Journal of Surgical Arts
ISSN NO: 1308-0709 Cerrahi Sanatlar Dergisi
Year 2019, Volume 12, Issue 2

Original study

Liver and kidney transplantation as treatments for type 1 primary hyperoxaluria

Tip 1 primer hiperoksalüri tedavisinde karaciğer ve böbrek nakli

Gökhan Ertuğrul

Medipol Universty Faculty of Medicine, 1. Hepatobiliary Surgery and Organ Tx Center, İstanbul, Turkey

Corresponding address: Dr. Gökhan Ertuğrul mdgertugrul@gmail.com

J Surg Arts (Cer San D), 2019;2:28-31.

ABSTRACT

Type 1 primary hyperoxaluria is an autosomal, recessive metabolic disease triggering calcium oxalate accumulation in tissues. The liver lacks the peroxisomal enzyme alanine-glyoxylate amino transferase. Clinically, patients develop kidney stones, urinary tract infections, and progressive renal failure. We evaluated liver and kidney transplantation to performed for type 1 primary hyperoxaluria in our study.

In this study, we retrospectively evaluated 7 patients with type 1 primary hyperoxaluria who underwent liver and kidney transplantation. Two main groups were established; Sequential and simultaneous liver and kidney transplantation group. Mortality rates were compared between these two groups.

Sequential liver and kidney transplantation was performed in 5 (71.4%) patients and simultaneous liver and kidney transplantation was performed in 2 (28.6%) patients. All patients died in simultaneous liver and kidney transplantation group.

Sequential liver and kidney transplantation group mortality rates were lower therefore treatment for type 1 primary hyperoxaluria more preferable.

Keywords: Type 1 primary hyperoxaluria, liver transplantation, kidney transplantation

ÖZET

Tip 1 primer hiperoksalüri dokularda kalsiyum oksalat birikimine neden olan otozomal resesif kalıtılan metabolik bir hastalıktır. Karaciğer de peroksizomal bir enzim olan alanin-gliyoksilat amino transferaz eksiktir. Klinik olarak böbrek taşları, üriner sistem enfeksiyonları ve ilerleyici böbrek yetmezliği ortaya çıkar. Bu çalışma ile Tip 1 primer hiperoksalüri tedavisi için yapılan karaciğer ve böbrek nakilleri değerlendirilmiştir.

Bu çalışmada tip 1 primer hiperoksalüri tanısı ile karaciğer ve böbrek nakli yapılan 7 hasta retrospektif olarak değerlendirdik. İki ana grup kuruldu; bunlar ardışık ve eşzamanlı karaciğer ve böbrek nakli yapılan gruplar idi. Bu iki grup arasında mortalite oranları karşılaştırıldı.

Beş (%71.4) hastaya ardışık karaciğer ve böbrek nakli, 2 (%28.6) hastaya eşzamanlı karaciğer ve böbrek nakli yapıldı. Eş zamanlı karaciğer ve böbrek nakli yapılan gruptaki tüm hastalar öldü.

Ardışık karaciğer ve böbrek nakli grubun mortalite oranları düşüktü, bu nedenle tip 1 primer hiperoksalüri tedavisinde daha fazla tercih edildi.

Anahtar kelimeler: Tip 1 primer hiperoksalüri, karaciğer nakli, böbrek nakli.

INTRODUCTION

Type 1 primary hyperoxaluria features the absence of alanine-glyoxylate aminotransferase, a liver peroxisomal enzyme; the condition is autosomal recessive (1). Endogenous oxalate overproduction and excessive urinary excretion follow. Calcium oxalate accumulation in tissues triggers end-organ damage. Particularly, kidney oxalate accumulation may cause renal failure (2). Oxalate crystals accumulate in bones, muscles, arteries, eyes, the skin, and nerves, causing various problems. Liver transplantation is the only definitive treatment (3). Depending on the extent of renal insufficiency, a kidney transplant may be required.

In early childhood, urinary tract stones and recurrent urinary tract infections should be carefully assessed in patients with a family history of primary hyperoxaluria.

In present study, we evaluated liver and kidney transplants to performed for type 1 primary hyperoxaluria.

MATERIAL AND METHODS

Between December 2014 and December 2018, we retrospectively evaluated seven patients with living donor liver and kidney transplantation due to type 1 primary hyperoxaluria in our center.

Two main groups were established; Sequential and simultaneous liver and kidney transplantation group. For each of these groups, the age, sex, e-GFR, morbidity and mortality rates were compared.

Donor selection

Seven patients underwent left lobe lateral segment living donor liver transplantation and living donor kidney transplantation to performed type 1 primary hyperoxaluria. Donor blood groups were identified. Intravenous, contrast-enhanced abdominal computed tomography (CT) was used to evaluate the donor hepatic artery, and the hepatic and portal veins; Magnetic resonance cholangio-pancreato-graphy (MRCP) was employed to explore the course of the biliary tract.

