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ALTERED SERUM BILE ACID POOL ASSOCIATE WITH INTESTINAL RESECTION AND LIVER INJURY IN PEDIATRIC INTESTINAL FAILURE

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Aim of the study. Bile acids serve as important signaling molecules regulating liver function. Modification by intestinal bacterial modulate bile acid's ability to activate their target receptors. In germ free animals lack of secondary bile acids promote liver injury. We studied serum bile acid pool in relation to intestinal resection and histological liver injury in pediatric intestinal failure (IF).

Methods. After an ethical approval, serum bile acids were measured with gas liquid chromatography in 45 IF patients [median age 5.1 (IQR, 2.3-10) years] and 27 age-matched healthy controls [6.3 (4.2-13), P=0.128]. Liver biopsies for histological analyses were available in 27 patients. Fourteen patients remained on parenteral nutrition (PN) after 36 (6.7-87) PN months and 31 patients had weaned off after 10 (4.4-16) PN-months.

Results. Absolute serum concentrations and percentages of primary bile acids, chenodeoxycholic acid and cholic acid, were increased and those of secondary bile acids, lithocholic acid, deoxycholic acid and ursodeoxycholic acid, were decreased in IF patients. (**Table**). During PN, lowered percentage of (bacterially modified) secondary bile acids lithocholic (r=-0.641, P=0.03) and deoxycholic acid (r=-0.720, P=0.008) associated closely with histological liver inflammation. Likewise, liver fibrosis was related decreased lithocholic acid percentage (r=-0.83, P=0.001) and increased concentration of primary bile acids, chenodeoxy (r=0.724, P=0.008) and cholic acid (r=0.679, P=0.0015). Serum cholic acid concentration was increased further in PN-dependent IF patients (**Table**) and in those without any remaining ileum [(72 (40-280) vs 25 (18-49), P=0.002)]. Remaining Ileum length correlated negatively with serum cholic acid concentration (r=-0.392, P=0.008).

Conclusions. The bile acid pool is altered in IF, characterized by profoundly decreased secondary bacterially modified bile acids and increased primary bile acids. These changes associated with intestinal resection and histological inflammation and fibrosis of the liver, suggesting that altered bile acid signaling may contribute to live injury in IF.

Table. Serum bile acids in intestinal failure patients and controls

Variable	All Patients N=45	Patients on PN N=14	Patients weaned off PN N=31	Controls N=27
Total bile acids (µg/100 ml)	232 (116-345)[1]	122 (97-364)[1]	237 (127-345)[1]	103 (79-131)
Primary bile acids				
Chenodeoxycholic acid (%)	51 (45-64)[1]	51 (43-52)[1]	58 (45-68)[1]	24 (18-33)
µg/100 ml	129 (52-212)[1]	56 (45-226)[1]	139 (58-210)[1]	27 (17-43)
Cholic acid (%)	23 (13-32)[1]	28 (22-36)[1,2]	17 (12-28)	14 (11-20)
µg/100 ml	43 (21-83)[1]	38 (26-115)[1]	44 (20-72)[1]	15 (8.6-19)
Secondary bile acids				
Lithocholic acid (%)	3 (2-8)[1]	7 (2-8)[1]	3 (2-7)[1]	18 (12-20)
µg/100 ml	8.5 (6.5-13)[1]	8.0 (6.6-13)[1]	9.2 (6.3-13)[1]	16 (12-21)
Deoxycholic acid (%)	7 (3-12)[1]	10 (5-13)[1]	6 (3-9)[1]	27 (23-35)
µg/100 ml	12 (8.3-17)[1]	13 (9.3-21)[1]	12 (8.0-17)[1]	27 (20-41)
Ursodeoxycholic acid (%)	3 (2-10)[1]	3 (2-6)[1]	4 (1-10)[1]	10 (7-14)
µg/100 ml	6.6 (2.3-22)	3.2 (2.2-23)[1]	20 (11-72)	9.6 (6.3-16)

Data are median (IQR). % percentage of total bile acids. Mann Whitney U-test [1]P<0.05 vs controls, [2]P<0.05 vs patients weaned off PN.