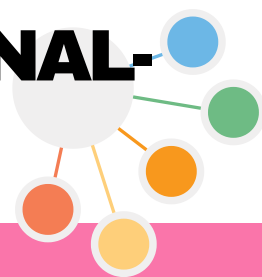


BETA-LACTAM ANTIBIOTICS IN ACUTE KIDNEY INJURY: IS IT TIME TO RETHINK OF RENAL-DOSE ADJUSTMENT?



Question of Interest

- **PK profile** of beta-lactam antibiotics can be altered dramatically in patients with **septic shock**.
- The **increases in volume of distribution (Vd)** and **total body clearance (TBCL)** causes **reduction in antibiotics absorption** - hence ineffective antibiotics activity.
- Hypothesis:
 - In the first **48 hours**, beta-lactam antibiotics usage **without renal-dose adjustment** would have improved vasopressor-free days

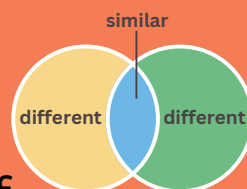
Study Population



- **Retrospective**, multicentre study in the US (Jan 2013 - Apr 2019).
- Patients received either **Cefepime / Pip-Tazobactam / Meropenem**.
- Patients had **AKI** (as per KDIGO criteria) during receipt of the antibiotics.
- **Septic shock** was also present as defined by SEPSIS-3 criteria.

The Outcomes

- Primary outcome:
 - There is **no significant difference** of **vasopressor-free days at 28 days** between the adjusted-dose group and the non-adjusted dose group. [27.15 days vs 27.55 days; mean difference 1.96 days]
- Secondary outcomes:
 - There is also **similar outcomes** in **ventilator-free days** and **in-hospital mortality**.



Discussion & Analysis

- The creatinine clearance (**CrCl**) in the dose adjustment group **was significantly lower** compared to the unadjusted-dose group. [37.6 mLs/min VS 48.9 mLs/min; p value = 0.015].
 - This may contribute to 'prescription-bias' in decision for the antibiotics dosing.
- Up to **40%** of the patients had **AKI recovery within 48 hours** - clinical effect of renal-associated toxicity would be presumably lower.
- About **30%** of the cohort had a **genitourinary source of sepsis**.
 - Dosing differences may have less an impact since BL antibiotics are concentrated in the urine.

Would this Change My Practice?

- **Full unadjusted dose may be considered** in the **first 48 hours**, even in the presence of AKI.
- However, other factors to consider would be **source of sepsis** and the **severity of the AKI**.
- Further prospective studies / RCTs would be helpful to delineate a causative effect of renal-dose adjustment in AKI patients.
- **TDM for beta-lactam** would be helpful to assist in further PK profiling in this cohort of patients.

