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Renal Transplantation in Children

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SYMMARY

With the purpose of discussing the specific problem of renal transplantation in children, we reviewed our experience. From May 1977 to April 1992, 407 transplants were performed, 50 (12.3 %) of them in 44 children between 2 and 15 years old. The mean age was 11.3 (SD= 3.3). Seven children were submitted to transplantation without previous dialysis (14 %). Cadaver donors were used in 11 cases (22 %), living related donors in 32 (64 %), and non-related or distant relatives in 7 (14 %). The immunosupression therapy used until 1986 was azathioprine and prednisone, and after this year, cyclosporine was added. OKT3 was used, in the treatment of steroid-resistant acute rejection (6 cases). The survival of the patient and of the allograft, in the first transplant with living donor, in the first year was, respectively, 94.9 % and 82.7 %. Four adolescents lost 5 allografts because of non-compliance. We concluded that there are certain peculiarities to transplantation in children, like technical diffilcuties owing to the size of the children, the greater frequency of obstructive uropathy as the underlying pathology, and non-compliance to treatment, specially in adolescents.

Introduction

The annual incidence of new pediatric patients accepted for renal replacement therapy in the state of Rio Grande do Sul (Brazil), was 0.58 per milion child population (PMCP) until 1975, and increased progressivily until 1988 when this incidence was 6.5 PMCP[1].

Despite significant advances in dialysis technology, successful renal transplantation remains the therapy of choice for children with end-stage renal disease[2,3]. Pediatric renal transplant recipients enjoy a better quality of life than children maintained on dialysis, because transplantation prevents the psychological and neurological impairment, promote a better growth rate and mental development[4]. However, there are a series of obstacles that make truly successful transplantation often difficult to achieve. There are a number of biological differences bewtween children and adults wich can affect the outcome of renal transplantation in childhood, mainly in cadaveric donor.

The aim of this analysis is to present our long term results and consider some points that are of particular interest in children transplantation as technical difficulties, noncompliance, growth retardation, and the preparation of the recipient who frequently needs a surgical correction of anatomical abnormalities of urinary tract, including obstructive uropathies.

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Patients and Methods

We have analysed all children who underwent a renal transplant at our institution from may 1977 to april 1992, with age less than 15 years at the time of transplantation. There was a 100 % complete follow-up in all patients, with a minimum follow-up of 6 months. No patients were excluded from analysis.

Outcome was analysed using actuarial survival data. We analysed the growth rate by means of the standard deviation score (SDS) wich is calculated from the formula: SDS=x−x1/SD1, where x is the parameter being measured, x1 and SD1 are the sex and age-specific mean and standard deviation, respectively, of the parameter in the reference population[5].

Results

In this period, 407 renal transplant were performed, in our transplant unit, 50 (12.3 %) of then in 44 children bet-

ween 2 and 15 years old. The mean age was 11.3 years (SD=3.3), sixteen were less than 10 years old, and three of them were younger than 3 years. The weight ranged from 8 to 46 Kg, with a mean of 27.53 Kg; twelve weighted less than 20 Kg, and only one less than 10 Kg. Twenty-five children (66.8 %) were female. The primary diagnoses of the recipients were: glomerulonephritis (27.3 %), obstructive uropathy (25 %), and reflux nephropathy (15.9 %). Five children with obstructive uropathy underwent a surgical correction before transplantation, one patient underwent augmentation cystoplasty and one had prior urinary diversion (bilateral urocutaneous ureterostomy). Cadaveric donor were used in 11 children (22 %), living related donor in 32 (64 %) and non-related or distant relatives in 7 (14 %). Seven children underwent transplantation without previous dialysis (14 %) and the mean time of waiting on dialysis was 14.5 ± 14.6 months. The inmunossupressive therapy used until 1986 was azathioprine and prednisone, and then cyclosporine was added to the regime. The mean initial dose of prednisone was 0.77 mg/Kg/day, 0.43 mg/Kg/d at 6 months and 0.27 mg/Kg/d at one year after transplantation. Episodes of acute allograft rejection were treated with methylprednisolone, 500 mg/day in children with more then 30 Kg and 15 mg/Kg/day in children with less then 30 Kg, for 3 to 5 days.

Considering all children, after a mean follow-up of 26.1 (+22.81) months, we lost 6 patients. Two died with functioning allografts, at 1 and 72 months after transplantation, due to renal bleeding and lip carcinoma, respectively. Three children died from septicemia, at 1, 31 and 38 months after transplant, and one child died in the transoperatory period from a ventricular fibrillation.

At the end of follow-up, twenty-one allografts were lost in twenty children, 6 due to acute cortic-resistent rejection, 11 owing to chronic rejection, 2 children died with functioning allograft, and 2 grafts were lost in the perioperatory, period (1 renal artery thrombosis and 1 child died due to ventricular fibrilation).

Rejection accounted for 80.9 % of graft failures. There were a total of 46 episodes of acute rejection (8.9 episode/patient). In the group treated with double therapy (n=10), three grafts were lost due to acute steroid-resistant rejection, 2 of them treated with radiation without success. In the group on triple therapy (n=40), there were 8 (20 %) episodes of acute steroid-resistant rejection, six of them were treated with OKT3 for ten days, with recovery of renal function in 5. Eleven grafts were lost due to chronic rejection (52.3 %), from this group, 4 children lost 5 allografts secundary to non-compliance, which represents 23.8 % of total grafts loses, 29.4 % of immunologic graft failure and 45.5 % of allograft lost in the first year after transplantation.

