Pediatric Transplantation

Liver transplantation for children – the Red Cross Children's Hospital experience

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Abstract: Liver transplantation for infants and children has been available in South Africa at a single centre, the only established service in Sub-Saharan Africa, for more than a decade. Current concerns have shifted from an initial target of early post-transplant survival to quality of life in the long-term. *Materials and methods*: Since 1985, 225 infants and children have been assessed, with 146 accepted for transplantation. Sixty-nine have had 71 orthotopic liver transplants (OLTx). Biliary atresia was the most frequent diagnosis (54%) followed by acute liver failure (ALF) (15%). Waiting list mortality has remained high (23%), particularly for the ALF group (50%). Forty-three were reduced size transplants with donor: recipient weight ratios ranging from 2:1 to 11:1. Twenty-seven were < 10 kg. *Results*: Fifty (74%) survive 1 month–12 years post-transplant. Actuarial survival after 1996 since HBV core antibody positive donor livers were refused and prophylactic IV ganciclovir used has been > 82%. Early post-OLTx mortality was low (5%), one primary non-function, one IVC thrombosis, one PV thrombosis, but late morbidity and mortality (20%) was mainly due to viral infection: de novo hepatitis B (five patients, three deaths), EBV-related post-transplantation lymphoproliferative disease (PTLPD) (eight patients, six deaths) and CMV disease (11 patients, five deaths). Tuberculosis prophylaxis, required in six cases, resulted in major morbidity in two and mortality in one. Poor compliance played a significant role in seven deaths. Hypertension requiring medication along with some compromise of renal function has been present in all but two patients. However, all those of school-going age (25) attend school normally and remain in good health and only three of the survivors have abnormal liver function tests. *Conclusions*: Successful liver transplantation is possible in a developing country with limited resources. Scarcity of virus-free donors (HBV and HIV) leading to waiting list mortality and infrequent re-transplantation along with long-term consequences of immunosuppression (infection, lymphoma and renal toxicity) remain problems. Intense education of the caregiver and close follow-up, particularly of those living at long distances has partly addressed the compliance problem.

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Abbreviations: AZA, azathioprine; CMV, cytomegalovirus; CyA, cyclosporin A; EBV, Epstein–Barr virus; HBV, hepatitis B virus; HIV, human immunodeficiency virus; INH, isoniazid; IVC, inferior vena cava; OLTx, orthotopic liver transplants; PCR, polymerase chain reaction; PTLPD, post-transplantation lymphoproliferative disease; PVT, portal vein thrombosis; TB, tuberculosis.

During the early and mid-1980s several South African children with end stage liver disease were sent abroad to the USA and UK at great expense, the money in most cases being raised by public appeal. It was during this time that preparations were made to develop liver transplantation for children at the Red Cross Children's Hospital, Cape Town. The first children were accepted on to a transplant waiting list as
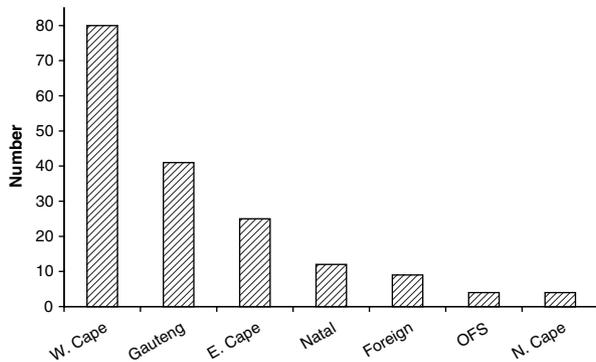
Fig. 1. Geographical origin of all patients, referred for consideration for liver transplant since 1985.

early as mid-1985. Since then 225 children have been referred for assessment (Fig. 1). The first transplant took place on 6 December 1987 on a 6-yr-old girl with end stage liver disease and cirrhosis from alpha I anti-trypsin deficiency. The patient survived the operation but died from complications in January 1988. A successful adult programme was commenced during that year at Groote Schuur Hospital and when this had become established, the paediatric programme was restarted in November 1991 (1).

