cholecystostomy, subtotal cholecystectomy or percutaneous cholecystostomy have been recommended in high risk patients with gallstones, but the number of these trials is limited (21-23).

In conclusion emergency operations on the biliary tract in patients with chronic liver disease are associated with a high rate of mortality and morbidity, and this increases with the Child class of the patient. Those patients with liver cirrhosis and symptomatic gallstones may be better managed by elective cholecystectomy at a stage where the functional reserve of the liver is acceptable (Child A or B) and where this "formidable" operation as it has been called by Aranha et al. may be better tolerated (24).

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