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Transfusion Timing and Volume in African Children with Severe Anemia

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To The Editor

In two articles, Maitland et al. (Aug. 1 issue) report the findings of the TRACT (Transfusion and Treatment of Severe Anemia in African Children) trial, in which they evaluated both the timing of transfusion administration[1] and transfusion volume[2] in children between the ages of 2 months and 2 years with uncomplicated severe anemia. The children in the trials had a history of fever during the illness that brought them to the hospital, and more than 60% hadevidence of malaria. Thus, treatment with anti-malarial agents could have affected the results of these trials.

Since immediate transfusion seemed to be beneficial in febrile patients and malaria-negative patients,[1] a cross-tabulation analysis for co-incidence of fever and malaria would be required. In the transfusion-volume trial,[2] in which the investigators compared two transfusion volumes (20 ml per kilogram of body weight vs. 30 ml per kilogram), among the 39% of children with fever at the time of screening, mortality was higher with the 30-ml volume than with the 20-ml volume. This finding suggests that higher-volume blood

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transfusion would not benefit children with anemia without proper treatment also being provided for infections other than malaria.

The use of pathogen-inactivation techniques would be reasonable for reducing transfusion-transmitted malaria, given the high prevalence of malaria, the high dependency on blood donated by family and friends, and the spread of drug-resistant malaria in the sub-Saharan area. Also helpful would be high-sensitivity malaria screening and establishment of a voluntary registry system for blood donors.[3] In addition, according to the guidelines for red-cell transfusion in children,[4] a whole-blood transfusion of 20 ml per kilogram can increase the hemoglobin level by 2 g per deciliter, which supports the recommendations of the World Health Organization.[5] Taken together, these two articles suggest the importance of treating underlying diseases in children with severe anemia.

The Authors Reply

At screening, all the children in the TRACT trial were tested for malaria by means of rapid diagnostic tests and were then treated if the results were positive. In the two trials, we found no evidence that *Plasmodium falciparum* malaria affected the relative difference in 28-day mortality (the primary end point in both trials) between immediate transfusion and no immediate transfusion (P=0.18 for heterogeneity) or between transfusion with 30 ml per kilogram or 20 ml per kilogram (P = 0.13 for heterogeneity). (Details are provided in Fig. S7 and Fig.S4 of the Supplementary Appendixes accompanying the respective articles.)

Furthermore, malaria positivity did not explain the strong interaction between fever at screening and the effect of the transfusion volume of 30 ml per kilogram on 28-day mortality. Among the children without fever, estimates of benefits regarding mortality at 28 days for the volume of 30 ml per kilogram, as compared with the volume of 20 ml per kilogram, were similar in those with malaria (hazard ratio, 0.66; 95% confidence interval [CI], 0.36 to 1.21) and in those without malaria (hazard ratio, 0.24; 95% CI, 0.10 to 0.53). Among the children with fever, estimates of harms regarding mortality at 28 days were also similar in those with malaria (hazard ratio, 1.99; 95% CI, 0.85 to 4.66) and in those without malaria (hazard ratio, 1.77; 95% CI, 0.75 to 4.18). Finally, in malaria-endemic regions, blood donors (predominantly adults and older children) are largely immune to malaria, so the prevalence of malaria among donors is low (<1.5%).[1] Consequently, the use of costly pathogen-inactivation techniques and high-sensitivity malaria screening is unlikely to add benefit.

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