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ORIGINAL ARTICLE

Clinical and histological outcomes following living-related liver transplantation in children

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Summary

Objectives: Living-related liver transplantation (LRLT) was developed to increase the donor pool of size-matched organs for children. In the UK only one centre performed LRLT between 1993 and 2008. This study reports the clinical and histological outcomes following adult-to-paediatric LRLT at our centre.

Methods: Forty-six LRLTs were reviewed. Recipients had a mean age, weight and PELD score of 2.4 years (range 0.5—11 years), 11.0 kg (3.7—32.3 kg) and 11.7 (—20.3 to 49.1) respectively. The incidence of post-transplant paediatric morbidity, abnormal liver function tests and histological abnormalities was reviewed.

Results: Patient and graft survival rates were 97.8%, 95.1% and 95.1%, and 97.8%, 92.1% and 71.7% at 1, 5 and 10 years post-transplant respectively. Three children were re-transplanted at 44, 100 and 119 months post-transplant. Nine children developed neuropsychological problems, 6 experienced educational difficulties, 5 developed post-transplant lymphoproliferative disorder and 5 suffered height or weight growth < 2 centile. Normal LFTs were found in 41.7%, 50%, 68% and 64.7% of children at median follow-up of 6, 13, 61 and 85 months respectively. Liver histology showed hepatitis, acute rejection, non-specific changes, biliary pathology, vascular pathology and chronic rejection in 32.9%, 29.5%, 13.4%, 10.1%, 6% and 2% of biopsies respectively.

Abbreviations: LRLT, Living-related liver transplantation; UK, United Kingdom; KCH, King's College Hospital; PTLD, Post-transplant lymphoproliferative disorder; EBV, Epstein Barr Virus; DNA, Deoxyribonucleic acid; LFTs, Liver Function Tests; INR, International Normalised Ratio; AST, Aspartate aminotransferase; ALP, Alkaline Phosphatase; γGT, Gamma Glutamyltransferase; Bil, Bilirubin; ACR, Acute cellular rejection; BA, Biliary Atresia; PFIC, Progressive Familial Intrahepatic Cholestasis; NANB, Non-A, non-B hepatitis; PELD, Paediatric End-stage Liver Disease; HAT, Hepatic Artery Thrombosis; MRI, Magnetic Resonance Imaging; NRH, Nodular regenerative hyperplasia; WLT, Whole-liver transplantation; SLT, Split-liver transplantation; UNOS, United Network for Organ Sharing; OLT, Orthotopic Liver Transplantation.

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Conclusions: The prevalence of paediatric morbidity and histological abnormalities emphasize the need for specialist and long-term follow-up following LRLT in children.

Introduction

The first successful series of living-related liver transplantations (LRLTs) was reported from Chicago in 1991 [1]. Since then the technique has become an accepted modality of liver transplantation to supplement the limited deceased donor pool [2—6]. This problem is nowhere more evident than in the paediatric population as a result of intense competition for a subgroup of small, high quality donor organs [7].

LRLT has a number of potential advantages over whole- and split-liver deceased donation transplantation [8]. It has significantly reduced the high rate of mortality seen in children waiting for a suitable donor on the transplant list [9,10]. LRLT offers recipients better quality grafts [11] resulting in improved graft and patient survival rates [8], the ability to schedule the operation to coincide with the recipient's optimum level of well-being and, importantly for children, better size-matched grafts compared with whole organ transplantation [1]. LRLT has been widely adopted by those countries in which the use of deceased donation organs for transplantation goes against religious and cultural preferences [3,5,12]. In such countries with extensive LRLT experience, 10-year patient and survival rates have been reported to be as high as 77.2% and 74.5% respectively [5]. Interestingly LRLT has not been associated with a reduced incidence of organ rejection [13—15], a phenomenon also seen with live-donor kidney transplantations [16]. The principal limitation of LRLT, apart from the procedure being technically more complex, is that it carries with it a small but significant risk of donor morbidity [17] and mortality [18,19]. Donor mortality has been reported in 0.15—0.2% of published cases [19].

