PROJECT: Proton Pump Inhibitors and *Clostridium difficile* Infection in Children

ABSTRACT

The purpose of this grant application is to determine whether use of proton pump inhibitors (PPIs) predisposes children to *Clostridium difficile* infection (CDI), a highly morbid form of infectious colitis. Proton pump inhibitors are potent suppressors of gastric acid, and use of PPIs has increased 20-fold in children during the past two decades. *C. difficile* infection, has also increased substantially in incidence among ambulatory, relatively healthy children. In adults, PPIs double the risk of CDI, but the impact of PPIs on the risk of CDI in children is unknown. We hypothesize that exposure to PPIs is associated with an increased risk of *C. difficile* infection in infants and children. We have performed preliminary analyses using data on over two million infants and children within The Health Improvement Network (THIN), an ambulatory, cross-sectional database comprised of records from general medical practices in the United Kingdom. We found a dramatically increased risk of CDI among PPI users, and this relationship between PPIs and CDI depended on child age. Using the complete THIN dataset, we propose a nested case-control study to determine: 1) the relationship between pediatric PPI use and CDI, and whether this relationship depends on PPI dose or duration, 2) the influence of age on the relationship between pediatric PPI use and CDI, and 3) demographic and clinical factors associated with pediatric *Clostridium difficile* infection, among PPI users and non-users. Although both pediatric CDI and PPI prescribing in children are steadily increasing, there are no previous population-based studies focusing on PPIs as a risk factor for pediatric CDI. The results of this study will have an immediate impact by improving clinical decision-making with regard to the pharmacological management of childhood GERD and will lead to future studies investigating targeted interventions related to the use of PPIs in children. Furthermore, this work will serve as the foundation for NIH grant applications to investigate the relationship between PPIs, the colonic microbiome, and *C. difficile* infection in children, potentially leading to the development of novel approaches for the prevention and treatment of PPI-associated pediatric CDI.