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Updates in Hospital Medicine

Updates in Hospital Medicine: Antibacterial Stewardship and Infectious Diseases

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UPDATE I

ORAL ANTIBIOTIC TRANSITION IN UNCOMPLICATED GRAM-NEGATIVE BACTEREMIA

Gram-negative bacteremia (GNB) is a common reason for hospital admission and prolonged hospitalization.[1] Although there are no official Infectious Diseases Society of America (IDSA) guidelines regarding GNB, a consensus statement has endorsed transitioning patients with uncomplicated GNB from intravenous to oral antibiotics, with a preference for fluoroquinolone (FQ) or trimethoprim- sulfamethoxazole (TMP-SMX).[1] Recent evidence suggests that the clinical practice of transitioning to oral antibiotics for GNB is frequently delayed or does not occur altogether.[2] A recent randomized trial of over 900 patients with uncomplicated GNB provided further support in favor of transition to oral agents, however, no guidance on which oral antibiotics to use was given.[3]

A new systematic review and meta-analysis attempts to address the question of whether oral β-lactams (BL) (including cephalosporins) could be used safely as oral transition therapy for GNB, compared to the more commonly recommended oral treatment of FQ or TMP/SMX.[4] The authors included 8 retrospective cohort studies with a combined total of 7500 patients. Studies were included if adults had uncomplicated GNB (defined as source control within 48 hours) and were initially treated with IV antibiotics before transitioning to an oral regimen. They excluded patients with immunocompromise, polymicrobial infection, endocarditis, abscess, infected hardware/foreign body, or osteomyelitis. One group was transitioned to oral FQ or TMP-SMX (n= 4998) and the second group to an oral BL (n=2482); the most common BL choices were cephalexin (31%), amoxicillin/clavulanic acid (30%), amoxicillin (14%), cefuroxime (10%), and cefpodoxime (10%). The two groups were similar in mean age (70 versus 71), sex distribution, Charleston comorbidity index, and duration of IV antibiotics (4.2 versus 4.5 days). There was no statistical difference in either primary outcome. For 30-day all-cause mortality, 103 patients (2.09%) died in the FQ/TMP-SMX group, and 47 patents (1.89%) died in the BL group. For antibiotic failure (defined as recurrence of infection with same bacteria), rates were 2.08% versus 3.42%, respectively, corresponding to 104 versus 85 patients.

This study has several limitations, primarily due to its observational design. While patient demographics were largely similar between groups, unmeasured confounding factors may have influenced the selection of specific oral antibiotic classes. When considering the generalizability of the results, it is worth noting that the patient population was largely GNB due to a urinary source (~80%). Additionally, the BL group included antibiotics with a wide range of bioavailability, and there are important differences between members of that group. The total antibiotic duration, the dosing of the oral agents, along with the adverse effects of antibiotics were not included. The safety and efficacy of oral BL depends greatly on the dose and frequency of administration, tailored to the infection at hand. In line with this, recent IDSA guidelines for complicated urinary tract infections (with or without

GNB) recommend considering higher-dose oral regimens for BLs and cephalosporins and explicitly favor oral third-generation cephalosporins with high bioavailability.[5]

Take-away: For patients with uncomplicated gram-negative bacteremia for whom the current first-line oral transition treatment of FQ or TMP/SMX is not appropriate or carries unacceptable side effect profiles, oral BLs are a reasonable option when dosing is optimized.

UPDATE 2

BEING LABELED AS ALLERGIC TO B-LACTAM ANTIBIOTICS MAY PUT PATIENTS AT AN INCREASED RISK OF HEALTHCARE-ASSOCIATED INFECTIONS

β-lactams (BL) are a commonly reported drug allergy, with 10-15% of patients carrying this label.[6] However, most of these patients are not truly "allergic," either due to mischaracterization of the original reaction or the waning of the immune response and thus are ultimately tolerant of BL on testing.[7] Due to the threat of a true anaphylactic allergy and subsequent altered prescribing practices, mischaracterized BL allergies may expose patients to unnecessarily broad-spectrum (and in many cases, inferior) antibiotics and of greatest concern, potentially worse clinical outcomes.[8,9]

A new systematic review and meta-analysis aimed to better understand patient-centered, unintended clinical outcomes of a reported BL allergy as compared to patients who do not carry this label.[9] The authors ultimately included 62 observational studies (most were retrospective cohort) and 1 experimental study. Most studies focused on inpatients only, and 95% were in high-income countries. Authors found that being labeled with a BL allergy had negative impacts on several clinical outcomes: patients had higher rates of surgical site infection (OR 1.6), infection or colonization with multidrug-resistant organisms (OR 1.4), and C. difficile infection (OR 1.3). They also experienced increased length of hospitalization (statistically significant, albeit of unclear clinical significance, of 0.06 days). There was no impact on overall, in-hospital, or 30-day mortality, although there was an association with higher mortality at 180 days or greater (OR 1.4; notably only six studies examined this outcome). An important limitation of this review is that 62 of the 63 included studies were observational, meaning the reported health outcomes should be interpreted as "associations" rather than "causations".

Take-away: Most patients with a label of BL allergy do not have a true anaphylactic allergy. This study provides evidence that a mischaracterization of a BL allergy may be associated with health risks at the level of the individual patient. Healthcare systems should put more resources into accurately managing patients' antibiotic allergy labels, with benefits to patient-centered outcomes as well as quality metrics.

UPDATE 3

DO RESPIRATORY SYNCYTIAL VIRUS (RSV) INFECTIONS CONFER A HIGHER RISK OF CARDIOVASCULAR EVENTS?

Respiratory syncytial virus (RSV) infection is now recognized as both an important cause of acute respiratory illness as well as associated with cardiac complications, especially congestive heart failure (CHF), in hospitalized adults.[10,11] This retrospective study of 471 adult patients hospitalized with RSV from 2017-2020 builds upon their prior surveillance work, and sought to better understand the relationship of this infection with cardiovascular events (CVEs), i.e., myocardial infarction (MI), new-onset CHF or CHF exacerbation, new or decompensated arrythmia, stroke, venous thromboembolism.[10,12] The authors compared CVE rate in the 6 months leading up to admission ("pre-infection") against the 28-day period post-admission ("acute infection") and against the late period post-admission (29 days to 6 months; "post-infection"). The authors found that 37% of patients had CVEs in "acute infection" stage (most common CVEs were CHF, atrial fibrillation (AF), and MI), with highest risk in the first 7 days. Almost half of these events occurred in patients with no prior history of these medical conditions. The incidence rate ratio of CVEs was 18.5 during "acute infection" and 1.6 during "post-infection", compared to "pre-infection". Patients with pre-existing history of hypertension, CHF, AF, and CAD, and ≥ 3 classic cardiac risk factors had higher risk of CVEs. Older age also conferred higher risk of CVEs: Prevalence was 23% for patients < 65 years of age, 41% for 65-85 years, and 60% for > 85 years. Importantly, one-month mortality was higher for patients with ≥ 1 CVE in "acute infection" period compared to patients with none (12% versus 3%).

Take away: Adults hospitalized with RSV are at markedly increased risk of CVEs. Although older patients with cardiac comorbidities have higher rates of CVEs, patients without traditional risk factors are also at risk. Hospitalists should increase their pre-test probability for these acute conditions in this patient population and encourage patients to obtain RSV vaccination if appropriate.

Disclosures/Conflicts of Interest

The authors have no conflicts of interest to disclose.

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