Pediatric Renal Transplantation: A Single-Center Experience in Northeast Thailand

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Objective: *To clarify the demographic data, outcomes and complications of renal transplantation in children at Srinagarind (university) Hospital.*
Material and Method: *The authors reviewed the medical records of children with end-stage renal disease (ESRD) who received renal transplantation at Srinagarind Hospital, Khon Kaen, between August 2001 and July 2008.*
Results: *Eight male and seven female patients were identified. Their mean age was 12.8 ± 3.2 years (range, 5.0-17.6). The major cause of ESRD was a congenital anomaly of the kidneys (53%). All of the children received cadaveric transplantations and none received induction therapy. Triple immunosuppressive drugs comprising cyclosporine, prednisolone and mycophenolate mofetil were administered to 12 patients. Tacrolimus, instead of cyclosporine, was given to three patients who had received a renal transplant since January 2008. The median follow-up time was 15 months (3 to 82 months). The most frequent complication was urinary tract infection (40%). Acute graft loss was found in one patient (6.7%) due to graft infarction. Other complications included herpes viral infection, chronic rejection, acute rejection, severe gingival hyperplasia, myopathy, lymphocele and transitional cell carcinoma of the bladder. Two patients returned to dialysis due to graft infarction and chronic rejection, respectively. The mean serum creatinine at the last follow-up of the remaining cases was 1.2 ± 0.5 mg/dL (range, 0.6-2.3). All of the patients survived. The 1- and 5-year graft survival rates were 93.3% and 86.7%, respectively.*
Conclusion: *The present study demonstrates the potential for successful outcomes of pediatric renal transplantation in this resource-limited area.*

Keywords: *Renal transplantation, Children, Complication, End-stage renal disease*

J Med Assoc Thai 2009; 92 (12): 1635-9
Full text. e-Journal: *http://www.mat.or.th/journal*

Renal transplantation is currently the most effective treatment for children with end-stage renal disease (ESRD), especially better growth and quality of life over dialysis. The high expense of performing the procedure and the sophisticated care needed for renal transplantation in children are the most important limitations in developing countries.

Pediatric renal transplantation was first performed in Thailand at Siriraj Hospital (Bangkok) in 1996. In Thailand's Northeast, the region with the greatest population and lowest average income, a pediatric renal transplant program, adapted to limited resources, has been in development at Srinagarind Hospital, Khon Kaen University since 2001. The purpose of the present study was to clarify the demographic data, outcomes and complications of renal transplantation in children at Srinagarind (university) Hospital.

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Material and Method

The authors reviewed the medical records of children under 18 with ESRD who received renal transplantation at Srinagarind Hospital, Khon Kaen, between August 2001 and July 2008.

Table 1. Characteristics of patients at the time of renal transplantation

Patient	Gender	Age (year)	Cause of ESRD	Mode of dialysis
1	M	9.3	Hypoplastic-dysplastic kidneys	CAPD
2	F	14.4	Hypoplastic-dysplastic kidneys	HD
3	F	5.0	Hypoplastic-dysplastic kidneys	CAPD
4	M	10.2	Hypoplastic-dysplastic kidneys	NIPD
5	M	13.7	Hypoplastic-dysplastic kidneys	NIPD
6	F	16.6	Unknown	CAPD
7	M	14.4	Hypoplastic-dysplastic kidneys	NIPD
8	M	11.2	Hemolytic uremic syndrome	CAPD
9	M	12.7	Chronic glomerulonephritis	CAPD
10	F	15.9	IgM nephropathy	CAPD
11	M	12.8	Chronic glomerulonephritis	CAPD
12	F	14.9	FSGS	NIPD
13	F	10.1	Hypoplastic-dysplastic kidneys	CAPD
14	F	17.6	Lupus nephritis	CCPD
15	M	12.6	Hypoplastic-dysplastic kidneys	CAPD

CAPD = continuous ambulatory peritoneal dialysis; CCPD = continuous cycler-assisted peritoneal dialysis; F = female; FSGS = focal segmental glomerulosclerosis; HD = hemodialysis; M = male; NIPD = nocturnal intermittent peritoneal dialysis

Table 2. Complications after renal transplantation

Complications	Number of patients
Infection	
Urinary tract infection	6 (40.0%)
Herpes viral infection	3 (20.0%)
Non-infection	
Chronic graft rejection	3 (20.0%)
Acute graft rejection	2 (13.3%)
Severe gingival hyperplasia	2 (13.3%)
Lymphocele	1 (6.7%)
Graft infarction	1 (6.7%)
Myopathy	1 (6.7%)
Bladder carcinoma	1 (6.7%)

Results

Eight male and seven female patients were identified. The major cause of ESRD (53%) was a congenital anomaly of the kidneys (hypoplastic-dysplastic kidneys) (Table 1). Most of the patients (93.3%) received peritoneal dialysis before transplantation.

