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The incidence and management of biliary complications following liver transplantation in children

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Abstract Biliary complications following liver transplantation are a cause of significant morbidity and mortality. During the period 1988–1993 ten cases of biliary complications occurred after 98 transplantations in 78 children. The complications were four bile leaks, three intrahepatic biliary strictures (one with recurrent cholangitis), two anastomotic biliary strictures (one with recurrent cholangitis) and one recurrent cholangitis. All leaks occurred within 6 weeks of transplantation whereas all strictures and cholangitic episodes occurred after 3 months. Two biliary complications (20 %) – one intrahepatic and one anastomotic stricture – developed secondary to hepatic artery thrombosis. The incidence of biliary complications was 13.2 % with whole liver grafts as compared to 6.7 % with partial liver grafts and it was 4.3 % with duct-to-duct anastomosis as compared to 12.0 % with Roux-en-Y hepatico-jejunostomy. Seven children required intervention for management of biliary complications and three were managed conservatively. There were no deaths related to the biliary complications.

Key words Biliary complications, liver transplantation, children

Introduction

Liver transplantation is now the accepted treatment for a variety of conditions leading to end-stage liver disease in children. There are a number of factors, related to both technique and immunosuppression, that influence the long-term results of liver transplantation. Mortality after liver transplantation in children is high (20 %–30 %) and particularly so in younger children [4]. Among long-term survivors, considerable morbidity is produced by infective and biliary complications [2]. In this study we have analysed the incidence and management of biliary complications in children following liver transplantation.

Materials and methods

During the period 1988–1993, 98 liver transplantations were performed in 78 children with end-stage liver disease, including chronic and fulminant liver failure. Sixty-two children underwent one transplantation, 12 children received a second transplant and 4 children received a third transplant. There were 32 male and 46 female children. The ages ranged from 1 month to 16 years (median 5 years). A whole liver was used in 53 transplants and partial liver grafts were used in 45 transplants; the right lobe in 2, the left lobe in 19 and the left lateral segment in 24 transplants. Biliary reconstruction was carried out by end-to-end hepatico/choledocho-choledochostomy in 24 transplants (without a stent in 6 and with a stent in 18) and by Roux-en-Y hepatico-jejunostomy in the other 74 transplants (without a stent in 17 and with a stent in 57). We use a paediatric 4 FG NG tube inserted as a stent. The decision to

use a stent is dependent on the small size of the duct or a significant discrepancy in the size of the donor and recipient ducts. Duct-to-duct anastomoses were performed in children with a median age of 13 years (range 2–16 years), whereas Roux-en-Y anastomoses were performed in children with a median age of 3 years (range 15 days–16 years). Primary immunosuppression was provided by a combination of cyclosporin, azathioprine and steroids. Steroid-resistant rejection was treated with OKT3 or FK 506. Doppler ultrasound (US) studies of the vessels of all paediatric patients were done during the 1st post-transplant week. If no arterial Doppler signal was detected or if it was abnormal, a selective visceral angiogram was performed. Imaging of biliary complications included US studies to assess possible bile duct dilatation, endoscopic retrograde cholangiopancreatography (ERCP) to assess duct-to-duct biliary reconstructions, percutaneous cholangiography (PTC) to assess Roux-en-Y hepatico-jejunostomies and di-isopropyliminodiacetic acid scan (DISIDA) to assess Roux loop emptying in cholangitis without identified intrahepatic pathology. The records of these patients were reviewed for biliary complications. Data were analysed with the chi-square test and Student's *t*-test.

Results

Ten biliary complications occurred after 98 transplants for an overall incidence of 10.1 % and included four bile leaks, three intrahepatic biliary strictures (one with recurrent cholangitis), two anastomotic biliary strictures (one with recurrent cholangitis) and one recurrent cholangitis. Of these ten patients, seven received a whole liver; a reduced graft was transplanted in the other three children. The incidence of biliary complications was 13.2 % (7/53) for full-size grafts and 6.7 % (3/45) for partial grafts ($P = 0.29$, NS). Three children with biliary complications in reduced-size grafts, had Roux-en-Y hepatico-jejunostomy reconstructions over an indwelling stent. Of the seven patients with biliary complications in full-size grafts a Roux-en-Y hepatico-jejunostomy was performed in six and an end-to-end hepatico-choledochostomy without a stent in one. Biliary complications were identified in 1/24 (4.2 %) of the patients with duct-to-duct anastomoses and 9/74 (10.8 %) patients with a Roux-en-Y hepatico-jejunostomy ($P = 0.26$, NS).

The mean cold ischaemia time in patients with biliary complications was 12.8 h, not statistically different from those without biliary complications (12.8 vs 12.9 h; $P = 0.97$).

All bile leaks occurred within 6 weeks of transplantation. All strictures and cholangitic episodes occurred more than 3 months after transplantation.

Seven of the ten children required surgical or radiological therapeutic procedures. In one child, the biliary stricture was dilated percutaneously. One child with anastomotic stricture and recurrent episodes of cholangitis underwent surgical revision of the Roux loop after percutaneous dilatation of the stricture. The biliary-enteric anastomosis was revised in three children because of a bile leak, recurrent cholangitis and biliary stricture, respectively. Laparotomy was performed in one child with a bile leak, and retransplantation was required in one child with multiple intrahepatic strictures for which no cause was identified. In two children, the bile leak stopped spontaneously and one child with in-

Table 1 Details of ten patients with biliary complications following liver transplantation

