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Our Initial Experiences and Outcomes of Pediatric Kidney Transplantations

Çocuk Hastalara Yaptığımız Böbrek Nakilleri ile İlgili İlk Deneyimlerimiz ve Sonuçlarımız

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Abstract

Objectives: Kidney transplantation is the best treatment method associated with improved quality of life and better survival for both adult and pediatric patients with end stage renal disease. We have performed a total of 117 kidney transplantations from living or deceased donors between November 2010 and May 2014. Thirteen of these were pediatric kidney transplantations. Here, we present our initial experiences and outcomes of these pediatric kidney transplantations.

Materials and Methods: One of the pediatric recipients who underwent en bloc and dual-kidney transplantation from a deceased donor was excluded from this study. This recipient was a 40-month-old patient whose donor was an eleven-month-infant. Her allograft kidneys were explanted because of vascular thrombosis on the first postoperative day. We collected and retrospectively analyzed the data of the other twelve pediatric transplantation recipients and their donors. Seven of these kidney transplantations were from deceased donors and five from living donors. All recipients and the five living donors underwent a thorough examination and their clinical history was studied with in detail.

Results: Deceased to living donor ratio was 7:5, respectively. The mean follow up period was 31.8 (1-42) months from living donors group and 16.8 (2-28) months from deceased donors group, respectively. Graft survival was 100% during this period. No kidney was lost from rejection, technical causes, infection or recurrent diseases. The living donors are also still alive without any problems.

Conclusion: For pediatric end stage renal disease patients, kidney transplantation should be done from deceased or living donors as soon as possible.

Keywords: Pediatric; Kidney; Transplantation.

Öz

Amaç: Hem çocuk hem de erişkin böbrek yetmezliği hastaları için en iyi tedavi seçeneği yaşam süresini ve kalitesini de artıran böbrek naklidir. Kasım 2010 ile Mayıs 2014 tarihleri arasında toplam 117 hastaya böbrek nakli yaptık bunların 13'ü çocuk hastalardı. Çocuk hastalara yaptığımız böbrek nakilleri ile ilgili ilk deneyimlerimizi ve sonuçlarımızı burada sunmayı amaçladık.

Materyal ve Metot: En bloc ve dual böbrek nakli yaptığımız bir olgumuz bu çalışmanın dışında bırakıldı. Geriye kalan 12 hasta ve donörlerinin kayıtları geriye doğru toplanarak incelendi.

Bulgular: Hastalarımızın 7'sine kadavradan, 5'ine canlı donörlerinden nakil yaptık. Canlı donörden nakil yaptığımız alıcıların ortalama takip süreleri 31.8 ay(dağılım; 1-42 ay), kadaverik donörden nakil yaptığımız alıcıların ise16.8 aydı (dağılım; 2-28 ay).

Takip süresince greft sağkalım oranı %100'dü. Teknik nedenlerden, altta yatan hastalıkların tekrar etmesi, infeksiyon ya da rejeksiyon nedeni ile organ kaybetmedik.

Sonuç: Çocuk yaş grubundaki kronik böbrek yetmezliği olan hastlara kadaverik ya da canlı donörden olabildikçe erken böbrek nakili yapılmalıdır. Çocuklara; hem kadavradan hemde canlıdan nakiller nakil merkezi yeni kurulmuş olsada güvenli bir şekilde yapılabilinir.

Anahtar Kelimeler: Çocuk; Böbrek; Nakil.

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INTRODUCTION

Kidney transplantation (KT) is the most effective treatment method associated with improved quality of life and better survival since it enables satisfactory physical, social and psychological rehabilitation for pediatric patients with end stage renal disease (PPESRD) (1-5). We have performed a total of 117 kidney transplantations form living or deceased donors between November 2010 and May 2014. Thirteen of these operations were pediatric kidney transplantations. The aim of this study is to share our initial experiences and outcomes of these pediatric kidney transplantations.

MATERIALS and METHODS

We performed thirteen pediatric KTs between November 2010 and May 2014. One pediatric recipient had en bloc and dual-kidney transplantation from a deceased donor and, thus, was excluded from this study. This recipient was a 40-month-old infant with an eleven-month-donor. Her allograft kidneys were explanted because of vascular thrombosis on the first postoperative day. We collected and retrospectively analyzed the data of the remaining twelve pediatric transplantation recipients and their donors. Seven of these kidney transplantations were from deceased donors and five from living donors. All recipients and the five living donors underwent detailed examination as we also accuretely collected data about their clinical history. All living donors were evaluated according to the criteria of Amsterdam Forum (6). Human Leukocyte Antigen (HLA) typing and tissue cross match between donors and their recipients were also carried just before transplantation.

