2296. Hypoglycemia Risk with Antibiotics: An Epidemiologic Surveillance Study of the FDA Adverse Event Reporting System (FAERS)
Kaitlin E. Kennedy1; Chengwen Tang, PharmD, MS2; Taylor M. Patel1;
Christopher R. Frei, PharmD, FCGR, BCPSP3; The University of Texas at Austin, San Antonio, Texas; South Texas Veterans Health Care System, UT Health San Antonio, UT Austin College of Pharmacy, San Antonio, Texas
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Background. In July of 2018, the FDA published a drug safety warning for the potential risk of developing hypoglycemia with fluoroquinolones. Some studies have evaluated the potential risk of developing hypoglycemia with linezolid and ticagrelor. A few case reports have also been published that report hypoglycemia from cefditoren, doxycycline, and trimethoprim-sulfamethoxazole use. Since data comparing various antibiotics and the risk of developing hypoglycemia is limited, the objective of this study was to evaluate the association between hypoglycemia and antibiotics using the FDA Adverse Event Reporting Systems (FAERS).

Methods. FAERS reports from January 1, 2004 to December 31, 2017 were included in the study. The Medical Dictionary for Regulatory Activities (MedDRA) was used to identify cases of hypoglycemia. Reporting odds ratios (ROBs) and corresponding 95% confidence intervals (95% CI) for the association between antibiotics and hypoglycemia were calculated. An association was considered to be statistically significant when the lower limit of the 95% CI was greater than 1.0.

Results. A total of 2,334,959 reports (including 18,466 hypoglycemia reports) were considered, after inclusion criteria were applied. Cefditoren had the greatest proportion of hypoglycemia reports, representing 10% of all cefditoren reports. Statistically significant hypoglycemia ROBs (95% CI) for antibiotics were: cefditoren 6.10 (95% CI 5.99–6.23), tigecycline 3.12 (95% CI 2.99–3.27), ertapenem 2.10 (95% CI 2.04–2.16), levofloxacin 2.06 (95% CI 2.01–2.12), and linezolid 1.54 (95% CI 1.50–1.59).

Conclusion. Cefditoren, tigecycline, clarithromycin, ertapenem, moxifloxacin, levofloxacin, and linezolid were all significantly associated with hypoglycemia. The ertapenem association had not been reported in prior literature. Levofloxacin and moxifloxacin were the only fluoroquinolones significantly associated with hypoglycemia, even though the FDA drug safety warning was issued for all fluoroquinolones. Doxycycline and trimethoprim-sulfamethoxazole were not significantly associated with hypoglycemia, even though case reports have reported hypoglycemia with doxycycline and trimethoprim-sulfamethoxazole.

Disclosures. All authors: No reported disclosures.

2297. Epidemiology of Antibiotic-Resistant Pathogens and Empiric Treatment Patterns in Community-Onset Sepsis
Chana Rhee, MD, MPH1; Sameer S. Kadri, MD, MS2; John P. Dekker, MD, PhD3; Robert L. Danner, MD4; Hui-Chun Chen, PhD5; David Fram, BA, Michael Klopman, MD, MPH6; Harvard Medical School / Harvard Pilgrim Health Care Institute, Boston, Massachusetts; NIH Clinical Center, Bethesda, Maryland; National Institute of Allergy and Infectious Diseases, Bethesda, Maryland; National Institutes of Health, Bethesda, Maryland; Commonwealth Informatics, Walham, Massachusetts; Harvard Medical School and Harvard Pilgrim Health Care Institute, Boston, Massachusetts
Session: 246. Clinical Outcomes of Infections with Resistant Organisms
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Background. Guidelines recommend immediate empiric broad-spectrum antibiotics for all patients with suspected sepsis. Understanding the epidemiology of antibiotic-resistant pathogens and empiric treatment patterns in sepsis could inform improvements in antibiotic utilization and outcomes.

