2296. Hypoglycemia Risk with Antibiotics: An Epidemiologic Surveillance Study of the FDA Adverse Event Reporting System (FAERS)

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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 tigecycline. 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 (RORs) 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 ROs (95% CI) for antibiotics were: cefditoren 2.14 (1.93–2.38), tigecycline 2.14 (1.93–2.38), linezolid 1.14 (1.07–1.20), ertapenem 2.07 (1.14–3.75), moxifloxacin 2.06 (1.59–2.65), levofloxacin 1.66 (1.37–2.01), linezolid 1.54 (1.07–2.20).

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.

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2297. Epidemiology of Antibiotic-resistant Pathogens and Empiric Treatment Patterns in Community-Onset Sepsis

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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 excess empiric therapy (empiric MRSA or VRE coverage, extended spectrum β-lactam, or carbapenem therapy when targeted organisms were absent), adjusting for baseline characteristics and severity-of-illness.

Results. The cohort included 17,962 patients with culture-positive sepsis; 2,965 (16.5%) died in hospital. The most common culture-positive sites were urine (51.2%), blood (41.8%), and respiratory (16.6%). The most common pathogens were E. coli (33.0%), S. aureus (20.9%), and Strepococcus (13.2%) (Figure 1). Most (81.6%) patients received empiric antibiotics active against all isolated pathogens. Empiric therapy was directed at resistant organisms in 67.5% of cases (primarily vancomycin and extended spectrum β-lactams, Figure 2), but resistant organisms were isolated in only 25.2% (MRSA 11.5%, CRO 12.9%, VRE 2.0%, ESBL 0.8%). Both inappropriate empiric therapy and excessively broad empiric therapy were associated with higher mortality on multivariable analysis (OR 1.30, 95% CI 1.14–1.48 and OR 1.20, 95% CI 1.13–1.38, respectively).

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.

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2298. Infections in Patients Receiving TVEC Therapy

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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 [3E–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 have been reported 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 adult patients 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 (30%) grade 1–2 cutaneous reactions were deemed probable or definitely related to TVEC and described as pruritis or rash. 12 (23%) patients had any microbiologically confirmed infection identified following TVEC therapy; 6 were bacterial (3 UTI, 1BSI, 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.

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