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Utility of liver biopsy in the evaluation of pediatric total parenteral nutrition cholestasis

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ABSTRACT

Background: Cholestasis is a serious complication of total parenteral nutrition (TPN) in neonates. Liver biopsies may be requested to assess the severity of cholestasis and fibrosis. We hypothesized that liver biopsy would not lead to changes in management or improved patient outcomes.
Methods: A single institution retrospective review of infants with TPN cholestasis from January 2008 to January 2016. Outcomes: length of stay, complications, change in management and mortality. Statistical analysis was performed using Fisher's exact test.
Results: Twenty-seven out of 95 patients with TPN cholestasis underwent liver biopsy. Liver biopsy was associated with increased utilization or ursodeoxycholic acid ($p = 0.001$). There were no differences in length of stay (LOS) or mortality. One patient had a complication following anesthesia for liver biopsy, there were no bleeding complications recorded.
Conclusions: Liver biopsy in patients with TPN cholestasis was associated with an increase in utilization of ursodeoxycholic acid. The effects of this are not fully understood; however, liver biopsy was not associated with improved patient outcomes such as LOS or mortality.
Summary: The utilization of liver biopsy in the evaluation of TPN cholestasis in neonates is unknown. The only change in management after liver biopsy was an increase in the use of ursodeoxycholic acid; however, did not lead to changes in patient outcomes.

Introduction

Total parenteral nutrition (TPN) cholestasis, also referred to as parenteral nutrition-associated liver disease, is a common and serious complication of prolonged parenteral nutrition in neonates with an incidence of 40–60%.[1–4] Cholestasis occurs when there is stagnation of bile formed by hepatocytes, causing impairment in the secretion of bile. Since the 1960s, parenteral nutrition has revolutionized the care of patients unable to receive adequate enteral feeding; however, cholestasis and hepatic injury were quickly recognized as significant complications.[3,5–8] Over time, there have been several advancements in the highly sophisticated nutrient solution in order to optimize the combinations of macro and micronutrients while minimizing the harmful effects.[2,3,9,10] Despite the technical improvements and preventative strategies employed, TPN cholestasis remains a significant life threatening complication of long-term parenteral nutrition use.[1,2,5,10,11]

The pathogenesis of TPN cholestasis is likely multifactorial; however, still remains poorly understood.[2,4,8,10–13] Continued parenteral therapy can cause cholestasis, fibrosis and even cirrhosis over the course of several months.[2] Liver biopsies may be requested to assess the severity of cholestasis and fibrosis; however, the utility of this has not been defined. To elucidate the utility of liver biopsy in the evaluation of TPN cholestasis, this study aims to assess the impact on treatment strategies and patient outcomes in neonates with the disease.

Material and methods

Study population: All patients with a diagnosis of TPN cholestasis

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at a single institution tertiary care children's hospital from January 2008 to January 2016 were screened for eligibility. We utilized the institution's electronic medical record reporting workbench to query any pediatric patient with the following diagnosis titles: cholestasis, cholestasis in newborn, cholestasis intrahepatic, cholestasis of parenteral nutrition, intrahepatic cholestasis, neonatal cholestasis, fatal intrahepatic cholestasis, and TPN-induced cholestasis. We identified a total of 355 patients. Each medical record was examined to exclude patients with cholestasis not associated with parenteral nutrition use (viral hepatitis, congenital hepatic fibrosis, biliary atresia, previous liver transplant). Ninety-five patients were found to have TPN cholestasis during this time period. Institutional Review Board approval was obtained prior to the initiation of this retrospective chart review.

Data Collection: Clinical parameters collected by chart review included: date of birth, gender, race/ethnicity, primary insurance provider, zip code, gestational age, birth weight, chronic medical diagnoses, laboratory values (albumin, total bilirubin, gamma-glutamyl transferase [GGT], aspartate aminotransferase [AST], alanine aminotransferase [ALT]), indication for TPN, duration of TPN, duration of enteral feeds and type, infectious history, liver biopsy pathology results, post-procedural complications, use of ursodeoxycholic acid (UDCA), use of lipid minimizing strategies, history of abdominal surgery, length of stay (LOS), and date of death.

