ORIGINAL ARTICLE

Endoscopic retrograde cholangio-pancreatography in the management of biliary complications after paediatric liver transplantation – a retrospective study

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SUMMARY

The published paediatric experience with endoscopic retrograde cholangio-pancreatography (ERCP) in the diagnosis and management of biliary complications following liver transplantation (LT) is limited. We describe our experience with ERCP in the management of children following LT who presented with biliary complications, over a 20-year period (1995–2014). The retrospectively reviewed data are summarized descriptively. Of 94 children (47 boys) who received 102 liver transplants at our centre, seven children (five boys, two girls) underwent ERCP after liver transplantation. In total, 25 ERCP procedures were carried out in these patients. The median age at liver transplantation was 10.7 (3.9–16.2) years. The median interval between LT and the first ERCP was 28 days (12 days–6.8 years). All patients were on standard calcineurin-inhibitor-based immunosuppression regimens. Six of the seven patients underwent ERCP on more than one occasion [median number of ERCP sessions per patient- 4, (1–6)]. Seventeen procedures were carried out under conscious sedation, remaining eight under general anaesthesia. Sedation was achieved employing a standard regimen (Midazolam 5 mg with Pethidine 50 mg) and occasionally Fentanyl. ERCP is an effective and safe intervention from both diagnostic and therapeutic point of view, in the management of post-LT biliary complications in children.

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Introduction

Liver transplantation (LT) is the definitive treatment for end-stage liver disease in children [1]. Rapid advances in transplant hepatology have resulted in continually improving patient outcomes that have made a positive impact on patient and graft survival. Biliary complications have been well described following paediatric liver transplantation [2]. It is also known that their incidence is higher after living donor transplants as compared to transplantation using deceased donor grafts [3]. Biliary complications can be early (occurring within 4 weeks after liver transplantation) or late post-transplant. They include bile leaks, biliary strictures/stenosis and biliary stones. Both anastomotic and nonanastomotic strictures are described. The latter are more challenging in terms of

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management and often follow as a consequence of vascular complications involving mainly the hepatic artery. Endoscopic retrograde cholangio-pancreatography (ERCP) is an established modality in the diagnosis, and management of biliary complications following liver transplantation and its diagnostic yield, therapeutic utility as well as safety profile has been validated in adult recipients of liver transplants [4]. However, published paediatric experience with ERCP postliver transplantation is limited not only for its use but also for follow-up assessment [5]. Our objective was to describe our experience with ERCP in the management of children who have undergone LT and presented with biliary complications.

Methods

We retrospectively reviewed the case records of children who had undergone LT and subsequently underwent ERCP for biliary complications. Approval was obtained from the Hospital Institutional Review Board. We obtained relevant demographic details, age at LT, indications for LT, pre-ERCP investigations including radiological investigations, ERCP procedures performed and outcomes in terms of findings, complications post-ERCP and long-term outcomes focusing particularly on graft function.

Results

During the 20-year study period (1995–2014), 94 children (47 boys) received 102 liver transplants at a single centre. Of these 94 children, 20 children (21%) developed biliary leaks and/or strictures postliver transplant. Thirteen had a bilio-enteric anastomosis, and ERCP was not feasible in this group of patients. Of these 13, three children had simple bile leaks with no radiological evidence of intrahepatic biliary dilatation or strictures and they underwent radiologically guided percutaneous drainage. The other 10 children, all of whom had a bilio-enteric anastomosis, underwent PTC for active management of biliary complications. The remaining seven children with a duct-to-duct biliary anastomosis (five boys and two girls) underwent ERCP after liver transplantation. In total, 25 ERCP procedures were carried out for this group of patients. The median age at liver transplantation was 10.7 years (range: 3.9–16.2). The median interval between LT and the first ERCP procedure carried out was 28 days (range: 12 days–6.8 years). All patients were on standard calcineurin-inhibitor-based immunosuppression regimens.

All the procedures were carried out by two experienced operators employing standard side-viewing duodenoscopes (Olympus, Tokyo, Japan, TJF 260 V series), under prophylactic antibiotic cover.

Six of the seven patients underwent ERCP on more than one occasion (median number of ERCP sessions per patient- 4; range: 1–6). Seventeen procedures were carried out under conscious sedation and the remaining eight under general anaesthesia. Sedation was achieved employing a standard regimen (Midazolam 5 mg with Pethidine 50 mg) and occasionally Fentanyl.