Liver disease has been generally underestimated as a cause of death in children in South Africa as elsewhere. This is probably because many liver conditions in children have led to rapid deterioration and death in the past (2). However, it has taken at least a decade of hard work to publicize amongst medical colleagues the fact that in most cases the only chance of a cure is liver transplantation and that this service was available locally (3). Also, that, liver transplantation should be considered as an option for chronic liver disease *before* the condition of end stage liver disease is realized; thus allowing time for a thorough assessment of the child and the family, for full and frank discussions of treatment options and assessment of the family's capacity to sustain long-term compliance after transplantation, which is so crucial to the success of this endeavour (4–9).

Materials and methods

Since 1985, 225 children have been referred to our unit for assessment for transplantation. Initially they predominantly came from the Western Cape Province and were few but numbers have increased over the last 6 yr, on average 16 referrals a year, with a greater proportion coming from elsewhere in South Africa (Fig. 1). In addition, several families have migrated from other provinces so that they could be managed before and after transplantation in close proximity to our centre. Of these 225 patients, 146 were accepted for transplant. Reasons for refusal included

psychosocial factors (parental substance abuse, psychiatric problems), rarely socio-economic factors and parental decision, but most importantly poor compliance with pre-operative therapy. Compliance was most difficult to predict in children with acute hepatic failure as time from presentation to transplant was so much shorter. Indications for early transplant were evidence of poor synthetic liver function including prolonged prothrombin time, low serum albumin and cholesterol, presence of ascites, bleeding from oesophageal varices not controlled by sclerotherapy and failing nutritional status (3, 7, 8). Those with acute hepatic failure who developed encephalopathy, hypoglycaemia, a prothrombin time of greater than 100 s, and factor five level less than 20% were considered for transplant, as almost all die without transplantation. There were few medical contra-indications, however children with disseminated TB, severe cardiac, renal or pulmonary disease, marked neurological impairment, chronic Hep B infection and HIV infected patients were not accepted. All patients accepted underwent intensive medical and nutritional resuscitation to treat complications of liver disease, portal hypertension and nutritional deprivation (3, 10). Immunization status was reviewed and supplemented with Hepatitis A and B, H influenza and pneumococcal vaccine in most cases. The decision as to which waiting list patient to transplant was taken at the time a donor presented. In principle, the sickest patient was transplanted first with a blood group compatible donor but also taken into account was the best possible use of the donor organ. This resulted in some patients remaining on the waiting list until their medical condition had deteriorated to the extent that they were considered too sick to withstand the transplant operation. Of the 146 children accepted, 33 have died prior to transplant (23%). These included 17 with biliary atresia and nine with acute hepatic failure. Most of the biliary atresia deaths occurred in the early years of our programme, current waiting list mortality being less than 15%.

At the time of writing, of the 32 children accepted and awaiting transplant only 14 are considered urgent cases. The others have established liver disease but 18 are in good health at present and would not be transplanted until deterioration of growth velocity or complications became evident. Six patients have had transplants abroad, three in USA and three in the UK, four of whom survive, 5 months to 17 yr after transplant.

