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ORIGINAL ARTICLE

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Raised pressure in the bile ducts after orthotopic liver transplantation

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Abstract Biliary complications are common after orthotopic liver transplantation. Bile leakage in the immediate postoperative period and on removal of the T-tube could possibly be caused by a raised bile duct pressure. In order to test this hypothesis, bile duct pressure was studied in seven consecutive liver transplant patients. During the operation, the common bile duct was anastomosed end-to-end over a T-tube. The initial bile duct pressure measurement was performed a median of 12 days (range 10–17 days) after the transplantation and on one or two more occasions during the following 3 months. Seven cholecystectomized gallstone patients with indwelling T-tubes were used as controls. The bile duct pressure at the level of the xiphoid process in the transplanted group was 7.7 ± 1.4 cm H_2O and in the control group 0.5 ± 0.8 cm H_2O ($P < 0.001$). The initially increased bile duct pressure after liver transplantation decreased with time ($P < 0.05$) towards normal during the following 3 months. The raised pressure may increase the risk of bile leakage in the postoperative period.

Key words Liver transplantation, bile duct pressure · Bile duct pressure, liver transplantation

Introduction

Today, orthotopic liver transplantation (OLT) is a well-established treatment for end-stage liver disease. Biliary tract complications after OLT have caused significant morbidity as well as mortality [4, 10, 17]. A variety of methods have been used to reconstruct the bile ducts, and although a reduced frequency of biliary tract complications has been reported, it is still a major cause of morbidity after OLT [8]. Bile duct stenosis or bile leakage is reported to occur in 10%–30% of the patients. The underlying cause may be either technical or ischemic. Most transplantation centers currently use a duct-to-duct anastomosis over a T-tube, except in cases where the recipient common bile duct is affected by the underlying disease. Bile leakage may also occur after the removal of the T-tube, but the optimal time to remove the T-tube after OLT has yet to be established. A few reports have discussed the management of this complication, but the possible background pathophysiology has attracted little attention [2, 4, 13].

Recent advances in our understanding of biliary tract physiology [12, 19, 23] indicate that bile duct pressure may be increased after OLT, due to interference with the reflex control of the sphincter of Oddi, and this may augment the risk of bile leakage and influence liver function.

The aims of this study were (1) to measure the bile duct pressure after OLT and compare it with that in a group of cholecystectomized gallstone patients with an indwelling T-tube and (2) to investigate whether there was a correlation between bile duct pressure and serum bilirubin, alkaline phosphatase, or liver enzymes in liver graft recipients.

Table 1 Data on the transplanted patients

Age[a]	Sex	Diagnosis	Manometry (Days after surgery)
23	F	Acute liver failure	10
35	F	Liver cancer	17
30	M	Amyloidosis	12
49	M	Chronic hepatitis	11
59	F	Primary biliary cirrhosis	10
41	F	Alcoholic cirrhosis	13
52	M	Alcoholic cirrhosis	13

[a] Median age of patients was 41 years

Table 2 Data on the control group

Age[a]	Sex	Diagnosis	Manometry (Days after surgery)
60	F	Choledocholithiasis	21
42	F	Choledocholithiasis	28
62	F	Choledocholithiasis	8
40	F	Choledocholithiasis	16
67	M	Choledocholithiasis	8
29	F	Choledocholithiasis	5
29	F	Choledocholithiasis	14

[a] Median age of patients was 42 years

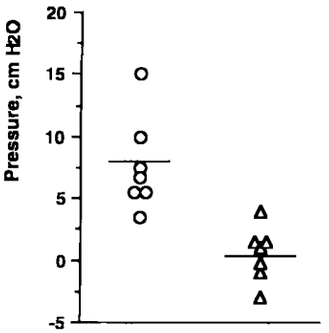

Fig. 1 The bile duct pressure in seven liver transplant patients (O) and seven cholecystectomized controls (△). The mean bile duct pressures *(line)* were significantly different ($P < 0.001$)