Recipient blood groups were determined and creatinine clearance and the estimated glomerular filtration rate (e-GFR) were measured in 24 hours urine. Tissue typing, cross-flow matching, and panel reactive antibody (PRA) and donor specific antibodies (DSA) were performed using immunological tests. Intravenous, contrast-enhanced abdominal CT was used to evaluate the renal arteries, renal veins, and ureters of all donors. Five liver donors also donated kidneys, but two did not because both kidneys had multiple arteries and ureters.

Surgical procedure

Each recipient underwent bilateral subcostal incision. After total hepatectomy, the donor left lobe lateral liver segment was removed from ice and placed in the abdomen. The left middle and right hepatic veins of the recipient were ligated to obtain a single hepatic vein. The graft and recipient left hepatic veins were anastomosed using 5/0 polydioxanone (PDS) stitches. The recipient main portal vein and the graft left portal vein were anastomosed using 6/0 PDS stitches. The vascular clamps were opened to allow reperfusion. The donor and recipient left hepatic arteries were microscopically anastomosed using individual 7/0 prolene sutures. All vascular structures were normal on intraoperative Doppler USG. We pre-prepared standard Roux-en-Y for bile duct anastomosis. The graft left bile duct was connected to the jejunum. Using individual 6/0 PDS stitches, the anterior and posterior wall were anastomosed. The left lobe lateral segment was attached to the abdominal wall using individual 2/0 silk sutures.

For kidney transplantation, we preferred the iliac fossa to the subcutaneous route. In patients who did not undergo simultaneous liver/kidney transplantation, kidney transplantation was performed 1 week after liver transplantation.

The kidney from a living donor was removed from ice and warmed and the external iliac vein was clamped inferiorly. The renal vein and external iliac vein were stapled using 6/0 Prolene stitches and anastomosis was completed. An external iliac artery side-clip was placed. The renal artery and external iliac artery were connected using 6/0 Prolene sutures and anastomosis was completed. Reperfusion was achieved by opening the clamps. The vascular structures were normal on intraoperative Doppler ultrasonography. We then performed ureteroneocystostomy. Using individual 5/0 PDS stitches.

Statistical analysis

SPSS 22.0 (SPSS for Windows, 2007, Chicago) was used for statistical analysis. Con-tinuous variables wich have normal distribution, were presented as mean ± Standard deviation. Statistical analysis fort he parametric variables was performed by the Student' s T-test. The qualitative variables were given as percent and the correlation between categorical variables was investigated by the chi-square test and Fisher's exact test. Statistical significance level was defined as $P < 0.05$.

RESULTS

Mean age of the Sequential group was 93 (11-156) months; Simultaneous group was 48 (24-72) months, 5 (71.4%) of the 7 patients were male. Mean e-GFR was 11.2 (9-14) (ml/min/1.73m^2). All this patients were on preoperative peritoneal dialysis.

The first two patients underwent simultaneous liver and kidney transplantation in our clinic. This two patients died within 15 days after surgery. Sepsis related multiorgan failure caused death. We have changed strategy and next five patients (sequential group) underwent liver transplantation, followed by kidney transplantation when liver enzyme and bilirubin levels had normalized. No patient died in this group.

Two (28.5%) patients developed complications in the early postoperative period. The morbidities due to hemorrhage.

The mean follow-up time was 29.2 (0.1–62) months. Table 1 shows the comparison of demographic and clinical findings of the sequential and simultaneous patient groups.

DISCUSSION

We evaluated seven patients undergoing liver and kidney transplantation to performed type 1 hy-

peroxaluria. The condition is inherited in an autosomal recessive manner, and is rare (1-3). The prevalence is 1-3 people per million (4). Half of all patients exhibit symptoms before 5 years of age (5). The infantile form of the disease often exhibits rapid progression to end stage renal disease by 5 years of age (6). Such disease develops in 50% of patients by the age of 15 years (7), and in 80% by the age of 30 years (8). There was history of urinary tract stones and recurrent urinary tract infections and rapid end stage renal disease in our patients. The mean age of our patients was 80.4 months (11-156).

Table 1: Demographic and clinical findings of the two patient groups.

	Sequential (n=5)	**Simultaneous (n=2)**
Age (months)	93 (11-156)	48 (24-72)
Male/ Female (n, %)	4 (80%) / 1 (20 %)	1 (50%) / 1 (50%)
eGFR (ml/min/1.73m^2)	11 (9-13)	12 (10-14)
Morbidity (n/%)	1 (20%)	1 (50%)
Mortality (n/%)	-	2 (100%)

Combined liver and kidney transplantation should be scheduled when the eGFR is in the range 15–40 mL/min/1.73 m^2 because, in this range, oxalate retention increases rapidly (9). Combined liver and kidney transplantation, either sequential or simultaneous, is the treatment of choice for children with type 1 primary hyperoxaluria when the eGFR is 15–40 mL/min/1.73 m^2. In this study mean e-GFR was 11.2 (9-14) (ml/min/1.73m^2). All this patients were on preoperative peritoneal dialysis.