Thirty-two children were followed for 1 to 8 years after transplantation. The mean height at transplantation was 3.09 SD below the normal mean. After one year of transplantation, the mean heigh was −3.36 SD, and at the second and third year, −2.93 SD and −2.65 SD, respectively (Fig. 1). Growth was nevertheless very different from one patient to another. The mean height gain for children transplanted with less than 10 years was 5.33 cm/year at the first year, and 3.08 cm/year for children with more then 10 years at transplantation (Fig. 2).

The one year actuarial patient survival for first transplantation with living donor was 99.4 %, and the graft survival was 82.7 %.

Discussion

We performed 7 (17.9 %) transplants without prior dialysis, and we believe that any children with end stage renal disease is an active candidate for transplantation, but unfortunately this approach is not suitable for all children. Forty seven percent of children who had a living donor

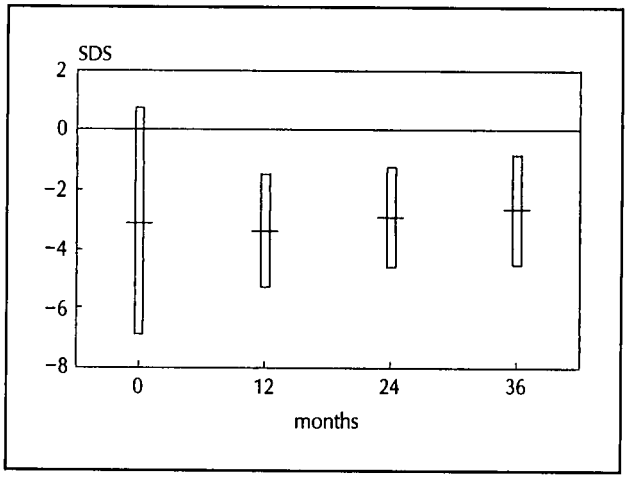

Fig. 1.—Standard deviation score (SDS) profiles for height in 32 children at transplantation and after three years of follow-up.

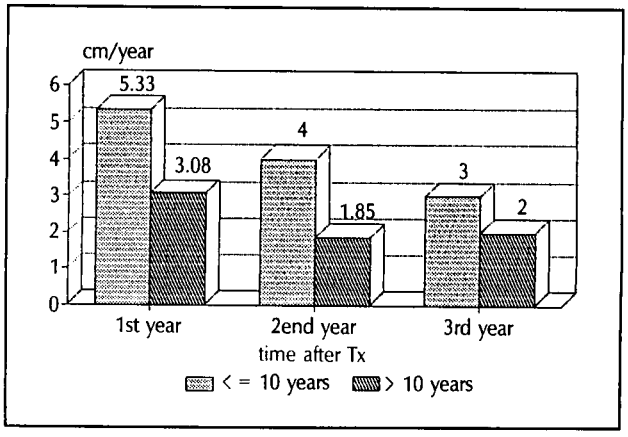

Fig. 2.—The mean growth velocity (cm/year) in 32 transplanted children considering age at transplantation.

were transplanted before completing 6 months on dialysis. In contrast, the children who underwent a cadaveric donor transplant, 54 % had to wait on dialysis for more then one year.

Most of the grafts were from living related donors (64 %), in contrast to other countries[6]. Cadaveric donation is increasing but still insufficient in our country, so cadaveric grafts were used primarily in cases in which the patients didn't have a relative donor. There were 5 grafts from non-related living donor in this survey, all of them from adoptive parents, grandparents or friends. The sale of organs is forbidden in Brazil by legislation[1].

Among the factors that seem to play an important role in the success of renal transplantation in children, non compliance must be emphasized. Non compliance was admitted by more than 40 % of patients with chronic rejection in this series, a proportion greater than reported by Broyer[6], and the Los Angeles group[7], but similar to that referred by Colón in his review[8]. We must attempt to identify the children at risk for non compliance.

Infection following transplantation in pediatric patients accounts for approximately half of the reported morbidiy and mortality in this population as reported for many authors[6, 9, 10]. In our series, we lost 6 children, and the most frequent cause of death was infection. Three children died from septicemia in differents periods after transplantation.

Growth remains the main concern in the transplanted child, since most of them remain with height below the normal mean. Our results, as well as McEnery's[11], suggest that delaying transplantation beyond the 10th year of age for children who need a transplant is a disadvantage in terms of improvement in height. In orden to maximize post-transplant growth, not only a transplant should be performed as soon as possible, but also the dosage of corticosteroids should be minimal, and the allograft function must be excellent. It is probable that these three factors act synergistically, and therefore an adverse effect on growth can occur if any one is suboptimal[8, 12]. However, the reduction of the dose of corticosteroids increase the risks of rejection, and the development of new immunosupressive drugs, will probably produce better results in terms of growing.

In conclusion, we believe that transplantation has been a successful treatment for children with chronic renal failure, and better results will be achieved with advances in immunology, immunosuppressive therapy, and adequade patient management.

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