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Lower Vancomycin Serum Trough Concentrations Might Not Be the Answer

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To the Editors,

We read with interest the manuscript published by Frymoyer et al(1) regarding desired vancomycin trough serum concentrations for treating invasive methicillin-resistant staphylococcal (MRSA) infections. In their manuscript, the authors suggest that vancomycin serum trough concentrations of 7–10 µg/mL should be sufficient for treatment of invasive MRSA infection in more than 90% of children when the MIC of vancomycin is 1.0 µg/mL or less. The revelation that the current clinical practice guidelines by the Infectious Disease Society of America could be so misguided in recommending vancomycin serum trough concentrations of 15–20 µg/mL for the treatment of invasive MRSA seemed astonishing.(2)

We recently performed a validation study of a pediatric population pharmacokinetic model of vancomycin at our institution. Hospitalized children 0–18 years of age receiving vancomycin therapy were invited to participate. Subjects had two additional vancomycin serum concentrations drawn (peak and random) in addition to troughs obtained as part of clinical care and at the discretion of the physician. A previously published pediatric population PK model was validated in our population using Bayesian estimation in MW/Pharm (Mediware, Groningen, The Netherlands).(3) Of 15 subjects enrolled, 12 subjects had vancomycin peak, random, and trough serum concentrations obtained. A 24 hour area under the curve (AUC 24) was calculated to correspond with the serum concentrations in these subjects. (4)

While the simulation by Frymoyer et al was performed using a 25 kg base patient, our subjects' weights ranged from 12.3–52.5 kg, and encompassed children aged 1.2–17.3 years. Fifty-eight percent of the subjects were male, and the actual dosage range around the time of the vancomycin serum trough concentration ranged from 45–102 mg/kg/day.

Two subjects who had a vancomycin serum trough concentration < 5 µg/mL had a corresponding AUC 24 = 280. The four subjects who had a vancomycin serum trough concentration = 14.5 µg/mL had a corresponding AUC 24 > 694. Only 67% of the remaining

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subjects with a vancomycin serum trough concentration between 8 and 10 µg/mL had a corresponding AUC 24 > 400. This is important, as data from adults suggest that successful treatment is less likely if the ratio of AUC/minimal inhibitory concentration (MIC) < 400.(5)

While the study published by Frymoyer et al brings up important topics for discussion, we would not recommend a change in clinical practice that simply sought lower vancomycin serum trough values. Instead, personalizing medical treatment and using information about the AUC and the MIC for each person requiring vancomycin for invasive staphylococcal disease could provide the best outcomes for our patients.

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