Renal Transplantation in Children with Lower Urinary Tract Dysfunction: A Single-Center Experience

Alt Üriner Sistem Disfonsiyonu olan Çocuklarda Renal Transplantasyon: Tek Merkez Deneyimi

Hakan Sözen[1], Kibriya Fidan[2], Onur Özen[3], Oğuz Söylemezoğlu[2], Aydın Dalgıç[1,4]

[1] Gazi University Faculty of Medicine, Transplantation Center, Ankara, Turkey
[2] Gazi University Faculty of Medicine, Pediatric Nephrology, Ankara, Turkey
[3] Gazi University Faculty of Medicine, Department of Pediatric Surgery, Ankara, Turkey
[4] Gazi University Faculty of Medicine, Department of General Surgery, Ankara, Turkey

ABSTRACT

Aim: To evaluate patient and graft survival, as well as the surgical risks of LUTD patients treated at Gazi University Transplantation Center. Renal transplantation in patients with lower urinary tract dysfunction (LUTD) of various origins remains challenging in the field of pediatric transplantation.
Patients and Methods: Of 42 pediatric transplantation recipients treated since 2006, LUTD developed in five (12%). Videourodynamic tests were performed on all patients preoperatively, and postoperatively if required. The causes of urological disorders were: Posterior urethral valve (PUV) (n=3), PUV with a neurogenic bladder (n=1), and a meningiomyocele plus a neurogenic bladder (n=1). Continual intermittent catheterization (CIC) was required by three patients for bladder emptying. Three patients received kidneys from deceased donors and two patients received kidneys from living donors. All patients underwent calcineurine-based triple immunosuppressive therapy. No patient underwent pre-transplantation augmentation. Only one patient (with PUV and a neurogenic bladder) underwent an augmentation operation during transplantation surgery. We used the Haberal corner-saving suture technique for ureteral stenting combined with ureteroneocystostomic anastomosis.
Results: The mean age at transplantation was 12.2±1.6 years (10-14 years). The median follow-up duration after transplantation was 101 months (68 to 110 months). Two of the five recipients developed BK virus nephropathy (BK). One of the grafts was lost to BK but the other retained normal functioning. No recipient developed urological or surgical complications after transplantation. Three grafts were lost [BK (n=1); chronic allograft nephropathy (n=2)] but the remaining two patients are doing well with median creatinine levels 1.1 mg/dL. The 1-, 3-, and 5-year patient and graft survival rates were: 100%, 100%, 100% and 100%, 100%, 60% respectively.
Conclusion: Renal transplantation in children with a LUTD can yield long-term successful outcomes comparable to those in children with non-LUTD. Because of the high complication rates associated with these transplants, careful evaluation, surveillance, and management of pre/post-transplantation periods are essential to optimize these outcomes.

Key Words: Pediatric, renal transplantation, outcome

Received: 07.21.2017 **Accepted:** 09.25.2017

ÖZET

Amaç: Pediatrik böbrek transplantasyonu alt üriner sistem disfonksiyonu (AÜSD) olan hastalarda zorlayıcı olmaya devam etmektedir. AÜSD olan hastalardaki greft ve hasta sağ kalımları sonuçları ile cerrahi açıdan Gazi Üniversitesi Transplantasyon Merkezi olarak sonuçlarımızı sunmayı amaçladık.
Yöntem: 2006 yılından sonra toplam 42 pediatrik renal transplantasyon yapılmış olup bunların 5 (%12) tanesi AÜSD grubundadır. Tüm hastalara preoperatif bazı gerekli durumlarda postoperatif dönemde de videoürodiamik testler yapıldı. AÜSD etiyolojisi: posterior üretral valv (PUV) (n=3), PUV+nörojenik mesane (=1) ve Meningiomiyosel+nörojenik mesane (n=1). Temiz aralıklı kateter (TAK) kullanımı 3 hastada mesane boşaltılması için kullanıldı. Böbrek transplantasyonu 3 hastada kadavradan, 2 hastada ise canlı donörden gerçekleştirildi. Tüm hastalara kasinörin inhibitör içeren üçlü immünsüpresyon kullanıldı. Augmentasyon işlemi sadece 1 (PUV+ nörojenik mesane) hastaya transplantasyon sırasında yapıldı. Transplantasyon sırasında ureteroneosistostomi anastomozu, double J stent + Haberal Corner Saving yöntemi kullanılarak gerçekleştirildi.
Bulgular: Transplantasyon olduklarında ortanca yaş 12.2±1.6 yıldır (10-14 yıl). Transplantasyon sonrası ortanca takip süresi 101 aydır (68-110 ay). İki hastada BK nefropatisi gelişmiş olup, bunlardan bir tanesi medikal tedavice cevap verdi fakat diğerinde greft kaybı gelişti. Bu çalışmada hiçbir hastada cerrahi veya ürolojik komplikasyon gelişmedi. Toplam 3 greft kaybı görüldü: kronik rejeksiyon (n=2) ve BK (n=1). Diğer 2 hasta ortanca kreatin 1.1mg/dL seviyesinde sorunsuz olarak izlenmektedir. 1-, 3- ve 5-yıllık hasta ve greft sağkalım oranları sırasıyla% 100,% 100,% 100 ve% 100,% 100,% 60'tır.
Sonuç: LUTD'li çocuklarda böbrek transplantasyonu, LUTD'siz çocuklarla karşılaştırılabilir uzun vadeli başarılı sonuçlar verebilir. Bu nakillerle ilgili yüksek komplikasyon oranları nedeniyle, nakil öncesi / sonrası dönemlerin dikkatli bir şekilde değerlendirilmesi, gözlemlenmesi ve yönetimi bu sonuçları en iyi duruma getirmek için şarttır.