All of the children received cadaveric transplantations. Their mean age at the time of transplantation was 12.8 $\pm$ 3.2 years (range 5.0-17.6). The mean donor age was 25.2 $\pm$ 12.9 years (range, 2.9-45). The mean cold ischemic time was 20.2 $\pm$ 5.7 hours (range, 5.9-27.7). The mean HLA mismatch score was 4.1 $\pm$ 0.8 (range, 3-5). None of the patients received induction therapy.

Triple immunosuppressive drugs comprising cyclosporine, prednisolone and mycophenolate mofetil (MMF) were administered to 12 patients. Tacrolimus, instead of cyclosporine, was initially given to three patients who had received a renal transplant since January 2008. Diltiazem was given to all patients in order to control hypertension and to reduce the calcineurin inhibitor dosage. The median follow-up time was 15 months (range, 3-82). The respective cyclosporine and tacrolimus dosages, which gave the desired serum drug level within the first month period post-transplantation, were 8.08 $\pm$ 2.49 and 0.19 $\pm$ 0.04 mg/kg/day.

The most frequent complication was urinary tract infection (40%) (Table 2). Acute rejection was found in two patients; however, it was successfully treated by using pulse methylprednisolone. Chronic rejection occurred in three patients and the cyclosporine was replaced by tacrolimus in those patients. Graft loss was found in two patients. The first graft loss occurred in patient No. 9 due to graft infarction 20 days post-transplantation. Chronic hemodialysis was introduced in this patient after his acute graft loss. The second graft loss occurred in patient No. 6 due to chronic rejection 16 months

post-transplantation, which did not improve after tacrolimus replacement. The patient had to return to continuous ambulatory peritoneal dialysis.

Other complications included herpes viral infection (20%), severe gingival hyperplasia (13.3%), myopathy (6.7%), lymphocele (6.7%) and transitional cell carcinoma of bladder (6.7%). The post-operative lymphocele in patient No. 5 resolved spontaneously. Patient No. 4 developed transitional cell carcinoma of bladder 18 months post-transplantation: he presented with painless gross hematuria and underwent bilateral nephro-ureterocysto-urethrectomy and transplanted ureterostomy with ileal conduit. The cyclosporine dosage was reduced in this patient after diagnosis.

Cyclosporine was changed to tacrolimus in five patients diagnosed with severe gingival hyperplasia (2 patients), chronic rejection (2 patients) and myopathy with chronic rejection (1 patient). Gingival hyperplasia and myopathy gradually improved and then resolved after tacrolimus replacement.

The mean serum creatinine at the last follow-up of the remaining thirteen patients was 1.2 $\pm$ 0.5 mg/dL (range, 0.6-2.3). Non-adherence did not occur in this study. All of the patients survived. The 1- and 5-year graft survival rates were 93.3% and 86.7%, respectively. The mean graft survival time was 5.5 (95% CI; 4.0-7.0) years. Of those eight patients who received transplantation more than 1 year ago, seven (87.5%) returned to continue their education.

Discussion

Renal transplantation is the most effective treatment for ESRD. Due to the financial constraints, a small number of children with ESRD in Thailand receive renal transplantation. In the past few years, pediatric renal transplantation in Thailand has increased due to government and charity support.

In the present study, the etiology of ESRD was congenital disease of the kidneys, which was similar to a report from the North American Pediatric Renal Trials and Collaborative Studies (NAPRTCS)[1]. Peritoneal dialysis is preferable to hemodialysis in Thai children with ESRD due to its being a non-complicated technique.

All patients in the present study received kidneys from deceased donors because of local beliefs toward taking live kidney transplants. Despite there being no induction therapy in the present study, the patient and graft survival were not worse than those from other studies[1-9]. This may be attributed to the authors' using the MMF regimen which has an excellent outcome even without induction therapy[10,11].

Surgical complications were few in the present study. Due to immunosuppression, urinary tract infection was the most common type of complication. Decreased dwelling time of urinary catheters and ureteric stents in these patients might reduce this complication.