In the UK, adult-to-paediatric LRLT was established in London at King's College Hospital (KCH) in 1993 and for the subsequent 15 years was the only centre that performed this surgery. Our previous paper has reported on the surgical outcomes [20]. This paper focuses on the medium- to long-term clinical and histological outcomes.

Subjects and methods

Our centre performed forty-six adult-to-paediatric LRLT operations on 46 patients under the age of 12 years between October 1993 and April 2006. The medical records (paper and electronic) were retrospectively reviewed to obtain data on pre-transplant demographics, long-term graft and patient survival, long-term graft function and the prevalence of post-transplant neurological, psychological, educational, oncological and growth problems. A semi-structured proforma was used to facilitate data collection. The records of patients with hepatoblastoma and post-transplant lymphoproliferative disorder (PTLD) were further reviewed for the dates and regimes of chemotherapy. PTLD was defined histologically, radiologically and by the presence or absence of Epstein Barr Virus (EBV) DNA. Liver Function Tests (LFTs) (International Normalised Ratio (INR), Aspartate aminotransferase (AST), Alkaline Phosphatase (ALP), Gamma Glutamyltransferase (γGT) and Total Bilirubin [Bil]) performed at 6 months, 1, 5 and 7 years post-transplant (or as close to these time points as available) were assessed and abnormal LFTs were defined as surrogate markers of graft dysfunction. Normal values for LFTs at our unit were defined as an AST 10—50 units/L, ALP < 350 units/L, γGT 5—55 units/L and Bil 3—20 μmol/L. 'Mildly raised' LFTs were defined as an INR > 1.2, AST > 50 units/L, ALP > 350 units/L, γGT > 55 units/L or Bil > 20 μmol/L. 'Significantly raised' LFTs were defined as an AST > 100 units/L, ALP > 700 units/L, γGT > 110 units/L or Bil > 40 μmol/L. Histology from patients who had undergone liver biopsy was reviewed by a Consultant Pathologist (AQ) using an approach similar to that described by Evans et al. [21]. Briefly, an overall diagnostic assessment was carried out to classify biopsies samples into the following categories: normal, mild and non-specific changes, non-specific hepatitis, acute cellular rejection (ACR), chronic rejection, changes of biliary or vascular pathology and other pathology. Rejection was graded according to the Banff grading system [22]. Hepatitis was graded semi-quantitatively as none, mild, moderate and severe, and fibrosis was staged semi-quantitatively as none, mild without bridging, bridging and cirrhosis. Donor demographics were obtained from data held by the surgical transplant team. Actuarial patient and graft survivals were calculated using the Kaplan-Meier method.

Recipient, donor and transplant demographics

The forty-six recipients, 16 of whom were female, had a mean age of 2.4 years (range 0.5—11), a mean weight of 11.0 kg (range 3.7—32.3) and consisted of 24 children with biliary atresia (BA) (18 with previous Kasai portoenterostomy), 6 with metabolic liver disease (1 tyrosinaemia, 1 propionic acidaemia, 2 type I Crigler-Najjar syndrome, 1 Wilson's disease and 1 factor VII deficiency), 6 with hepatoblastoma, 5 with progressive familial intrahepatic cholestasis (PFIC) and 5 with other causes of liver disease (1 Alagille syndrome, 2 neonatal sclerosing cholangitis and 2 with acute liver failure non-A, non-B hepatitis [NANB]). Nineteen recipients were White British, 5 were White European and 18 were Middle-eastern. Using a scoring system based on bilirubin, albumin, INR and severity of ascites and encephalopathy (all components scored 1 to 3), 14 children were classified preoperatively as low-risk (score 3—6), 15 as medium-risk (score 7—9) and 17 as high-risk (score 10—15). These categories correlated with mean Paediatric End-stage Liver Disease (PELD) [23] scores of 2.8, 9.6 and 21.8 respectively (range —20.3 to 49.1 for all children). Mean PELD score