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P0147 Sulfamethoxazole/trimethoprim-associated acute kidney injury: real or a mirage?

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Background: Sulfamethoxazole/trimethoprim (SMX/TMP) is a commonly used antimicrobial; however use is sometimes limited because of nephrotoxicity concerns. Evidence supporting these concerns is limited to small, noncomparative case series and historical concerns with less soluble sulfonamides. These concerns are further complicated by small rises in creatinine caused by trimethoprim due to inhibition of tubular secretion of creatinine. The primary objective of this analysis is to determine if there is a true association between SMX/TMP use and acute kidney injury (AKI) in a patient population matched for baseline risks for AKI.

Materials/methods: A retrospective matched cohort study in patients receiving treatment with SMX/TMP or a non-nephrotoxic comparator agent was performed. Patients were included if they received a target antimicrobial for ≥48 hours and excluded if creatinine clearance (CrCl) was < 30 mL/min or had a pre-existing need for renal replacement therapy. Patients were matched 1:1 based on antibiotic indication, severity of illness, number of concomitant nephrotoxins, duration of therapy, and ICU status. The primary outcome was AKI defined as meeting at least the "Injury" stage of the RIFLE criteria in order to avoid misclassification due to insignificant rises in creatinine caused by trimethoprim.

Results: 328 (164 in each group) patients were included in the analysis. Baseline characteristics were similar except that patients receiving SMX/TMP were younger (mean age 54 years [standard deviation (SD) 18] vs. 61 years [SD 14], (p=0.0001), more likely to be male 63% vs. 52% (p=0.04), had higher mean baseline CrCl 87.7 mL/min [SD 29.4] vs. 75.7 mL/min [SD 28.9] (p=0.02), and more likely to have AIDS 13% vs. 1%, (p=0.0001). Indications for treatment were systemic infections (60%), SSTI (21%), and UTI (9%) in both groups. AKI occurred in 4.3% treated with SMX/TMP vs. 2.4 % with comparator agents, p=0.54. Any stage of the RIFLE criteria (≥1.5-fold increase in serum creatinine) occurred in 11% of SMX/TMP patients and 3.7% of the comparator agents (p=0.02).

Conclusions: Although TMP-SMX was associated with an increase in small (1.5 x baseline) rises in creatinine, rates of AKI were comparable between the groups.