

### **American Society for Apheresis Guidelines Support Use of Red Cell Exchange Transfusion for Severe Malaria With High Parasitemia**

TO THE EDITOR—The American Society for Apheresis (ASFA) Special Issue Writing Committee read the article “Exchange transfusion for severe malaria: evidence base and literature review” by Tan et al with much interest [1]. The article concludes that exchange transfusion (ET) is not indicated in the setting of severe malaria. This recommendation contrasts with our evidence-based review, which supports ET as an adjunctive therapy [2]. Tan et al’s conclusion was based on analysis of cases of severe malaria reported to the US National Malaria Surveillance System from 1985 to 2010, supported by a literature review. They used a propensity score matching technique to select and compare 101 individuals with severe malaria who received ET with 314 who did not. The overall mortality rates of those receiving and not receiving ET were 17.8% and 15.9%, respectively, resulting in no statistically significant

association between ET and survival outcomes; however, the study was underpowered to detect a difference in mortality of <10%. The expected difference in the mortality rate between no ET and ET to make it beneficial was set at 4.6% with 15.9% overall mortality. This implies that to consider ET as efficacious, one would need to see a 3-fold decrease in mortality (about 60%).

We would like to highlight differences between these 2 publications, and indicate continued support of our conclusion. First, the vast majority of cases reviewed for the Special Issue had severe malaria and >10% parasitemia. By comparison, Tan et al studied cases of malaria infection plus at least cerebral malaria, renal failure, acute respiratory distress syndrome, severe anemia, parasitemia >5%, acidosis, hypotension, or disseminated intravascular coagulopathy. Their Table 1 reports that parasite density was unknown in >90% of cases [1]. Therefore, the assignment of malarial severity was predominantly based on clinical findings, rather than parasitemia. Given the importance of high parasitemia in the decision to perform ET, and in support of the therapeutic rationale of this modality, the effect of ET on mortality cannot be reliably judged in the absence of this pathological correlate. Next, there is a lack of important data, including the 38% of cases not having survival data (thus not being included in the study), and exclusion of 5 ET cases that resulted in survival. Last, the Special Issue uses literature published in English only, whereas Tan et al used literature published in multiple languages, utilizing an online translating service of potentially unproven accuracy [3].

The study by Tan et al resulted in the revision of the Centers for Disease Control and Prevention's malaria treatment guidelines, in which ET is no longer recommended as an adjunct procedure for the treatment of severe malaria [4]. The recently published Special Issue designates ET (including automated and manual methods) for severe malaria and parasitemia >10% as a category II indication, that is, a disorder for which apheresis is accepted as second-line therapy, either as a stand-alone treatment or in conjunction with other modes of treatment; and assigned a grade 2B recommendation (ie, a weak recommendation with moderate quality evidence) [2]. The Writing Committee continues to support our grade and categorization, given the substantive shortcomings of the study by Tan et al.

## Notes

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