Anesthesia management of liver transplantations in pediatric patients with metabolic disorders: a case series

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INTRODUCTION

Pediatric patients with metabolic disorders presenting for liver transplantation (LT) represent a unique population of patients in the world of liver transplant. They tend to present early in life without the myriad of clinical manifestations of liver failure,[6] however, they do require modification in anesthesia monitoring and management. Current literature on this topic is scarce and the goal of this clinical case series is to highlight the anesthetic implications and develop a guideline for management of such patients.

BACKGROUND

Metabolic diseases make up about 22% of LT in pediatric population with urea cycle disorders being the most common.[5,9] Such patients are medically managed with dietary restrictions and medications aimed at reducing the accumulation of toxic metabolites and supplementation of essential products downstream of the defect.[5,6] However, some of these diseases such as ornithine transcarbamylase deficiency (OTCD) are poorly managed medically and LT prior to first year of life is required.[3,9] LT provides a mean of replacing the activity of the deficient enzyme. It is not always curative, but reduces the risk of metabolic decompensation and the need for strict dietary adherence.[5] Ultimately, it improves quality of life.[5]

CASE SERIES DESCRIPTION

At our institution, 28 pediatric patients underwent orthotopic LT for metabolic disorders between 2004 and 2020; 7 patients received concurrent kidney transplant and 1 received concurrent pancreas transplant.

Underlying pathology (Figure 2):

- 8 Urea cycle disorder (UCD)
- 5 Hyperoxaluria
- 4 Organic acidemia (OA)
  - 2 methylmalonic acidemia (MMA)
  - 2 propionic acidemia (PA)
- 3 Maple syrup urine disease
- 2 Tyrosinemia
- 2 Glycogen storage disease (GSD)

IRB approval was obtained to evaluate these patients retrospectively. Four anesthesia records could not be located and were excluded. At the time of surgery, the mean age and weight was 5 years and 21 kg (Figure 1).

Figure 1

Demographics		Range
Average age (years)	5.4	0.4 - 18
Average weight (kg)	21	7 - 57
Percent male	54	
Average length of stay (days)	48	14 - 162
Number of patients pre-admitted > 1 day	2	0-9

