Custom Parenteral Nutrition for Critically Ill Patients with Aminoacidopathies

Ann & Robert H. Lurie Children's Hospital of Chicago®

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Objective

To review the use of a non-formulary parental nutrition (PN), from Integrity Compounding Pharmacy, in patients with aminoacidopathies admitted at Ann & Robert H. Lurie Children's Hospital of Chicago (LCH)

Background/Methods

Phenylketonuria (PKU) and Maple Syrup Urine Disease are two rare aminoacidopathies caused by an inborn error of metabolism (IEM) in phenylalanine (PHE) for PKU and branched chain amino acids (BCAA), leucine, isoleucine and valine for MSUD. If improperly treated, PKU can lead to severe mental disabilities. Lack of proper treatment, MSUD can also lead to severe mental and physical disabilities and coma or death. While early initiation of treatment prevents the most severe outcomes in both conditions, providing appropriate nutrition, particularly during catabolic stress, is essential to prevent further sequalae. Treatment during catabolic stress includes, reducing offending amino acids (AA) while providing appropriate protein supplementation, and correcting catabolism with sufficient calories. If enteral nutrition (EN) is not feasible to prevent catabolism, parental nutrition (PN) must be considered. Standard PN relies on protein mixtures that contain both PHE and BCAA and are not appropriate with this patient population.

In 2018, Integrity Compounding Pharmacy began suppling specially compounded AA solutions for PN use in patients with an IEM. This custom PN is tailored for each specific IEM and do not contain the offending AA. Between August 2018 and July 2019, Integrity, and the LCH pharmacy and metabolic team collaborated to create a standard operating procedure for obtaining this specially PN when a patient with an IEM is admitted and unable to meet nutrition goals utilizing EN alone.

A retrospective chart review identified four critically ill patients with aminoacidopathies who were treated at LCH. All four patients were unable to meet nutrition goals solely through EN.

Patient A: 4 day old female (CGA 31 0/7 wks) admitted to outside hospital due to prematurity and respiratory failure, and history of twin-to-twin transfusion (donor). The patient had two plasma amino acids (PAA) revealing very elevated phenylalanine levels, leading to presumed diagnosis of PKU.

Patient B: 4 day old female (CGA 31 0/7 wks, twin of patient A), admitted to outside hospital due to prematurity, respiratory failure, ductal dependent pulmonic stenosis, and history of twin-to-twin transfusion (recipient).

Patient A and B both had two PAA revealing very elevated phenylalanine levels, leading to presumed diagnosis of PKU. Due to prematurity, Integrity PN was initiated to meet nutrition goals. The patient had an older sibling that was identified to have PKU on newborn screening, and family was in communication with clinic leading up to delivery with plan to collet PAA shortly after birth.

Patient C: 26 year old male with MSUD admitted for metabolic decompensation and respiratory failure with novel Covid-19 virus. In the setting of worsening respiratory status, Integrity PN was started.

Patient D: 8 year old female with MSUD presenting with nausea and vomiting in the setting of novel Covid-19 virus. Continuous enteral feeds were attempted but discontinued due to ongoing emesis, leading to Integrity PN being started.

Based on the critical nature of all four patients' conditions and their inability to meet nutrition needs through EN, all patients received custom PN from Integrity Compounding Pharmacy to prevent further catabolism and achieve good metabolic control until full enteral nutrition (EN) tolerance could be achieved.

Results

Three of the four patients received enteral nutrition support during their hospitalizations (A, B, & D), and all patients received intravenous nutrition support during their stays, including custom PN from Integrity Compounding Pharmacy (Integrity PN).

In all cases, supplies of Integrity PN were available for use within 24 hours of consenting the patient, and the LCH standard operating procedure was followed in all cases. For three patients (A, B, & D) Integrity PN was initiated the same day it was delivered to LCH pharmacy. For patient C, Integrity PN was started 48 hours after delivery in the setting of rising leucine levels despite meeting PO supplementation goal.

