THALASSEMIA MANAGEMENT CHECKLISTS

Guidelines for Managing Transfusion Therapy for Thalassemia

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PRE-TRANSFUSION HEMOGLOBIN LEVEL	ACTION	RATIONALE
<8.5 g/dL*	• Increase transfusion volume by 15 to 20% for children and by 1 unit for adults; do not exceed 20 ml/kg • Consider scheduling next transfusion 1 week early if patient/family schedule permits • If hemoglobin level consistently in this range, increase frequency of transfusions	This hemoglobin level is well below the target
8.5 to 9.4 g/dL	• Increase transfusion volume by 15 to 20% for children and consider increase by 1 unit for adults; Do not exceed 20 mL/kg per transfusion • If hemoglobin consistently in this range, consider increase frequency of transfusions	This hemoglobin level is below the target
9.5 to 10.5 g/dL**	• Maintain current transfusion volume and frequency: – Typical transfusion volumes are ~15 mL/kg for children (range 10 – 20 ml/kg) and ~2 to 4 units for older children and adults	This hemoglobin level is in the target range
>10.5 g/dL	• Reduce transfusion volume by 15 to 20% • Consider increasing interval between transfusions if hemoglobin consistently in this range	To minimize disruptions to patient/family schedules, it is generally preferred to administer a smaller volume of transfusion rather than postponing transfusion

**If hemoglobin level unexpectedly low, investigate for causes such as recent illness, new red cell antibody, and splenomegaly.*

***This is generally considered the ideal pre-transfusion hemoglobin target range. Some patients may require higher hemoglobin levels due to clinical complications such as heart failure or symptoms as noted below.*

Regular red cell transfusions are indicated in the presence of severe anemia (hemoglobin level <7 g/dL). In addition, regular transfusions should be initiated for clinical complication of ineffective erythropoiesis including facial bone changes (frontal bossing and maxillary hyperplasia), poor growth, and symptomatic extramedullary hematopoiesis. The goal of transfusion therapy in thalassemia is to relieve the anemia and to reduce the ineffective erythropoiesis.

For most patients, it is recommended that the target hemoglobin level be maintained in the 9.5 to 10.5 g/dL range, typically accomplished by administering transfusions every 3 to 4 weeks. This hemoglobin level generally adequately suppresses bone marrow activity and is associated with a reduction in bony abnormalities. In addition, this regimen promotes normal growth and physical activity.[1,2,3,4,5,6] A higher pre-transfusion hemoglobin target may needed in individuals with clinical complications such as heart failure, clinical or laboratory evidence of ineffective erythropoiesis, or fatigue. Maintaining lower pre-transfusion hemoglobin levels (below 9 g/dL) is not recommended because it is associated with increased ineffective erythropoiesis, which can lead to bony deformities, masses of extramedullary hematopoiesis, splenic enlargement, and impair growth and physical functioning.

For patient/family convenience, in general, it is recommended to schedule transfusions at regular intervals, such as every 3 weeks, rather than changing the transfusion schedule based on the pre-transfusion hemoglobin level. Rather, hemoglobin levels outside of the recommended target can be addressed by adjusting the transfusion volume.

Lowering the pre-transfusion hemoglobin level should not be used as a strategy to reduce iron overload. Splenectomy is not generally recommended as a strategy to manage transfusions, given the long-term risks of thrombotic complications and pulmonary hypertension, but may be considered in the setting of a very high transfusion burden (>200 ml/kg/year of pure red cells). Rather, chelation therapy should be titrated to balance the ongoing transfusional iron intake. Higher pre-transfusion hemoglobin levels (11 - 12 g/dL) may be indicated for certain complications such as heart failure or for patients who are symptomatic (such as fatigue, bone pain) at lower hemoglobin levels.

Patients should receive leukoreduced packed red blood cells. A red cell antigen profile (serologic and or molecular typing) should be sent prior to initiating transfusions and patients should receive a product that at a minimum is matched for Rh (Cc,D,Ee) and Kell antigens, the most common antigens implicated in alloimmunization in this patient population.[9] Molecular typing is helpful to predict the red cell antigen phenotype in patients who have recently received transfusion and also aids in the identification of Rh variants.

Supplementary Material:
Findings from Research Studies to Assess Optimal Pre-transfusion Hemoglobin Levels

The goal of transfusion therapy in thalassemia is to relieve the anemia and to reduce the ineffective erythropoiesis, thereby reducing complications of thalassemia. Randomized controlled trials comparing target hemoglobin levels are lacking.

Similarly, long-term observational studies comparing the effects on growth, development, bony changes, extramedullary hematopoiesis and other thalassemia complications of a variety of pre-transfusion hemoglobin levels are not available. Rather, the majority of data regarding optimal pre-transfusion hemoglobin levels are derived from assessing the impact of a different hemoglobin levels on laboratory outcomes, such as the soluble transferrin receptor levels, as a marker of ineffective erythropoiesis.

In general, a pre-transfusion hemoglobin level of 9 to 10 g/dL has been associated with suppression of erythroid activity to one to four times normal. Clinical outcomes, including improved growth and reduction in bony abnormalities have been seen with transfusions targeting a hemoglobin level of 9.0 to 10 g/dL. Maintaining higher hemoglobin levels (>10.5 g/dL) was associated with increased blood consumption and iron loading compared with maintaining hemoglobin levels in the 9 to 10.5 g/dL range, though this unwanted effect seems most pronounced soon after initiation of the higher target level. Lowering the pre-transfusion hemoglobin target (below 9 g/dL) is not recommended as a method to control iron loading.

HEMOGLOBIN (g/dL)	OUTCOMES
> 9	• Erythroid activity suppressed in majority[1]
9 - 10	• Erythroid activity suppressed (1 - 4 X normal)[2]
9 - 10	• Significantly lower blood consumption (iron loading) compared with trough Hb>10[3]
~9.5	• Good growth, regression of bone deformities, and hepatosplenomegaly[5]
10	• Improved growth in 1st decade of life[6]
11 - 12	• Higher pre-transfusion hemoglobin level not associated with increased transfusion requirements • Initial increase in transfusion requirements but returned to prior requirement after 1 - 4 months; normalization of plasma iron turnover[7]
12.3	• Transient increase in blood consumption which subsequently returned to baseline • Better bone marrow suppression (nucleated RBC & reticulocyte count) compared with Hb 10.2 g/dL[8]

References for this checklist can be found online at the Cooley's Anemia Foundation's website: ***www.thalassemia.org/checklists-references****. The Cooley's Anemia Foundation encourages doctors to utilize this information in treating thalassemia patients.*

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