Methods. We identified adults admitted during 2009–2015 to 104 US hospitals in the Cerner HealthFacts dataset who met CDC Adult Sepsis Event criteria and had positive clinical cultures within 2 days of admission. We characterized prevalence and empiric treatment rates for methicillin-resistant S. aureus (MRSA), vancomycin-resistant enterococcus (VRE), ceftriaxone-resistant Gram-negative organisms (CRO) (including P. aeruginosa), and extended-spectrum β-lactamase Gram-negative organisms (ESBL). We evaluated associations between in-hospital mortality and either inappropriate empiric therapy (antibiotics inactive against any isolated pathogen) or excessively broad empiric therapy (empiric MRSA or VRE coverage, extended spectrum β-lactam, or carbapenem therapy when targeted organisms were absent), adjusting for baseline confounders.

Results. Among 1,854,525 adults admitted during 2009–2015 to 104 US hospitals in the Cerner HealthFacts dataset who met CDC Adult Sepsis Event criteria and had positive clinical cultures within 2 days of admission, we characterized prevalence and empiric treatment rates for methicillin-resistant S. aureus (MRSA), vancomycin-resistant enterococcus (VRE), ceftriaxone-resistant Gram-negative organisms (CRO) (including P. aeruginosa), and extended-spectrum β-lactamase Gram-negative organisms (ESBL). We evaluated associations between in-hospital mortality and either inappropriate empiric therapy (antibiotics inactive against any isolated pathogen) or excessively broad empiric therapy (empiric MRSA or VRE coverage, extended spectrum β-lactam, or carbapenem therapy when targeted organisms were absent), adjusting for baseline confounders.

Conclusion. Most patients with community-onset sepsis do not have resistant pathogens, yet empiric broad-spectrum antibiotics are frequently prescribed. Both inappropriate empiric therapy and excessively broad therapy are associated with worse outcomes.

Disclosures. All authors: No reported disclosures.

2298. Infections in Patients Receiving TVEC Therapy
Elizabeth Robilotti, MD MPH; Mini Kamboj, MD; Memorial Sloan Kettering Cancer Center, New York, New York
Session: 247. Clinical Virology/Viral Epidemiology
Saturday, October 5, 2019: 12:15 PM

Background. Oncolytic viral immunotherapy is an emerging cancer treatment, but the infectious complications are not well described outside of clinical trials. Genetically engineered replication competent herpes simplex virus (HSV-1), commercially known as IMLYGIC® (AmGen) or talimogene laherparepvec (TVEC) was the first FDA approved agent in this class and is used for the local intralesional treatment of unresectable melanoma. TVEC is derived from a wild-type(WT) strain of HSV-1 (JS—1), which is modified to attenuate off-target effects and promote selective proliferation within cancer cells. Despite these changes local and systemic infection with HSV are known to occur from trials and is the subject of an FDA mandated post-market review. Here we review the infectious complications of the first cohort of patients treated at our institution post-FDA approval.

Methods. Demographic and clinical information for 52 adults treated for unresectable melanoma with TVEC following FDA approval in 2015 was extracted from the EMR for the period October 1, 2015–June 30, 2018. EMR and microbiologic data were reviewed for evidence of local site reaction and disseminated infection.

Results. No cases of disseminated HSV infection were identified during the study period. Of cutaneous reactions, none were documented as greater than severity grade 2, based on standard adverse event reporting criteria. 3 (50%) grade 1–2 cutaneous reactions were deemed probable or definitely related to TVEC and described as pruritus or rash. 12 (23%) patients had any microbiologically confirmed infection identified following TVEC therapy; 6 were bacterial (3 UTI, 1BLI, 2 wound). 8 episodes of viral infections occurred (5 respiratory and 3 GI). A single patient was noted to have localized HSV dermal lesions more than one year after the final TVEC.
2300. Incidence, Complications, and Recurrence of Herpes Zoster in Unvaccinated Adults ≥50 Years of Age
Bradley Ackerson, MD; Katia Bruzovsk, PhD, MPH; Lisa S. Sy, MPH; Yi Lu, MD; Hsin-Hsiung Lin, MD, MS; Tien-Tun Yu, MD; Chengyi Zheng, PhD, MS; Biana P. Cheung, MS; Brandon J. Patterson, PharmD, PhD; Desiree Van Oorschot, MSc; Hung Fu Tseng, PhD, MPH; Kiser Permanente, South Bay Medical Center, Harbor City, California; Kaiser Permanente Southern California, Pasadena, California; GSK Vaccines, Waver, Vlaams-Brabant, Belgium