Surgical technique

The surgical techniques used for donor retrieval and recipient liver removal and engraftment have been previously described in detail (1, 4, 5). Because of donor recipient height and weight mismatch, reduced sized livers have been used since 1992 (Fig. 2) (11). With all reduced size livers and in patients with biliary atresia, choledochojejunostomy has been used for biliary drainage without stents or T-tubes. In most cases of reduced size grafts, the hepatic venous outflow was anastomosed to the preserved recipient inferior vena cava with a large, flush, triangular anastomosis to avoid venous outflow obstruction (Fig. 2) (12). To overcome the disparity in size of the often small and hypoplastic recipient portal vein, the right and left bifurcation of the recipient vein was preserved and opened to make a trumpet-shaped orifice to anastomose to the larger donor portal vein or else the anastomosis was done at the confluence of the splenic and superior mesenteric veins (13). The arterial anastomoses were in most cases from the recipient common hepatic artery to the base of the donor coeliac trunk. The various
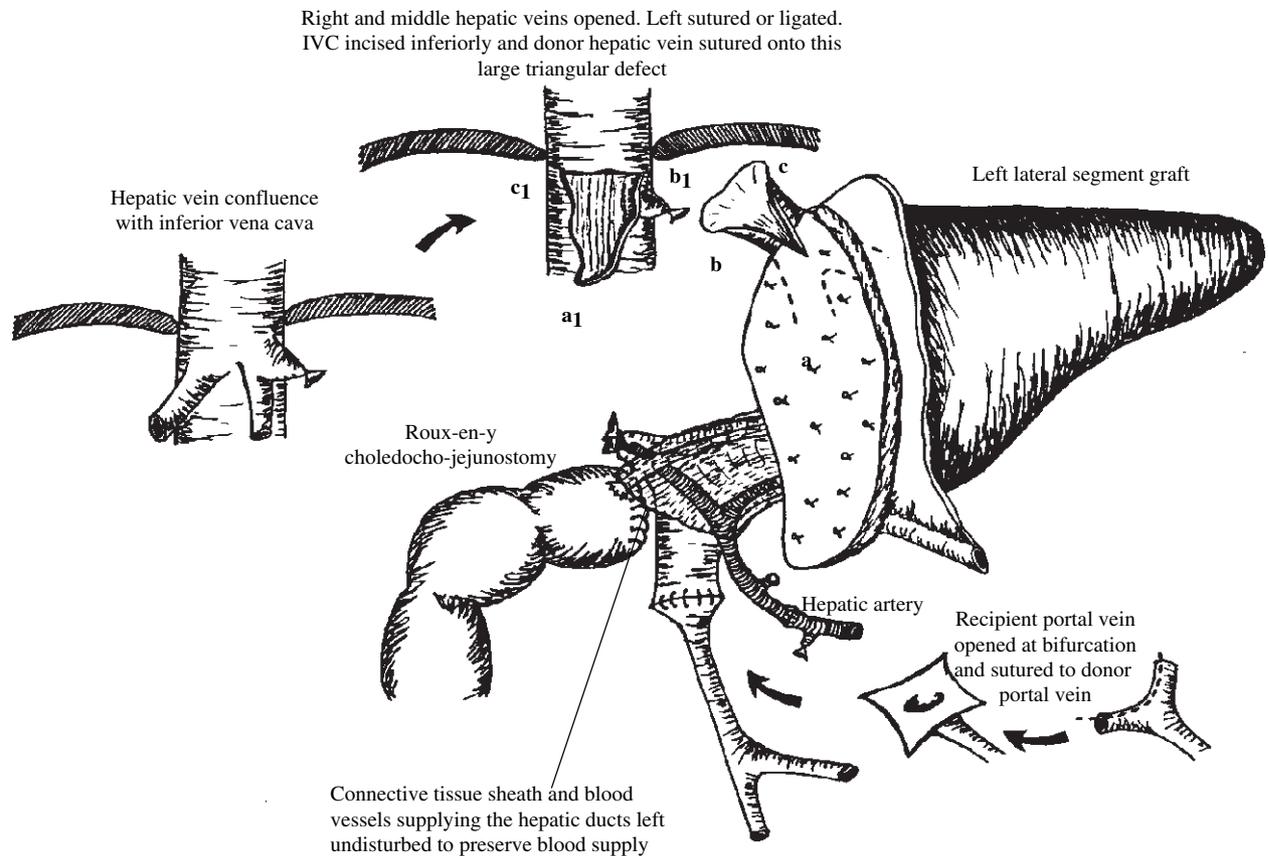
Fig. 2. The surgical technique of a left lateral segment reduced size liver transplant.

types of interposed grafts described in other series were not used in any of our cases. Crucial to the success of the operative procedure was good anaesthetic support (14, 15).

Medical management

Immunosuppression

CyA (5 mg/kg) was given immediately prior to the operation and was continued in the post-operative period initially intravenously but since 1997 as an oral dose using cyclosporin emulsion (Neoral) (Novartis), given as a three times a day dosage aiming for a trough level of around 350 ng/mL initially and currently a 2 h peak level of > 1000 ng/mL (17–19). Dosage was adjusted frequently in the post-operative period as particularly in small children, absorption was erratic with diarrhoea and rejection and low CyA levels being a recognized association. AZA (1–2 mg/kg) and methylprednisolone (10 mg/kg) were given at the time of reperfusion of the graft. The methylprednisolone doses were reduced over the first week to 1 mg/kg for the first month and then further reduced to a level of 0.2 mg/kg as maintenance. This was later reduced in some patients to alternate day therapy or even withdrawn. The AZA dose 0.5–1 mg/kg was monitored keeping the leukocyte count above 4000/mm (2) and was continued for at least 6 months. Tacrolimus was used as rescue therapy if an acute rejection did not respond to three or four daily pulses of methylprednisolone 10 mg/kg/dose and recently with compatible but not identical blood types. Mycophenolate mofetil was used

instead of AZA in three patients because of persistent rejection with conventional therapy and rapamycin has been used in two patients with chronic rejection and high EB virus levels. In the last 2 yr anti-CD25 antibodies have been used (basiliximab 20 mg/dose weight > 40 kg, 10 mg/dose weight < 20 kg, daclizumab 1 mg/kg/dose) both as a two dose regimen (20). Later conversion from cyclosporin to tacrolimus was prompted in a few cases because of cosmetic side effects of gingival hyperplasia and hirsutism.

