ORIGINAL PAPERS

Liver-kidney simultaneous transplantation in adult patients with primary hyperoxaluria. Experience at Hospital Universitario 12 de Octubre

Javier Martínez-Caballero, Alberto A. Marcacuzco-Quinto, Iago Justo-Alonso, Oana Anisa-Nutu, Alejandro Manrique-Municio, Jorge Calvo-Pulido, Félix Cambra-Molero, Óscar Caso-Maestro and Carlos Jiménez-Romero

HBP and Abdominal Organ Transplant Surgery Unit. Hospital Universitario 12 de Octubre. Madrid. Surgery Department. Universidad Complutense de Madrid. Madrid, Spain

Received: 19/04/2017 · **Accepted:** 28/08/2017

Correspondence: Javier Martínez-Caballero. HBP and Abdominal Organ Transplant Surgery Unit. Hospital Universitario 12 de Octubre. Avda. Córdoba, s/n, 28041 Madrid, Spain. **e-mail:** j.mtnezcaballero90@gmail.com

ABSTRACT

Primary hyperoxaluria (PH) is a metabolic liver disease with an autosomal recessive inheritance that results in oxalate overproduction that cannot be metabolized by the liver. Urinary excretion of oxalate results in lithiasis and nephrocalcinosis leading to a progressive loss of renal function that often requires renal replacement therapy despite medical treatment. Type 1 PH is the most common form and is due to a deficiency in the alanine-glycolate aminotransferase enzyme found in hepatic peroxisomes. Therefore, a liver-kidney simultaneous transplant (LKST) is the definitive treatment for end-stage renal disease (ESRD) patients. However, some studies suggest that the morbidity and mortality rates are greater when this procedure is performed instead of only a kidney transplant (IKT). Herein, we report five patients with PH and a mean glomerular filtration rate of 20.2 ± 1.3 ml/min/1.73 m^2 who received a LKST between 1999 and 2015 at the Hospital Universitario 12 de Octubre. Recurrence and liver or kidney graft loss was not observed during the postoperative period and only one case of late acute rejection without graft loss was diagnosed. The recipient survival rate was 100% with a median follow up of 84 months. As LKST is a curative and safe procedure with a low mortality and high survival rate, it must be considered as the treatment of choice in adults with HP and ESRD.

Key words: Primary hyperoxaluria. Transplant. Liver transplantation. Kidney transplantation. Simultaneous. Combined and adult.

INTRODUCTION

Primary hyperoxaluria (PH) is an autosomal recessive disease caused by an overproduction of hepatic oxalate. The estimated prevalence is 1-3 per million and the incidence in Europe is 1:120,000 births per year (1). There are 3 types and 80% are classified as type 1. The disease is caused by a mutation in the gene that codes for the alanine-glycolate aminotransferase (AGT) enzyme that is found solely in hepatic peroxisomes (2).

The initial symptoms of type 1 PH appear around an average age of 5-6 years and the disease is characterized by early and recurrent nephrolithiasis, nephrocalcinosis and urinary tract infection (UTI). This leads to a progressive renal damage which may result in end-stage renal disease (ESRD) between 25 and 35 years of age (2-4).

Initially, PH type 1 patients may benefit from medical treatment and renal replacement therapy, even though these are generally ineffective treatments. When patients develop ESRD, the treatment of choice for the simultaneous correction of the enzymatic defect and ESRD is a liver-kidney transplant.

There are numerous studies in the literature regarding pediatric patients. However, information with regard to adult patients is limited. The aim of this study was to analyze a series of five patients with PH treated with a liver-kidney simultaneous transplant (LKST).

MATERIAL AND METHODS

This retrospective series included 5 adults who had received a LKST due to PH that were selected from the 42 liver-kidney transplant patients from the Hospital Universitario 12 de Octubre from 1999-2015. The study included three women and two men; four were diagnosed with type 1 PH and the final patient had type 2 PH. Patients were referred to our center after a diagnosis in other centers during childhood. Four patients were diagnosed via a genetic study and one patient with first degree relatives affected by PH was diagnosed by a renal biopsy which showed a calcium oxalate deposit.

Martínez-Caballero J, Marcacuzco-Quinto AA, Justo-Alonso I, Anisa-Nutu O, Manrique-Municio A, Calvo-Pulido J, Cambra-Molero F, Caso-Maestro O, Jiménez-Romero C. Liver-kidney simultaneous transplantation in adult patients with primary hyperoxaluria. Experience at Hospital Universitario 12 de Octubre. Rev Esp Enferm Dig 2018;110(2):82-87.