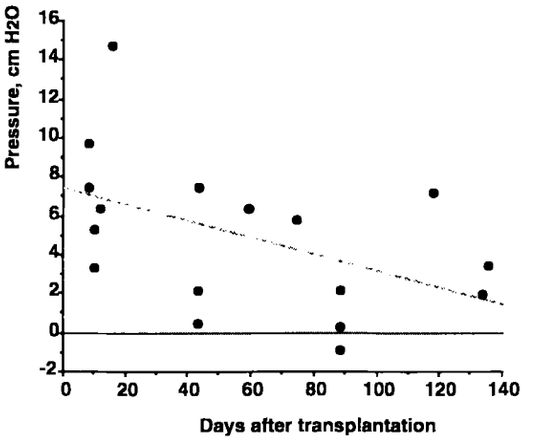

Fig. 2 Bile duct pressure correlated to postoperative time ($y = -0.04 \times + 7.4$, $r = 0.45$, $P = 0.033$) in seven liver transplant patients. Bile duct pressure was measured three times in four patients and twice in three patients

Patients and methods

The investigation was approved by the Ethics Committee of the University of Gothenburg for investigations involving human subjects. The age and sex distributions of the two groups are presented in Tables 1 and 2. Seven consecutive liver transplant patients were studied. The common bile duct was anastomosed end-to-end over a silicon 9 Fr T-tube. The T-tube was kept open the 1st week and was then clamped until the manometry.

Bile duct pressure was measured 10–17 days after the operation (median 12 days) and on one or two more occasions during the following 3 months. The last manometry was done on the day the T-tube was removed. Seven cholecystectomized gallstone patients were used as controls. These patients had been operated on due to choledocholithiasis and had an indwelling T-tube postoperatively. The T-tube was clamped at least 24 h before the manometry, which took place 5–30 days after the operation (median 13 days). Liver function was assessed using standard laboratory tests.

Manometry

The manometry was performed in the morning after 12 h of fasting. The patient was resting in the supine position on a firm bed. The T-tube was opened and the bile duct pressure was measured with a pressure transducer (EMT-34, Siemens Elema) connected to the T-tube. The T-tube was kept open by infusion of saline at a constant rate of 0.1 ml/min. The zero level of the pressure registration was set to the level of the xiphoid process. The bile duct pressure was continuously recorded on a polygraph (Mingograph 82, Siemens Elema). The manometry was continued for 30 min and the bile duct pressure was determined every 5 min.

Statistics

Manometry values are given as mean ± SEM, age and time as median and range. Of the six recorded pressures of each patient, the maximum and minimum values were left out and the mean of the remaining four was used in the later calculations. Statistical analyses were performed using the unpaired Student's *t*-test to compare means and least square linear regression to analyze any correlation between bile duct pressure and postoperative time. A P value less than 0.05 was considered significant.

Results

The average bile duct pressure at the first measurement was 7.7 ± 1.4 cm H_2O in the OLT group and 0.5 ± 0.8 cm H_2O in the control group ($P < 0.001$, Fig. 1). The variation in bile duct pressure within each individual during the pressure recording was 1.4 ± 0.3 cm H_2O in the liver transplant group and 0.7 ± 0.3 cm H_2O in the control group. There was no correlation between age and bile duct pressure. The bile duct pressure in the transplant group decreased ($P < 0.05$) with time and at 90–130 days after transplantation was not different from that in the control group (Fig. 2).

After the removal of the T-tube, a major bile leak was noted in three patients in the transplant group. The bile

duct pressure in these three patients was not elevated compared to those who did not leak.

There was no significant correlation between the bile duct pressure in the transplant group and bilirubin, alkaline phosphatase, or liver enzymes in serum. In the transplant group, the alkaline phosphatase was elevated in most patients at first manometry and there was a tendency towards a correlation with the bile duct pressure ($P = 0.11$). With time, the alkaline phosphatase decreased and was close to normal in most transplanted patients.