Patient 1 had presented with jaundice secondary to occlusion of his original choledocho-enterostomy. He had needed creation of a secondary choledochal anastomosis to facilitate biliary flow. He had jaundice, and imaging revealed intrahepatic biliary dilatation with calculi. The hepatic calculi were secondary to the biliary obstruction. This obstruction was eventually relieved with the placement of a hepatic drainage tube that not only established good biliary flow but also resulted in rapid improvement in graft function and resolution of jaundice. The patient has not had any further sequelae. Although he has mild graft dysfunction, synthetic liver function has been well preserved.

Patient 2 needed a sphincterotomy followed by placement of a biliary stent. Repeat cholangiogram was necessary in view of persistent cholestasis that showed a biliary stricture, which was managed by re-stenting. Six months later, the biliary stent was found to have migrated within the common bile duct. This was retrieved successfully. Cholangiogram showed a stricture that needed re-stenting. Five months after this, the child presented with fever and cholestasis. Repeat ERCP was carried out, with a diagnostic intent, did not show any evidence of obvious abnormalities and the stent was patent with biliary flow. Blood and biliary fluid cultures were negative. The child had the final ERCP session (6 ERCP's in total), at 13 years of age (nearly 2 years post-LT), which showed significant improvement. After a few uneventful years, the child moved abroad. Although not under regular follow-up at our centre, the child is alive and well with good graft function.

Patient 3 had a biliary stricture, initially addressed by stenting without any need for sphincterotomy at his first ERCP. However, subsequent ERCP after 10 months revealed that the stent had migrated proximally in to the bile duct. After failed attempts at conventional removal, a generous biliary sphincterotomy was carried out for access. Unfortunately, this was complicated by bleeding that stopped after local adrenaline injection, and the procedure was terminated. ERCP was repeated

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on two successive occasions within the next 3 days, and the stent was eventually successfully extracted without any complications. Postextraction cholangiogram showed no residual anastomotic stricture. The patient remains well with good graft function and has not required any further intervention.

Patient 4 had his initial ERCP after more than 5 months post-LT. This revealed a tight stricture at the duct-to-duct anastomosis. Serial ERCP sessions (four in total) revealed slow improvement with the deployment of bigger sized stents. Finally, after just under 2 years post-LT, the stents were removed with a normal postextraction cholangiogram. However, this patient sadly died at 16 years of age, while awaiting re-LT for chronic allograft rejection, which was secondary to poor compliance with immunosuppressant medication.

Patient 5 had an anastomotic stricture at the hilum with upstream intrahepatic biliary duct dilatation. Following an adequate biliary sphincterotomy, a stent was placed across the hilar stricture. Six months later, she underwent repeat ERCP. Cholangiogram revealed a nondilated biliary system with no residual stricture. Although there were no concerns after this from the biliary system per se, the child developed chronic allograft rejection that culminated in re-LT, which was successful. She remains well.

Patient 6 underwent her first ERCP 3 week's post-LT with a clinical suspicion of bile leak. This revealed near normal cholangiographic appearances although a small stent was placed to promote bile flow. This stent was removed at the next ERCP session. At this stage, the cholangiogram was completely normal. The child remains very well with normal graft function.

Patient 7 had an initial ERCP early post-LT for a suspected bile leak, and this revealed a biliary anastomotic stricture that required stent placement. ERCP was repeated after 2 weeks, and this revealed persistence of the previously documented stricture with upstream intrahepatic duct dilatation. Sphincterotomy and re-stenting were achieved with good bile drainage. The third ERCP session involved replacement of the biliary stent. Unfortunately following the procedure, the patient developed a self-limiting episode of acute pancreatitis of moderate severity with an uneventful recovery, remaining very well with good graft function. Subsequently, one more ERCP intervention involving re-stenting was required. Finally, about 1-year post-LT, the final ERCP examination revealed a normal cholangiogram.

None of the patients had any general anaesthesia or sedation-related complications. After a median follow-up period of 13 months postfinal ERCP, six patients (including the child who underwent re-transplantation) are alive and well with good graft function.