DOI: 10.17235/reed.2017.5016/2017

Statistical analysis

Categorical variables are expressed as frequencies and quantitative variables are expressed as a mean and standard deviation or range. The survival was calculated in months from the day of the surgery to death.

RESULTS

Pre-transplantation recipient characteristics

The mean age at diagnosis was 16.6 ± 10 years and the time between the first symptoms and diagnosis was 14.6 ± 6 months. The most frequent symptoms were nephrocalcinosis and lithiasis. A presentation of oxalosis was observed in one patient as a respiratory failure secondary to pulmonary bleeding and peripheral arterial disease (Table 1). Four patients received medical treatment with a high fluid intake, pyridoxine and intensive hemodialysis (HD). The mean time in HD prior to transplantation was 13.7 ± 15.6 months (range 3-36). The median time to LKST was 14 years. All patients had preserved liver function and were in dialysis or in a pre-dialysis situation when the transplantation was performed. The mean glomerular filtrate rate was 20.2 ± 1.3 ml/min/1.73 m^2 and the mean serum creatinine value was 4.7 ± 2.7 mg/dl.

Liver-kidney transplantation and follow-up

Firstly, a hepatectomy with vena cava preservation was performed (piggy-back technique). A liver graft was implanted in the orthotopic position. All the liver-kidney grafts were from the same deceased donor. Later, a kidney graft was implanted during the same procedure in the right iliac region. All the patients were older than 18 years of age and the mean age was 34 ± 14 years. The mean age of the donor was 30 ± 13.3 years, four of them were brain dead and there was one case of a donation after cardiac death (DCD) Maastricht Type III. Intraoperative HD was performed in all cases.

Five patients required post-transplant HD during 9.8 ± 4.5 days. HD was administered on non-consecutive days and short HD intervals were used until the serum oxalate and renal function were optimized. All patients received preoperative induction therapy with thymoglobulin. After transplantation, the initial immunosuppressive therapy included IV tacrolimus, MMF and methyl-prednisolone and the monitoring of liver enzymes, renal function and the tacrolimus valley concentration. Maintenance immunosuppression was based on tacrolimus, MMF and prednisone. The target levels of the tacrolimus valley point concentration was between 5-10 ng/ml during the first 0-6 months and between 10-15 ng/ml during the following 6-12 months.

The mean glomerular rate filtration (GRF) was 27.6 ± 10.1 ml/min/1.73m^2 and the serum creatinine was 2.64 ± 0.8 mg/dl on the 7th post-transplant day. Four out of five patients developed acute kidney failure post-transplantation and acute tubular necrosis was the main cause in three cases. The liver function remained normal in all cases. At discharge, the mean GRF was 47.3 ± 22.2 ml/min/1.73 m^2 and the mean serum creatinine was 2.24 ± 1.0 mg/dl.

The vascular, immunologic and infectious complications during the transplant procedure and follow-up are described in table 2. One patient presented with hypovolemic shock due to hemoperitoneum and compartment syndrome which required emergency surgery. Pulmonary embolism secondary to deep vein thrombosis was observed 59 months post-transplant and another patient developed a late acute rejection grade IIA of the kidney graft 124 month post-transplant that was resolved with corticosteroids. The median follow up time was 84 months. During this period, the recipient and graft (liver and kidney) survival rates at 1 and 5 years were 100%. There was no oxalate lithiasis, nephrocalcinosis or a need for dialytic therapy after LKST.

DISCUSSION

PH is a rare disease due to a glyoxalate metabolic disorder that causes an oxalate overproduction. Type 1 is the most common and severe form (2,3) of the disease, which is caused by an AGT enzyme defect that causes an increase of serum oxalate and glycolate levels (4). Onset of the disease during childhood or adolescence with recurrent episodes of lithiasis and nephrocalcinosis, as in the series described here, is a milder form of the disease that results in a delay in diagnosis and treatment. In addition, 80% of patients will require HD during the third decade of life and consequently a kidney transplant during adulthood. Type 2 is usually a more indolent form of presentation and represents 10% of all cases that is caused by a defect or absence of glycolate/hydroxypyruvate reductase (GRHPR) activity which generates excessive oxalate and pyruvate (5). Type 3 accounts for 5-10% of cases and originates from a mutation in the HOGA1 gene and is a very early but indolent form of the disease and ESRD does not usually develop (6).

