Title: Vancomycin Troughs Before and After Implementation of a Standardized NICU Dosing Protocol

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Background: Vancomycin is commonly used in neonates for empiric coverage in late-onset sepsis. Predicting the kinetics of vancomycin in neonates can be particularly challenging due to wide variations in developmental age and body composition. Many different dosing strategies exist for calculating an initial dose in these patients. Wesley Medical Center implemented a dosing protocol in 2019 based on internal data from their own neonatal intensive care unit (NICU) in order to standardize and optimize the approach for choosing an initial dose. The purpose of this study is to assess the facility's NICU vancomycin dosing protocol and ensure the protocol efficiently achieves therapeutic troughs.

Methods: This is a single-center, retrospective, cohort study. One cohort was comprised of patients whose initial dose was based on the new protocol. The second cohort consisted of neonates who received vancomycin prior to protocol implementation. The primary outcome was percent of initial, steady-state troughs that were between 10-20mg/L. Secondary outcomes included: incidence of acute kidney injury (AKI), average length of therapy, and number of dose adjustments prior to first therapeutic trough. Thirty-five patients per group were needed to achieve 80% power to detect a 30% increase in initial therapeutic troughs. A 1:1 ratio of patients in each group was maintained. Patients were included if they had at least one steady-state trough while in the NICU or neonatal special care unit. Notable exclusions included patients with known renal dysfunction within 7 days prior to first dose or patients who did not receive an initial dose based on the NICU vancomycin dosing protocol (post implementation group). Acute kidney injury was defined as an increase in serum creatinine of at least 0.5mg/dL in a 7-day time period or a single serum creatinine level of 1.5 mg/dL or greater. Study eligibility was determined through review of patients' electronic health records.

Results: A total of 38 patients were included in each group. Therapeutic troughs were achieved with the initial dosing regimen in 24 patients in the post-protocol group vs 13 in the pre-protocol group (63.2% vs 34.2%; p=0.0248). No difference was found in rate of AKI in the post-protocol group compared to the pre-protocol group, occurring in 2 of 38 vs 3 of 38 respectively (5.2% vs 7.9%; p=0.304). Average length of therapy was similar after and prior to protocol implementation at 8.6 and 8.2 days respectively (p=0.719). The average number of dose adjustments needed prior to achieving a therapeutic trough was significantly less after implementation of the protocol compared to before implementation (0.45 vs 0.92; p=0.0048).

Conclusion: The implementation of the NICU vancomycin dosing protocol was associated with a significant increase in number of initial therapeutic trough levels. The number of dose adjustments needed prior to achieving a therapeutic trough was decreased by 51% after the protocol was implemented. The protocol did not show any effect on the rate of AKI or total length of therapy. These results support the use of the protocol to more efficiently achieve desired vancomycin troughs without increasing adverse effects.