Immunosuppression has led to an increasing incidence of malignancy in post-transplanted patients. The incidence and type of post-renal trasplantation malignancies are geographically dependent; the incidence varying between 6.7 and 13.3%[12-18]. Among those malignancies, transitional cell carcinoma occurs frequently in the Asian population and the most common presentation of transitional cell carcinoma in renal recipients is painless gross hematuria[12,16-20]. In contrast to caucasians, skin cancer is less frequent. Therefore, post-renal transplant patients who present with this symptom should receive prompt and careful urologic examination and treatment.

In conclusion, the present study demonstrates the potential for successful outcomes of pediatric renal transplantation in this resource-limited area. More financial support and organ donations, however, would help other end-stage renal disease children in this area to receive renal transplantation for an improved quality of life.

Acknowledgements

The authors wish to thank families and patients for their cooperation, the Department of Pediatrics and Faculty of Medicine at Khon Kaen University for their support and Mr. Bryan Roderick Hamman for assistance with the English-language presentation of the manuscript.

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ผลการปลูกถ่ายไตในผู้ป่วยเด็กภาคตะวันออกเฉียงเหนือของไทย

สุวรรณี วิษณุโยธิน, อภิชาติ จิระวุฒิพงศ์

วัตถุประสงค์: *เพื่อศึกษาผลการปลูกถ่ายไตในเด็กและภาวะแทรกซ้อนที่เกิดขึ้นใน รพ.ศรีนครินทร์ คณะแพทยศาสตร์ มหาวิทยาลัยขอนแก่น*

วัสดุและวิธีการ: *รวบรวมข้อมูลย้อนหลังจากเวชระเบียนของผู้ป่วยเด็กที่เป็นไตวายเรื้อรัง ระยะสุดท้ายที่ได้รับการปลูกถ่ายไตใน โรงพยาบาลศรีนครินทร์ ตั้งแต่สิงหาคม พ.ศ. 2544 ถึงกรกฎาคม พ.ศ. 2551*

ผลการศึกษา: *ผู้ป่วยเด็กที่ได้รับการปลูกถ่ายไตมีทั้งสิ้น 15 คน (ชาย:หญิง = 8:7) มีอายุเฉลี่ยขณะได้รับการปลูกถ่ายไต 12.8 $\pm$ 3.2 ปี (5.0-17.6) สาเหตุส่วนใหญ่ของการเกิดไตวายเรื้อรังระยะสุดท้ายคือ ความผิดปกติแต่กำเนิดของไต (ร้อยละ 53) ผู้ป่วยทุกคนได้รับไตจากผู้บริจาคไตที่เสียชีวิตและไม่มีผู้ใดได้รับ induction therapy ยากดภูมิต้านทานที่ใช้ในผู้ป่วย 12 รายแรก ประกอบด้วย cyclosporine, prednisolone และ mycophenolate mofetil ยา tacrolimus ถูกใช้แทน cyclosporineในผู้ป่วยที่ได้รับการปลูกถ่ายไตตั้งแต่มกราคม 2551 (3 ราย) ค่ามัธยฐานของระยะเวลาในการติดตามการรักษาคือ 15 เดือน (3-82 เดือน) ภาวะแทรกซ้อนที่พบบ่อยที่สุดคือ การติดเชื้อระบบทางเดินปัสสาวะ (ร้อยละ 40) acute graft loss พบในผู้ป่วย 1 ราย (ร้อยละ 6.7) เนื่องจาก graft infarction ภาวะแทรกซ้อนอื่นที่พบคือ การติดเชื้อไวรัส herpes, chronic rejection, acute rejection, severe gingival hyperplasia, myopathy, lymphocele และ transitional cell carcinoma ของกระเพาะปัสสาวะ ผู้ป่วย 2 ราย ต้องกลับไปล้างไตใหม่เนื่องจาก graft infarction และ chronic rejection ตามลำดับระดับครีอาตินีนในเลือดเฉลี่ยในผู้ป่วย 13 รายที่เหลือคือ 1.2 $\pm$ 0.5 มก./ดล. (0.6-2.3) ผู้ป่วยทุกคนยังมีชีวิตอยู่ และอัตราการรอดของ graft ที่ 1 และ 5 ปี เท่ากับร้อยละ 93.3 และร้อยละ 86.7 ตามลำดับ*

สรุป: *ผลการปลูกถ่ายไตในเด็กในโรงพยาบาลศรีนครินทร์เป็นที่น่าพึงพอใจเทียบเท่ากับการศึกษาอื่น แม้ว่ามีความจำกัดทางทรัพยากรและเงินทุน*