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Biosketch

Kathleen M. Gura, is the Clinical Research Program Manager and a clinical pharmacist with the Clinical Nutrition Service in the Division of Gastroenterology, Hepatology, and Nutrition at Boston Children's Hospital. She is also an Associate Professor of Pharmacy Practice at the MCPHS University in Boston. Her professional focus is on academic clinical pharmacy and research, and her topics of expertise include parenteral nutrition associated liver disease, nutritional support for the critically ill pediatric patient, nutritional support in intestinal failure, sterile products preparation, aluminum toxicity, and drug-nutrient interactions. Certified as a Nutritional Support Pharmacist, Dr. Gura is a Fellow of the American Society of Health-System Pharmacists, the Pediatric Pharmacy Advocacy Group, and the American Society for Parenteral and Enteral Nutrition. She is also a member of many pharmaceutical societies, including the ASHP, ASPEN, the American Society for Nutrition, and the European Society for Parenteral and Enteral Nutrition. She has numerous awards including the 2012 Distinguished Pharmacist award from the American Society for Parenteral and Enteral Nutrition (ASPEN) and the 2008 ASPEN Serlick Award for safe practice in the field of parenteral nutrition. She was also awarded the 2009 Drug Therapy Research Award of the American Society of Health Systems Pharmacists.

Dr. Gura is the author of several book chapters on pediatric nutrition and has written more than 100 peer-reviewed articles on topics such as the parenteral nutrition associated cholestasis, clinical practice guidelines for parenteral nutrition, and the use of parenteral nutrition in the neonate. Along with Drs. Tom Jaksic and Christopher Duggan, she is a co-editor of the textbook, Clinical Management of Intestinal Failure. Her research in the area of PN associate liver injury has been funded by the March of Dimes with additional funding coming from the FDA's Orphan Drug Development Program.

Abstract: Liver disease among infants receiving parenteral nutrition - challenges in identifying clinically relevant biomarkers

Parenteral nutrition-associated liver disease (PNALD) is complex and diagnosed by concurrent use of parenteral nutrition, clinical presentation, and alterations in hepatic biomarkers exclusive of other causes of liver disease. Some consider it a form of drug-induced liver injury (DILI). In adults, threshold criteria based on upper limits of normal (ULN) for alanine transaminase (ALT), alkaline phosphatase (ALP) and total bilirubin may not be appropriate for children whose hepatic function is immature. Using a pre-existing database of children treated for PNALD, our aim was to determine if the adult DILI criteria could be applied to this population.

Methods: Adult DILI criteria were applied at baseline, when treatment for PNALD (defined as a direct bilirubin ≥2.0 mg/dL) was initiated.

Results: A total of 214 children with PNALD treated at Boston Children's Hospital were identified; 168 subjects were eligible for analysis. Most subjects analyzed were male (61%) and preterm (87%). ALP≥2×ULN captured the least amount of DILI (11%), while GGT≥1×ULN accounted for the most (62%). Using the adult DILI criteria, 60 (39%) subjects with PNALD were found to have DILI. Substituting GGT≥1×ULN for ALP≥2×ULN improved the sensitivity, with 105 (69%) of subjects meeting at least one criterion for DILI.

Discussion/Conclusion: Numerous challenges made it difficult to apply adult DILI criteria to pediatric patients with PNALD. Direct bilirubin, fractionated ALP and perhaps gamma-glutamyltransferase may be more suitable. Given its complex etiology, perhaps a more appropriate term, multifactorial induced liver injury (MILI) should be used when diagnosing PNALD and potentially other hepatic conditions in this population.