Anti-infectious agents (3, 21–24)

Fungal prophylaxis was given prior to transplant as mycostatin orally and after transplant, amphotericin B lozenges were added and continued over a period of several months. Infants in poor condition with prolonged pre-transplant in-hospital treatment received intravenous amphotericin for 2–3 wk. From 2–3 wk after transplant for at least the first year, trimethoprim/sulphamethoxazole was given at a dose of 6 mg/kg a day in two divided doses 3 days a week for prevention of pneumocystis carinii infection. As oral therapy has been found to be less effective, intravenous gancyclovir 5 mg/kg per dose 12 hourly was given as viral prophylaxis against CMV and EBV infection, initially for 2 wk but currently this is continued for up to 3 months in high risk patients not previously exposed to EBV in an attempt to prevent post-transplantation lymphoproliferative disease (PTLPD). (25) Either hyperimmune CMV globulin or immunoglobulin in the form of Polygam (Natal Blood

Transfusion Service) was given to assist viral prophylaxis. Leucocyte filtered blood products were used since 1995 to reduce CMV viral load. Prophylactic antibiotics were given with induction of anaesthesia and continued for 3–5 days. These were changed according to cultures taken of blood, secretions, sputum and urine. Anti-TB prophylaxis was given only if the reason for transplant was a reaction to anti-TB drugs, where evidence of TB was found prior to surgery or if close family contact was recorded. Ofloxacin, rifampicin and ethambutol or ethionamide was used in addition to INH but very careful monitoring of liver function tests was required because of both drug induced hepatic toxicity and decrease in levels of cyclosporin or tacrolimus due to enzyme p450 induction with increased drug metabolism (26, 27).

Post-operative care

Post-operative management was according to protocol (3, 28). Patients were usually weaned off the ventilator within the first 48 h. Liver ultrasound with a colour flow doppler was performed frequently to confirm vascular patency and absence of biliary dilatation. Liver biopsies were performed if indicated by increasing serum liver enzyme activity or bilirubin levels by means of the Menghini technique [Hepafix needle (Braun) diameter 1.4 mm] unless biliary dilatation was observed on ultrasonography. Biopsies were routinely assayed for viral and bacterial activity.

Diagnosis of rejection was made on the basis of clinical, biochemical and histologic criteria (29). The grade of rejection was according to established histologic criteria being graded from 0 to 4. Rejection was treated with four doses of methylprednisolone 10 mg/kg, the first three on successive days and then the fourth dose on the fifth day after commencing treatment. If rejection persisted, the immunosuppressive protocol was changed to tacrolimus at a starting dose of 0.3 mg/kg per day in two divided doses to obtain a trough level of 10–15 ng/mL initially.

Hypertension, which was present in all of our patients was managed initially with nifedipine as required in conjunction with diuretic agents and subsequently enalapril or amlodipine in the appropriate dosage (30). Aspirin 3 mg/kg was given on alternate days as prophylaxis against hepatic arterial thrombosis along with sucralfate initially and latterly omeprazole for gastric mucosal protection (31).

Nutrition and vitamin supplementation was commenced usually within 72 h of surgery and was supplemented by nasogastric feeding or parenteral nutrition in the early phase if there was delay in restoration of bowel function. Magnesium and phosphate deficiency required replacement therapy in nearly all patients.

