619. Intestinal Microbiome Changes Associated with Immune Status and Clostridium difficile Colonization in Hospitalized Children
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Background. The intestinal microbiome modulates local and systemic immune responses and may impact clinical outcomes. However, there are few studies in pediatric patients. We conducted a cross-sectional study of fecal microbiomes in hospitalized children on a single inpatient unit at Children’s Hospital at Montefiore, Bronx, New York in 2016–2017 to test the hypothesis that “high-risk” children with chronic illnesses (cancer, transplant and sickle cell disease [SCD]) have decreased microbial diversity and higher rates of asymptomatic colonization with C. difficile compared with children hospitalized on the same ward but without similar risk factors.

Methods. Stool was collected within 72 hours of admission from patients who provided consent and assayed for C. difficile colonization by glutaamate dehydrogenase (GDE); microbiome analysis was performed by 16S rRNA sequencing. Clinical and demographic data were obtained from the EHR.

Results. One hundred and six unique patients provided a sample for analysis. Sixty-nine were categorized as high-risk, including 32 SCD patients. C. difficile colonization rates were 22% and 19% in the high-risk and low-risk groups, respectively, but highest in the subset of SCD patients on penicillin prophylaxis (33%). The high-risk group had a trend toward lower microbial diversity than controls, and SCD patients exhibited a diversity index greater than other high-risk patients. Antibiotic use in the last 3 months and PPI use were associated with decreased microbial diversity across the entire study population (P = 0.004, P = 0.007, respectively). Among children with SCD, those on penicillin prophylaxis had a trend toward decreased alpha diversity while folic acid was associated with increased diversity (P = 0.02). SCD patients had greater quantities of Bacteroides and Parabacteroides and fewer Escherichia and Shigella than the other cohorts.

Conclusion. SCD and penicillin prophylaxis might be risk factors for C. difficile colonization and intestinal dysbiosis. The implications of these findings require further longitudinal study.

Disclosures. All authors: No reported disclosures.

620. Oral β-Lactamase Therapies Prevent Microbiome Damage and Attenuate Antibiotic Resistance From IV and Oral Antibiotics in Large Animal Models of Antibiotic-Mediated Gut Dysbiosis
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Background. Antibiotics can damage the gut microbiome leading to overgrowth of pathogens and provide selective pressure for emergence of antibiotic resistance. SYN-004 (ribaxamase) is a clinical-stage β-lactamase formulated for oral delivery intended to degrade certain β-lactam antibiotics in the GI tract to preserve the gut microbiome. Ribaxamase was evaluated in a phase 2b clinical study that met its primary endpoint of significantly reducing C. difficile infection in patients treated with IV ceftriaxone and demonstrated protection of the gut microbiome with reduced emergence of antibiotic resistance. Ribaxamase is intended for use with IV penicillins and cephalosporins, but does not degrade carbapenems. β-lactamase-mediated microbiome protection was expanded to include oral and carbapenem antibiotics.

Methods. For use with oral β-lactams, a ribaxamase formulation, SYN-007, was engineered for release in the lower small intestine, distal to the site of antibiotic absorption. For use with IV carbapenems, SYN-006, a novel metallo-β-lactamase, was formulated for oral delivery. SYN-007 (10 mg, PO, TID) was evaluated in dogs treated with oral amoxicillin (100 mg/kg, PO, TID) for 5 days. SYN-006 (50 mg, PO, QID) was evaluated in pigs treated with ertapenem (30 mg/kg, IV, SID) for 4 days. Serum antibiotic levels were measured and fecal DNA whole-genome shotgun sequence analyses were performed.

Results. In dogs and pigs, systemic antibiotic levels were not significantly different (SYN-006 vs. SYN-007). In pigs, 16S rRNA metagenomics analyses demonstrated that oral amoxicillin and IV ertapenem resulted in significant changes to the gut microbiome. SYN-007 and SYN-006 attenuated microbiome damage and reduced emergence of antibiotic resistance.

Conclusion. Ribaxamase, SYN-007, and SYN-006 have the potential to protect the normal gut microbiota from antibiotic-mediated collateral damage and to mitigate emergence and spread of antibiotic resistance, thereby broadening the utility of this prophylactic approach to include all classes of β-lactam antibiotics, delivered both systemically and orally. Antibiotic inactivation represents a new paradigm for preservation of the gut microbiome and reduction of antibiotic resistance.

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