Reply to Shaz et al

To the Editor—We appreciate the comments from Shaz et al [1] regarding the limitations of our article [2] on the use of exchange transfusion (ET) for severe malaria. We would like to take this opportunity for further discussion considering the differences in recommendations between our article and that of the American Society for Apheresis (ASFA) special issue [3]. The ASFA drew its evidence from a limited pool of literature, mostly case studies. Our recommendations were based on the results of our study and the findings of a comprehensive literature review.

Our study was underpowered, as was mentioned in our article. Given the 1.9% difference in mortality rates, a sample size of 5071 ET patients and 20,284 non-ET patients would have been needed to see a significant difference, but this is not feasibly achieved. In the 25 years of US national surveillance data examined, there were only 176 patients receiving ET for severe malaria.

Further analysis shows that inclusion of missing data does not change our observations. Imputing missing data for 5 ET patients who survived, mentioned as a limitation in the Shaz et al letter, resulted in similar results for survival as when these 5 cases were excluded (odds ratio = 0.87 [95% confidence interval, 0.46–1.63]). To examine the impact of including the 38% of severe malaria cases with missing survival data, we assumed that all ET patients and 84.1% of non-ET patients survived (proportions observed among those with a known survival outcome) and reanalyzed the data with these patients included. There was no significant difference in survival outcomes ($\chi^2 = 1.18; \text{df} = 1; P = .28$). We attempted to control for missing parasite density by matching those with known parasitemia. For those with unknown parasitemia, we matched on clinical criteria to achieve some parity of severity of illness. Furthermore, 1 retrospective cohort study since the Riddle et al meta-analysis found that of patients with parasitemias at >10%, survival among those with ET versus those without ET was not statistically different [4].

Online translation was required for only 8 of the 193 articles, of which 5 had an English-language summary available on PubMed. Of the 3 that did not, 2 were case reports, and the other was a general review of malaria treatment. Therefore, using online translation for those few articles would not have affected the findings of the comprehensive literature review.

ASFA suggests that ET should be a second-line therapy, either as a standalone treatment or in conjunction with other modes of treatment (category II) [3], and cites the Centers for Disease Control and Prevention as recommending ET for the treatment of malaria, which we have since revised [5]. Our data analysis and literature review do not demonstrate any positive impact of ET on mortality. ASFA lacked an evidence-based review of the safety of
ET and the adverse events associated with its use. We suggest that ASFA explicitly include information on the frequency and severity of adverse events associated with ET and revise its recommendation to category IV—disorders in which the published evidence demonstrates or suggests apheresis to be ineffective or harmful.

Note

Potential conflicts of interest. All authors: No reported conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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References


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