

Paediatric renal transplantation: a single centre experience

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ABSTRACT

Introduction: Renal transplantation (RT) is the therapy of choice for children with end-stage renal disease (ESRD). Hospital de Santa Maria's Paediatric Nephrology Unit RT programme began in 1995 and its living related donor transplantation programme in 2003. Our study evaluates the Unit's performance over 12 years. **Subjects and Methods:** We retrospectively analysed data on the kidney recipients followed at our centre from September 1995 to September 2007. **Results:** Fifty patients were studied, mean recipient age was 12 ± 3 years (2 to 18 years) and mean RT/year was 4. Uropathy (obstructive and refluxive) was the most prevalent ESRD aetiology; (46%). All patients underwent dialysis before transplantation and mean time on dialysis was 20 ± 20 months (1 to 84 months). Transplantation from living related donor was performed in 5 (10%) patients. Immediate graft function occurred in 48 (96%) patients. Episodes of acute rejection were observed in 15 (30%) patients. Urinary tract infections were diagnosed in 17 (34%) patients, CMV infection in 21 (42%) and tuberculous meningitis in one (2%) patient. One (2%) patient developed a lymphoproliferative disease. Graft survival from living related donor transplant was 100% at 1 year and graft survival from cadaveric donor transplant was 94%, 84% and 50% at 1, 5 and 10 years, respectively. In adolescents treatment noncompliance was the main cause of graft loss (71%). Global patient survival was 96%. **Discussion:** Although these results are similar to those of other paediatric units, specific measures to optimise compliance in adolescents, and increased

live donation and the implementation of surgical techniques to transplant younger children would contribute to improving the health-related quality of life of our patients.

Key-words:

Children; end-stage renal disease; renal transplantation.

INTRODUCTION

Renal transplantation (RT) is the therapy of choice for children with end-stage renal disease (ESRD)¹⁻³, allowing a return to a fairly normal way of life. Dialysis is considered a transitory therapeutic choice while waiting for RT or between transplantations⁴.

In Portugal the incidence of ESRD in paediatric patients is about 2 to 3 new cases per million inhabitants per year⁵. Twenty to 30 ESRD children aged below 18 years per year are expected.

The Hospital de Santa Maria (HSM)'s Paediatric Nephrology Unit RT programme began in September 1995 and its living related donor transplantation programme in 2003. Our centre provides facilities for RT patients aged below 18 years old in a paediatric setting and is the reference centre for the south and islands.

Our study evaluates the Unit's performance, aiming to improve the quality of healthcare for the paediatric ESRD population.

SUBJECTS AND METHODS

Retrospective, descriptive study reviewing the clinical records of patients followed in our Unit and who underwent RT between September 1995 and September 2007.

Demographic data, ESRD aetiology, type and time on dialysis, priority on the waiting list, donor characteristics, HLA mismatch, immunosuppression, infection prophylaxis, graft function, rejection episodes, surgical complications, infectious complications, recurrence of primary disease, graft survival and patient survival were studied.

Data are expressed as mean±SD. We used Student's unpaired t-test to compare means between groups, with a $p < 0.05$ indicating statistical significance. Kaplan Meier plots were used for calculating graft survival.

RESULTS

Fifty patients were followed during the 12 years of the RT programme. Forty six were transplanted at HSM, three at Hospitais da Universidade de Coimbra (two hepatic-renal transplantations) and one infant at Hôpital Necker in Paris. Forty nine patients received a first transplant and one had a second graft.

There was a mean of 4 RT/year over the study period as a whole. The mean was 2 RT/year for the first five years of activity which then increased to 5 RT/year for the rest of the study period. In 2007 9 RT were performed (Fig. 1).

Twenty eight patients (56%) were male, eight (16%) were non-Caucasian and seven (14%) from African countries whose official language is Portuguese. Mean recipient age was 12 ± 3 years (2 to 18 years). Eleven (22%) patients were below 10 years old. Sixteen (32%) weighed under 25 kg at transplantation and only three (6%) weighed under 15 kg.

Uropathy (obstructive and refluxive) was the most prevalent ESRD aetiology, occurring in 23 (46%) children (Fig. 2).

