Impact of intravenous antimicrobial dose reductions on clinical outcomes in patients presenting with sepsis-induced acute kidney injury (AKI)

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Background
Sepsis-induced acute kidney injury (AKI) requires early, effective antimicrobial therapy to reduce mortality1. Pathophysiological changes in sepsis lead to altered antimicrobial pharmacokinetics2. Sepsis increases capillary permeability, resulting in increased volume of distribution of hydrophilic antimicrobials and the possibility of subtherapeutic concentrations3. Treatment of sepsis-induced AKI requires a balance between treatment failure and toxicity. No validated guidelines exist regarding antimicrobial dosing in this state4. Current guidelines regarding antimicrobial dosing adjustments are obtained from pharmacokinetic studies in patient populations with normal kidney function or chronic kidney disease (CKD)5. These populations have stable kidney function and do not reflect the acute changes seen in AKI patients. We aimed to investigate the effect of antimicrobial dose reductions on clinical outcomes in patients with sepsis-induced AKI. Secondary objectives were to determine the impact of development of AKI, severity of AKI and effect of antimicrobial dose reductions.

Method
Retrospective single-centre cohort study conducted at Chelsea and Westminster Hospital including patients >18 years with microbiological confirmation of sepsis, defined as blood culture indicating Gram-negative bacteraemia, between December 2015 to March 2018. Institutional databases were used to collect data on patient demographics, comorbidities, admission/discharge dates, transfer to ITU, date of death and prescription of dose of antimicrobials. Data collected on kidney function included serum creatinine values and estimated glomerular filtration rate (eGFR) values. Acute rise in serum creatinine was used to identify and stage patients with AKI according to RIFLE classification. There were 109 patient cases of AKI. Collected data was compared between groups based on development of AKI, severity of AKI and effect of antimicrobial dose reductions.

Results
Table 1: Comparison of demographic and clinical data for Gram-negative septic patients who received a reduced dose of antimicrobial compared to those who received full dose for the first 24 hours of treatment. Patients received the following antimicrobials: beta-lactam (75%), aminoglycoside (37.5%), glycoprotein (12.5%), nitroimidazole (12.5%), macrolide (5%) and fluoroquinolone (5%)

Table 2: Comparison of demographic and clinical data for Gram-negative septic patients who did and did not develop AKI in 2017

Table 3: Comparison of demographic and clinical data between Gram-negative septic patients with a 'risk' severity of AKI compared to patients with an 'injury or failure' severity according to RIFLE classification

Conclusions
A trend for worse clinical outcomes is seen with antimicrobial dose reductions in patients with sepsis-induced AKI
Patients with a lower eGFR at time of sepsis diagnosis were more likely to receive a reduced antimicrobial dose
Use of eGFR values to guide dosage adjustments has been validated in CKD patients but do not accurately reflect drug clearance in patients with acute kidney dysfunction
Administration of full-dose antimicrobials for the first 24 hours of treatment in patients with sepsis-induced AKI did not worsen kidney function and no cases of beta-lactam induced seizures were reported
Development of AKI and more severe AKI in a septic patient led to longer length of hospital stay.
The results of this study will need to be replicated in a prospective multicentre study

References

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