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Empiric Antibiotic Regimens and the Incidence of Acute Kidney Injury in Hospitalized Black Patients

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Abstract

The selection of inpatient empiric antibiotic regimens is a significant challenge for hospitalists and clinicians today. Much is known about the increased incidence of acute kidney injury associated with the use of vancomycin and piperacillin-tazobactam in combination compared to vancomycin and other beta-lactam combinations. What is less clear is the incidence of antibiotic associated acute kidney injury and outcomes in Black patients. Incidence rates of acute kidney injury are already known to be higher in Black patients compared to white patients, which makes extrapolating the risks of antibiotic associated acute kidney injury challenging. In addition, only one research paper has included a study population with greater than 50% Black patients.

Keywords:

Vancomycin • Piperacillin-tazobactam • Antibiotic induced acute kidney injury

Introduction

Antibiotic induced AKI is often dependent on several pathways and specific to each antibiotic. These pathways are summarized in Figure 1. Due to the increasing burden of antimicrobial resistance, empiric antibiotic coverage for hospitalized patients with suspected infection must be broad. Often, a regimen will include vancomycin, a glycopeptide, for coverage against potential methicillin-resistant Staphylococcus aureus. In 2018, the Medicare Expenditure Panel calculated over 600,000 vancomycin orders in the United States alone [2]. In one survey, vancomycin was administered in 34.9% of critical care patients [3]. The risk of nephrotoxicity with vancomycin monotherapy is well documented [4], and recently, several studies have investigated whether combination beta lactam and vancomycin therapies cumulatively increase the risk of AKI, even with beta lactams that are not shown to cause AKI when used as monotherapy [5-7]. This has been most well studied with piperacillin-tazobactam (PTZ), a combination ureidopenicillin and beta-lactamase inhibitor, and the second most common antibiotic administered in critical care patients [3], and cefepime, a fourth-generation cephalosporin. Both have not been shown to be associated with AKI when used as monotherapy [7-8]. Both have broad gram-negative and gram-positive coverage, including pseudomonas species, but one notable difference is that while PTZ generally demonstrates good susceptibility against anaerobic species, CPE does not. When these regimens are used empirically, a lack of anaerobic coverage could be affecting treatment failure rates.

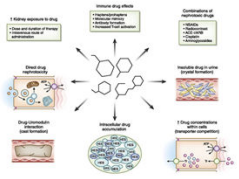

Figure 1. Perazella 2018, Mechanisms of drug induced acute kidney injury.

VAN-CPE versus VAN-PTZ

In one study of 558 hospitalized patients comparing the incidence rates of AKI in each treatment arm, 29% of VAN-PTZ patients developed an AKI, compared to 11% of VAN-CPE patients [9]. This significant result from these patients--matched and stratified on severity of illness, critical care status, and other factors—caused many clinicians to question the appropriateness of the use of VAN-PTZ as a first-line empiric option in many different disease states. Since then, several more studies have been published, reporting an increased incidence of AKI with VAN-PTZ regimens when compared to VAN combined with other beta-lactams [10-11].

VAN and PTZ associated AKI in black patients

Black patients have been shown to have higher incidences of vancomycin associated AKI, and higher incidences of AKI during hospitalization with diabetes compared to white patients [12-13]. There are many hypotheses for these differences, including socioeconomic differences, health access, and differences in genetic variances such as the APOL1 gene that is nearly non-

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existent in white patients but prevalent in Black patients [14]. To date, there is no consensus on the cause of the increased incidence of AKI in this patient population. Many studies have been conducted to analyze the occurrence of AKI in hospitalized patients. Demographic information is often collected, and most studies do not report a percentage of Black patients included in their study. See Figure 2 below. Only one study was identified in reporting the percentage of Black patients, included a majority of patients who identified as Black [9]. This study demonstrated an almost three-fold increase in the incidence in AKI in VAN-PTZ regimens compared to VAN-CPE regimens. Therefore, it is not unreasonable to hypothesize that the incidence rate of combination VAN-PTZ associated AKI is higher in Black patients than white patients. However, this needs to be confirmed in order for clinicians to confidently adjust empiric prescribing practices. An interesting finding of this study is that there was no significant difference in all-cause mortality. Few studies have examined clinical cure rates when comparing these antibiotic regimens. On the opposite side, if there is little difference in the occurrence of AKI observed between VAN-PTZ and VAN-CPE, this would potentially support the continued use of VAN-PTZ due to its enhanced anaerobic coverage in empiric prescribing, since there is not universal adoption of the addition of metronidazole to cefepime and vancomycin in empiric therapy for all indications.

Conclusion

The choice of empiric antibiotics is one of the most important decisions that clinicians must make today in the care of hospitalized patients. In the era of personalized medicine, clinicians need to consider racial differences when evaluating standards of care. Though current evidence indicates that the increased risk of AKI exists in the general population of the United States, and in one study with a majority of Black patients, a better understanding of the mechanisms and magnitudes of risk is sorely needed. According to the United States Census Bureau, 42 million American citizens are Black. When the outcomes of this many people are at stake, clinicians need to ensure that they are providing the best care possible.

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