All patients underwent dialysis before transplantation. The mean time on dialysis was 20 ± 20 months (1

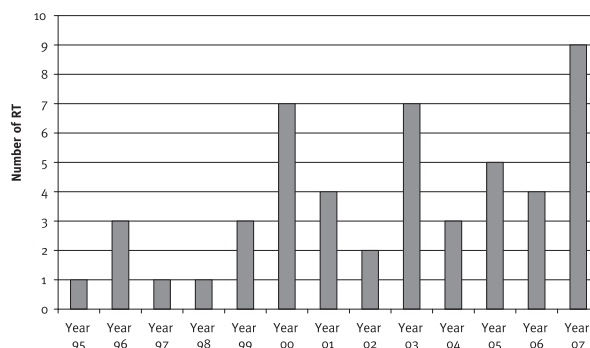


Figure 1
Number of RT per year

to 84 months). The mean time on dialysis for children aged below 10 years old was 30 ± 26 months (3 to 84 months), and for children aged over 10 was 16 ± 16 months (1 to 72 months). This difference attained statistical significance ($p = 0.01$). Prior to RT, 30 patients (60%) underwent peritoneal dialysis, 11 (22%) haemodialysis and nine (18%) both techniques. Two (4%) patients were maximum priority on the waiting list when the RT was performed. Only one patient presented high (>80% PRA) serum HLA antibodies.

Five (10%) patients received grafts from living related donors. The donor was the mother in three patients and the father in two.

Mean cadaveric donor age was 19 ± 9 years (5 to 37 years). Nineteen donors were aged below 18 years old, with mean recipient age 11 ± 4 years (5 to 18 years).

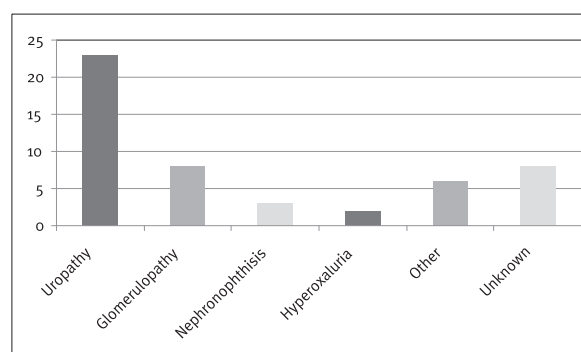


Figure 2
ESRD aetiology

Most patients had four (23-46%) or three (12-24%) HLA mismatches.

From September 1995 to May 2000 induction immunosuppression was with polyclonal anti-lymphocytes immunoglobulin and methylprednisolone. After May 2000 basiliximab and methylprednisolone were used for maintenance and 38 (76%) patients received this therapy. Triple immunosuppression was used for maintenance in all cases. Prednisolone was used in all patients, starting with 60 mg/m²/day with subsequent tapering over 6 months, to 10 mg/m² every other day. Ciclosporin was used until April 2006, and after that date changed to tacrolimus (0.1-0.2 mg/kg/day adjusted by trough levels). For cosmetic adverse side effects 14 (28%) patients on ciclosporin were switched to tacrolimus. The third immunosuppressive drug was azathioprine in 1995-1996 and mycophenolate mofetil (1.2 g/m²/day) after that time.

Immediate graft function occurred in 48 (96%) grafts. Two had acute tubular necrosis, one needing dialysis. Both recovered normal function.

Episodes of acute rejection were diagnosed, based on raised (>10%) serum creatinine, in 15 (30%) patients. Needle graft biopsies were performed in 12 (24%) cases showing two acute rejections (Banff I), four chronic rejections, one recurrent focal segmental glomerulosclerosis, one focal C4D positive, one acute tubular necrosis, one tacrolimus toxicity and two with nonspecific interstitial changes.

Patients with uropathy received prophylaxis for urinary tract infections with trimethoprim for six months after RT. Prophylactic protocols for viral infections started in 1996 for CMV and in 2003 for EBV. Both consisted of immunoglobulin and ganciclovir followed by valganciclovir in all negative recipients with a positive donor. After RT, patients received nystatin for four weeks and co-trimoxazol for six months as prophylaxis against candidiasis and *Pneumocystis jirovecis* respectively.

Urinary tract infection was diagnosed in 17 (34%) cases, mainly in the first six months after RT. Three patients developed other bacterial infections: *Staphylococcus* coagulase negative sepsis in the second day after RT, pneumonia one year after RT and tuberculous meningitis diagnosed three years after RT.

CMV serology "mismatch" donor/recipient is shown in Table I. CMV infection occurred in 21 (42%) cases of which seven (33%) were CMV negative before RT. One patient had systemic serious infection with pneumonitis. All the other had minimal (fever, leucopaenia or mild transaminases elevation) or absent clinical signs with significant viral replication detected by polymerase chain reaction (PCR).

Table I

CMV serology "mismatch" donor/recipient

CMV Donor/Recipient	Number of patients
+/+	24
-/-	2
+/-	19
-/+	5

Varicella infection with pericarditis and hepatic dysfunction occurred in one patient.

Surgical complications were observed in 10 (20%) cases. Three were major: intestinal necrosis, haemoperitoneum (hepatic-renal transplantation) and vascular anastomosis disruption. The others were minor: three ureteral obstructions, two lymphoceles and two renal vein thrombosis (partial obstruction of the lumen without functional significance and total recovery).