In patients A & B, Integrity PN was utilized in combination with standard TPN, while enteral trophic feeds were slowly advanced. Patient A received 8 days of Integrity PN, while Patient B received 9 days of Integrity PN, related to longer NPO status for procedure at 5 days of life. Patient C received Integrity PN for 6 days while also tolerating PO formula to help meet leucine free protein goal as well as Valine and Isoleucine supplementation. Patient D received Integrity TPN for 8 days, while also receiving Valine and Isoleucine supplements via gastrostomy tube.

Conclusion/Discussion

Integrity PN provided appropriate amino acid supplementation to optimize nutrition until full enteral and/or oral nutrition could be tolerated. This essential nutrition therapy helped reverse catabolism, achieve metabolic control and prevent further metabolic decompensation. In all four cases, a source of enteral nutrition was available to utilize to some degree. However, during metabolic crisis, there are times when enteral nutrition therapy may not be enough to meet all nutrition needs. Specifically in Patient C, who was able to take his oral formula supplement, and yet blood Leucine levels continued to rise. Only when Integrity PN was utilized, in addition to his oral supplement, was metabolic control obtained.

These cases demonstrate the unique role that specialty PN can play in the care of patients with inborn errors of metabolism. Additionally, having a standard operating procedure in place prior to the need arising greatly increased efficiency, leading to quick accessibility of Integrity PN and less delay in achieving metabolic control.

Establishing standard operating procedures for utilizing non-formulary and/or custom blends of parental nutrition can improve patient care, decreasing burden of obtaining these supplies in the event a need arises. The custom blends of parental nutrition available from Integrity Compounding Pharmacy should be considered in critically ill patients with aminoacidopathies that are not able to meet nutrition goals through enteral route alone.

Children's Hospital of Chicago Medical Center			Children's Hospital of Chicago Medical Center		
Standard Operating Procedure			Standard Operating Procedu	are	
s	dures for obtaining specially compounded Amino from Integrity Compounding Pharmacy : Pharmacy	Effective Date: 7/29/19 Page 1 of 2	Procedures for obtaining specially compounded Amino Acids from Integrity Compounding Pharmacy Scope: Pharmacy	Effective Date: 7/29/19 Page 2 of 2	
	Purpose		IV. Procedures		
	To outline the process for the procurement and ordering of specially compounded amino acid solutions obtained from an external pharmacy for inpatient use in patients with inborn errors of metabolism.		A. Call Integrity pharmacy to notify them of potential need: 1. Business hours (M-F 9 am to 5:30 pm): 404-815-1610 2. Off-Hours a) Call Casey Gaetano: 678-571-2835 b) If Casey Gaetano is unavailable, call the regular pharmacy to activate the on-call		
[.	Definitions		system: 404-815-1610		
	<u>Compounding</u> : the preparation, mixing, assembling, alterir drug, drug-delivery device, or device in accordance with a laprescription, medication order, or initiative based on the prapharmacist/compounder relationship in the course of profes	icensed practitioner's ctitioner/patient/	B. The patient or the patient's representative must sign delivery of medication to the inpatient pharmacy (A Integrity Pharmacy are willing to consent the patien phone but may require facilitation of this discussion 1. Consent form should be sent by the Genetics LI patient's chart. The paper copy can also be deliv	Appendix A) Representatives of nt or patient's representative over the n by the onsite Genetics Team. IP to HIM to be scanned into the	
<u>Compounding pharmacy:</u> a pharmacy that has made an investment in equipment and training to safely compound medications. These are classified as 503a (patient specific compounds) and 503b (bulk compounding) pharmacies.			Director who will deliver the form to HIM. C. A LIP from the Genetics Team must complete the Custom Amino Acid IV Requisition Form (Appendix B) and fax the form to 404-815-1609. D. Integrity will review the Custom Requisition Form for appropriateness and fax back a		
	<u>Inborn Errors of Metabolism:</u> rare genetic disorders in the metabolize nutrients and generate energy. Examples include syrup urine disease (MSUD), and methylmalonic academia	phenylketonuria (PKU), maple	completed IMD Rx Form. 1. IMD Rx Form must be signed by an authorized E. Integrity will coordinate deliveries of supply to the 1. For normal deliveries:	LIP and faxed back to Integrity.	
	<u>Licensed Independent Practitioner (LIP):</u> An individual permitted by law and by the organization to provide care, treatment, and services without direct supervision. A licensed independent practitioner operates within the scope of his or her license, consistent with individually granted clinical privileges.		 a) The product will be delivered to the main dock via FedEx priority overnight (estimated delivery time 10:30 am during the week week and noon on weekends) b) For emergent deliveries on weekends/holidays, the product will be delivered to the main dock via a FedEx same-day courier service 		
[.	Policy Statements		F. The pharmacist should place an order in EPIC unde prepared solution" so the administration can be char	rted in the electronic medical record.	
	A. A prescription is required to obtain specially compound Integrity pharmacy.	ed amino acid solutions from	G. The Pharmacy Clinical Director or designee, will co Integrity.	oordinate duration of therapy with	
	B. Integrity pharmacy can ship same-day for crisis situation stable for 72 hours. After December 1, 2019, the product being compounded.		Date Written: 6/1/2019 Date Reviewed/Revised: 6/18/2019; 7/29/2019 Approved by: Jenny Elhadary, Senior Director, Pharmacy Se	ervices	
	C. A LIP from the Genetics team must order specially com	pounded amino acid solutions.			
	D. The patient or patient's representative must sign a conse solutions to the inpatient pharmacy.	nt form to authorize delivery of			
ite	AIMER: This policy was developed solely for the use of Children's Hospi is ("Medical Center"). The information contained herein shall not be reli Medical Center for accuracy, timeliness, or any other purpose.		DISCLAIMER: This policy was developed solely for the use of Children's Paffiliates ("Medical Center"). The information contained herein shall not be outside Medical Center for accuracy, timeliness, or any other purpose.		

