968. Effect of Outpatient Antibiotic Ordering Restrictions on Antibiotic Prescribing Patterns at a State-wide VA Healthcare System

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Session: 124. Out of the Box and Out of the Hospital: Stewardship Outpatient Services Friday, October 4, 2019: 11:00 AM

Background. Approximately 30% of antibiotics prescribed in the outpatient setting are inappropriate, mostly due to unnecessary prescriptions (Rx) for upper respiratory infections. Ordering restrictions is one approach to curtail inappropriate use. However, this approach may cause unintended consequences, such as increases in Rx of higher level antibiotics. This study evaluated the downstream effect of an azithromycin (AZM) ordering restriction.

Methods. This was a pre–post evaluation of the impact of an AZM removal (October 2017) on prescribing patterns of common outpatient antibiotics at the VA Maryland Healthcare System. AZM restriction was placed >10 years ago for concerns of higher level antibiotics. This study evaluated the downstream effect of an azithromycin ordering restriction.

Results. Of 2,893,413 visits by adults during 2012–2016, 1,866,145 (66%) resulted in antibiotic prescriptions. ARIs accounted for 46% of urgent care, 17% of medical office, and 14% of retail health visits for acute respiratory infections (ARIs) for which antibiotics are not needed. We aimed to quantify antibiotic prescribing rates to adult patients in a large retail health clinic chain using electronic health records and to identify future stewardship targets.

Methods. We included visits by adults ≥18 years to network retail health clinics from 2012 to 2016. We classified diagnoses by ICD codes. We calculated the percent of visits with systemic antibiotics prescribed among all visits, by individual diagnosis, and for ARIs as a group (e.g., pneumonia, sinusitis, pharyngitis, acute otitis media [AOM], bronchitis, and viral upper respiratory infections [URI]). We also assessed the percent of visits for sinusitis and pharyngitis with first-line antibiotics prescribed.

Results. Of 2,893,413 visits by adults during 2012–2016, 1,866,145 (66%) resulted in antibiotic prescriptions. ARIs accounted for 2,039,423 (72%) of visits and 1,475,069 (79%) of antibiotic prescriptions. The most common diagnoses regardless of antibiotic prescription were sinusitis (31% of visits), pharyngitis (15%, of which 81% were coded as streptococcal pharyngitis), urinary tract infection (9%), viral URI (8%), AOM (7%), and bronchitis (5%). Antibiotics were frequently prescribed for sinusitis, urinary tract infection, pharyngitis, and AOM but not for viral URI and bronchitis (Figure 1). First-line antibiotics were prescribed in the majority of sinusitis and pharyngitis visits (Figure 2).

Conclusion. ARIs are major drivers of visits by adult patients and of antibiotic prescribing to adults in this retail clinic network. Inappropriate antibiotic use was low in this setting for viral URI and bronchitis and first-line antibiotic selection was high for sinusitis and pharyngitis, although additional opportunities for improvement exist. Future antibiotic stewardship efforts may target examining adherence to guideline–recommended diagnostic criteria for sinusitis, AOM, and pharyngitis and increasing use of watchful waiting for sinusitis and AOM.

Disclosures. All Authors: No reported Disclosures.

969. Antibiotic Prescribing in a Large Retail Health Clinic Chain: Opportunities for Stewardship

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Background. Retail health is a growing outpatient setting. Research using claims data found that antibiotics were linked with 46% of urgent care, 17% of medical office, and 14% of retail health visits for acute respiratory infections (ARIs) for which antibiotics are not needed. We aimed to quantify antibiotic prescribing rates to adult patients in a large retail health clinic chain using electronic health records and to identify future stewardship targets.

Methods. We included visits by adults ≥18 years to network retail health clinics from 2012 to 2016. We classified diagnoses by ICD codes. We calculated the percent of visits with systemic antibiotics prescribed among all visits, by individual diagnosis, and for ARIs as a group (e.g., pneumonia, sinusitis, pharyngitis, acute otitis media [AOM], bronchitis, and viral upper respiratory infections [URI]). We also assessed the percent of visits for sinusitis and pharyngitis with first-line antibiotics prescribed.

Results. Of 2,893,413 visits by adults during 2012–2016, 1,866,145 (66%) resulted in antibiotic prescriptions. ARIs accounted for 2,039,423 (72%) of visits and 1,475,069 (79%) of antibiotic prescriptions. The most common diagnoses regardless of antibiotic prescription were sinusitis (31% of visits), pharyngitis (15%, of which 81% were coded as streptococcal pharyngitis), urinary tract infection (9%), viral URI (8%), AOM (7%), and bronchitis (5%). Antibiotics were frequently prescribed for sinusitis, urinary tract infection, pharyngitis, and AOM but not for viral URI and bronchitis (Figure 1). First-line antibiotics were prescribed in the majority of sinusitis and pharyngitis visits (Figure 2).

