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LETTER TO THE EDITOR

Is Alternate-Day Therapeutic Drug Monitoring in the Intensive Care Unit Not Intensive Enough?

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We thank Fournier et al. (1) for their contribution to the important subject of therapeutic drug monitoring (TDM) in the intensive care unit (ICU). Additionally, we appreciate their assessment of the feasibility of an alternate-day strategy. However, their study raised a number of questions with regard to their approach.

We question why the authors chose alternate-day monitoring of antibiotic levels. It was suggested that this approach would account for the time it takes to achieve steady state after dose adaption. However, they themselves highlight the rapid changes in pharmacokinetics to which burns patients are subject, leading other studies toward utilizing a daily-level protocol (2). We note from their previous work (3) that the frequency of same-day availability of drug levels has been increasing at their institution. Therefore, does their methodology reflect their own institutional laboratory practice, a concern regarding cost-effectiveness, or a true belief that alternate day is best (despite limited evidence as to the optimal frequency)? This is an important consideration for those who intend to utilize TDM at ICUs given the current wide range in practice (4).

We were surprised that the authors allowed breaks in protocol enabling clinicians to review drug levels in the standard-care group. While it is reassuring that the authors have great faith in the role of TDM, in allowing these protocol breaks, have they exposed a significant bias toward TDM, undermining the conclusion of their paper? Unlike other investigators (5), the authors attempted to prove that TDM is both feasible and useful without assessing any beneficial clinical effect. As such, would this make their study inappropriate for future meta-analyses? It is rational that breaks in protocol occur if patient safety is at risk. However, we would question whether that is applicable here, since the authors are attempting to evaluate the feasibility of TDM, presumably in preparation for future work on assessing clinical outcomes. Surely, at such an early stage, we are working out how to obtain the antibiotic concentration and what to do to change it, rather than assessing whether the availability of antibiotic concentrations would benefit the patient.

The authors have also highlighted an ongoing problem in antibiotic dosing in ICU patients: the time taken to achieve the MIC after the first dose and the frequency with which trough levels fall below this despite TDM. The administration protocol moved from a 30-min to a 2-h infusion during the time frame of this study. Therefore, do the authors believe that we should be moving toward using loading boluses followed by TDM-guided continuous infusions? Moreover, this mode of antibiotic delivery is now used extensively for glycopeptides (6) and carbapenems (7). While the research to date is equivocal (8), might this not minimize the frequency at which trough levels fall below the MIC?

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In summary, further research evaluating the practicality of daily TDM, as well as the clinical benefits and cost-effectiveness of TDM compared to routine practice, is encouraged.

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