Effects of Delayed Second Dose Antibiotic Administration in Patients with Septic Shock

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Background
Sepsis is a dysregulated host response to infection causing life-threatening organ dysfunction; septic shock manifests as circulatory and metabolic abnormalities. Prompt initial antibiotic administration in sepsis has demonstrated a significant impact on mortality. Kumar and colleagues found a 7.5 percent decrease in survival for every hour in delay of initial antibiotics. Presently, there is a paucity of data describing the implications of delay in administration of second dose antibiotics in patients with septic shock. This study evaluated the impact delay of second dose antibiotics may have on vasopressor duration.

Methods
This was an institutional review board approved, retrospective cohort study comparing vasopressor duration in septic shock patients with and without delayed second dose antibiotic administration. Patients between January 1, 2018 to August 31, 2019 were included if they were 18 years of age or older diagnosed with septic shock. Patients initially treated at an outside hospital, antibiotics not administered within 24 hours of presentation, discontinuation of antibiotics prior to second dose, inpatient death within 24 hours, and pregnancy were excluded. Patient demographics, clinical data, and hospital admission information were collected retrospectively from the electronic health record. Acute Physiology and Chronic Health Evaluation (APACHE II) scores were calculated. The primary outcome was comparison of vasopressor duration between delay and no delay second dose antibiotic administration. Delay was defined by first-to-second dose time greater than or equal to 50% of the recommended interval. Secondary outcomes included vasopressor duration between no delay and moderate delay and vasopressor duration between moderate and major delay. No delay was defined by first-to-second dose time less than or equal to 24% of the recommended interval and any delay occurred at greater than or equal to 25% of the recommended interval. Additional secondary outcomes included frequency and duration of mechanical ventilation, length of intensive care unit (ICU) stay, hospital length of stay (LOS), and hospital mortality. It is hypothesized that major delay in administration of second dose antibiotics will increase duration of vasopressor requirements in patients with septic shock.

Results
In total, 126 admissions were included in the final analysis and 63 patients were included in the no delay and delay groups. No difference in vasopressor duration was seen between no delay and delayed antibiotic groups (median [IQR], 22.2 hours [10.8-39.0] vs 17.9 hours [7.1-38.9], p=0.376). No difference was found for vasopressor duration <25% delay and ≥25% delay (median [IQR], 22.2 hours [10.8-45.3] vs 18.6 hours [7.2-36.2], p=0.380). No significant differences were found between ICU LOS, hospital LOS, inpatient mortality, or duration of mechanical ventilation.

Conclusions
Vasopressor duration was not statistically impacted by major delay in second dose antibiotic administration. Further research, with a larger sample size, is necessary to determine impact of second dose antibiotic administration delay in this patient population.