Pediatric Kidney Transplantation : Siriraj Hospital Experience

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Abstract

We reported six children with end stage renal disease (ESRD) who received kidney transplantation in our unit from 1996 to 2000. They were 5 boys and 1 girl and their mean age was 9.7±2.7 years (range 6.8 to 13.2). Etiologies of ESRD were congenital anomalies (3 patients), chronic glomerulonephritis (2 patients), and rapidly progressive glomerulonephritis (1 patient). Prior to the transplantation, chronic peritoneal dialysis was used in 5 patients, including one who had to switch to hemodialysis due to chronic exit site infection and 1 had preemptive kidney transplantation.

All children received a kidney from living-related donors, 4 from their fathers, 1 from his mother, and 1 from his elder brother. Triple immunosuppressive drug therapy (prednisolone, azathioprine, and cyclosporine A) was initially given to all patients. Serum creatinine returned to normal within the first week in all patients and 4 patients were discharged home by the end of the second week post operation. Immediate complications included severe hypertension (all patients), ureteral leakage (2 patients), neutropenia (3 patients) and nephrotic syndrome (1 patient). Azathioprine was discontinued in 2 patients due to persistent neutropenia. Cyclosporine A was discontinued in 1 patient due to hepatotoxicity, this patient was maintained on mycophenolate mofetil and prednisolone. Serum creatinine levels at last follow-up (mean 24.3±19.0 months, range 8-55) were normal in 5 patients and slightly increased (1.5 mg/dl) in one. Five patients returned to school full time within 1 year after kidney transplantation. Height standard deviation score improved markedly as early as 6 months post transplant. The cost of maintenance of the immunosuppressive drugs was similar to adults, i.e. 6,859.1±1,151.8 Baht per month at 6 months post kidney transplantation.

We concluded that kidney transplantation can be performed successfully in selected Thai children with very good results and similar cost of treatment as for adults.

Key word : Pediatric Kidney Transplantation, Renal Replacement Therapy, End Stage Renal Disease

SUMBOONNANONDA A, LERTAKYAMANEE J,
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J Med Assoc Thai 2001; 84: 1084-1089

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End-stage renal disease (ESRD) is unfortunately not rare in children. During 1997, the incidence of ESRD patients under 19 years old was 13 per million US population[1]. The true incidence of ESRD in Thailand was not known but at least 238 children with moderately severe chronic renal failure and ESRD were diagnosed between 1996 and 1998[2]. Renal replacement therapy is necessary in children with ESRD and the 3 most preferred modes of therapy are peritoneal dialysis, hemodialysis, and kidney transplantation.

Pediatric kidney transplantation was first performed in the late 1960's[3]. Experience has increased dramatically to such an extent that kidney transplantation has become the treatment of choice for children with end-stage renal failure in developed countries[4-6]. Pediatric kidney transplantation was first reported in Thailand in 1996[7]. Since then, more patients have received kidney transplantation in our unit. We described the management and outcome of these patients.

PATIENTS AND METHOD

From 1996 to 2000, 6 pediatric patients received kidney transplantation at the Department of Pediatrics, Siriraj Hospital. All of them were from living related donors (1 from his brother, 1 from his mother, and 4 from their fathers). Demographic data is shown in Table 1. The mean age was 9.7±2.7 years (range 6.8 to 13.2 years). Etiologies of ESRD

Table 1. Pediatric kidney transplant : Siriraj Hospital experience 1996-2000.

Pt	Sex	Age (yr)	Cause	RRT	Drugs	Last Scr (mg/dl)
1	F	8.0	CGN	CPD	PCA/PA	0.7
2	M	7.3	PUV	APD	PCA/PM	1.0
3	M	11.0	VUR/NB/Hyp	CPD	PCA	1.0
4	M	13.2	VUR/CBN	CPD	PCA	1.1
5	M	11.8	RPGN	CPD/HD	PCA/PC	1.0
6	M	6.8	FSGS	CPD	PCA/PC	1.5

Note : RRT = renal replacement therapy, Scr = serum creatinine, CGN = chronic glomerulonephritis, PUV = posterior urethral valve, Hyp = hypoplastic/dysplastic kidney, VUR = vesico ureteral reflux, NB = neurogenic bladder, CBN = contracture bladder neck, RPGN = rapidly progressive glomerulonephritis, FSGS = focal segmental glomerulosclerosis, CPD = chronic peritoneal dialysis, APD = acute peritoneal dialysis, HD = hemodialysis, P = prednisolone, C = cyclosporine, A = azathioprine, M = mycophenolate mofetil

Table 2. Medical complications post transplant in 6 patients.

Complications	< 1 month %	1-6 month %	> 6 month %
Hypertension	100	83.3	66.7
Rejection	-	83.3	50.0
Infection	16.7	66.7	33.3
Hepatotoxic	-	-	16.7
Neutropenia	16.7	50.0	16.7

were congenital anomalies (3 patients), chronic glomerulonephritis (2 patients), and rapidly progressive glomerulonephritis (1 patient). Chronic peritoneal dialysis was utilized in 5 patients including one patient who had to switch to hemodialysis afterward due to a chronic exit site problem.