Conclusion. ARIs are major drivers of visits by adult patients and of antibiotic prescribing to adults in this retail clinic network. Inappropriate antibiotic use was low in this setting for viral URI and bronchitis and first-line antibiotic selection was high for sinusitis and pharyngitis, although additional opportunities for improvement exist. Future antibiotic stewardship efforts may target examining adherence to guideline–recommended diagnostic criteria for sinusitis, AOM, and pharyngitis and increasing use of watchful waiting for sinusitis and AOM.
therapy was completely protective in mice depleted of a single effector. While dual depletion resulted in diminished MAb efficacy in terms of survival, mice retaining neutrophils had marked improvements in survival with MAb therapy compared with other dual-depletion groups. The dissociation of bacterial density and survival suggested that inflammation was a primary driver of host outcome. Levels of IL-10 and TNFα and a reciprocal relationship in mice across effector depletion groups and were lower in mouse groups with higher survival when adjusted for bacterial density. IL-10 disruption completely abrogated the survival benefit of MAb therapy without altering bacterial clearance mediated by MAb. In contrast, TNFα disruption enhanced MAb efficacy for survival, and the presence of TNFα was antagonistic to MAb efficacy. Conclusion. These results confirm that host outcomes from A. baumannii infection are driven by host inflammatory response rather than bacterial density alone. Furthermore, novel therapeutic approaches seeking to improve outcomes from such infections must seek to shift the balance of pro-/anti-inflammatory cytokines to favor a down-modulated inflammatory response.

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972. A Mycobacterium tuberculosis Secreted Lipid Triggers Cough through a Neuronal Cough Receptor

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Session: 125. Pathogenesis and Inflammatory Response
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Background. A hallmark symptom of active pulmonary tuberculosis vital for disease transmission is cough. The current paradigm for tuberculosis-related cough is that it results from airway damage or irritation. However, there is limited experimental data to support this theory, and whether Mycobacterium tuberculosis (MtB) induces cough to facilitate its own transmission has not been explored. The cough reflex is a complex and coordinated event involving both the nervous and musculoskeletal systems initiated by particulate or chemical molecules activating nociceptive neurons, which sense pain or irritation. This activation induces a signaling cascade ultimately resulting in a cough. Respiratory nociceptive neurons innervate the airways of humans and most mammals and thus are poised to respond to noxious molecules to help protect the lung from damage. Because MtB is a lung pathogen, cough is a primary mechanism of MtB transmission, and respiratory nociceptive neurons activate cough; we hypothesized that MtB produces molecules that stimulate cough thereby facilitating its spread from infected to uninfected individuals. We previously identified a cough molecule produced by MtB, and in this work characterize its neuronal receptor using genetics, biochemistry, and pharmacology.

Methods. We used an in vitro neuronal activation bioassay to study MtB cough-inducing molecules. We also used a biochemical assay to identify the cough receptor. Finally, we used gene silencing, biochemistry, and pharmacologic inhibition to validate and characterize the activity of the newly discovered cough receptor.

Results. We isolated a complex lipid produced by MtB that activates nociceptive neurons. Both an organic MtB extract and the purified molecule alone were sufficient to induce cough in a conscious guinea pig cough model and guinea pigs infected with wild-type MtB cough much more frequently than guinea pigs infected with MtB strains unable to produce nociceptive molecules. Using genetics, biochemistry, and pharmacologic techniques, we identified and validated a cough receptor for the MtB lipid expressed on nociceptive neurons.

Conclusion. We conclude that MtB produces a molecule that activates nociceptive neurons and induces cough through a specific neuronal receptor. These findings have significant implications for our understanding of MtB transmission.

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973. Single-cell RNA Sequencing Analysis of Zika Virus Infection in Human Stem Cell-Derived Cerebral Organoids

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Session: 125. Pathogenesis and Inflammatory Response
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Background. The molecular mechanisms underpinning the neurologic and congenital pathologies caused by Zika virus (ZIKV) infection remain poorly understood. One barrier has been the lack of relevant model systems for the developing human brain; however, thanks to advances in the stem cell field, we can now evaluate ZIKV central nervous system infections in human stem cell-derived cerebral organoids which recapitulate complex 3-dimensional neural architecture.

Methods. We applied Seq-Well—a simple, portable platform for massively parallel single-cell RNA sequencing—to characterize cerebral organoids infected with ZIKV. Using this sequencing method, and published transcriptional profiles, we identify

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