Anahtar Sözcükler: Pediatric, renal transplantasyon, sonuç

Geliş Tarihi: 21.07.2017 **Kabul Tarihi:** 25.09.2017

Address for Correspondence / Yazışma Adresi: Hakan Sözen M.D., Gazi University Hospital, Transplantation Center, B Blok kat:1, Besevler, 06510, Ankara, Turkey E-mail: mhakansozen@gmail.com

doi:http://dx.doi.org/10.12996/gmj.2017.74

INTRODUCTION

Up to 30% of pediatric end-stage renal disease (ESRD) patients exhibit lower urinary tract dysfunction (LUTD). Concerns about renal transplantation in children with LUTD are not new. Developments over the past decades have shown that it may now be possible to achieve results in such patients comparable to those obtained after other pediatric transplantations (1, 2, 3). However, the best way to manage such patients remains controversial; no established criteria for reconstructive surgery are available and both the optimal surgical procedure and timing remain unclear.

MATERIALS and METHODS

Of the 42 pediatric transplantation recipients treated since 2006, LUTD developed in five (12%). Videourodynamic tests were performed on all patients preoperatively, and postoperatively if required. The causes of urological disorders were: Posterior urethral valve (PUV) (n=3), PUV with a neurogenic bladder (n=1), and a meningiomyocele plus a neurogenic bladder (n=1). Continual intermittent catheterization (CIC) was required by three patients for bladder emptying. Three patients received kidneys from deceased donors and two patients received kidneys from living donors. All patients received calcineurin-based triple immunosuppressive therapy.

We used a standard surgical technique for pediatric kidney transplantation (4). Briefly, we employed the retroperitoneal approach for recipients with body weights over 25 kg. However, intra-abdominal placement was preferred for patients with body weights below 20 kg. Graft renal artery and vein anastomoses were performed using monofilament non-absorbable sutures (7/0 for arteries and 6/0 for veins). For neoureterosistostomy anastomosis, we employed the Haberal "Corner-Saving Open Loop Continuous Suture Technique" with a 5/0 PDS suture accompanied by placement of a double-J stent (DJS) (5). DJS catheter was removed 4 weeks after transplantation. No patient underwent pre-transplantation augmentation. Only one patient (with PUV and a neurogenic bladder) underwent an augmentation operation (from the native ureter) during the transplantation surgery.

Our immunosuppression protocol has been described earlier (4, 6). Briefly, following induction treatment with IL-2 receptor antagonists, calcineurin inhibitors (CNI), tacrolimus, mycophenolic acids (MPAs), and prednisolone were prescribed. Prednisolone was tapered to 5 mg/daily by 2 weeks after transplantation. No patient received a steroid-free regimen. In those exhibiting delayed graft function, an antilymphocyte antibody (ATG Fresenius) was preferred to CNI until the graft function attained an acceptable level (normovolemic urine output, and a 50% decrease in the 24-h serum creatinine level or a creatinine level less than 3 mg/dL). Rejection episodes were treated with a corticosteroid bolus and repeat corticosteroid therapy, as previously described by our group (4, 6). Corticosteroid-resistant rejection episodes were treated with antilymphocyte antibody therapy and/or plasmapheresis.