Urinary tract anomalies were corrected prior to transplant. The anesthesiologist, pediatric urologist, and pediatric nephrologist communicated and co-operated closely throughout the perioperative period. All patients received triple therapy (prednisolone, azathioprine, and cyclosporine A) for immunosuppression initially. Intravenous methylprednisolone and cyclosporine A were given immediately pre-operation and shifted to orally as tolerated. Azathioprine was given orally from day 1 post-operation.

Height standard deviation score (HSDS) was calculated according to Tanner et al[8].

Statistical methods

All data were analyzed using the SPSS statistical package. Comparison of HSDS change was performed using the 2-tail Student's *t*-test. A p value of less than 0.05 was regarded as significant.

RESULTS

Serum creatinine levels returned to normal with good urine flow by the end of the first week post operation in all patients and four patients were discharged home by the end of the second week post-operation. One patient (pt. 1) remained in the hospital for 4 weeks due to severe hypertension. Another one (pt. 6) had nephrotic-range proteinuria which resolved after plasmapheresis and oral cyclophosphamide. Neutropenia in pt. 2 and 5 resolved after discontinuation of azathioprine. Hepatotoxicity due to cyclosporine A was also found in patient 2 and resolved after cyclosporine A discontinuation, mycoplenolate mofetil was added for immunosuppressive in this patient.

Short and long-term complications are shown in Table 2. Patient 1 and 6 had urinoma requiring surgical drainage at 2 and 8 months post transplant, respectively. Patient 6 also had graft artery stenosis which was corrected by surgical revision. Average cost of maintenance of immunosuppressive agents at 6 month post kidney transplant was 6,859.1±1,151.8 Baht (range 5,042.3-8,556.3), about the same as the cost of medications for adult kidney transplants. Serum creatinine levels at last follow-up (mean 24.3±19.0 months, range 8-55) revealed good to excellent renal function. Five patients returned to normal school full time within one year after kidney transplant. Height standard deviation score was markedly improved as early as 6 months post transplant as shown in Table 3.

DISCUSSION

A recent report from the North American Pediatric Renal Transplant Cooperative study (NAPRTCS) showed living donor graft survival

Table 3. Height standard deviation score (HSDS) in the patients.

Patient	Height Standard Deviation Score		
	At transplant	6 months post transplant	1 year post transplant
1	-2.20	-1.97	-2.43
2	0.52	0.34	-0.20
3	-1.91	-1.52	-1.83
4	-2.08	-1.99	-1.95
5	-1.57	-1.33	-1.44
6	-3.95	-3.94	-
Mean ± SD	-1.86 ± 1.4	-1.74 ± 1.38*	-1.57 ± 0.84*

*P < 0.05

rates of 90 per cent at 1 year, 85 per cent at 2 years and 75 per cent at 5 years post transplant, respectively[9]. Our results, although in a much smaller group of patients, are comparable with that report.

The five most common primary renal disease diagnosis in American transplanted children were aplastic/hypoplastic/dysplastic kidneys (17.2%), obstructive uropathy (17.1%), focal segmental glomerulosclerosis (11.1%), reflux nephropathy (5.6%) and systemic immunological disease (4.6%)[9]. The etiologies of renal diseases in this study are also similar; i.e. reflux nephropathy, obstructive uropathy, chronic glomerulonephritis, focal segmental glomerulosclerosis and rapidly progressive glomerulonephritis.

Anesthesia and transplantation surgery required a variety of pediatric subspecialists including a pediatric urologist and anesthesiologist, and good communication with the pediatric nephrologist throughout the critical period[10]. The main causes of acute failure of a transplanted kidney in the early post transplant period are ischemic damage (acute tubular necrosis), rejection, infection, and cyclosporin A toxicity[11]. Meticulous care in intraoperative fluid management and aseptic techniques are therefore very important. Less common causes include bleeding, ureteral obstruction, urinary leakage, venous thrombosis, and stenosis or occlusion of the renal transplant artery.

Most NAPRTCS centers prefer triple immunosupperessive drug therapy (prednisolone, azathioprine, and cyclosporine A)[9] as used initially in this study. Azathioprine had to be discontinued in 2 patients due to persistant neutropenia and the recommended dose of (1-2 mg/kg/day) had to be reduced in another patient. Bone marrow suppression is the main side effect of this drug as in other reports[12]. Hepatotoxicity due to "normal trough level" cyclosporine A was found in 1 patient, he also had persistent neutropenia due to azathioprine so his immunosuppressive regimen was subsequently changed to prednisolone and mycophenolate mofetil 1 g/M^2/day with good renal function on follow-up.

