TRANSPLANT INTERNATIONAL

LETTER TO THE EDITORS

Liver donation after ethylene glycol overdose: when is it safe?

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Ethylene glycol is a sweet tasting compound found in high concentrations in substances like automotive antifreeze, brake fluids, and industrial solvents [1] and is often used as an alcohol substitute by alcoholics, or as a means of suicide. Ethylene glycol gets metabolized by alcohol dehydrogenase into glycoaldehyde which is then converted into glycolic acid, the main cause of the metabolic acidosis which characteristically develops. Glycolic acid gets converted through glyoxylic acid into oxalic acid, which precipitates with calcium into calcium oxalate crystals. These crystals are primarily responsible for the cerebral edema and renal failure which are characteristic late sequelae of ethylene glycol overdose [2]. We recently made a decision to utilize a liver from a donor who overdosed on ethylene glycol.

The donor was a 26-year-old B-positive male with schizophrenia, who was otherwise healthy. He was found unresponsive and taken to the emergency department, where his anion gap was 26 with a bicarbonate of 12 mmHg, sodium of 142 mEq/l, potassium of 5.2 mEq/l, glucose of 84 mEq/l, and creatinine of 2.7 mg/dl. His toxicology work-up came back positive for ethylene glycol and he was then dialyzed until the toxicology screens came back negative. Despite aggressive attempts at saving his life, the donor succumbed to the damage from his overdose 4 days later.

Prior to procurement, the donor's labs revealed a total bilirubin of 0.5 mg/dl, direct bilirubin of 0.1 mg/dl, aspartate transaminase (AST) of 28 IU/l, alanine transaminases (ALT) of 7 IU/l, and gamma-glutamyl transpeptidase of 23 IU/l. He was, however, in renal failure with a creatinine ranging from 4.5 to 5 mg/dl. Both kidneys were biopsied and discarded at procurement because of bilateral crystallization. The liver was biopsied twice at procurement and both specimens showed no evidence of crystallization, hepatitis, centrilobular necrosis, carcinomas, granulomas, or alcohol-induced injury. It was orthotopically transplanted using standard technique [3] without bypass into a 51-year-old male patient with end-stage liver disease secondary to hepatitis C, complicated by hepatocellular carcinoma. His Model for End-Stage Liver Disease score was 25 prior to the transplantation and during the case he was hemodynamically stable.

To the best of our knowledge, this is the third case of orthotopic liver transplantation from an ethylene glycol overdosed donor (Table 1) [4,5]. In the prior examples, the recipients recovered without any published renal injury. Our patient developed acute renal failure post-transplantation that has progressed to chronic kidney disease (defined as a GFR of less than 60 ml/min/1.73m^2 for ≥3 months). During and after liver transplantation, the patient was hemodynamically stable. His pre-operative creatinine of 0.97 mg/dl rose to 3.95 mg/dl by postoperative day 4, at which point it began to slowly recede. At 6 months postop, the patient's creatinine stabilized at approximately 2 mg/dl, with an estimated glomerular filtration rate (GFR) consistently falling between 40 and 50 ml/min/1.73 m^2.

This led us to ask when it should be considered safe to transplant a liver from an ethylene glycol overdosed donor. The half-life of ethylene glycol in humans has been estimated at 3–8.4 h in untreated adults [6], and renal failure has been demonstrated to occur up to 72 h after ethylene glycol ingestion [7]; however, considering the estimated half-life of oxalic acid of 92 ± 8 min [8], this damage most likely depends on the continued presence of oxalic acid precursors in the blood stream multiple days after the patient's initial presentation. With dialysis, ethylene glycol and glycolic acid levels are typically reduced to concentrations less than 5 mmol/l within the first 10 h [9]. As glycolic acid causes metabolic acidosis in these patients, this may be a useful surrogate marker for the levels of residual toxic chemicals in the patient's system. Waiting for at least 12 h after a negative ethylene glycol and glycolic acid toxicology screen or for 12 h after the metabolic acidosis has been corrected should allow ample time for the body to rid itself of excess oxalic acid.

Fomepizole therapy without dialysis increases the ethylene glycol half-life in the body from 3 to 8 h up to 19.7 ± 1.3 h [10]. As conversion to GA will occur at a slower rate, but for a longer period of time, both GA and

Table 1 Summary of liver transplantation from donors with ethylene-glycol-induced brain death.

Characteristics	Dy-Liacco *et al.*	Wolff *et al.*	McClain *et al.*
Age/gender of donor	Male – age 41	Female – age 44	Male – age 26
Time from overdose to brain death	48 h	8 days	4 days
Liver function tests at procurement:			
Aspartate aminotransferase (AST), U/l	36	59	28
Alanine aminotransferase (ALT), U/l	27	35	7
Gamma-glutamyltransferase, U/l	–	49	23
Alkaline phosphatase, U/l	48	–	52
Total bilirubin mg/dl	1	0.9	0.5
Prothrombin time (PT), s	12.3	–	12.1
sINR	–	0.9	1
Liver biopsy findings	Normal hepatocytes with no evidence of inflammation or crystal deposition	Mild perivenous microvesicular steatosis, scarce periportal round cell infiltration. No crystals	No evidence of hepatitis, centrilobular necrosis, carcinomas, granulomas, or alcohol induced injury
Age/gender of recipient	Male – age 54	Unknown – age 32	Male – age 51
Recipient liver injury and complications	Alcoholic cirrhosis, ascites & encephalopathy	Hemophilia A, hepatitis C, HIV	Hepatitis C, hepatocelluar carcinoma
Model for end-stage liver disease (MELD) score at transplant	28	18	22
Peak postop liver function tests:			
Aspartate aminotransferase (AST)	345	–	1798
Alanine aminotransferase (ALT)	197	375	430
Alkaline phosphatase	35	–	39
Total bilirubin	3.3	–	6.7
Prothrombin time (PT)	23.2	–	–
Days until normal liver function tests:	2	8	9
Days until discharge	7	15	10

OA may be present at potentially damaging levels for longer than the 72 h seen without intervention. In view of this, more time should be allowed before organ donation is attempted from a patient treated with fomepizole. The exact time would depend on the potential donor's clinical picture, but like a dialyzed patient, the donor should be free from metabolic acidosis or exhibit a negative toxicology screen for at least 12 h prior to transplant allowing time for oxalic acid clearance from the system.

In either case, the proposed recipient should be informed about the nature of the liver they are about to receive. It would be appropriate to tell them that the liver is coming from an individual who overdosed on a toxic substance, and that this might pose some degree of increased risk to them. However, they should also be told that every published case of such a procedure has been successful. They should be aware of the time that has passed since the overdose, and be informed whether or not this is sufficient for clearance of the toxic substances. It should be emphasized that the overdose does not change the nature of the procedure that will be performed.

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