Session: 247. Clinical Virology/Viral Epidemiology
Saturday, October 5, 2019: 12:15 PM

Background. More recent baseline epidemiological data for Herpes Zoster (HZ) in adults ≥50 years of age, obtained before the introduction of the adjuvanted Recombinant Zoster Vaccine (RZV), are needed for future evaluations of the impact of RZV on HZ epidemiology.

Methods. The study comprised five elements: (1) The incidence of HZ was estimated from immunocompetent adults ≥50 years of age not vaccinated with Zoster Vaccine Live who had incident HZ between 2011–2015. HZ was identified by International Classification of Diseases (ICD) codes from electronic health records (EHR) of 4.6 million Kaiser Permanente Southern California members; (2) Postherpetic neuralgia (PHN) was identified by validated survey and medical record review of laboratory-confirmed incident HZ cases recruited during 2012–2015 for HZ-related pain ≥90 days after initial HZ diagnosis; (3) HZ Ophthalmicus (HZO) with complications was identified by ICD codes and keyword search in EHR among patients identified with HZO using a validated natural language processing algorithm; (4) The proportion of HZ-related non-PHN and non-HZO cutaneous, neurological or other complications was assessed by double abstraction of EHRs from a sample of 600 incident HZ cases; (5) Recurrent HZ was identified by having an HZ diagnosis with HZ antiviral medication in a cohort initially diagnosed with HZ between 2007 and 2008 and followed through 2016.

Results. We identified 40,893 incident HZ cases with an overall incidence of 9.92 (95% CI: 9.54–9.89%), which increased by age to 14.42% (95% CI: 13.82–15.02%) and 21.84% (95% CI: 20.46–23.23%) for those ≥60 years of age. The proportion of incident HZ cases with PHN and HZO with ocular involvement was 18.37% (95% CI: 14.90–21.84%) and 8.06% (95% CI: 7.70–8.32%), respectively. The incidence of recurrent HZ was 10.96/10,000 person-years (95% CI: 10.18–11.79%).

Conclusion. HZ is common among unvaccinated US adults ≥50 years of age, with PHN and HZO occurring most frequently among incident HZ cases.

Disclosures. All authors: No reported disclosures.

2301. Increased Risk of Varicella-Associated Hospitalizations Among Adult Immigrants From Temperate and Tropical Countries After the Introduction of the Childhood Varicella Vaccination Program in Quebec, Canada
Jordan Mah, MD; Anthony Liu, MD; Zoe R. Greenwald, MS; Azaz Akaberi, MSc; Sunny Song, MSc; Laurent Azoulay, PhD; Marc Brisson, PhD; Caroline Quach, MD; Christin Greenaway, MD, MSc; 1Faculty of Medicine, McGill University, Montreal, QC, Canada; 2McGill University, Montreal, QC, Canada; 3Centre for Clinical Epidemiology, Lady Davis Institute for Medical Research, Montreal, QC, Canada; 4Research Group in Mathematical Modeling and Health Economics of Infectious Disease, Université Laval, Québec, QC, Canada; 5Department of Microbiology and Immunology, CHU Sainte-Jusante, Montreal, QC, Canada; 6Jewish General Hospital, McGill University, Montreal, QC, Canada

Session: 247. Clinical Virology/Viral Epidemiology
Saturday, October 5, 2019: 12:15 PM

Background. Varicella zoster virus (VZV) hospitalizations are an uncommon, severe and costly consequence of VZV. Childhood VZV vaccination leads to decreased VZV rates across all age groups through herd immunity but increases the age of VZV acquisition and the potential risk of severe VZV in non-immune adults. A large proportion (~15%) of young adult immigrants from tropical regions are susceptible to VZV due to different transmission dynamics in their countries of origin and lack of vaccination. We aimed to describe the impact of the childhood VZV program introduced in 2006 in Quebec on VZV hospitalizations in immigrants and nonimmigrants.