Statistical Analysis: Patients were divided into two groups; 1) those with liver biopsy and 2) those without. Primary outcome was a change in management after biopsy. Secondary outcomes included length of stay (LOS), mortality, and complication after biopsy. All data were analyzed using SAS version 9.4 (SAS Institute, Cary, NC). Comparisons between groups were compared using Fisher's exact test for categorical data. Statistical tests were 2-sided, with a p value < 0.05 considered statistically significant.

Results

Included in the analysis were 95 patients with TPN cholestasis, of which 27 (28.4%) had a liver biopsy. Of the patients with TPN cholestasis, 39% were hypoalbuminemic, 60% had short bowel syndrome and 4 patients (4%) had an active infection at the time of diagnosis. The underlying diagnoses for patients with short bowel syndrome included necrotizing enterocolitis (63%), gastroschisis (16%), intestinal atresia (14%), intestinal perforation (3.5%), and malrotation (3.5%).

Patient characteristics

First, we investigated which patients were selected for liver biopsy. Table 1 compares demographics between patients who had liver biopsy and those who did not. There was a significant difference in race (Asian, African American, Hispanic, Caucasian or other) between patients who received liver biopsy and those who did not ($p = 0.047$) (Table 1). Upon further analysis, 52% of African American patients underwent liver biopsy while only 20% of non-African American patients were chosen for the procedure ($p = 0.002$). Additionally, a higher percentage of patients with government insurance underwent liver biopsy than patients with private insurance (43% and 21%, respectively; $p = 0.03$) (Table 1).

Table 2 compares patient characteristics between patients who had liver biopsy versus those who did not. Patients with short bowel syndrome received more liver biopsies than those without ($p = 0.04$). There was a significant difference between the cohorts with regards to peak ALT and AST levels ($p = 0.01$ and 0.02, respectively). Seventy percent of patients who underwent liver biopsy had a peak total bilirubin level greater than ten times the normal range.

There was no difference between cohorts with respect to pre-

Table 1
Demographics.

Variable	No Liver Biopsy n = 68	Liver Biopsy n = 27	p value
Gender			0.82
Male	40 (58.82%)	17 (62.96%)	
Female	28 (41.18%)	10 (37.04%)	
Gestational Age			0.70
> 37 weeks	16 (23.53%)	5 (18.52%)	
33–37 weeks	17 (25.00%)	5 (18.52%)	
28–32 weeks	11 (16.18%)	7 (25.93%)	
< 28 weeks	24 (35.29%)	10 (37.04%)	
Birth Weight			0.87
Normal (>2500 g)	19 (30.16%)	6 (26.09%)	
Low (1500–2500 g)	12 (19.05%)	3 (13.04%)	
Very low (1000–1500 g)	9 (14.29%)	4 (17.39%)	
Extremely low (<1000 g)	23 (36.51%)	10 (43.48%)	
Unknown	5	4	
Great Circle Distance[a]			0.26
0–5 miles	10 (14.71%)	4 (14.81%)	
5–10 miles	16 (23.53%)	11 (40.74%)	
10–20 miles	11 (16.18%)	4 (14.81%)	
20–40 miles	23 (33.82%)	4 (14.81%)	
40–60 miles	5 (7.35%)	1 (3.70%)	
60 + miles	3 (4.41%)	3 (11.11%)	
Race			0.047
Asian	8 (11.76%)	1 (3.70%)	
African American	12 (17.65%)	13 (48.15%)	
Hispanic	17 (25.00%)	4 (14.81%)	
Caucasian	28 (41.18%)	9 (33.33%)	
Other	3 (4.41%)	0	
Insurance Status			0.03
Private	49 (75.38%)	13 (52.00%)	
Government	16 (24.62%)	12 (48.00%)	
None	3	2	

[a] The distance in miles between the patient's residence and the hospital.

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