Children With Steatosis and Fibrosis Have a Blunted Postprandial FGF19 Response to a High-Fat Meal

Christina Sciarrillo,[1] Stephen Clarke,[1] Destinee Elliott,[1] Sam Emerson,[1] Bryant Keirns,[1] Sirish Palle,[2] and Kevin Short[2]

[1]Oklahoma State University and [2]University of Oklahoma

Objectives: The standard for early screening of NAFLD in children is circulating liver enzymes, but those measures lack clinical specificity and sensitivity for NAFLD. As an alternative candidate, we tested the hypothesis that the postprandial fibroblast growth factor-19 (FGF19) response to an abbreviated fat tolerance test (AFTT) may discriminate pediatric patients with NAFLD from obese and normal weight peers.

Methods: In this cross-sectional study, 15 normal weight controls (6M/9F; age: 17 ± 2y; BMI: 49 ± 24%ile), 13 controls with obesity without NAFLD (5M/8F; age: 17 ± 2y; BMI: 98 ± 1%ile), and 9 patients with NAFLD (7M/2F; age: 15 ± 2y; BMI: 99 ± 0%ile) completed an AFTT. Following an overnight fast, participants consumed a high-fat meal (73% fat; 9 kcal/kg) and FGF19 was measured at baseline and 4h post-meal. Liver steatosis (controlled attenuation parameter (CAP)) and fibrosis (stiffness) were measured via Fibroscan.

Results: Two-way ANOVA revealed no group × time interaction, time effect, or group effect (p's > 0.05) for FGF19. Similarly, FGF19 tAUC and ΔFGF19 did not differ across groups (p's > 0.05). There was a medium effect size between the OB control and NAFLD groups (d = 0.57) and the normal weight and NAFLD groups (d = 0.47) and a large effect size between the normal weight and NAFLD groups (d = 0.80) for 4h FGF19, suggesting that a larger sample size may reveal statistically lower values in children with NAFLD. Across all groups, fasting FGF19 was not different between children with high (≥ 220 dB/m) vs. low steatosis (≤ 220 dB/m; $p = 0.09$), however 4h FGF19 was 256% higher in children with lower steatosis (1406 ± 1371 pg/mL) compared to higher steatosis (394 ± 352 pg/mL; $p = 0.007$). Likewise, across all groups, fasting FGF19 did not differ between children with no fibrosis (kPa < 6) and children with evidence of fibrosis (kPa > 6; $p = 0.11$); however, children with no fibrosis had 4-fold higher 4h FGF19 compared to children with evidence of fibrosis (kPa > 6; $p = 0.04$).

Conclusions: The postprandial rise in FGF19 was blunted in children with higher liver steatosis and fibrosis. A major role of FGF19 is to promote fatty acid oxidation and inhibit triglyceride synthesis in the liver, thus this finding provides insight on how hepatic fat accrues in pediatric NAFLD.

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