We used routine methylprednisolone (MP) and induction immunosuppressive drugs just before surgery. We used prophylactic antibiotic and low molecular weight heparin in all patients. Bladders of recipients were lavaged with gentamycine plus serum physiologic.

There are only two transplant surgeons in our kidney transplant team. Because of this reason, we started off with donor nephrectomy procedure from living donor transplantations. After completing dissections, we gave a break to donor nephrectomies. Then, we prepared implantation areas, which was mainly extraperiotenal area in right or left iliac fossas in the recipients. After completing this procedure, we gave a break to recipient operations. Then, we turned to the donor nephrectomies again. After the donor nephrectomies, we immediately started implantation procedures in the recipients.

Six left and six right kidneys were transplanted. Ten kidneys were placed in the right iliac fossa of the recipients. The other two kidneys were placed in the left iliac fossa of the recipients who underwent native nephroureterectomy. Renal vessels were anastomosed to external iliac vessels in ten recipients. Renal vessels were anastomosed to common iliac vessels in the other two recipients. Ureteroneocystostomy (UNC) was performed extravesically, using Lich-Gregoir technique over a double J (DJ) stent in all cases (7). The urethra was prepared by removing redundant urethral length, preserving adequate distal blood supply, and spatulating posterior by at least 10 millimeters. We used 6/0 or 7/0 polydioxanone surgical (PDS) suture for anastomosis. The detrusor muscle was closed exteriorly to create an antireflux mechanism by one-by-one 3/0 absorbable sutures. The recipients and the five living donors were followed up in our transplant clinic during hospitalization. Fluid replacement was given according to urine output at postoperative first night and balance was ensured at about + 500 (fluid input more than urine + drainage fluid). Oral fluid intake was ensured within the postoperative 6-8 hours. Intravenous fluid replacement was decreased on the postoperative first day and was generally stopped on the second day.

Complete blood count, profile of coagulation and routine biochemistry tests including renal function tests were performed at the postoperative first night and daily during patients' stay at the hospital. Immunosuppressive drug level was controlled and regulated on postoperative second day and then daily during this period. Transplanted kidney wasn't imaged routinely in the postoperative hospitalization period. All patients were followed by the Pediatric Nephrology outpatient clinic after discharge. As two of these patients turned 18, they started to be followed up by the Nephrology outpatient clinic.

RESULTS

We performed seven KTs from deceased donors and five from living donors. Male to female ratio was 9:3 in the recipients and 4:8 in the donors, respectively. The mean age of living donors and their recipients were 42.8 (33-50) and 11.6 (4-17) years, respectively. The mean age of deceased donors and their recipients were 15.5 (4-46) and 12.7 (9-17) years, respectively. All transplantations from living donors were performed to their related recipients. Three of these living donors were recipients' fathers, one was recipient's mother and one was recipient's grandmother. In the deceased donor group, the recipients and their donors were not related.

The relationship between the recipients and donors with regards to mismatched HLAs is presented in Table 1. All patients and their donors had compatible blood groups. Demographic traits of donors and their recipients and also the causes of end stage renal disease (ESRD) in patients are shown in Table 1.

The mean warm ischemic time was 91.4 (67-110) seconds and the mean totally ischemic time was 88.4 (55-108) minutes in the living donors group. The mean cold/totally ischemic time was 1284.8 (850-1628) minutes in the deceased donors group. The mean time of discharge from hospital was postoperative 5.8 (5-7) days in the living donors group and 8.1 (5-13) days in the deceased donors group, respectively. The mean follow up times were 31.8 (1-42) months in the living donor

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group and 16.8 (2-28) months in the deceased donors group, respectively (Table 1).

Left kidney donor nephrectomy was preferred as much as possible for the living donors. If there were vascular problems or a condition in favor of the donor, we preferred right kidney nephrectomy. The left donor nephrectomy to right donor nephrectomy ratio was 4:1 in the living donor transplantations. The left kidney to right kidney ratio was 2:5 in the deceased donor transplantations (Table 1).

Right iliac fossa was usually preferred for implantation in the recipients. If there was a vascular problem, surgical necessity such as native nephrectomy, we preferred left iliac fossa. Ten kidneys were placed in the right iliac fossa of the recipients. The other two kidneys were placed in the left iliac fossa of the recipients who underwent native nephroureterectomy (Table 1).

Table 1. Demographic traits of recipients and donors.