In one patient an EBV-driven post-transplant lymphoproliferative disease (PTLD) was diagnosed two years after RT. The disease remitted with progressive reduction of immunosuppression and the graft still survives with near normal function five years after diagnosis.

Thirty three (67%) patients have arterial hypertension, which started before RT in 24 (73%).

Graft survival from living related donors was 100% (5/5) at 1 month and 100% (2/2) at 1 year. Graft survival from cadaveric donors was 94% (36/38) at 1 month and at 1 year, 84% (16/19) at 5 years and 50% (2/4) at 10 years (Fig. 3). The main cause of graft loss in adolescents was non-compliance, occurring in 71% (5/7) of cases. Four of these patients lost their grafts after transition to the adult clinic. One patient had graft failure following a vascular

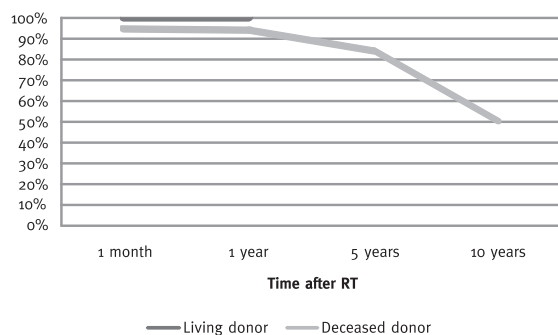


Figure 3
Graft survival (Kaplan-Meier)

anastomosis disruption and another due to acute vascular rejection.

Global patient survival is 96% (48). One patient died from a major surgical complication in the second week after RT and the other from sepsis five years after transplantation at the age of 24 years.

DISCUSSION

Paediatric renal transplantation poses numerous challenges. These include not only the conventional problems of rejection, infection and long-term complications, but also the need for technically creative surgery to accommodate the significant size range of paediatric patients⁶.

Despite the increased number of RT per year in our centre, probably related to the April 2007 changes in organ allocation⁷ – paediatric age is now the first priority criteria when donors are under 18 years old – we are still falling short of our goals of reducing the RT waiting list and performing preemptive RT, goals achieved in other paediatric centres⁸⁻¹². This study showed that in our population this problem is worse in younger children, who have a significantly longer time on dialysis than older children. The implementation of the living related programme (started in our Unit in 2003) should help us to achieve these objectives.

Acute rejection became less frequent with the use of new immunosuppressant agents, as we can ver-

ify when comparing our results with previous studies performed in the Unit^{13,14}. However, the consequences of increased immunosuppression need to be evaluated in terms of new infections and long-term consequences, including malignancies, diabetes, and cardiovascular disease^{8,9,11,15,16}.

Urinary tract infection was the most prevalent bacterial infection in our study, with an incidence similar to other paediatric units^{8-10,17}; uropathies are still a major aetiology of ESRD in paediatric patients. The high number of CMV positive recipients is probably related to the relatively ‘old’ age of this paediatric group. CMV infection was frequent, as in other centres^{6,8,10,17}, but in our cases was almost never serious, even with a high prevalence of CMV negative recipients. This is probably because our practice of periodic determination of viral replication using the PCR technique led to early diagnosis allowing preemptive therapy and also because of our use of prophylaxis in CMV negative recipients when donors are CMV positive.

One patient developed *varicella* complicated by hepatic dysfunction and pericarditis, but maintained normal graft function and recovered completely after treatment. Nowadays *varicella* immunisation is recommended before transplantation for all patients with negative serology for *varicella-zoster*.

Another patient developed severe tuberculous meningitis, despite having had BCG, and this was related to close contact with an adult with untreated pulmonary tuberculosis.

De novo malignancies are a potential complication in these immunocompromised patients^{6,9,11,16}. EBV-driven PTLD is a particular problem in the young patient with no previous EBV exposure who receives a donor organ-recipient mismatch⁶. In our population a 12 year-old boy developed PTLD two years after RT. He made a total recovery with reduction of immunosuppression to a very low level and still maintains normal graft function eight years after RT.

Although overall results are comparable with those of several other paediatric Units^{6,8,10,11,15-20}, we need to implement several measures to optimise the quality of life and to provide a better life expectancy to adult age for children with ESRD. Adolescents are the highest risk group for graft loss,

mainly related to non-compliance with treatment^{6,11,15,21,22}. We are now focussing on improving the care of adolescents and their families, using new strategies of therapeutic self-monitoring, home visits, individualised treatment schedules adjusted to social and academic activities, psychological counselling and preparation for transition to the adult clinic²³.

Conflict of interest statement. None declared.

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