

Enteric pathogens detected in intussusception cases and surgical controls

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Background

Since the withdrawal of first generation rotavirus (RV) vaccines in 1999, intussusception (ISS) has been temporally linked to RV vaccines and associated with an elevated risk in the first seven days after RV vaccine administration in some settings. While the exact cause of intussusception is unknown, infectious pathogens including adenovirus (AdV), RV and human herpesvirus 6 have been implicated. The aim of the study was to identify enteric pathogens in intussusception cases and matched controls.

Methods

Post-marketing ISS surveillance was established in eight hospitals across South Africa between 2013 and 2018. In children <3 years, intussusception cases were defined using the Level 1 Brighton criteria and matched on age, site and admission date to hospitalized non-intussusception surgical controls (SC). Stools specimens were collected after obtaining consent. Nucleic acid was extracted using the QIAamp® Fast DNA Stool Mini kit (Qiagen) on a Qiacube extractor with upstream mechanical disruption. The nucleic acid was screened on a custom Taqman array card (designed by University of Virginia) using the Ag-Path-ID One Step RT-PCR Kit (ThermoFischer Scientific) and appropriate controls.

Results

A total of 340 specimens were included (170 cases and 170 surgical controls). At least one dose of RV vaccine was administered in 93.8% (319/340) of children. The odds of any RV (odds ratio (OR)=0.7; 95% CI 0.27-1.84; p=0.47; 4.1% ISS vs 5.9% SC) or RV vaccine (OR=0.17; 95% CI 0.02-1.38; p=0.097; 0.6% ISS vs 3.5% SC) detection was not significantly higher in ISS cases compared to controls. Conversely, AdV and AdV type C detection was higher in ISS cases compared to surgical controls (52.4% ISS vs 25.3% SC; OR=3.42; 95% CI 2.05-5.7; p<0.001 and 37.1% ISS vs 19.4% SC; OR=2.58; 95% CI 1.52-4.38; p<0.001, respectively). Selected pathogens (enterovirus, *Clostridium difficile*, enteropathogenic *Escherichia coli* (EPEC), norovirus GII and *Helicobacter pylori*) were detected more often in surgical controls compared to ISS cases (prevalence range in cases 0-14.1%, prevalence range in SC 3.5-31.2%; p<0.05).

Discussion

In this study, RV infections and RV vaccine detection were not associated with intussusception. In contrast, AdV type C infections were detected more frequently in ISS cases compared to surgical controls suggesting a potential role in the pathogenesis of intussusception.