Results

Survival and retransplantations

Since 1991, 71 transplants have been carried out on 68 patients of whom 46 were black and 22 white (Fig. 3). Thirty-three were female and 25 male. The mean weight was 18 kg with a range of 4–53 kg. Twenty-five were less than 10 kg in weight (37%). The mean age was 5.3 yr with a range of 6 months to 14 yr. Patient diagnoses and survival are listed in Table 1. There were three retransplants, one for acute fulminant rejection and two for chronic rejection. The mean anaesthetic time was 10 h with a range of 7–16 and the mean volume of blood transfused was 2.5 blood volumes with a range of 0.5–5.7. Blood group crossmatch was identical in 53, compatible in 15 and blood group B to O in three. The mean donor liver ischaemic time was 8 h with a range of 5–16 h. Reduced size liver transplants were performed on 42 occasions, which included the left lateral segment in 23, the left lobe in 15 and the right lobe in four. Donor recipient weight ratios averaged 3.4:1 with a range of 2:1 to 11:1. Three patients received a whole liver and a kidney graft for primary hyperoxaluria in two, and polycystic disease in one. We have performed one living related transplant (mother to child).

All patients survived the operative procedure. Currently, of the 68 patients transplanted, 50 survive (74%), 2 months to 12 yr post-transplant. Forty-seven of these are in excellent health (Fig. 4). Three have persistent liver dysfunction but are keeping well at home and one is convalescing after recent transplant. The causes and timing of deaths are listed in Table 2 and can be divided into those occurring early after transplant which were predominantly related to the operative procedure itself and those occurring later on, which were predominantly due to the consequences of immunosuppression or of immunosuppressive failure but in one case of

Fig. 3. The number of transplants performed per year from November 1991 until January 2003.
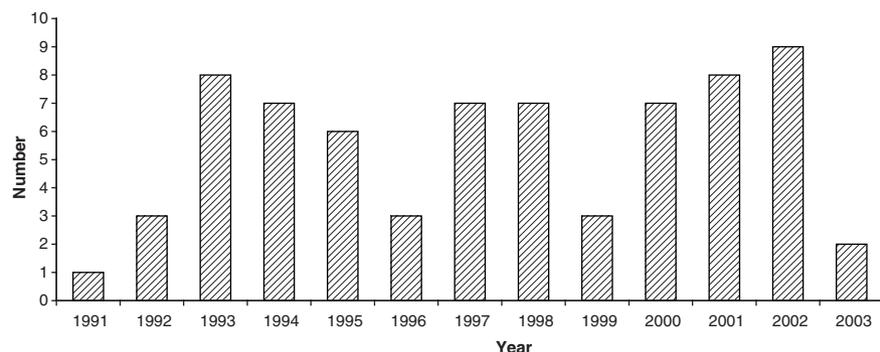
Table 1. Primary diagnosis of recipients from 1991 to 2003. Sixty-eight patients requiring 71 transplants with 50 surviving (74%)

Diagnosis	Number of transplants	Survivors (%)
Biliary Atresia	37	24 (65)
Fulminant hepatic failure	10	6 (60)
Autoimmune hepatitis	5	4 (80)
Alpha-1-antitrypsin deficiency	4	3 (75)
Neonatal hepatitis	3	3
Chronic rejection	2	1
Hyperoxaluria (+ kidney)	2	2
Alagille	2	2
Acute rejection (fulminant)	1	1
Idiopathic cirrhosis	2	1
Polycystic disease (+ kidney)	1	1
Hepatoblastoma	1	0
Budd Chiari	1	1

Table 2. Current status of transplant patients 1991–2003, n = 68

Survivors [n = 50 (74%)]	
Excellent quality of life	47
Persistent liver dysfunction	2
Convalescing	1
Deaths (n = 19)	
Timing	Causes
Early (≤ 1 month; n = 3)	IVC thrombosis, severe rejection, sepsis, haemorrhage
	Primary non-function
	Bleeding oesophageal ulcer
Intermediate (≥1–6 months; n = 2)	Rejection/infection
	Technical, late consequences, portal vein thrombosis and variceal bleed
Late (≥6 months–7 yr; n = 14)	Infection (bacterial, viral, fungal) (n = 6)
	PTLPDs (n = 6)
	Chronic rejection (n = 2)

bleeding oesophageal varices, the consequence of a PVT which occurred shortly after transplant.

