Children with acute hepatitis and human adenovirus infection (N Engl J Med. 2022 Jul 13)

Human adenoviruses typically cause self-limited respiratory, gastrointestinal, and conjunctival infections in healthy children. In late 2021 and early 2022, several previously healthy children were identified with acute hepatitis and human adenovirus viremia. In this series 9 children who had hepatitis without a known cause were identified, of which 8 (89%) tested positive for human adenovirus. These 8 patients plus one additional patient referred to their facility for follow-up were included in this case series (median age, 2 years 11 months). Liver biopsies indicated mild-to-moderate active hepatitis in 6 children, some with and some without cholestasis, but did not show evidence of human adenovirus on immunohistochemical examination. PCR testing of liver tissue for human adenovirus was positive in 3 children (50%). Sequencing of specimens from 5 children showed three distinct human adenovirus type 41 exon variants. Two children underwent liver transplantation; all others recovered with supportive care. The authors concluded that human adenovirus viremia was present in the majority of children with acute hepatitis of unknown cause, but whether human adenovirus was causative remains unclear. Sequencing results suggest that if human adenovirus was causative, this was not an outbreak driven by a single strain.

Effect of three days of oral azithromycin on young children with acute diarrhea in low-resource settings (JAMA Netw Open. 2021;4:e2136726)

World Health Organization (WHO) guidelines do not recommend routine antibiotic use for children with acute watery diarrhea. However, recent studies suggest that a significant proportion of such episodes have a bacterial cause and are associated with mortality. This multicentric, randomized, double-blind, clinical trial was conducted to determine whether the addition of azithromycin to standard case management of acute non-bloody watery diarrhea for children aged 2 to 23 months who are dehydrated or undernourished could reduce mortality. A total of 8266 children (4463 boys [54.0%]; mean [SD] age, 11.6 [5.3] months) were randomized to receive either oral azithromycin, 10 mg/kg, or placebo once daily for 3 days in addition to standard management. A total of 20 of 4133 children in the azithromycin group (0.5%) and 28 of 4135 children in the placebo group (0.7%) died (relative risk, 0.72; 95% CI, 0.40-1.27). The study did not detect a survival benefit for children from the addition of azithromycin to standard WHO case management of acute watery diarrhea in low-resource settings. Therefore, expansion of antibiotic use is not warranted in low-resource settings.

Effect of open-label placebo on children and adolescents with functional abdominal pain or irritable bowel syndrome (JAMA Pediatr. 2022;176:349-56)

Although, it is widely believed that concealment is required to elicit a placebo response, recent studies with adults suggest that open-label placebo (OLP) can yield significant benefits. This multi-center crossover randomized clinical trial evaluated the efficacy of OLP for the treatment of children and adolescents with functional abdominal pain or irritable bowel syndrome. Thirty patients [mean (SD) age, 14.1 (3.4) years; 24 female participants (80%)] completed the study. The mean (SD) pain scores were significantly lower during OLP treatment compared with the control period [39.9 (18.9) vs 45.0 (14.7); difference, 5.2; 95% CI, 0.2-10.1; P =0.03)]. The authors concluded that open-label placebo may be an effective treatment for children and adolescents with functional abdominal pain or irritable bowel syndrome.

Clinically meaningful BMI change impacts pediatric non-alcoholic fatty liver disease (J Pediatr. 2022. S0022-3476(22)00623-0)

In this retrospective single center study, the authors investigated the prevalence and characteristics of children with non-alcoholic fatty liver disease (NAFLD) who reduce their body mass index (BMI) *z*-score (BMIz) by >-0.25, a goal reached for in obesity medicine, and to determine the BMIz decrease needed for serum aminotransferase normalization. Of the 784 children that met study criteria (median age 13 years, 66% male, 24% Hispanic), 168 (31%) changed their BMIz>-0.25 from baseline over a median 367 days (IQR: 201-678). Decreases in serum aminotransferase and lipid levels were seen in both groups (with/without BMIz change>-0.25); however, these were more pronounced in children who achieved BMIz drop>-0.25. The BMIz decrease associated with an ALT normalization was 0.27. The authors concluded that a BMIz reduction of >-0.25 is associated with significant changes in serum aminotransferase levels. These findings can further guide the clinical management of children with NAFLD.

Odevixibat treatment in progressive familial intrahepatic cholestasis (Lancet Gastroenterol Hepatol. 2022:S2468-1253(22)00093-0.)

Progressive familial intrahepatic cholestasis (PFIC) is a group of inherited pediatric liver diseases resulting from mutations in genes that impact bile secretion. In this study, the authors evaluated the effects of Odevixibat, an ileal bile acid transporter inhibitor, versus placebo in children with PFIC. Patients eligible for this 24-week, randomized, double-blind, phase 3 study were pediatric outpatients diagnosed with PFIC1 or PFIC2 who had pruritus and elevated serum bile acids at screening. Sixty-two patients (median age 3·2 [range 0·5-15·9] years) were randomly allocated to placebo (n=20), odevixibat 40 µg/kg per day (n=23), or odevixibat 120 µg/kg per day (n=19). It was found that odevixibat effectively reduced pruritus and serum bile acids versus placebo and was generally well tolerated. Odevixibat, administered as once a day oral capsules, is a non-surgical, pharmacological option to interrupt the enterohepatic circulation in patients with PFIC.

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