Number	Sex	Age (years)	Diagnosis	Graft size	Graft cold ischaemia time (hours)	Complication	Treatment
Leaks							
1	M	6	Biliary atresia	Full	6.5	Anastomotic bile leak	Revision of anastomosis
2[a]	M	14	Wilson's disease	Full	4.0	Anastomotic bile leak	Conservative
8	F	6	Non-A, non-B viral hepatitis	Partial	9.0	Bile leak from cut surface	Laparotomy and suture
9	M	3	Chronic rejection (retransplant)	Full	15.0	Bile leak from segmental duct	Conservative
Strictures							
3	F	5	Alagille's syndrome	Full	12.5	Anastomotic stricture + recurrent cholangitis	Dilatation + revision of anastomosis
7	M	3	α-1-antitrypsin deficiency	Full	15.2	Anastomotic stricture due to HAT	Revision of anastomosis (retransplant for chronic rejection)
4	M	11	Acute Budd-Chiari syndrome (retransplant)	Partial	10.0	Intrahepatic stricture + recurrent cholangitis	Conservative
6	F	16	Cryptogenic cirrhosis	Full	13.5	Intrahepatic strictures	Retransplantation
10	F	1.5	Biliary atresia	Full	13.0	Intrahepatic strictures due to HAT	Dilatation
Cholangitis							
5	F	3.5	Cryptogenic cirrhosis	Partial	12.0	Recurrent cholangitis	Revision of Roux loop

[a] Biliary reconstruction by duct-to-duct anastomosis; all others by Roux-en-Y hepatico-jejunostomy

trahepatic stricture and recurrent cholangitis was managed conservatively.

One child developed intrahepatic biliary strictures secondary to hepatic artery thrombosis (HAT), which had been managed conservatively. Another child developed an anastomotic biliary stricture secondary to HAT. He underwent revision of the hepatico-jejunostomy but required retransplantation later due to chronic rejection. HAT occurred in five other children, four of whom received successful second transplants. One child died 3 days after the occurrence of HAT without retransplantation. The interval between HAT and retransplantation was 2 days, 3 days, 14 days and 6 months, respectively.

There were no deaths resulting from biliary complications.

Discussion

Biliary complications following liver transplantation are a cause of considerable morbidity in adults and children [1, 2] and may lead to loss of the graft [2]. The incidence of biliary complications in children has been reported to be 10 %–30 % [1, 2, 4, 5]. In this series the overall incidence of biliary complications was 10 % and was not associated with mortality.

There is no reported difference in the incidence of biliary complications when either the whole organ or part of it is used for liver transplantation [3, 4, 5]. In this series the incidence of biliary complications in children receiving full size grafts (13.2 %) was twice that for partial livers (6.7 %). However, this difference does not reach statistical significance. In two patients with full-size grafts, the biliary complications resulted from HAT, and this may account for the apparent difference. The incidence of HAT with full-size grafts is known to be greater than with reduced grafts [7]; however, three children in this study with early HAT received retransplants before they could develop biliary complications.

No difference has been reported in the incidence of biliary complications after biliary reconstruction either by duct-to-duct anastomosis or Roux-en-Y hepatico-jejunostomy [1, 4]. In this series the Roux-en-Y anastomoses were associated with a higher rate of biliary complications. However, this may be because Roux-en-Y hepatico-jejunostomies were performed in much younger children with smaller ducts.

Biliary strictures are the commonest biliary complication after paediatric liver transplantation [1, 2, 5], particularly after Roux-en-Y hepatico-jejunostomy [2]. Strictures accounted for half the biliary complications in our patients and occurred only in those children with Roux-en-Y hepatico-jejunostomy. This may be a reflection of the small size of the bile duct. In two cases they were associated with recurrent episodes of cholangitis. Bile leaks were almost as common as strictures in this series, although others have reported a lower incidence [2, 5]. Bile leaks occur either from the biliary anastomosis, the cut surface of a reduced graft [2, 3, 4, 6], or from divided segmental ducts. There is an equal incidence with duct-to-duct and Roux-en-Y anastomoses [2]. In our series, one bile leak occurred from the cut surface of a reduced graft. There was an unrecognised accessory segment VIII duct in another patient, and there were two anastomotic leaks.

In this series, one patient developed intrahepatic strictures and another developed an anastomotic stricture secondary to HAT. HAT has been reported to be the cause of up to 25 % of all biliary complications [5] and about 20 % of all bile leaks due to necrosis of the bile ducts [1, 3, 6]. It has also been reported to be a cause of biliary stricture and cholangitis [4]. The bile leaks in this series were not associated with HAT and were possibly related to technical complications.

The majority of biliary complications are reported to present in the first 3 months after the transplant [2, 5]. In general, bile leaks are reported to occur early (by the 1st month) [2, 3, 6], and strictures usually develop late, up to 1 year after the transplant [2, 3]. Our experience has been similar.

Prolonged cold ischaemia time has been associated with biliary complications and, in particular, with non-anastomotic strictures. However, in our series, there was no such association.

Interventional procedures were required for 70 % of our patients, which is similar to other reported series [1]. Procedures for management have consisted of initial percutaneous drainage of the biliary tract or placement of transanastomotic stents followed by operative repair [5] Suture and drainage of generalised bile leaks (whether from the anastomosis, Roux loop or cut surface) [3, 4, 6] US-guided percutaneous drainage for localised bile leaks [6] Laparotomy and formal repair for T-tube removals resulting in late biliary peritonitis [6] Roux-en-Y hepatico-jejunostomy for stenosis after duct-to-duct anastomosis [4] Revision of the Roux loop for kinking of the bile duct [4]. Strictures were managed either by percutaneous transhepatic dilatation or by surgical repair [1]. Biliary complications following HAT required retransplantation in the majority of cases [1, 3, 5], particularly if recurrent cholangitis or multiple intrahepatic strictures developed [4].

Refinements in surgical techniques for biliary reconstruction have reduced the incidence of biliary complications [2]. It is hoped that this improvement will continue and will help to reduce the morbidity and mortality in patients undergoing liver transplantation.

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