A270 - Identifying synergistically nephrotoxic antimicrobial regimens in patients with sepsis: two nationwide multicenter registries in Japan

N Meguro¹; J Yoshimura¹; K Yamakawa²; Y Umemura²; S Fujimi¹; H Ogura²; T Abe²; S Gando²; Y Otomo²

¹Division of Trauma and Surgical Critical Care, Osaka General Medical Center, emergency, Osaka, Japan, ²Japanese Association for Acute Medicine Sepsis Prognostication in Intensive Care Unit and Emergency Room (SPICE) study group, emergency, Tokyo, Japan

Introduction:
Acute kidney injury (AKI) is a serious complication in sepsis and associated with high morbidity and mortality. The combination antimicrobial regimens with vancomycin (VCM) and broad-spectrum beta-lactams (BSBL), such as piperacillin tazobactam and cefepime, have been identified as potentially nephrotoxic combinations, but existing studies have not provided sufficient evidence. The aim of this study was to evaluate detailed association between the combination antimicrobial therapy and the risk of AKI in septic patients.

Methods:
This investigation was a post hoc analysis of 2 prospective nationwide cohorts enrolling consecutive adult patients with sepsis in intensive care units in Japan. In this study, progression of AKI was defined as one or more elevation of renal sub-score in Sequential Organ Failure Assessment score from day 1 to day 4. We regarded anti-pseudomonal penicillins, fourth generation cephalosporines, and carbapenems as BSBL. Multivariable logistic regression analysis including a two-way interaction term (VCM x BSBL) was performed to assess the add-on effects of each antimicrobial agent on the progression of AKI.

Results:
The final study cohort comprised 1837 patients with sepsis. Among them, 45 received VCM without BSBL, 1055 received BSBL without VCM, 249 received both VCM and BSBL, and 488 received other type of antimicrobials. The administration of VCM was associated with an increased risk of AKI in patients with BSBL [odds ratio (OR), 1.57 (0.96-2.57); p=0.072]. However, the tendency was not evident in patients without BSBL [OR, 0.23 (0.03-1.56); p=0.133]. The interaction effect on the progression of AKI between VCM and BSBL were statistically significant (p for interaction=0.038).

Conclusion:
The regression model including two-way interaction term suggested that the combination of VCM and BSBL might synergistically increase the risk of AKI in patients with sepsis.