Oxalate overproduction in the liver is eliminated via the urine resulting in hyperoxaluria. Insoluble calcium oxalate precipitate in the urine lead to symptoms and the progressive loss of renal function (7). When the glomerular filtration rate (GFR) is below 30-40 ml/min/1.73 m^2, systemic oxalate deposition (oxalosis) occurs in the retina, bone, nerves, skin, blood vessels and the heart (8). The most frequent symptoms are nephrocalcinosis and recurrent nephrolithiasis, hyperuricemia or recurrent UTI are less common. None of the patients in this series had ESRD at diagnosis, unlike patients suffering from the infant form of the disease.

Early diagnosis is crucial in order to prevent ESRD (9). Twenty-four hours oxalate and glycolate measurements in serum and urine are necessary and a renal biopsy could be performed in unclear cases. Furthermore, in the absence of a family history, a genetic analysis is essential in order to confirm the diagnosis (9,10).

Renal failure is associated with a worse prognosis in patients on the liver transplant waiting list or when this condition develops after the transplant (11,12). Therefore, medical treatment based on a high fluid intake, pyridoxine and calcium crystalizing inhibitors must be started as soon as a diagnosis is made or is suspected (2,4,13). However, these treatments are insufficient when ESRD is established. In these cases, renal replacement therapy by hemodialysis prior to a kidney transplant must be initiated. It is essential to reduce the time between ESRD diag-

Table 1. *Recipient and donor features and liver-kidney transplant outcome*

	Case 1	Case 2	Case 3	Case 4	Case 5
Recipient feature					
Age at transplantation	18	45	53	27	29
Gender	W	M	M	W	W
BMI	22.1	32.7	27.5	25.3	23.7
PH type	1	1	2	1	1
Age at diagnosis	4	14	11	26	28
ESRD at diagnosis	No	No	No	-	No
Systemic disease	Yes	No	No	No	No
Prior nephrectomy	No	No	Yes	No	Yes
Pre-transplantation					
HD time pre-Tx (months)	3	-	3	13	36
Intensive medical treatment	Yes	Yes	Yes	Yes	Yes
GFR (ml/min/1.73 m2)	22.4	26	16.5	24.2	11.8
Creatinine (mg/dl)	5.7	8	7	2.4	4.4
Time to Tx (years)	14	22	42	1	1
Donor feature					
Donor age (years)	23	23	55	26	24
Donor type	BD	BD	BD	BD	DCD type III
HLA histocompatibility	6	-	3	4	2
Transplant					
Year of transplant	1999	2009	2009	2014	2015
Transplant type	Simultaneous	Simultaneous	Simultaneous	Simultaneous	Simultaneous
Cold ischemia (min)	175	350	395	360	330
Warm ischemia (min)	50	80	75	50	45
Intraoperative HD	Si	Si	Si	Si	Si
Post-trasplantation					
Post-transplant HD	Yes	Yes	Yes	Yes	Yes
HD time (days)	9	9	15	4	-
Acute renal kidney	Yes	Yes	Yes	No	Yes
Acute tubular necrosis	Yes	Yes	Yes	No	No
Follow-up					
Time (months)	206	85	84	27	13
Liver graft rejection	No	No	No	No	No
Kidney graft rejection	Yes	No	No	No	No
Liver graft survival (months)	206	85	84	27	13
Kidney graft survival (months)	206	85	84	27	13
1-year recipient survival	Yes	Yes	Yes	Yes	Yes
5-year recipient survival	Yes	Yes	Yes	-	-

BMI: body mass index; PH: primary hyperoxaluria; ESRD: end-stage renal disease; HD: hemodialysis; Tx: transplant; GFR: glomerular filtration rate; BD: brain death; DCD: donor after cardiac arrest.

nosis and the transplant in order to avoid systemic oxalate deposits (7,14,15).

Hemodialysis must be intensive and aims to reduce oxalemia, delay renal impairment and therefore the risk of developing oxalosis. The time spent in dialysis prior to transplant is related to a shorter time to hyperoxaluria resolution according to the European Register (15). Although, some studies (7) did not observe a significant reduction with respect to graft survival. These differences may be

Table 2. *Complications during the post-transplant and follow-up period*

Complication	Case 1	Case 2	Case 3	Case 4	Case 5
Hemorrhage	-	Yes	-	-	-
Compartment syndrome	-	Yes	-	-	-
Pyelocaliceal stenosis	-	-	-	-	Si
Acute kidney rejection	Yes	-	-	-	-
Infections	-	*C. glabrata*	-	*E. coli*	*Klebsiella* sp. BK Virus
DVT/PE	-	-	Yes	-	-

DVT/PE: deep vein thrombosis/pulmonary embolism.

related to the mean time in dialysis (three *vs.* one year, respectively) (7).