RESULTS

Figure 2

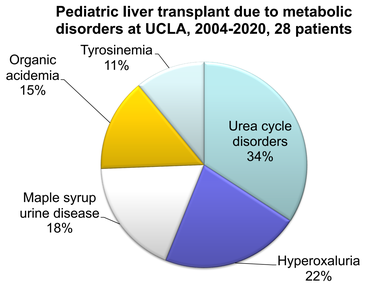

Figure 3

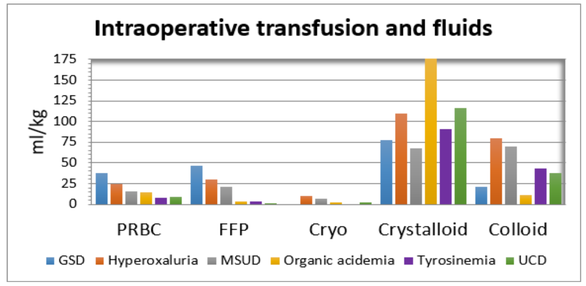

Figure 4

Diagnosis	Pre-operative			Intra-operative									
	Genetics consult	Dextrose	Management	Pre-med	Induction		NMBA	NaCO3	Adjuncts	Dextrose	Plasmalyte	NS	Albumin
GSD: Type 9C		X	Cornstarch	M	P	F	Sux + Panc	X			X		X in 25% LR
GSD: Type I		X	DDAVP for Von Willebrand	M	P	F	Vec	X		D50	X		X
Hyperoxaluria			Dialysis 8 hrs pre-transplant	M	P	F	Roc				X		X
				M	P	F	Roc	X		D50	X		X
				M	P	F	Roc	X		D10		X	X
				M	P	F	Roc	X			X	X	X
		X		M	P	F	Roc					X	X
Maple syrup urine disease	X		Dip urine for ketones once NPO, if positive, to start intralipid Skipped mealtime valine and isoleucine x 2 meals	M	P	F	Roc	X		D10	X		X
	X		Home isoleucine/valine			F	Roc				X		X
						F	Roc			D50		X	X
Methylmalonic acidemia		X	Home levocarnitine held	M	P	F	Roc				X		X
		X		M	P	F	Roc			D5		X	X
Propionic acidemia	X	X	IV levocarnitine + intralipid started for NPO >8hr Ammonia q4h while NPO and in OR; Ammonul as needed		P		Roc	X	Intralipid Levocarnitine	D10	X	X	
	X	X	Home levocarnitine			K	Roc		Levocarnitine	D10	X		
Tyrosinemia	X	X	Home nitisinone	M	P	F	Roc				X		X
					P	F	Roc			D5	X		X
UCD: argininosuccinic aciduria		X	Ammonul load and maintenance if hyperammonemia	M	P		Roc	X	Arginine		X		X
		X	Home arginine + phenylbutyrate	M	P	F	Roc				X		X
UCD: citrullinemia		X	Home arginine + phenylbutyrate Pre-op accuchecks and ammonia levels		P	F	Roc					X	X
UCD: probable		X			P	F	Roc			D5	X		X
UCD: OTCD		X	Home arginine + benzoate		P	F	Roc		Arginine Benzoate	D10	X		
	X	X	Continue diet until OR time confirmed Home phenylbutyrate until NPO, Ammonul + arginine started		P	F	Roc	X	Arginine Benzoate/ Phenylacetate	D10	X		X
		X				F	Roc					X	X
	X	X	IV levocarnitine Home benzoate + citrulline**	K (IM)	P	F + T	Roc + Vec	X	Intralipid Benzoate	D10	X		X
Total:	7	16			20			10		D5%: n=6 D10%: n=7 D50%: n=3	18	8	21

GSD: glycogen storage disease
UCD: urea cycle disorder
OTCD: ornithine transcarbamylase deficiency
**Ammonul not started due to lack of IV access

Key: M- midazolam, K- ketamine, IM- intramuscular, P- propofol, F-fentanyl, T-thiopental, Sux- succinylcholine, Panc- pancuronium, Roc- rocuronium, D%- Dextrose fluid %, NS- normal saline

DISCUSSION

General Perioperative Principles:

- Limit NPO time and perioperative stress [3,5,7]
- Dextrose infusion [4,5,6,7] +/- lipids once NPO to avoid catabolism [5]
- Close monitoring of intra-operative glucose, acid/base status, electrolytes [5]
- Continuation of home supplements and ammonia scavengers [4,5]

Pre-operative considerations (Figure 4):

- Patients who had genetics consultation on admission were more likely to have home medications continued perioperatively.
- Dialysis 8 hours prior to transplant was recommended by the nephrology team in all 5 patients with hyperoxaluria. While intraoperative continuous renal replacement therapy (CRRT) is recommended[1], none of the 5 patients received such intervention.

Medication considerations:

- **Dextrose** 4-8 mg/kg/min is often recommended to prevent catabolism.[5,6,8] A dextrose infusion was started pre-operatively in 16 patients and continued in 10 intraoperatively; 3 patients not on an infusion required D50% for hypoglycemia. For hyperglycemia, dextrose should not be held, and insulin should be initiated.[8]
- **Carnitine** may be deficient in patients with OA[4] and UCD and was given intraoperatively to two patients with OA, and one with UCD.
- **Ammonia scavengers** (sodium benzoate, phenylacetate) are often employed in management of UCD[5], and were administered intraoperatively in ¾ patients with OTCD. Ammonia levels were not routinely assessed during surgery, but have been suggested for surgeries lasting > 2 hours.[5,8]
- **Propofol** is metabolized to propionyl-CoA and its use, particularly prolonged infusions, should be used with caution in patients with OA.[4,6,7] Of the 4 patients with OA, 3 received propofol without significant acidosis on the initial blood gas post-induction.
- **NMBAs** is metabolized by ester hydrolysis (succinylcholine, cisatracurium, mivacurium) form organic metabolites and should be used with caution in patients with OA.[4,6,7]
- **Albumin** may serve as an occult source of protein in OA and UCD patients.[6,8]
- **DDAVP** was given in a GSD Type 1 patient. Studies have shown in-vitro correction of bleeding time after glucose and total parenteral nutrition in patients with GSD-associated VWD.[2] Transfusion requirement was highest in GSD followed by hyperoxaluria. However, this may be attributed to a longer operations given multi-organ transplants with the average anesthetic times being 160 minutes longer than LT alone.

CONCLUSION

Perioperative management of metabolic disorders in pediatric patients presenting for liver transplantation require a multidisciplinary approach.[3,9] Special considerations are taken by the anesthesiologist for optimization of such patients. [9]

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