Indian J Hematol Blood Transfus (July-Sept 2018) 34(3):591–592
https://doi.org/10.1007/s12288-018-0923-3

CORRESPONDENCE

Can Exchange Transfusions Using Red Blood Cells from Donors with Hemoglobin E Trait Prevent or Ameliorate Severe Malaria in Patients with Multi-drug Resistant *Plasmodium falciparum*?

Ryan P. Jajosky[1] · Audrey N. Jajosky[2] · Philip G. Jajosky[1]

Received: 17 October 2017 / Accepted: 15 January 2018 / Published online: 18 January 2018

Dear Editor,

Malaria continues to be a devastating parasitic disease. In 2015, an estimated 212 million new infections caused 429,000 deaths across the world—about 70% of these deaths were children less than 5-years-old [1]. The *Plasmodium falciparum* parasite was responsible for 99% of all deaths [1]. Unfortunately, in 2017, multi-drug resistant strains of *P. falciparum* are spreading throughout the Greater Mekong subregion. Because of multi-drug resistance, new therapeutic options are needed. We recently proposed that a selective or "therapeutically-rational red blood cell exchange" (T-REX) strategy using Southeast Asian ovalocytosis (SAO) RBCs may reduce the morbidity and mortality of patients infected with multi-drug resistant *P. falciparum* malaria [2]. Here we propose an alternative strategy using RBCs with hemoglobin E trait (HbAE), which may be feasible in regions where SAO is not prevalent.

Hemoglobin E (HbE) is a hemoglobin variant caused by a point mutation in codon 26 of the β-globin gene which substitutes lysine for glutamic acid. HbAE is most common in Southeast Asia, especially northeast and eastern India and eastern Thailand [3] where more than 50% of some populations have HbAE [4]. In addition, HbAE is also prevalent in Myanmar, Indonesia, and Malaysia [3]. Fortunately, HbAE protects against severe *P. falciparum* malaria [5] and explains why this variant is common in malaria-endemic regions. HbAE is characterized by microcytosis without anemia and has no clinical significance for carriers. HbAE can be screened-for/diagnosed using high-pressure liquid chromatography (HPLC), acid/alkaline hemoglobin electrophoresis, isoelectric focusing, or DNA-based tests.

Instead of using routine, "standard-issue" RBC units for exchange transfusion to ameliorate severe malaria (by removing infected, cytoadherent RBCs and replacing them with "standard-issue" RBCs), we suggest evaluating the efficacy of selective HbAE-RBC T-REX. In hospitals without an automated RBC-exchange machine, manual RBC exchange can be performed. Fortunately, HbAE RBCs are already commonly and safely used to treat blood loss. Because clinical studies have shown that HbAE-RBCs are protective against severe *P. falciparum* malaria, HbAE-RBC T-REX could prove to be life-saving. Fortunately, HbAE-RBC T-REX is feasible because (1) individuals with HbAE are generally asymptomatic, not anemic, and qualify as blood donors, (2) up to 50% of individuals in regions of India and Thailand have HbAE, and (3) blood banks can identify units as HbAE by testing the donors or a blood-tubing segment for low mean corpuscular hemoglobin (MCV), followed by confirmatory testing. Of course, severely anemic patients could receive HbAE-RBC blood transfusions before undergoing HbAE-RBC T-REX.

Because more than 400,000 *P. falciparum* malaria patients still die each year due to delayed drug administration or multi-drug resistance, non-drug cell therapies warrant serious consideration. Fortunately, compelling clinical data and modern public health infrastructures mean

Ryan P. Jajosky, Audrey N. Jajosky, Philip G. Jajosky have equally contributed to the literature review and manuscript editing/production.

✉ Ryan P. Jajosky
rjajosky@gmail.com

[1] Biconcavity Inc, 1106 Spring Mill Dr. SW, Lilburn, GA 30047, USA

[2] Pathology Department, University Hospitals Cleveland Medical Center, Case Western Reserve University, 11100 Euclid Avenue, Cleveland, OH 44106, USA

that selective HbAE-RBC T-REX can—and should—be evaluated for the prevention or amelioration of severe malaria in high-risk patients in regions where HbAE donor blood is available.

Compliance with ethical standards

Conflict of interest Ryan Jajosky is the CEO and part-owner of Biconcavity Inc. Philip Jajosky is CFO and part-owner of Biconcavity Inc, a biotechnology research and development company exploring drug-linked-erythrocytes. This company does not have any interest in Hemoglobin E or malaria.

References

1. World Health Organization (2016) World malaria report 2016. World Health Organization, Geneva
2. Jajosky RP, Jajosky AN, Jajosky PG (2017) Can exchange transfusions using red blood cells from donors with Southeast Asian ovalocytosis prevent or ameliorate cerebral malaria in patients with multi-drug resistant *Plasmodium falciparum*? Transfus Apher Sci 56:865
3. Colah R, Gorakshakar A, Nadkarni A (2010) Global burden, distribution and prevention of β-thalassemias and hemoglobin E disorders. Expert Rev Hematol 3:103–117
4. Sikdar M (2016) Hemoglobin E in Northeast India: a review on its origin, distribution, migration and health implication. Anthropol Rev 79:241–263
5. Chotivanich K, Udomsangpetch R, Pattanapanyasat K (2002) Hemoglobin E: a balanced polymorphism protective against high parasitemias and thus severe *P. falciparum* malaria. Blood 100:1172–1176