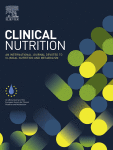
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Original article

Do functional gut parameters predict enteral autonomy and chronic cholestasis in pediatric intestinal failure?

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ABSTRACT

Background & Aims

Parenteral nutrition (PN) dependency in patients with intestinal failure (IF) can lead to complications including liver disease. Therefore, IF management strives to wean patients off PN. In adult IF, chronic cholestasis is predicted by the functional gut parameters citrulline (CIT) and enteroendocrine fibroblast growth factor 19 (FGF19), which inhibits hepatic bile salt synthesis. We investigated 1) whether CIT, FGF19 and a marker for enterocyte damage (urinary intestinal fatty acid-binding protein (I-FABP)) are associated with enteral autonomy within 60 days after intestinal surgery in neonates, and 2) the longitudinal patterns of CIT, FGF19, total bile salts and C4 (marker for bile salt synthesis) in subgroups of children on long-term PN (short bowel syndrome (SBS) and functional IF).

Methods

A prospective two-center cohort study, including 1) neonates with PN-need after intestinal surgery and 2) children (aged <18y) with >6 months PN-dependency. CIT, FGF19, and I-FABP were measured post-surgery in neonates. CIT, FGF19, total bile salts and C4 were assessed on inclusion in children with long-term PN-dependency. Associations were analyzed using Cox regression models. Longitudinal patterns were analyzed using linear mixed-effects models.

Results

Of 50 neonates, 52% reached enteral autonomy. Residual small bowel length <75 cm (hazard ratio 0.23, p=0.046), but not CIT, FGF19 or I-FABP concentrations, was negatively associated with 60-day enteral autonomy. Children with SBS (n = 20) had dysregulated bile salt synthesis with lower FGF19 (24.4 vs 108.8 pg/mL, p=0.004) and higher C4 concentrations (110.3 vs 30.9 pg/mL, p=0.024) than children with functional IF (n = 20). In children with long-term PN, CIT concentration significantly increased with decreasing PN-dependency and total bile salt concentration significantly increased with increasing PN-duration.

Conclusion

Functional gut biomarkers provided no additional value in predicting enteral autonomy in neonates post-intestinal surgery over residual small bowel length. In children on long-term PN, enhanced bile salt synthesis was observed in those with SBS.

Clinical Trial Registration

Overview of Medical research in the Netherlands (OMON) NL-OMON27840 (previously NTR6080), <https://trialsearch.who.int/Trial2.aspx?TrialID=NL-OMON27840>

Keywords

parenteral nutrition

short bowel syndrome

citrulline

bile salt

FGF19

Abbreviations used

ALP

alkaline phosphatase

ALT

alanine aminotransferase

AST

aspartate aminotransferase

CIT

citrulline

C4

7α-hydroxy-4-cholesten-3-one

C-statistic

concordance statistic

EA

enteral autonomy

FGF19

fibroblast growth factor 19

GGT

gamma-glutamyl transferase

IF

intestinal failure

I-FABP

intestinal fatty acid-binding protein

PN

parenteral nutrition

SBS

short bowel syndrome

SDS

standard deviation score

TBIL

total bilirubin