Surgical complications

Fortunately these have been relatively few. Hepatic artery thrombosis occurred on one proven occasion and one suspected. The first patient developed a bile leak 1 month post-transplant, which was successfully treated with revision Roux-en-Y hepaticojejunostomy. The other child, an infant of under 10 kg in weight, developed fulminant hepatic failure 3 wk post-transplant and no cause was identified. The hepatic artery was seen to be pulsating on ultrasound. Post-mortem examination was refused. Histology of a needle biopsy showed a massive fallout of liver cells, which was in keeping with either an ischaemic, toxic or viral injury. PVT occurred on three occasions, two of which were repaired successfully and the third led to portal hyperten-

sion and subsequent uncontrollable bleeding varices 6 months post-transplant. Two other bile leaks occurred. The first patient developed a bile leak on the 8th day post-surgery which was successfully repaired and another reduced size liver transplant had bile stained ascites, which resolved spontaneously. Two patients developed IVC thrombosis, the first, 6 months post-transplant probably secondary to chronic rejection and enlargement of the donor graft with distortion of the IVC anastomosis. The second developed an IVC thrombosis in the immediate post-operative period shortly after an acute rejection episode, which had resulted in significant graft swelling. Both patients were treated with thrombolytic therapy, the first successfully but the second developed significant bleeding from the cut edge of the reduced size graft and sepsis and died
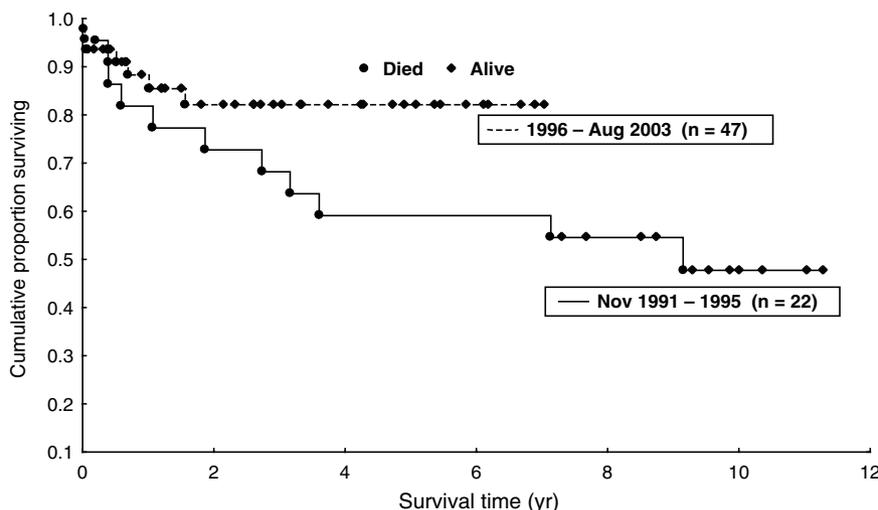

Fig. 4. Pediatric liver transplantation: cumulative proportion surviving (Kaplan–Meier), Nov 1991–1995 vs 1996–2003. The cumulative survival of patients transplanted since 1991 (n = 68) divided into those receiving transplants before 1996 and after. Current expected 5 yr survival is >80%.

shortly after. At post-mortem, however, there was no visible thrombus in the vena cava. Post-operative gastrointestinal bleeding occurred in three patients. One ceased spontaneously, another required laparotomy and was found to be bleeding from the Roux-en-Y anastomotic site and the third bled uncontrollably from a large ulcer in the lower oesophagus secondary to pretransplant sclerosant injection for control of bleeding varices.

Medical follow-up

Most could be discharged from the intensive care unit within the first week after transplantation although in practice this was delayed because logistical problems of a full surgical ward. Bacterial infection in the post-transplant period was frequent but had surprisingly little morbidity and only one suspected mortality. The only systemic fungal infection was the first transplant in 1987 who died of a ruptured mycotic (Candida) aneurysm at the hepatic arterial anastomosis. Minor skin infections have been frequent and have been treated with local anti-fungal agents and fluconazole. Viral infections, however, have been a problem with major morbidity and late mortality (25, 30, 32–34). CMV is endemic in our population and 90% of donors carried the virus (34). CMV disease occurred in 11 patients (13 transplants) and CMV infection in a further 12. Five of 11 patients with CMV disease died. The site of the CMV disease was the lung in four, liver in seven and pancreas and gastrointestinal tract in one each. Initially the diagnosis was made using serology and cultures but from 1995, the CMV PP65 antigen test became available. Particularly at risk were patients with poor clinical status prior to transplantation and those who required steroid pulses for more than one rejection episode. EBV infection has also resulted in significant morbidity and mortality. Ten children developed EBV infection and eight subsequent PTLPD. All were transplanted for biliary atresia following a failed Kasai procedure. The development of PTLPD in five patients followed a typical acute membranous tonsilitis with associated cervical lymphadenopathy. Mean time to development of PTLPD in these children was 9.2 months, with a range of 3–30 months post-transplant. Three of the eight children were EBV nuclear antigen positive at the time of transplant and all were positive at the time of diagnosis of PTLPD. Subsequent development of PTLPD included four tonsillar, one intestinal, two gastrointestinal tract and one central nervous system involvement. Histology confirmed the diagnosis, which was described as polyclonal in four, monoclonal in two and T-cell lymphoma in two.