Number of Patient/ Follow up period (months)	Age and Gender	Donor (Living or Deceased)	Side of Transplanted Kidney/ Implantation area	Age and Relation of Donors to the Recipients	HLA MM	Cause of ESRD	Renal Replacement Options and duration
1/ 42	4, M	Living	Left/ Right	Grandmother, 50	2 MM	Idiopathic	Preemptive
2/ 40	17, M	Living	Left/ Left	Father, 43	3 MM	VUR	PD, 9 months
3/ 40	10, M	Living	Right/ Left	Father, 33	2 MM	Renal Tubular Acidosis	Preemptive
4/ 36	13, M	Living	Left/ Right	Father, 47	3 MM	VUR	PD, 5 years
5/ 28	17, M	Deceased	Right/ Right	Unrelated, 5	5 MM	MPGN (Type 2)	HD+PD, 2 years
6/ 26	9, F	Deceased	Left/ Right	Unrelated, 4	4 MM	Idiopathic	PD, 2 years
7/ 25	16, F	Deceased	Right/ Right	Unrelated, 46	4 MM	VUR	HD+PD, 3 years
8/ 22	13, F	Deceased	Right/ Right	Unrelated, 5	5 MM	Neurogenic bladder	PD+HD, 7 years
9/ 11	9, M	Deceased	Right/ Right	Unrelated, 9	4 MM	Idiopathic	PD, 1.5 years
10/ 4	14, M	Deceased	Right/ Right	Unrelated, 27	4 MM	VUR	HD+PD, 1 year
11/ 2	11, M	Deceased	Left/ Right	Unrelated, 13	5 MM	Idiopathic	HD+PD, 9.5 years
12/ 1	14, M	Living	Left/ Right	Mother, 41	3 MM	Idiopathic	HD, 2 years

M; Male, **F;** Female, **HLA;** Human Leukocyte Antigen, **MM;** Mismatch, **ESRD;** End Stage Renal Disease, **VUR;** Vesicoureteral Reflux, **MPGN;** Membranoproliferative Glomerulonephritis, **PD;** Peritoneal Dialysis, **HD;** Hemodialysis.

Renal vessels were anastomosed to external iliac vessels in ten recipients. Renal vessels were anastomosed to common iliac vessels in the other two recipients. Nine patients' arteries were anastomosed in end-to-side fashion, using a continuous 6/0 polypropylene suture. One patient's artery was anastomosed in end-to-side fashion, using a continuous 7/0 polypropylene suture. In the other two recipients, we anastomosed one face of the renal artery with continuous 6/0 polypropylene suture and the other face of the renal artery with one by one 7/0 polypropylene suture technique. We performed artery anastomosis with donor aortic patch from all deceased donor kidney transplantations except for one patient. Except one patient, having two renal arteries, all other patients' kidneys had one renal artery. Two renal arteries were anastomosed with common aortic patch of the deceased donor's abdominal aorta wall.

We used induction immunosuppressive drugs as corticosteroids, Anti Tymosit Globulin (ATG) in ten patients, and Basiliximab in two patients. Tacrolimus, mycophenolate mofetil (MMF), and corticosteroid were given to recipients as postoperative immunosuppressive drugs.
We performed two native nephroureterectomies due to potential recurrent urologic infection. One of these patients had incurable vesicoureteral reflux (VUR), and the other had incurable vesicoureteral stenosis. The causes of renal failures were idiopathic in 5 patients, VUR in 4 patients, renal tubular acidosis in 1 patient, Membranoproliferative Glomerulonephritis (MPGN) in 1 patient and neurogenic bladder in 1 patient. The causes of renal failures are also shown in Table 1.

One patient suffered from ureteral stenosis two months after the transplantation. For this patient, we inserted a percutaneous nephrostomy catheter though balloon dilatation couldn't be achieved. He was treated with surgical intervention.

BK virus nephropathy occurred in only one recipient. The patient's creatinine level is higher than 2 mg/dl; fortunately, the graft function is now stable. After the BK virus infection, he suffered from VUR with the transplanted kidney. He was treated with endoscopic surgical intervention at the Department of Urology. A tephlon was injected into the submucosal area of UNC. This patient is our only patient whose creatinine level is still higher than 2 mg/dl. There were two Cytomegalovirus (CMV) cases associated with acute rejection episode in two recipients. Both of them were treated with high dose MP and parenteral ganciclovir.

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One of these patient's creatinine level is still higher than 1.5 mg/dl; fortunately, the graft function is currently stable. Our ten patients' creatinine levels are lower than 1.5 mg/dl currently. The recipients' creatinine levels in discharge time and currently are shown in graphic 1.

The graft survival rate was 100% during this period (Figure 1). No kidney was lost due to rejection, technical causes, infection or recurrent diseases.