Methods. A population-based cohort of all medically-attended VZV cases in Quebec identified in administrative health databases and linked to immunization data. VZV-attributable hospitalizations included those with primary or secondary ICD-9 or ICD-10 codes for VZV. Overall age-standardized and age-specific rates of hospitalizations were calculated during pre- (1996–98), private (1999–2005) and public vaccination (2006–14) periods and by immigrant status and pregnancy. Relative risk (RR) and 95% CI for immigrants vs. nonimmigrants were estimated.

Results. 5873 hospitalizations occurred among 230,052 VZV cases. Hospitalization rates decreased dramatically in the public vaccination period (6.6 to 1.3/100,000 population); however, the proportion of hospitalized varicella cases increased from 1.7% to 3.9% (P < 0.01). Immigrants only accounted for 3.6% of hospitalizations (N = 213) however, the proportion of all hospitalizations among immigrants increased in the pre- vs. public-vaccination periods in those aged 10–18 years (2.9% to 13.7%) and 20–39 years (8.8% to 22.7%). The RR was higher in these age groups in the public vaccination period [RR = 1.36 and RR = 1.67] (Table 1). Adults (≥20 years) accounted for 52% (CI: 45–59%) and pregnant women 18% (13–25%) of all hospitalizations among immigrants compared with only 14% (13–15%) and 1.6% (1.3–2.0%) in nonimmigrants, respectively.

Conclusion. Young adult and pregnant immigrants bore a disproportionate burden of VZV hospitalizations after the introduction of childhood VZV vaccination. Susceptible immigrant adults would benefit from targeted VZV vaccination.

Disclosure. All authors: No reported disclosures.

Table 1: Overall age-standardized and age-specific rates of varicella-attributable hospitalizations and proportion of cases by immigrant status in Quebec, Canada (1996–2014).

| Age Group | Vaccination Period | Immigrants Cases | Non-Immigrants Cases | Immigrants vs. Non-Immigrants Rate difference (95% CI) |
|-----------|--------------------|------------------|---------------------|-----------------------------------------------|
| 0–4 years | 1996–1998          | 17               | 71                   | -0.55 (95% CI: -1.10 to 0.01)                   |
| 5–14 years| 1996–1998          | 15               | 58                   | -0.55 (95% CI: -1.10 to 0.01)                   |
| 15–19 years| 1996–1998       | 3                | 39                   | -0.55 (95% CI: -1.10 to 0.01)                   |
| 20–24 years| 2009–2014       | 8                | 77                   | 0.87 (95% CI: 0.43–1.31)                        |
| 25–34 years| 2009–2014       | 9                | 72                   | 0.87 (95% CI: 0.43–1.31)                        |
| 35–44 years| 2009–2014       | 9                | 69                   | 0.87 (95% CI: 0.43–1.31)                        |
| 45–54 years| 2009–2014       | 5                | 68                   | 0.87 (95% CI: 0.43–1.31)                        |
| 55–64 years| 2009–2014       | 3                | 63                   | 0.87 (95% CI: 0.43–1.31)                        |
| 65–74 years| 2009–2014       | 5                | 65                   | 0.87 (95% CI: 0.43–1.31)                        |
| 75–84 years| 2009–2014       | 3                | 66                   | 0.87 (95% CI: 0.43–1.31)                        |
| 85+ years  | 2009–2014       | 2                | 67                   | 0.87 (95% CI: 0.43–1.31)                        |

Disclosures. All authors: No reported disclosures.