There were no major complications in the transplant group during the study period.

In all patients in the cholecystectomized group, the alkaline phosphatase was normal at the time of the first manometry and no complications were registered.

Discussion

The bile duct pressure in a group of liver transplant patients was elevated compared with that in a group of gallstone patients subjected to cholecystectomy and common bile duct exploration.

The manometric method used in this study has been evaluated in previous studies [7, 21] in which the bile duct pressure after cholecystectomy was close to zero when the xiphoid process was used as the zero level. This is in good agreement with the present results. By using a slow infusion, the T-tube is kept open and this infusion does not interfere with the pressure recording [9].

Bile duct pressure is determined by the rate of bile secretion from the liver and the flow resistance in the sphincter of Oddi. This pressure is normally also influenced by the compliance of the gallbladder, but the gallbladder was removed in all patients in this study. The basal bile duct pressure after cholecystectomy is reported to be close to preoperative values [18].

Bile flow is a sensitive parameter of liver graft function. The initial bile flow is normally low after OLT but increases during the first 14 postoperative days [1, 5]. The bile flow after 2–3 months is still reduced when compared with that in cholecystectomized controls [3]. Hence, the elevated bile duct pressure after OLT cannot be explained by an increased bile flow but rather by a raised flow resistance in the sphincter of Oddi. The sphincter of Oddi is innervated by tonic inhibitory nerves running along the bile ducts [20]. A possible explanation for the increased flow resistance may be a reduced nervous inhibition of the sphincter of Oddi after division of the nerves running along the bile ducts of the removed liver. Distension of the bile ducts and the gallbladder [19], the pancreatic duct [21], the duodenum [21] and stomach [24] decreases flow resistance in the sphincter of Oddi. A similar nervous arrangement is suggested by the finding in humans that distension of the gallbladder decreases sphincter of Oddi activity [23].

In a recent preliminary publication [15], sphincter of Oddi manometry was performed in nine patients after OLT. The authors could not see any major disturbances in the function of the sphincter since the basal pressure, amplitude, and frequency of phasic contractions and the response to cholecystokinin seemed normal. One transplanted patient, however, had a raised pressure in the sphincter. In the quoted study, however, no controls were used. Sphincter of Oddi manometry has mainly been used to study postcholecystectomy pain, and in these studies normal bile duct pressure has been found when reported. This may indicate that the suggested dysfunction of the sphincter of Oddi in this study may be overlooked with sphincter of Oddi manometry. Indirect support for a raised biliary pressure after OLT is the radiological finding that the common bile duct was dilated in 15 of 28 patients after OLT [11]. Liver function tests in the present study were not correlated to the bile duct pressure and, hence, do not provide any information on the bile duct pressure after OLT.

In the present study, the average bile duct pressure decreased with time and was not significantly different from that of the control group when the T-tube was removed after 3 months. This finding may be explained by an adaptation of the sphincter of Oddi to the nervous inhibition from the pancreatic duct and the duodenum. Reinnervation from the bile ducts is also a possibility. In three patients there was bile leakage after removal of the T-tube. These three patients did not exhibit a higher bile duct pressure than the other four transplanted patients. However, after the manometry, all of the transplanted patients were premedicated with an opiate before the removal of the T-tube. As opiates increase sphincter of Oddi activity [6, 22] and bile duct pressure [14], the pressure recording can not be expected to foresee the risk of bile leakage in the individual case. As a consequence of this observation, this premedication has been abandoned.

One biliary complication reported to occur after OLT is papillary or ampullary stenosis [17, 25]. In view of our findings, this condition may be attributed to papillary dyskinesia due to post-transplant denervation of the sphincter [16]. The results of the present study show an initially high bile duct pressure, which may explain the dilatation of both the recipient and donor bile ducts reported in the literature [11].

Our findings support the use of a T-tube for at least 3 months. Moreover, sphincterotomy is usually not necessary in cases of suspected ampullary stenosis as the bile duct pressure may normalize within 3–4 months.

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