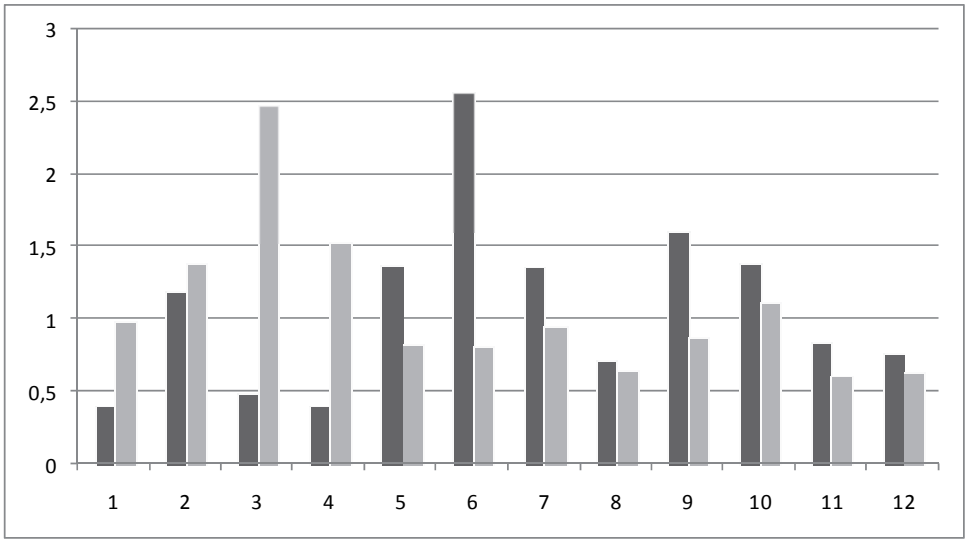

Figure 1. Recipients' current creatinine levels (light columns) and their creatinine levels at the time of discharge (dark columns). The living donors are alive and in good health without any problems.

DISCUSSIONS

KT improves quality of life and better survival as it also enables satisfactory physical, social, potential normalization growth and psychological rehabilitation for PPESRD (1-5). It reduces rate of mortality seen with dialysis (4). It liberates PPESRD patients from dialysis while it is also more cost-effective than dialysis. This treatment option has been performed less in the past, but its popularity is increasing worldwide day by day (4).

We used triple (Tacrolimus, corticosteroid and MMF) immunosuppressive drugs as they are used worldwide (1, 8, 9). Non-compliance of immunosuppressive is high among pediatric recipients (2). We didn't encounter non-compliance or use of discontinuation of immunosuppressive drugs.

Infections are an important cause of post-transplant mortality and morbidity in pediatric kidney transplant recipients (PKTR) in developing countries (1). Also, according to Garcia et al' study, infection is the main cause of death of PKTRs (5). We encountered three important viral infections. Two of these were CMV infections and one was BK virus infections. The CMV infections triggered acute rejection in these patients. Both of them were treated by high dose MP and parenteral ganciclovir. The BK virus infection occurred due to the BK virus associated with nephropathy in the allograft kidney. Treatment of BK virus nephropathy since the most common cause of renal failure in patients has been reported to be congenital lesions (14). We advised our patients to visit Pediatric Nephrologists in later periods for a check-up for potential kidney diseases.

consists of reduction of immunosuppression (10, 11). We reduced amounts of immunosuppressive drugs in our patient. Two of these three patients' creatinine levels are higher than 1.5 mg/dl to this day. All our PKTRs live their lives with stable graft functions.

According to Fraser et al' study, indications for native nephrectomy prior to renal transplantation have included the following causes: chronic renal parenchymal infection with high grade VUR, hydronephrosis or calculi, glomerulopathy with heavy proteinuria, uncontrollable hypertension, symptoms arising from large polycystic kidneys, acquired renal cystic disease, and malignancy (12). We performed two native nephroureterectomies with concerns of possible recurrent urologic infection. One of these had incurable VUR, and the other had incurable vesicoureteral stenosis.

According to Singh et al' study, vascular thrombosis remains a major cause of graft failure, accounting for 12.2% of failed index transplants and 19.2% of repeat transplants (13). We encountered vascular thrombosis in one patient who underwent en bloc and dual kidney transplantation from a deceased donor and thus was excluded from this study. We didn't encounter any vascular complications in our 12 patients, who were transplanted a single kidney.

The most causes of renal failure were idiopathic in 5 patients in our series. This is different from the literature

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The small number of patients and short follow up period were the limitations of our study.

In conclusion, the best treatment option for PPESRD is KT. However, it is necessary to increase awareness and educate patients and their relatives for KT. KT for PPESRD should be performed as soon as possible either from deceased or living donors.

This study was presented as a poster presentation at the 10th Congress of the Society for the Coordination of Turkish Organ Transplantation Institutions (Bodrum, Turkey, 15-18 October 2014).

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