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Association for the Advancement of Blood & Biotherapies

Association Bulletin #23-02

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To: AABB Members

From: Brian Gannon, MBA – President
Debra BenAvram – Chief Executive Officer

Re: Pretransfusion Hemoglobin Thresholds for Chronic Nonemergent Red Blood Cell Transfusions in β Thalassemia

Association Bulletins provide a mechanism for publication of documents approved by the Board of Directors for distribution to individual and institutional members, such as:

- Standards that were adopted after publication of the most recent edition of *Standards*
- Statements of AABB policy intended for distribution to members.
- Guidance, recommendations, and reports that have been developed by AABB Committees or National Office staff for distribution to members.

Summary
In individuals with thalassemia syndromes who are transfusion-dependent, Red Blood Cell (RBC) components should be transfused to maintain pretransfusion hemoglobin levels of 9.5-10.5 g/dL. The higher transfusion threshold in thalassemia is recommended to reduce ineffective erythropoiesis (IE) and symptoms from anemia. This threshold for RBC transfusions in transfusion-dependent thalassemia (TDT) patients is different from the generally recommended transfusion threshold of 7.0 g/dL.

This Association Bulletin, developed by the Transfusion Medicine Section Coordinating Committee (TMSCC), provides background information and recommendations to AABB members regarding the rationale and clinical benefit for maintaining higher hemoglobin levels in chronically transfused patients with thalassemia.

Background
Approximately 1,100 patients with thalassemia are cared for at 10 large thalassemia centers in the United States, while an estimated additional 1,500 patients receive care at other hospitals.

Chronic transfusions are essential for the survival of individuals with severe anemia and marked IE, with patients generally receiving 1-3 RBC components every 2-5 weeks. The goals of transfusion therapy are twofold:

- Correct anemia: to improve the patient's day-to-day functioning and quality of life, as well as to facilitate normal growth and development in children.

- Reduce IE: central to many pathologic features of thalassemia, including changes in skull bones (osteopenia, frontal and parietal bossing, and maxillary hyperplasia), and extramedullary hematopoiesis (splenomegaly, paraspinal masses of hematopoietic tissue).

Although symptomatic anemia can be ameliorated by maintaining hemoglobin levels above 7.0-8.0 g/dL, reducing the consequences of IE requires maintenance of higher hemoglobin levels to suppress endogenous red cell production. Unlike other transfusion-dependent anemias, such as Diamond-Blackfan anemia where IE is not a major component of the disease, patients with thalassemia should be maintained at a higher hemoglobin level to suppress this devastating complication.

Disease-specific tailoring of transfusions is not a novel practice. In patients suffering from sickle cell disease, the goal of achieving hemoglobin S <30% requires an individualized hemoglobin target, often above the general 7.0 g/dL threshold.

With the improved safety of the blood supply and reduced rates of alloimmunization by providing phenotypically matched RBCs for chronically transfused individuals, iron overload remains the major long-term complication of transfusion in thalassemia patients. Although maintaining the hemoglobin at 9.0 g/dL or higher effectively suppresses the increased intestinal absorption of iron seen in non-transfusion-dependent or inadequately transfused patients with thalassemia, chelation therapy is essential to manage iron overload in chronically transfused thalassemia patients.

Recommendations for Transfusion Threshold in Chronically Transfused Patients with Thalassemia

Chronically transfused patients with thalassemia should be managed on a regular transfusion schedule, administered every 2-4 weeks, designed to maintain a pretransfusion hemoglobin level between 9.5 and 10.5 g/dL. This corresponds to a posttransfusion hemoglobin level of 13.0 to 15.0 g/dL. This should adequately reduce IE and maintain appropriate hemoglobin levels to sustain an adequate quality of life and minimize other complications.

In special circumstances, such as rapidly growing children and individuals with evidence of extramedullary hematopoiesis, leg ulcers, or heart failure, higher minimum hemoglobin levels (above 10.0 g/dL) may be maintained for variable periods as needed. These treatment goals should be reviewed on a regular basis. Routinely maintaining hemoglobin levels above 10.5 or 11.0 g/dL may require additional transfusion of blood initially for 1-4 months, but these higher thresholds can usually be maintained with fewer transfusions thereafter.

Additional Recommendations for RBC Transfusions in Thalassemia

For chronically transfused patients who receive a large number of life-sustaining RBC transfusions during their lifetime, it is imperative to maximize the survival of the transfused red cells, minimize the occurrence of transfusion reactions, and prevent alloimmunization as much as possible.

Thus, the following steps are recommended:

- Obtain a red cell genotype (preferred) or extended red cell phenotype for all thalassemia patients who will likely require chronic transfusions.
- Transfuse phenotypically matched RBCs for the following red cell antigens: Rh (D, C, c, E, e) and K.

Note: Few published data are available on the clinical impact, such as hemolytic transfusion reactions or mortality, of providing phenotypically similar RBC units for thalassemia patients.

- Transfuse leukocyte-reduced RBCs.
- Transfuse hemoglobin sickle negative RBCs.
- Although data related to the ideal age / "freshness" of the component are not currently available, transfusion of fresher RBCs may be preferred.
- If patients are to receive a transfusion at another institution, blood bank to blood bank communication is recommended to ensure historical transfusion medicine testing, blood product administration, and transfusion reaction information is relayed.

Note: Irradiation is not routinely required.

In general, patients receive 1-3 RBC components every 2-5 weeks based on body size and desired hemoglobin level. In routine care, higher-volume transfusions are discouraged, but in rare circumstances, patients may require additional transfusions based on their size or logistical considerations, such as when the patient will not have access to transfusion for an extended period. In general, maintaining a steady hemoglobin level is desirable and wide fluctuations with high volumes at longer intervals should be avoided.

Best Practice Recommendations

If chronically transfused patients with thalassemia are maintained with pretransfusion hemoglobin levels between 9.5 and 10.5 g/dL using appropriate phenotypically matched RBCs, complications related to anemia and IE can be reduced. AABB supports optimizing RBC transfusions in this population to achieve this goal.

References and Published Guidelines

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