Five patients had acute rejection within the first 6 months post transplant but all had good response to high dose corticosteroids. One patient (patient 6) developed nephrotic syndrome with normal serum creatinine within the first week after kidney transplantation. His condition resolved after plasmapheresis and an 8-week course of oral cyclophosphamide. He was maintained on cyclosporine and prednisolone afterward. His renal function, unfortunately, slowly deteriorated and renal biopsy result was compatible with non-specific chronic allograft glomerulopathy. Although he had no previous history of nephrotic syndrome, his condition was most likely recurrent focal segmental glomerulosclerosis as reported in others[13-15]. Height standard deviation score were markedly improved. The quality of life in our patients was very good as five patients returned to school full time within 1 year post kidney transplant.

Cost of maintenance of immunosuppressive drugs was similar to adults and much lower than other modes of renal replacement therapy[2].

Offner et al studied the long term outcome of pediatric kidney transplantation and showed calculated half-life of a first graft to be 10.5 years. The best graft survival rates were observed after living-related donation, preemptive transplantation, and immunosuppression with cyclosporine. The majority of their patients were rehabilitated in regard to education and socioeconomic status[5].

SUMMARY

Although our group of patients is small and the average period of follow-up is only 24.3 months, we believe kidney transplantation is a very cost-effective mode of treatment and with very good long term outcome in selected patients.

(Received for publication on April 21, 2001)

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การปลูกถ่ายไตในผู้ป่วยเด็ก : ประสบการณ์ของโรงพยาบาลศิริราช

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รายงานผู้ป่วยเด็ก 6 รายที่ได้รับการปลูกถ่ายไตที่โรงพยาบาลศิริราช ในระหว่างปี พ.ศ. 2539-2543 ผู้ป่วยมีอายุเฉลี่ย 9.7±2.7 ปี (พิสัย 6.8-13.2 ปี) เป็นชาย 5 คน หญิง 1 คน สาเหตุของภาวะไตวายเรื้อรังระยะสุดท้ายในผู้ป่วยเป็นภาวะผิดปกติของระบบทางเดินปัสสาวะแต่กำเนิด 3 ราย, โรคไตอักเสบเรื้อรัง 2 ราย และ rapidly progressive glomerulonephritis 1 ราย ก่อนทำการปลูกถ่ายไต ผู้ป่วยได้รับการรักษาทดแทนไตโดยวิธีล้างไตทางช่องท้องแบบเรื้อรัง (chronic peritoneal dialysis) 5 ราย, 1 รายต้องเปลี่ยนไปทำการฟอกเลือดโดยวิธีไตเทียม (hemodialysis) เนื่องจากมีการติดเชื้อเรื้อรังที่ผนังหน้าท้อง และอีก 1 ราย ไม่เคยได้รับการรักษาทดแทนไตแบบเรื้อรังมาก่อน

ผู้ป่วยทุกรายได้รับไตจากผู้บริจาคที่ยังมีชีวิตอยู่ โดยผู้บริจาคเป็นบิดา 4 ราย, เป็นมารดา 1 ราย และพี่ชาย 1 ราย ทุกรายได้ยากดภูมิต้านทานเริ่มแรกเป็น prednisolone, azathioprine และ cyclosporine A หลังปลูกถ่ายไตค่าซีรั่มครีอะตินีนลดลงมาเป็นปกติภายใน 1 สัปดาห์ทุกราย และ 4 รายสามารถจำหน่ายออกจากโรงพยาบาลได้ภายใน 2 สัปดาห์หลังผ่าตัด ภาวะแทรกซ้อนระยะแรกได้แก่ ความดันโลหิตสูงชนิดรุนแรง (ทุกราย), ท่อไตรั่ว (2 ราย), เม็ดเลือดขาวต่ำ (3 ราย) และ 1 รายต้องหยุดยา cyclosporine A เนื่องจากการทำงานของตับผิดปกติ ค่าซีรั่มครีอะตินีนเมื่อติดตามการรักษาไปนานเฉลี่ย 24.3±19.0 เดือน (พิสัย 8-55) เป็นปกติในผู้ป่วย 5 ราย และสูงเล็กน้อย (1.5 มก./ดล.) ในผู้ป่วย 1 ราย ผู้ป่วย 5 ราย สามารถกลับไปเรียนหนังสือตามปกติได้ภายใน 1 ปี ความสูงเฉลี่ยของผู้ป่วยเพิ่มขึ้นอย่างมีนัยสำคัญทางสถิติตั้งแต่ 6 เดือนหลังปลูกถ่ายไต ค่ายากดภูมิต้านทานในผู้ป่วยเมื่อเวลา 6 เดือนหลังปลูกถ่ายไตไม่แตกต่างจากในผู้ใหญ่ คือ เฉลี่ย 6,859.1± 1,151.8 บาท/เดือน

ผู้รายงานสรุปว่า การปลูกถ่ายไตสามารถทำได้ผลดีมากในกลุ่มผู้ป่วยเด็ก โดยใช้ค่าใช้จ่ายไม่แตกต่างจากผู้ใหญ่

คำสำคัญ : การปลูกถ่ายไตในเด็ก, การรักษาทดแทนไต, ภาวะไตวายเรื้อรังระยะสุดท้าย

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จดหมายเหตุทางแพทย์ ฯ 2544; 84: 1084-1089

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