In this series, the mean donor age (30 ± 13.3 years) is lower than in other series, as donors were selected for recipients of the same age, mainly to improve kidney graft survival. An appropriate donor selection is essential to optimize the outcome (8). With regard to our experience with donors after cardiac death (DCD) Maastricht Type III, the outcome was satisfactory.

Isolated kidney transplant (IKT) is associated with a poor outcome (8,16) due to oxalate deposit mobilization and high urinary excretion that lead to kidney graft injury (7,8,13,17). The 3 year survival rate is 20% in cadaver grafts and 35% at 10 years for live donors. Therefore, this is not recommended unless performed as an interim measure while planning a liver transplant and should be reserved for milder forms of HP (9).

As the source of the enzymatic defect is located in hepatic peroxisomes, the imperative and potentially curative treatment is a liver transplant. Since progressive and irreversible kidney damage is very common, sequential or simultaneous liver-kidney transplantation is the definitive treatment (4,13). The transplantation strategy will depend on the systemic involvement, the phenotype-genotype variability and experience within the medical center (4). Some authors (1,4) suggest a scheme based on renal function in order to select the therapeutic time sequence. LKST is indicated in patients with oxalate overproduction resistant to pyridoxine, with a GFR < 20 ml/min/1.73 m^2, under dialysis for an entire year, oxalosis or evidence of renal impairment due to oxalate deposits (14). LKST was considered as the treatment of choice, as all our patients were in ESRD with a GFR < 20 ml/min/1.73 m^2 or displayed oxalosis symptoms.

After LKST, there is a risk of nephrocalcinosis recurrence in the kidney graft due to calcium oxalate deposit mobilization and a high renal excretion which might persist for three years in 36% of the patients (7). In order to prevent this, it is essential to resume medical intensive treatment immediately post-transplant and to continue dialytic therapy during and after the surgery according to renal function deterioration. Nevertheless, as in other studies (13), we did not observe any recurrence when using LKST as the first therapeutic option.

In the European multicenter study (1984-2004), recipient survival with LKST at 5 and 10 years was 80 and 68%, respectively and the kidney graft survival rate was 72 and 60%, respectively (15). There are discrepancies with regard to the effect of LKST on the survival of patients with type 1 PH. Some authors (7,13,14) have observed an increase in morbidity and mortality when the liver transplant is associated with the kidney in comparison to when an IKT is performed. A reduction in serum oxalate one year or less after the graft loss has no greater efficacy. However, other authors have not observed significant differences between LKST and IKT with regard to short-term mortality (13) and a greater graft survival in LKST (13,17). Table 3 summarizes studies in adults or children and adults who underwent a transplant due to PH since 2000, except for studies that only included children. The summary table also includes data with regard to recipient and kidney graft survival at 5 years. In Spain, 17 transplants have been performed due to PH.

Sequential transplantation is a different approach, where a liver transplant is performed first, deferring the kidney transplant until the oxalate levels are reduced by dialysis. Significant oxalosis or pediatric cases with ESRD where an LKST is unfeasible due to anatomical reasons is also an indication. This approach might also be considered in living donors or older children with an impaired but maintained renal function (GRF: 15-25 ml/min/1.73 m^2) as it may result in an improved renal function (18). There is a greater risk of infectious disease as it is necessary to maintain dialytic therapy after transplantation (20).

In addition to these different techniques, an orthotopic auxiliary partial liver transplant (II-III segments) associated with a kidney transplant has also been used in adults with type 1 PH. This approach reduces the morbidity of a complete liver transplant and the risk of hepatic failure due to graft loss (19). Despite this, some authors consider auxiliary transplantation an ineffective treatment (20).

Pre-emptive liver transplantation is proposed to avoid ESRD and related complications (11,12). It might be taken into consideration in aggressive infant forms when the GFR is between 60-40 ml/min/1.73 m^2 or recurrent nephrolithiasis in spite of medical treatment (4,10). It has certain advantages over LKST, as dialysis might be discontinued and it shortens the waiting list time (21). Nevertheless, it has ethical implications, especially if the GFR is > 60 ml/min/1.73 m^2 as the time to the development of ESRD is variable and unpredictable (4,22), thus patient selection and timing still remain controversial. Unlike other metabolic diseases, domino liver transplantation it is not recommended and must not be performed as recipients will develop PH and subsequently ESRD in a short time period with an associated high mortality rate (23,24).

