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Ethylene Glycol Poisoning Should Not Contraindicate Liver Donation

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Abstract: As the number of patients waiting to receive transplants increases, there is a need to explore all possible donation opportunities. In this case report, we describe the transplantation of a liver from a donor who died after ethylene glycol poisoning into a woman with alcoholic liver disease with cirrhosis and associated ascites. Donor management, including ethanol, fomepizol and haemodialysis, hastened clearance of ethylene glycol from the circulation, and after liver transplantation, the recipient exhibited no adverse effects suggestive of ethylene glycol toxicity, although recipient hepatic artery dissection and thrombosis necessitated retransplantation. Our experience suggests that donor death due to ethylene glycol intoxication should not contraindicate liver transplantation, particularly after appropriate donor management.

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Ethylene glycol (EG) is an odorless, sweet-tasting liquid found in industrial solutions such as antifreeze and windshield wiper fluid. Due to its sweet taste, it is sometimes consumed accidentally by children. Adults tend to ingest it intentionally as a substitute for alcohol or in an attempt at committing suicide. The lethal dose of EG is thought to be 1.4 to 1.6 mL/kg[1]; it exerts most of its toxicity via its metabolites glycolate and oxalate. The liver metabolizes approximately 80% of EG (Figure 1), and the remaining 20% is excreted unchanged by the kidneys.[2] Ethylene glycol exerts its toxicity in 3 stages. In the first 12 hours, its effects are primarily neurological with central nervous system depression. This is followed by a metabolic acidosis, with associated cardiopulmonary effects, such as pulmonary edema and acute congestive cardiac failure. Finally, after 24 hours, acute renal failure occurs due to calcium oxalate deposition and metabolic acidosis.[3] Oxalate, a metabolite of EG, binds circulating calcium-forming crystals that deposit in the renal cortex, causing reduced glomerular filtration. Death usually occurs during the metabolic acidosis phase, which is associated with multiorgan failure and cerebral edema, the latter resulting in brain stem herniation and death.[4]

In this article, we present a case of transplantation of a liver from a donor with EG poisoning, and review the relevant literature.

CASE DESCRIPTION

The donor liver was recovered from a 26-year-old woman found collapsed at home after ingesting a bottle of windshield wiper fluid. She had a history of self-harm and previous EG overdose attempts. She was intubated upon arrival to the hospital and given ethanol. Her blood results on admission included a sodium of 148 mmol/L, potassium of 6 mmol/L, creatinine of 195 μmol/L (2.2 mg/dL), glucose of 14.9 mmol/L, aspartate aminotransferase (AST) of 58 iU/L, alanine aminotransferase (ALT) of 30 iU/L, alkaline phosphatase (ALP) of 209 iU/L, and a total bilirubin of 3 μmol/L (0.18 mg/dL). On day 2, fomepizole was given instead of ethanol, and she was started on intermittent hemodialysis. This was stopped on day 3, because there was no trace of EG or its metabolites in the blood sample. She was then transferred to intensive care, where she coned the same day, and brain stem death was confirmed. The liver was recovered for transplantation 5 days after ingestion of EG.

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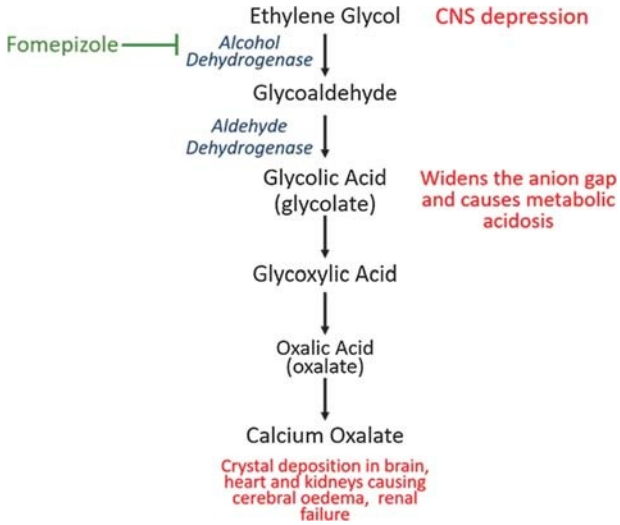

FIGURE 1. Metabolism of EG and the possible effect of its metabolites.

At the time of organ recovery, the serum AST was 26 iU/L, ALT was 26 iU/L, ALP was 109 iU/L, total bilirubin was 64 μmol/L (3.7 mg/dL), and prothrombin time (PT) at 13 seconds. A liver biopsy before transplantation showed no evidence of oxalate crystal deposition. The liver was orthotopically transplanted into a 62-year-old woman with alcoholic liver cirrhosis and ascites. Her Model of End-stage Liver Disease score was 26 before the transplantation, and her renal function was normal (creatinine, 42 μmol/L or 0.48 mg/dL). The operation was complicated by massive hemorrhage, estimated blood loss of 23 L, and she developed acute kidney injury perioperatively (peak creatinine, 127 μmol/L or 1.44 mg/dL on day 2). Her postoperative liver function tests on day 7 were ALT of 102 U/L, ALP of 74 U/L, total bilirubin of 37 μmol/L (2.2 mg/dL), and PT on day 8 was 12.1 seconds. A computed tomography scan on day 10 posttransplantation revealed she had an extensive dissection of the native hepatic artery proximal to the anastomosis to the donor for which she underwent retransplantation on day 22 posttransplant. At that time, she had recovered normal renal function.