Management strategies included adenotonsillectomy, reduction of immunosuppression and in two complete withdrawal (24, 25). Three received chemotherapy and these three died within 10 wk of diagnosis. Three died despite significant reduction in immunosuppression but two patients have made a complete recovery although one required retransplant for chronic rejection after total immunosuppression withdrawal. Thus overall there was a 14% incidence of PTLPD with a 75% mortality. Currently, pre-emptive intravenous gancyclovir therapy given for at least 3 months to high risk children and PCR viral monitoring only available in the last year, has so far been effective management (23, 25).

Hepatitis B *de novo* infection has occurred in five children and resulted in three deaths. Although not proven, these almost certainly were acquired from the donor liver as prior to 1996 donor livers were not tested for HBV core antibody and since excluding HBV core antibody positive donors, we have not seen a case (35). Of these five patients, three developed HBV hepatitis post-transplant and have died of severe progressive chronic active hepatitis. The other two survivors have responded very well to anti-viral therapy using initially famciclovir and currently, lamivudine with reduction of HBV DNA levels from more than 1000 pg/mL to below recordable levels (32, 36, 37). One patient however escaped initial control and being poorly compliant, developed DNA levels in excess of 700 pg/mL and died.

All children have received some form of anti-hypertensive therapy in the post-transplant period. As a degree of renal impairment is almost inevitable with patients suffering from severe chronic liver disease and with the additional burden of use of the nephrotoxic calcineurin inhibitors, cyclosporin and tacrolimus for immunosuppression, most children continue to require at least one anti-hypertensive agent (30). When the doses of steroids were reduced and cyclosporin and tacrolimus levels were allowed to settle to the lower therapeutic range, less anti-hypertensive therapy was required.

All surviving children of school-going age (25) attend school normally and participate in normal sporting and recreational activities. Three children transplanted for biliary atresia, have learning difficulties and attention deficit disorder and require special schooling but are physically fully rehabilitated (38). All eight children transplanted for fulminant hepatic failure made a complete neurologic recovery after transplant.

The overall cumulative 5 yr survival is around 60% but the projected survival since 1996 when aggressive anti-viral prophylaxis was started along with exclusion of HBV c AB +ve donors and a more pro-active follow-up programme is above 80% (Fig. 4).

Discussion

Careful planning, extensive preparation of personnel and a broad base of skills along with excellent team work between adult and paediatric health professionals allowed for the development of a successful paediatric transplant programme (3–5). Further improvements in surgical technique, anaesthetic skills, medical care and immunosuppressive therapy have increased our projected 5 yr survival to greater than 80% and much longer survival in good health is clearly possible and should become the norm in the future. These results are equivalent to other reported series (39, 40). However, liver transplantation remains an extremely demanding surgical procedure with many potential early and late complications (41, 42). Most of the serious complications occurred in the first few months after operation and many of these could have been avoided with meticulous attention to technical detail and intensive prophylactic measures. The regrettable need for immunosuppressive therapy with all its consequences along with immunosuppressive failure still remain major stumbling blocks to an uneventful post-operative course. After the first few months post-transplant complications usually resulted from immunosuppressive therapy whether this was infection, usually viral, or from the toxic effects of the drugs themselves (30). All three children receiving liver and kidney grafts have done well. One older child (10 yr) with hyperoxaluria continues to receive overnight hydration via button gastrostomy. The one child transplanted for multisectoral hepatoblastoma had portal vein tumour involvement at transplantation and despite apparent complete surgical clearance developed multiple hepatic metastases 3 months post-transplant. Her tumour showed evidence of vascular invasion on histology and did not respond well to cisplatinum and adriamycin chemotherapy. At the time of writing, she has an enlarging liver and no further anti-tumour therapy is contemplated.

