Background: Norovirus can cause chronic infections with serious morbidity and mortality in immunocompromised patients. While there are no FDA-approved medications for these infections, nitazoxanide, ribavirin, and enterally administered pooled immunoglobulin (IVIG) are used off-label on the basis of expert opinion. Nitazoxanide and ribavirin show antiviral activity in a murine norovirus infection model and an in vitro fusion model of genotype GI human norovirus RNA expression, respectively. However, these drugs have not been evaluated in in vitro infections with GI4 human noroviruses, responsible for most human norovirus disease. We used the stem cell-derived nontransformed human intestinal enteroid (HIE) system, which supports GI4 human norovirus replication, to evaluate the antiviral activities of nitazoxanide, ribavirin, and IVIG.

Methods: We inoculated HIEs with GI4 human norovirus in the presence of half-log dilutions of nitazoxanide (3 μM to 100 μM), ribavirin (10 μM to 10 mM), or IVIG (1:100 to 1:13,000) and a media control. One and 48 hours after inoculation, we extracted and quantified GI4 norovirus RNA from the HIEs. To demonstrate that replication inhibition was not due to cytotoxicity, we performed quantitative lactate dehydrogenase release assays on the HIEs across the therapeutic range of each compound.

Results: Nitazoxanide reduced GI4 replication at 48 hours in a dose-dependent manner, achieving a >90% reduction in viral replication at 10 μM without cytotoxicity. These findings were confirmed in multiple HIE lines representing different intestinal stem cell-derived enteroids established from different donors. IVIG completely inhibited GI4 replication at up to 1:1,000 dilution and was not cytotoxic at therapeutic concentrations. Ribavirin did not reduce GI4 replication at concentrations up to 10 mM, well in excess of levels achieved in human sera with standard doses.

Conclusion: Nitazoxanide and IVIG, but not ribavirin, potently inhibit GI4 human norovirus replication in a biologically relevant in vitro model of human norovirus infection. These data highlight the use of HIEs as a new pre-clinical model for developing therapeutics for human norovirus disease.

Disclosures. All authors: No reported disclosures.

272. Studies of Treatment and Prevention of Viral Disease
Saturday, October 5, 2019: 12:15 PM

Background: Healthcare-associated viral infections (HA-VI) are common in hospitalized children and are increasingly recognized as a cause of preventable harm. Yet, epidemiology and modifiable risk factors related to pediatric HA-VI are currently poorly understood.

Methods: We performed a prospective case–control study to identify the risk factors for HA-VI among children admitted to a quaternary care children’s hospital between November 2016 and August 2018. Prospective surveillance for HA-VI was performed hospital-wide by certified infection preventionists using NHSN definitions. Cases were matched 1:1 to controls by age, duration of hospitalization, and hospital unit. We abstracted data from the electronic medical record and conducted semistructured interviews with caregivers to identify potential exposures beginning 4 days prior to HA-VI identification date. We also measured length of antibacterial therapy (LOT) in the 7 days following enrollment.

Results: During the study period, we identified 143 eligible patients with HA-VI and enrolled 64 matched case–control pairs. In total, 79 viruses were identified among 64 case patients, of which 53 (67.1%) were respiratory viruses and 26 (32.9%) were gastrointestinal (GI). Case patients were more frequently exposed to a sick visitor, specifically either a caregiver or sibling, compared with controls (18.8% vs. 9.4%; P = 0.20, Fisher exact test). Inpatient exposure periods also had a significantly higher number of hospital procedures performed when compared with controls (n = 320 vs. 232; X² = 58.43, P < 0.001). Case, when compared with control, patients had a greater average LOT (2.89 vs. 1.08).

Conclusion: Results of study show that exposure to a sick visitor is a potentially modifiable risk factor for pediatric HA-VI. In addition, hospitalized children with HA-VI have increased exposure to antibacterial antibiotics when compared with matched controls. Prevention of pediatric HA-VI may have implications for antibiotic stewardship. Our findings suggest that hospital policies may need to be revised, with emphasis on visitor screening and partnership with families, to reduce the incidence of pediatric HA-VI during hospitalization.

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272. Epidemiology and Risk Factors for Healthcare-Associated Viral Infections in Children
Saturday, October 5, 2019: 12:15 PM

Background: Human cytomegalovirus (CMV) is the most common congenital infection worldwide. A CMV glycoprotein B (gB) subunit vaccine with MF59 adjuvant showed candidate immunogenicity. CMV infection is an important global health concern due to the risk of congenital infection and the potential for severe disease in immunocompromised patients. CMV gB vaccines have been shown to be protective in animal models and are under investigation in clinical trials for the prevention of CMV disease.

Methods: We conducted a retrospective cohort study to evaluate the efficacy of a CMV gB/MF59 vaccine in reducing CMV infection among immunocompromised patients. The study included a CMV gB/MF59 vaccine cohort, and a control cohort of patients who received the herpes zoster vaccine. We matched CMV gB/MF59 vaccinated patients who became infected and those who remained uninfected on a 1:1 ratio based on age, sex, and number of vaccine doses. The efficacy of the vaccine was assessed using a linear regression controlling for cohort.

Results: A total of 361 patients with viral infections were identified: CMV (n = 33), enterovirus (n = 147), herpes simplex virus (n = 83), varicella zoster virus (n = 28), and arboviruses (n = 70). CMV occurred more frequently in immunosuppressed patients [e.g., Acquired Immune Deficiency Syndrome (AIDS)], had more hypoglycemia (59%), and had worse clinical outcomes (61%) as compared with those with HSV, enterovirus, VZV and arboviruses. Additionally, CMV gB/MF59 vaccinees had higher CSF protein levels than enteroviral infections and had less CSF pleocytosis than HSV and VZV.

Conclusion: CMV gB/MF59 vaccinees are seen more frequently in immunosuppressed patients (e.g., AIDS), with more clinical outcomes when compared with other viral CNS pathogens. CMV gB/MF59 vaccinees had worse clinical outcomes compared with other viral CNS pathogens.

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252. Cytomegalovirus Meningoencephalitis: A Comparison to Other Viral CNS Infections
Saturday, October 5, 2019: 12:15 PM

Background: Cytomegalovirus (CMV) is a rare cause of meningoencephalitis (ME) with limited data to guide case reporting.

Methods: Retrospective observational study of all viral central nervous system (CNS) infections identified in 17 hospitals in the Greater Houston area from 2000 to 2017. CMV, herpes simplex virus (HSV), varicella zoster virus (VZV), and enterovirus were all identified by a positive cerebrospinal fluid (CSF) polymerase chain reaction (PCR) and all arboviruses were identified by serology.

Results: A total of 361 patients with viral CNS infections were identified: CMV (n = 33), enterovirus (n = 147), herpes simplex virus (n = 83), varicella zoster virus (n = 28), and arboviruses (n = 70). CMV occurred more frequently in immunosuppressed patients [e.g., Acquired Immune Deficiency Syndrome (AIDS)], had more hypoglycemia (59%), and had worse clinical outcomes (61%) as compared with those with HSV, enterovirus, VZV and arboviruses. Additionally, CMV gB/MF59 vaccinees had higher CSF protein levels than enteroviral infections and had less CSF pleocytosis than HSV and VZV.

Conclusion: CMV gB/MF59 vaccinees are seen more frequently in immunosuppressed patients (e.g., AIDS), with more clinical outcomes when compared with other viral CNS pathogens. CMV gB/MF59 vaccinees had worse clinical outcomes compared with other viral CNS pathogens.

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