TABLE 1.

Comparison of reported cases of liver transplantation from donors with EG poisoning

		Dy-Liacco	Wollf	McClain	Fujji	Current case
Donor	Age, y	41	44	26	31	26
	Sex	Male	Female	Male	Male	Female
	Blood group			B+		O+
	Time from overdose to brain death	48 h	8 d	4 d	5 d	3 d
	AST, U/l	36	59	28	32	26
	ALT, U/l	27	35	7	17	26
	GGT, U/l		49	23		48
	ALP, U/l	48		52		109
	Total bilirubin, mg/dL	1	0.9	0.5	0.6	3.7
	PT, sec	12.3		12.1		13
	Treatment for ingestion			Dialysis until toxicology is negative		Ethanol, fomepizole, dialysis until negative toxicology
	Creatinine, mg/dL			5		6.43
	eGFR, mL/min per 1.73 m^2					8
	Liver biopsy findings	Normal hepatocytes; no evidence of inflammation or crystal deposits	Mild perivenous microvesicular steatosis scarce periportal round cell infiltration; no crystals	No evidence of hepatitis, centrilobular necrosis, carcinomas, granulomas or alcohol induced injury, no crystals		No evidence of crystals
Recipient	Age	54	32	51	61	62
	Sex	Male		Male	Male	Female
	Liver injury	Alcoholic cirrhosis, ascites, encephalopathy	Haemophilia A, hepatitis C, HIV	Hep C, hepatocellular carcinoma	ESLD secondary to nonalcoholic steatohepatitis	Alcoholic cirrhosis, ascites
	MELD score at transplant	28	18	22	35	26
Peak postoperative LFTs	AST	345		1798		
	ALT	197	375	430		882
	ALP	35		39		47
	Total bilirubin	3.3		6.7		7.1
	PT	23.2				25.6
	Days until normal LFTs	2	8	9		
	Days until discharge	7	15	10		
Kidney function postoperative	Serum creatinine, mg/dL			3.95		1.44
	Creatinine (mg/dL) at 6 mo			2		
	eGFR at 6 mo			50		
	Complications			AKI that progressed to chronic kidney disease		Acute kidney injury; native hepatic artery dissection

eGFR, estimated glomerular filtration rate; MELD, Model of End-Stage Liver Disease; LFTs, liver function test; HIV, human immunodeficiency virus AKI; acute kidney injury; ESLD, end stage liver disease.

DISCUSSION

There have been 4 previous reports of liver transplantation from a donor who has died after ingestion of EG. Acute kidney injury is described in just one of the cases.[5] Renal failure in donors is due to metabolic acidosis secondary to glycolate and calcium oxalate deposition and can occur 24 to 72 hours after consumption.[6] One concern when accepting the liver from such a donor is the possibility of EG still being present which could result in renal failure in the recipient. This seems unlikely in our case, because after treatment at the donor hospital, there was no trace of EG in the donor at the time of donation.

After being rapidly absorbed by the gastrointestinal tract, serum level of EG peaks between 1 and 4 hours postingestion, and the elimination half-life with preserved renal function is 3 to 8 hours.[6] However, ethanol and fomepizole are often given to prevent the metabolism of EG into its toxic metabolites. Ethanol is the preferred substrate of alcohol dehydrogenase and is thus, metabolized in preference to EG, whereas fomepizole inhibits alcohol dehydrogenase activity, which is the rate-limiting step in EG metabolism. Because this slows down the conversion of EG into its metabolites, it changes the half-life of EG to 19.7 hours.[5] This is important to take into account when working out when EG is fully cleared and whether the organ is safe to transplant. Hemodialysis of the donor also reduces the levels of EG and its metabolites. It should be continued until the blood shows no traces of EG and its metabolites to prevent acute kidney injury and other pathologies attributed to EG metabolites in the recipient.

As the number of patients waiting to receive transplants increases, there is a need to explore all possible donation opportunities. Transplanting the liver from donors who died due to an EG overdose would appear to be safe, subject to appropriate donor management to eliminate EG and its metabolites before donation. The liver appears to be less susceptible to oxalate deposits.[2] Table 1 updates the table in a previous publication[5] and summarizes all the reported cases to date. In all cases, liver enzymes were normal before removal of the liver and the liver biopsies showed no evidence of oxalate crystal deposits. In addition, Fujii et al[2] showed that the allograft was still functioning 5 years after transplantation. As a result, so long as the donor is hemodynamically stable, and there are no contraindications to transplanting the liver, it is acceptable to use livers from donors who died from EG overdose. However, the recipient should be informed about the liver coming from an individual who had overdosed and the increased risks this may pose on them. The adverse result in our case was due to a dissection of the native hepatic artery extending back into the celiac trunk and compromising arterial flow into the graft. It was not related to the cause of donor death.

Although it seems safe to transplant livers, the safety of transplanting other organs from donors with EG poisoning is yet to be established. Because the third stage of EG toxicity involves calcium oxalate crystal deposition often in the renal cortex, causing acute kidney injury, one must be weary before using kidneys as allografts.[7] However, there have been reports of successful transplantation of a kidney[8] and of a kidney and pancreas[7] in this setting. Because there is a need for all viable allografts to be used, organs from EG overdosed donors should not be dismissed. Rather careful evaluation of their organs is needed on an individual basis to assess their suitability, because it is indeed possible to gain successful allograft function.

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