Table 3. *Comparison of the liver-kidney transplantation series in adults with type 1 PH*

Author	Year	Study type	n	Mean age	Patient	Primary outcome and 5-year Sv.
Monico et al. (15)	2001	Retrospective, unicentric	16	32.9 *vs.* 40.6	Adults	To compare kidney graft survival in IKT *vs.* LKST R. Sv.: 78%; KG: 52%
Cibrik et al. (18)	2002	Retrospective, unicentric	190	35 *vs.* 22	Adults	To compare kidney graft survival in IKT *vs.* LKST R. Sv.: 80%; KG: 75%*
Jamieson et al. (16)	2004	Retrospective, unicentric	135	16.5	Adults/children	LKST results in 35 countries R. Sv.: 80%, KG: 72%
Lorenzo et al. (10)	2006	Retrospective, unicentric	4	29.6	Adults	To compare liver-kidney sequential transplantation *versus* no transplant in type 1 PH
Bergstralh et al. (3)	2010	Retrospective, unicentric	203	28.2	Adults	To compare kidney graft survival in IKT *vs.* LKST R. Sv. : 67%, KG: 71%*
Malde et al. (2)	2011	Retrospective, unicentric	5	30.8	Adults	Recurrence and re-transplantation rate in IKT *vs.* LKST
Compagnon et al. (14)	2014	Retrospective, unicentric	54	20.3	Adults/children	To compare grafts, recipient and recurrence in IKT *vs.* LKST R. Sv.: 87.5%, LG: 88%, KG: 87%*
Hori et al. (25)	2015	Retrospective, unicentric	3	25	Adults/children	LKST and kidney after a domino liver transplant and living donor
12 de Octubre	2017	Retrospective, unicentric	5	34.4	Adults	Results in recipient, kidney and liver graft survival

Sv.: survival; LKST: liver-kidney simultaneous transplantation; IKT: isolated kidney transplantation; R: recipient; KG: kidney graft; LG: liver graft. *Censored death graft survival.

Type 2 PH can present at any age and the development of ESRD and oxalosis is rare (25). The treatment is based on a high fluid intake, citrates and dialysis and IKT is the treatment of choice in cases of ESRD (7,25). However, kidney graft loss by nephrocalcinosis has been reported and some authors suggest that LKST might improve the serum oxalate levels, especially in ESRD patients (5). However, there is insufficient experience in this matter.

In conclusion, due to the rarity of the disease and the current scientific evidence, the indication and timing of treatment remains controversial. However, LKST could be considered as a therapeutic option in patients with PH and ESRD.

REFERENCES

1. Van Woerden CS, Grothoff FJW, Wanders RJ, et al. Primary hyperoxaluria type 1 in the Netherlands: Prevalence and outcome. Nephrol Dial Transplant 2003;18:273-9. DOI: 10.1093/ndt/18.2.273
2. Malde DJ, Pararajasingam R, Tavakoli A, et al. Transplantation in adults with primary hyperoxaluria: single unit experience and treatment algorithm. Ann Transpl 2011;16(4):111-7. DOI: 10.12659/AOT.882227
3. Bhasin B, Urekli HM, Atta MG. Primary and secondary hyperoxaluria: Understanding the enigma. World J Nephrol 2015;4(2):235-44. DOI: 10.5527/wjn.v4.i2.235
4. Cochat P, Fargue S, Harambat J. Primary hyperoxaluria type 1: strategy for organ transplantation. Curr Opin Organ Transpl 2010;15(5):590-3. DOI: 10.1097/MOT.0b013e32833e35f5
5. Filler G, Hoppe B. Combined liver-kidney transplantation for hyperoxaluria type II? Pediatr Transplant 2014;18(3):237-9. DOI: 10.1111/petr.12243
6. Beck BB, Baasner A, Buescher A, et al. Novel findings in patients with primary hyperoxaluria type III and implications for advanced molecular testing strategies. Eur J Hum Genet 2013;21(2):162-72. DOI: 10.1038/ejhg. 2012.139
7. Bergstralh EJ, Monico CG, Lieske JC, et al. Transplantation outcomes in primary hyperoxaluria. Am J Transpl 2010;10(11):2493-501. DOI: 10.1111/j.1600-6143. 2010.03271.x
8. Millan MT, Berquist WE, So SK, et al. One hundred percent patient and kidney allograft survival with simultaneous liver and kidney transplantation in infants with primary hyperoxaluria: a single-center experience. Transplantation 2003;76(10):1458-63. DOI: 10.1097/01.TP.0000084203.76110.AC
9. Lorenzo V, Torres A, Salido E. Hiperoxaluria primaria. Nefrologia 2014;34(3): 398-412.
10. Cochat P SK, Schärer K. Should liver trasplantation be performed before advanced renal insufficiency in primary hyperoxaluria type 1? Pediatr Nephrol 1993;7(2):212-8. DOI: 10.1007/BF00864408
11. Brown RS, Lombardero M, Lake JR. Outcome of patients with renal insufficiency undergoing liver or liver-kidney transplantation. Transplantation 1996;62(12):1788-93. DOI: 10.1097/00007890-199612270-00018
12. Nair P, Al-otaibi T, Nampoory N, et al. Combined Liver and Kidney Transplantation in Primary Hyperoxaluria: A Report of Three Cases and Review of the Literature. Saudi J Kidney Dis Transpl 2013;24(5):969-75. DOI: 10.4103/1319-2442.118106
13. Compagnon P, Metzler P, Samuel D, et al. Long-Term Results of Combined Liver-Kidney Transplantation for Primary Hyperoxaluria Type 1: The French Experience. Liver Transplant 2014;20:1475-85. DOI: 10.1002/lt.24009