The only definitive treatment is combined liver and kidney transplantation (10,11). Liver and kidney transplantation is optimal when there is no systemic involvement; either combined liver and kidney transplantation or liver transplantation alone may be appropriate(12). Combined liver and kidney transplantation, introduced by Watts et al. in 1984, is now regarded as a valuable treatment option for patients with type 1 primary hyperoxaluria, with good long-term results (13). In our study, seven patients with type 1 primary hyperoxaluria who underwent liver and kidney transplantation.

Liver and kidney transplantation may be either sequential or simultaneous. Combined liver and kidney transplantation affords immunological advantages; the liver graft may protect the renal graft from rejection (14,15). The first two patients underwent simultaneous liver and kidney transplantation in our clinic. This two patients died due to sepsis related multiorgan failure. We have changed strategy and next five patients (sequential group) underwent liver transplantation, followed by kidney transplantation when liver enzyme and bilirubin levels had normalized. No patient died in sequential group.

Our study has several limitations. First, this study was retrospective. Second, the number of cases were small.

In conclusion, we evaluated liver and kidney transplantations to performed for type 1 primary hyperoxaluria in our study. We found sequential liver and kidney transplantation group mortality rates were lower. Therefore in our clinic, sequential liver and kidney transplantation to performed for type 1 primary hyperoxaluria more preferred.

Conflict of interest

No author has any conflict of interest.

REFERENCES

1. Cochat P, Fargue S, Harambat J. Primary hyperoxaluria type 1: strategy for organ transplantation. Curr Opin Organ Transplantation 2010; 15:590-3.
2. Scheinman JI. Liver transplantation in oxalosis prior to advanced chronic kidney disease. Pediatr Nephrol. 2010; 25:2217-22.
3. Jamieson NV, Jamieson KA. Primary hyperoxaluria type 1: gene therapy by liver transplantation. Transplantation. 2009; 87:1273-4.
4. Raju DL, Cantarovich M, Brisson ML, Tchervenkov J, Lipman ML.. Primary hyperoxaluria: clinical course, diagnosis, and treatment after kidney failure. Am J Kidney Dis. 2008; 51:e1–e5.
5. Cochat P, Deloraine A, Rotily M, Olive F, Liponski I, Deries N. Epidemiology of primary hyperoxaluria type 1. Nephrol Dial Transplant. 1995;10:3–7.
6. Cochat P, Liutkus A, Fargue S, Basmaison O, Ranchin B, Rolland MO. Primary hyperoxaluria type 1: still challenging! Pediatr Nephrol. 2006; 21:1075-81.
7. Danpure CJ. Molecular and clinical heterogeneity in primary hyperoxaluria type 1. Am J Kidney Dis. 1991;17:366-9.
8. Jamieson NV, Jamieson KA. Primary hyperoxaluria type 1: gene therapy by liver transplantation. Transplantation. 2009; 87:1273-4.
9. Gagnadoux MF, Lacaille F, Niaudet P, Revillon Y, Jouvet P, Jan D, et al. Long term results of liver-kidney transplantation in children with primary hyperoxaluria. Pediatr Nephrol 2001;16:946-50.
10. Jamieson NV. A 20 year experience of combined liver kidney transplantation for primary hyperoxaluria (PH1): The European PH1 transplant registry experience 1984-2004. Am J Nephrol. 2005; 25:282-9.
11. Ellis SR, Hulton SA, McKierman PJ, de Ville de Goyet J, Kelly DA, et al. Combined liver kidney transplantation for primary hyperoxaluria in

young children. Nephrol Dial Transplant. 2001; 16:348-54.
12. Latta K, Jamieson NV, Scheiman JI, Schärer K, Bensman A, Cochat P, et al. Selection of transplantation procedures and perioperative management in primary hyperoxaluria type1. Nephrol Dial Transplant. 1995;10 Suppl 8:53-7.
13. Watts RW, Calne RY, Williams R, Mansell MA, Veall N, Purkiss P, et al. Primary hyperoxaluria (Type 1): Attempted treatment by combined hepatic and renal transplantation. Q J Med 1985;57:697-703.
14. Rasmussen A, Davies HF, Jamieson NV, Evans DB, Calne RY. Combined transplantation of liver and kidney from the same donor protects the kidney from rejection and improves kidney graft survival. Transplantation. 1995; 59:919-21.
15. Tomohide H. Hiroto E. Toshimi K. Liver transplantation for primary Hyperoxaluria Type 1: A single-center experience during two decades in Japan. World J Surg. 2013;37:688-93.