There is little evidence to describe the optimal dosing regimen for surgical site infection prophylaxis in infants undergoing cardiac surgery, and a great deal of institutional variability exists in dosing prophylactic antibiotics" Ingrande et al (2019).

Abstract:

BACKGROUND: Gram-positive bacteria account for nearly three-quarters of all surgical site infections. Antibiotic prophylaxis against these bacteria with cephalosporins or, in select circumstances, with vancomycin is considered standard of care for prevention of surgical site infections. There is little evidence to describe the optimal dosing regimen for surgical site infection prophylaxis in infants undergoing cardiac surgery, and a great deal of institutional variability exists in dosing prophylactic antibiotics. We designed this study to describe an optimal dose regimen for cephalosporin and vancomycin based on pharmacokinetic evidence for infant open-heart surgery on cardiopulmonary bypass.

METHODS: Two separate cohorts of infants undergoing cardiac surgery with cardiopulmonary bypass were evaluated. Plasma concentrations of vancomycin (cohort 1, N = 10) and cefazolin (cohort 2, N = 10) were measured, and mixed-effects pharmacokinetic models were constructed for each drug. Simulations of various dosing regimens were performed to describe an appropriate dosing regimen necessary to maintain antibiotic concentrations above the susceptibility cutoff for staphylococci.

RESULTS: Both cefazolin and vancomycin plasma concentration versus time profiles were characterized by a 2-compartment model. Subject weight was a significant covariate for V1 for vancomycin. Subject age was a significant covariate for V1 for cefazolin. Cardiopulmonary bypass did not influence concentration versus time profiles. Simulations demonstrated that a 1-hour vancomycin infusion (15 mg·kg), repeated every 12 hours and a 10-minute infusion of cefazolin (30 mg·kg), repeated every 4 hours maintained plasma concentrations above 4 μg·mL and 16 μg·mL, for vancomycin and cefazolin, respectively. Both concentrations are above the minimum inhibitory concentration 90 for most susceptible staphylococci.

CONCLUSIONS: Prophylactic treatment of vancomycin 15 mg·kg infused >1 hour with 12-hour redosing and cefazolin 30 mg·kg infused >10 minutes with 4-hour redosing will

maintain serum levels of each antibiotic above the susceptibility cut-offs for susceptible staphylococci in infants undergoing cardiac surgery. Cefazolin levels may be adequate for some, but not all, Gram-negative bacteria. The effect of cardiopulmonary bypass on pharmacokinetics is negligible.

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Reference:

Ingrande, J., Gutierrez, K., Lemmens, H.J., Verma, A., Nicolau, D.P., Sutherland, C.A. and Ramamoorthy, C. (2019) Pharmacokinetics of Cefazolin and Vancomycin in Infants Undergoing Open-Heart Surgery With Cardiopulmonary Bypass. Anesthesia and Analgesia. 128(5), p.935-943. doi: 10.1213/ANE.0000000000003876.