14. Monico CG, Milliner DS. Combined liver-kidney and kidney-alone transplantation in primary hyperoxaluria. Liver Transplant 2001;7(11):954-63. DOI: 10.1053/jlts.2001.28741

15. Jamieson NV. The European Primary Hyperoxaluria Type 1 Transplant Registry report on the results of combined liver/kidney transplantation for primary hyperoxaluria 1984-1994. European PH1 Transplantation Study Group. Nephrol Dial Transplant 1995;10(8):33-7. DOI: 10.1093/ndt/10.supp8.33

16. Broyer M, Brunner FP, Brynger H. Kidney transplantation in primary oxalosis: data from the EDTA Registry. Nephrol Dial Transplant 1990;5(5):332. DOI: 10.1093/ndt/5.5.332

17. Cibrik DM, Kaplan B, Arndorfer JA, et al. Renal allograft survival in patients with oxalosis. Transplantation 2002;74(5):707-10. DOI: 10.1097/00007890-200209150-00020

18. Kemper MJ. Concurrent or sequential liver and kidney transplantation in children with primary hyperoxaluria type 1? Pediatr Transplant 2005;9(6):693-6. DOI: 10.1111/j.1399-3046.2005.00362.x

19. Onaca N, Sanchez EQ, Melton LB, et al. Cadaveric orthotopic auxiliary split liver transplantation and kidney transplantation: An alternative for type 1 primary hyperoxaluria. Transplantation 2005;80:421-4. DOI: 10.1097/01.tp.0000168147.88707.80

20. Trotter JF, Milliner D. Auxiliary Liver Transplant Is an Ineffective Treatment of Primary Hyperoxaluria. Am J Transplant 2014;14(1):24.

21. Perera MTPR, Sharif K, Lloyd C, et al. Pre-emptive liver transplantation for primary hyperoxaluria (PH-I) arrests long-term renal function deterioration. Nephrol Dial Transplant 2011;26(1):354-9. DOI: 10.1093/ndt/gfq353

22. Shapiro R, Weismann I, Mandel H, et al. Primary hyperoxaluria type 1: improved outcome with timely liver transplantation: a single-center report of 36 children. Transplantation 2001;72(3):428-32. DOI: 10.1097/00007890-200108150-00012

23. Hori T, Egawa H, Kaido T, et al. Liver transplantation for primary hyperoxaluria type 1: A single-center experience during two decades in Japan. World J Surg 2013;37(3):688-93. DOI: 10.1007/s00268-012-1867-7

24. Saner FH, Treckmann J, Pratschke J, et al. Early renal failure after domino liver transplantation using organs from donors with primary hyperoxaluria type 1. Transplantation 2010;90:782-5. DOI: 10.1097/TP.0b013e3181eefe1f

25. Milliner DS, Wilson DM, Smith LH. Phenotypic expression of primary hyperoxaluria: Comparative features of types I and II. Kidney Int 2001;59(1):31-6. DOI: 10.1046/j.1523-1755.2001.00462.x