Ann & Robert H. Lurie Children's Hospital of Chicago Chicago, IL 80611 Consent to Deliver Patient-Specific Prescription Drugs to Licensed Medical Practitioner	Medical Record No. Patient Name Birthdate Physician Please align patient label to the right				
INTEGRITY					
APPENDIX A: Consent to Deliver Patient-Specific Prescription Drugs to Licensed Medical Practitioner					
In accordance with GA Rule 480-1602(3), which reads "In order for a licensed medical practitioner to hold, administer, or deliver the partial at his or her office location, and the drug was previously dispert the practitioner's office by a pharmacy, the patient must first provid written authority to conduct such a delivery," I hereby consent to Compounding Pharmacy (the "Pharmacy") to deliver my prescription medical practitioner. This consent will apply to all prescription Pharmacy for me, indefinitely, unless revoked in writing at 8601 Du 750, Sandy Springs, GA 30350.	patient's prescription used and delivered to de the pharmacy with to allowing Integrity drugs to my licensed us dispensed by the				
I understand that I have the right to decline this method of delivery a assumed the risk of such delivery. I hereby release, discharge, inden and covenant not to sue the Pharmacy for, from and against any an damages, liabilities, losses, costs and expenses of any kind (including reasonable attorneys' fees) arising out of or in connection with the shimy prescription drugs. I understand that the Pharmacy has not assum for or made any representations as to the handling of the product one third-party courier.	nnify, hold harmless, ad all claims, actions, ng but not limited to ipment or delivery of ied any responsibility				
Name:					
Responsible Party's Name (if Minor):					
Date of Birth:					
Signature (or Responsible Party's Signature):					
Date:					
If you have questions, please contact Integrity Compounding Pharmacy at 4 Form 6490 Revised 6/19, HIM Approval 6/19	404.815.1610				