1. Neely and colleagues state that use of the fixed 200-mg dose may result in many concentrations considerably above or below a target trough of 1 μg/mL, and they question the tolerability of such a dose in the youngest children. The fixed dose also raises concerns about possible underdosing in the oldest children.

We examined 35 trough concentrations obtained from routine therapeutic drug monitoring in 21 hospitalized pediatric patients (age range, 7–18 years; mean age, 13.3 years) who received 200 mg of oral voriconazole twice daily between 2002 and 2008 (unpublished data from a multicenter French and Swiss database). Concentrations were measured at least 4 days after the dose was changed to 200 mg given twice daily or after therapy with this regimen was initiated. Trough concentration data were as follows: mean ± standard deviation, 1.66 ± 1.62 μg/mL; median, 1.29 μg/mL; range, <0.2 to 5.7 μg/mL. Seventeen levels (48.6%) were ≤1 μg/mL and may be considered suboptimal [4, 5]. Two levels were >5.5 μg/mL. Although limited, these data suggest that the fixed 200-mg dose is likely to expose a significant proportion of children to suboptimal voriconazole concentrations.

There is increasing evidence for exposure-effect relationships in patients treated with voriconazole [1, 4, 6]. Because voriconazole pharmacokinetics is highly variable, we agree with Neely and colleagues’ support of the need for therapeutic drug monitoring in children. We also believe that optimal dosage regimens of voriconazole, based on pharmacokinetic and pharmacodynamic end points, are still to be developed.

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