Patients have been referred from all over South Africa and clearly this dislocation from family, friends and workplace has had major emotional and financial implications. Initially referrals frequently occurred when the child was in very poor condition, however this has been less frequent in recent years. The premorbid clinical state had significant detrimental impact on the subsequent outcome following surgery (3, 7, 8, 41). The increasing evidence that patients with cholestatic liver disease early on in life have nutritional deficiencies which render them at risk for neuro-developmental impairment was confirmed being present in four of our longer-term survivors (38, 42). There is thus a need for earlier referral and transplantation in these children. We have made it an absolute requirement that any patient referred would need caring health professionals to take on the responsibility of looking after that patient on return to his/her home following successful transplantation. Current methods of electronic communication greatly facilitate improved management and long-term follow-up of patients.

Endemic viral and bacterial infections particularly CMV, EBV and TB have had a significant negative impact on our programme (32–34, 36, 43). Specifically the strategies of anti-viral protection have required extended hospital stay and are clearly expensive, but fortunately seem to be effective in preventing CMV disease and the consequences of EB virus infection or reactivation (21, 25).

Hepatitis B acquired after liver transplant is a tragic occurrence and in our experience is not a benign disease. Evidence that most were acquired from HBV core antibody positive donors is overwhelming. One published series quotes a greater than 80% conversion rate (35). In two of our five patients anti-viral therapy has been effective in reducing viral DNA levels but eAg remains positive in both (37). Since 1996, when we introduced HBV core Ab screening for liver transplants we have not seen a further case.

TB with its very high endemic incidence in the South African population (150–200 per 100 000) is a constant hazard to any immunosuppressed child. Careful screening of the child and family pretransplant is necessary. Prophylaxis or full treatment can be successfully carried out but hepatotoxicity and markedly reduced cyclosporin levels which may require up to five times increase in dosage are potential dangers and should be anticipated (43).

The costs of our transplant programme are difficult to quantify but detailed costing of some of our patients has indicated that an uncomplicated transplant costs in the region of 20 000 US$ for the first 3 months and thereafter approximately 500–1000 US$ per month for the first year. The costs of immunosuppression medication are significant but decrease, as smaller doses are required.

Complications after transplantation and retransplantation become very expensive thus we have attempted to transplant those children who would likely benefit most from the procedure. This has meant in some instances that patients on the waiting list in a poor medical condition have been overlooked in favour of those in better health but still with irreversible liver disease. Also retransplantation has rarely been an option because of donor scarcity. Compliance with regard to medication and follow-up is an absolute requirement for success. This is easier to predict pretransplant in those with chronic liver disease than those who present with fulminant hepatic failure. Poor socio-economic status has never been a contra-indication to transplantation and we have been frequently impressed by parents with relatively poor material resources who have been able to diligently care for their children. The value of a sympathetic social worker to provide support for distressed families cannot be overstated.

The need for paediatric liver transplants has been assessed at approximately one to two children per million per year and this would mean 20–30 transplants per year being required in South Africa (4, 5). In practical terms, this would be possible but clearly financial resources need to be allocated to such an endeavour. In recent years, more than 60% of children referred for transplantation come from outside of the Western Cape Province without at present any strategies in place to compensate the Western Cape Provincial Government and our centre for the costs involved. These costs are, however, very much less than those required for a South African child to receive a transplant overseas and it is distressing to still occasionally observe in the media of money being raised for this purpose when the facilities are available locally at one-tenth of the cost.

A most serious issue currently facing all transplant physicians, and we are no exception, is the major shortfall in donor organs needed to meet current demand. This is compounded in our country by endemic HBV infection and the increasing prevalence of HIV in the donor pool with current HIV infection rates in the 15–40 yr age group estimated at around 20–40%. This has to some extent been alleviated for children by use of reduced size livers (44, 45). As the numbers waiting for adult transplants becomes greater, we will have to proceed with more frequent living related donation (45–47). At present, split liver transplantation is beyond the capacity of our restricted human resource allocation (5, 46, 48–50). The potential of organ transplantation is great and the number of children requiring and receiving liver transplants is likely to increase. There will thus be an increasing need for a wider involvement of local medical and surgical teams and perhaps the development of other transplant centres in South Africa to cater for this demand. As with any new development, knowledge and experience improves, costs decline, application increases and success is ensured (51).

Acknowledgments

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