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AUTHOR REPLY

Reply to Sorooshian and Snow, "Is Alternate-Day Therapeutic Drug Monitoring in the Intensive Care Unit Not Intensive Enough?"

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We thank Parviz Sorooshian and Timothy A. C. Snow for their positive comments and their interest regarding our work (1–3).

We chose to monitor antibiotic levels every second day for two different reasons: (i) Roberts et al. concluded that a twice-weekly strategy was not sufficient to reach and maintain therapeutic antibiotic levels within the target (4); (ii) although our laboratory can provide same-day drug concentration measurements (3), we did not believe that once-daily therapeutic drug monitoring (TDM) would perform better than alternate-day monitoring, while adding much more work and costs. The minimum turnaround time to get the result is 6 h, which means that for blood samples withdrawn early in the morning, the dose adaptation would not occur sooner than in the evening. Having another antibiotic dosage early in the next morning (as per daily TDM) would not allow antibiotic concentrations to reach steady state in the majority of cases.

When we planned our study, TDM was already established at our institution, but not used routinely. We did not believe that depriving severe-burn patients of the possibility of TDM would have been ethically responsible and acceptable. Nevertheless, the results from the per-protocol analysis confirmed the results of the intention-to-treat analysis and the positive effect of the tested alternate-day TDM strategy.

The first predefined primary pharmacokinetic outcomes were the time to achieve serum anti-infective concentrations within the predefined target range and the proportion of serum antibiotic trough concentration measurements within the target range during a single course of treatment with a given anti-infective agent. We did not question the feasibility of TDM practice, since this strategy had already been used for more than a decade in our institution; rather, we were interested in its pharmacokinetic effect (3). Assessing clinical outcomes would have meant including >500 patients, something out of reach for our burn center, which admits fewer than 30 severe-burn patients a year. Noteworthy, Patel et al., though including a slightly higher number of patients, came to the same conclusion and reported that all enrolled patients achieved a positive clinical outcome (5).

The change in the administration protocol of beta-lactams from 30 min to 2 h occurred at the very end of the study. This decision was independent of us—the results from the study were still blinded at the time—and was the consequence of an update of the local ICU antibiotic stewardship protocol. We agree that current data are still equivocal on whether prolonged infusion results in better clinical outcomes (6, 7), but

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we do believe that optimizing the antibiotic prescription is important for overcoming hard-to-treat infections in particular populations, such as burn patients (2, 8, 9).

In summary, TDM proved to be a useful tool for monitoring antibiotic concentrations among severe-burn patients. Increasing the frequency of TDM to a daily practice appears far less beneficial from our point of view than evaluating its clinical benefits and cost-effectiveness in further research.

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