Discussion

Biliary complications following liver transplantation can potentially result in significant morbidity [3,6]. This is more relevant in the context of not only living donor LT but also with split and technical-variant grafts [3]. ERCP has been shown to be a safe and effective intervention tool for both diagnosis as well as simultaneous therapeutic management of biliary complications post-LT [5,6]. Experience in children post-LT, although described earlier, is limited and mainly from the West [5]. Our study from South-East Asia is the first from the Eastern Hemisphere, demonstrating the utility of ERCP in the management of biliary complications post-LT in children.

Biliary leaks with/without associated biliary strictures at the anastomosis were the predominant findings at initial ERCP in our series. A similar finding was revealed by Dechene *et al.* [5] in their series of seventeen patients. However, this series also reported ischaemia-type biliary lesions and more importantly a relatively higher incidence of biliary casts. Our series had only one patient with biliary casts. A study from Argentina, evaluating their overall experience with ERCP in general, also briefly described 12 children who underwent post-LT ERCP [7].

Although our series is relatively smaller, involving seven children, most patients underwent multiple ERCP examinations often necessitated by clinical need. The commonest indications for repeat ERCP were for re-stenting of anastomotic biliary strictures, retrieval of migrated biliary stents and finally for stent removal after satisfactory resolution of biliary complications. The German series also revealed a comparable trend with a mean of four ERCP sessions required per patient [5].

The majority of the procedures were carried out under general anaesthesia although a significant proportion was with conscious sedation. There were no complications attributable to the anaesthetic or sedative agents. With reference to the complications directly attributable to the ERCP procedure, there were no major complications apart from bleeding and the self-limited episode of pancreatitis.

Most of our patients underwent their first ERCP relatively early in the post-LT period. All patients were on variable weaning but significant doses of corticosteroids apart from aspirin (employed for prophylaxis against

hepatic artery thrombosis). This might, at least in theory, predispose them to a tendency for peri-procedural bleeding. The role of immunosuppression is not clear with some speculating that these medications might protect against or at least mitigate the severity of pancreatitis, but evidence remains anecdotal [8].

It is now well established that ERCP is probably the best choice for the diagnosis and management of biliary complications in the setting of LT, whenever the biliary tract is endoscopically accessible. Percutaneous transhepatic cholangiography (PTC) can also be useful as an alternative approach to the biliary tree, whenever endoscopic access is not feasible or there is extensive involvement of intrahepatic ducts with a dilated biliary system [9].

At our centre, all postliver transplant recipients who developed biliary complications with a duct-to-duct biliary anastomosis amenable to endoscopic approach were considered for ERCP. PTC was employed for the management of children in whom ERCP was not feasible and occasionally for children with peripheral nonanastomotic biliary strictures in our centre. We would recommend ERCP, whenever feasible, not only on account of very good patient outcomes but also with the aim to avoid surgical intervention.

In the past, surgical intervention in the form of revision of the hepatico-enterostomy or creation of a new bilio-enteric anastomosis was the preferred approach for the management of biliary anastomotic strictures [10]. Other options included percutaneous insertion of biliary drainage tubes [11]. Unfortunately, despite their success rates in achieving better biliary flow, complications were much more common and also associated with greater morbidity as compared to those reported with ERCP. ERCP at our centre in Singapore, in the management of children who have undergone LT, although noninvasive, has major limitations with therapy not being an option.

Our study has several important limitations. Firstly, the retrospective study design involving relatively small numbers of patients is a limiting factor. Secondly, the duration of follow-up post-ERCP is relatively shorter at just over a year. There are no long-term post-ERCP follow-up studies in paediatric LT recipients.

In conclusion, ERCP is an effective and safe intervention from both diagnostic as well as from the therapeutic point of view, in the management of post-LT biliary complications, specifically, duct-to-duct biliary anastomosis amenable to endoscopic intervention. ERCP would be recommended, whenever feasible, not only on account of very good patient outcomes but also with the aim to avoid surgical intervention. Further advances in endoscopy and positive experience with ERCP will hopefully translate into improved patient outcomes.

Authorship

SVK, S-HQ and MMA: contributed substantially to conception and design of the study, acquisition and interpretation of data. SVK: drafted the article. S-HQ and MMA: made critical revisions. SVK, S-HQ and MMA: approved the final version of the manuscript.

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Conflict of interest

All authors declare that they have no conflict of interest to declare.

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Ethics

The study was reviewed and approved by the local institutional review board, National Healthcare Group Domain Specific Review Board. The study being retrospective review of medical records involving no patient identifiers, the request for waiver of informed consent was granted by the IRB.

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