RESULTS

The mean age at transplantation was 12.2±1.6 years (10-14 years). The median follow-up duration after transplantation was 101 months (68-110 months). The two patients who had neurogenic bladders developed recurrent, symptomatic, curable urinary tract infections. In our series of five patients, only one patient with PUV+Neurogenic bladder, required an augmentation procedure because of a very low urinary bladder capacity (<30 mL). In this case, we performed right native nephrectomy during transplantation surgery under midline incision. Then, excessively dilated native ureter (attributable to grade V vesicoureteral reflux) of this nephrectomy material was used for augmentation.

Two of the five recipients developed BK viral infections (BK). One graft was lost to BK but the other retained normal function. The principal treatment for BK nephropathy is reduction of immunosuppression. The various strategies include reduction or discontinuation of the CNI and/or the adjuvant agent; changing from MMF to azathioprine, sirolimus, or leflunomide; and changing from tacrolimus to cyclosporine [7]. In our clinic, we first reduce immunosuppression and then prescribe cidofovire to treat the BK virus infection. One patient did not respond to medical treatment but the other did, and was cured. We did not encounter any surgical or urological complication after transplantation. During the median 101 months of follow-up, five rejection episodes were detected, of which two were humeral and three cellular. The latter rejections were successfully treated with pulsed steroids; the humeral rejections required plasmapheresis and ATG. Three grafts were lost due to BK nephropathy (n=1) and chronic allograft rejection (n=2). The two remaining patients are doing well with a mean creatinine level of 1.1 mg/dL after a median of 101 months of follow-up (Table-1). The 1-, 3-, and 5-year patient and graft survival rates were: 100%, 100%, 100% and 100%, 100%, 60% respectively.

Table 1: Demographics and outcomes of renal transplantation patients with LUTD.

#	Etiology	Tx	Sex	Age (yr)	Management	Cr (1 yr)	Cr (3 yr)	Cr (5 yr)	Cr (now)
1	PUV+VUR	L	M	14	Medical	1.4	4.1	ESRD	ESRD
2	PUV+VUR	C	M	11	Medical	0.9	1.2	0.8	1.2
3	PUV+ Neurogenic bladder	C	M	10	Intraoperative augmentation+ CIC	1.5	2.7	5.1	ESRD
4	Meningomyelocele+ Neurogenic bladder	C	M	13	CIC	1.3	4	ESRD	ESRD
5	PUV+VUR	L	M	13	Medical	0.9	0.9	0.9	1.1

L: living donor C: from deceased donors M: male Cr: creatinine (mg/dL) Yr: years ESRD: end-stage renal disease PUV: posterior ureter valve VUR: vesicoureteral reflux CIC: continual intermittent catheterization Tx: Transplantation

DISCUSSION

Nearly 50% of pediatric ESRD is congenital; most cases exhibit structural defects in the urinary tract and bladder (8). The best way to manage children with congenital abnormalities affecting the lower urinary tract, associated with ESRD, remains controversial (3, 8). All patients with LUTD and severe renal disease are potential candidates for kidney transplantation; the lower urinary tracts can be treated if necessary. If augmentation cystoplasty is intended, such surgery is preferably performed prior to renal transplantation to avoid the possible adverse effects of immunosuppressive treatment, such as delayed wound healing, severe infection, stone formation and/or cancer. Indications for the selection of particular interventions are unclear; more direct comparisons are required. In our series of five patients, only one patient required. In this case, we used an excessively dilated native ureter (attributable to grade V vesicoureteral reflux) for augmentation to avoid gastrointestinal complications after renal transplantation caused by collection of intestine/stomach material. We believe that, if a low intravesical pressure combined with adequate bladder drainage can be attained; other surgeons could achieve comparable results.

BK nephropathy has emerged as a significant complication after pediatric kidney transplantation in the era of increased immunosuppression. Our incidence of BK was as high as that in other published reports (7, 9). The two patients with BK had earlier developed humeral and acute rejection episodes. Thus, their immunosuppressive protocols changed more often than expected and intense immunosuppressive medications were used (ATG, pulse steroids) for treatment. We believe these may have triggered BK (7,10-11).

Despite the fact that our patient numbers were small, our patient and graft survival rates are similar to those of other reports (12-14). No patient or graft was lost to urological and/or surgical complications after transplantation.

CONCLUSION

Renal transplantation in children with a LUTD can yield long-term successful outcomes comparable to those in children with non-LUTD. Because of the high complication rates associated with these transplants, careful evaluation, surveillance, and management of pre/post-transplantation periods are essential to optimize these outcomes.

Conflict of Interest

There is no conflict of interest is declared by the authors.

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