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| **PROTOCOL TITLE:** Kidney and Pancreas Post Transplant: Management of Anemia |
| **APPLICABLE FACILITIES:**[ ] EHC [ ] EDH [ ] EHH [ ] EHI [ ] EHN [ ] EJCH [ ] ELTAC [x] ESJH[x] EUH [x] EUHM [ ] EUHS [ ] EUOSH [ ] EWWH [ ] RJV-ERH [ ] RJV-ESOP [x] TEC/ESA |
| **EFFECTIVE DATE:**  | **ORIGINATION DATE:** 01/03/2018 |

**SCOPE:** These guidelines are to be used by Emory Kidney and Pancreas Transplant clinicians for the management of anemia post transplantation.

**PURPOSE:**

Anemia is a common occurrence after renal transplantation. Multiple causes account for this problem, including:

* **Relative erythropoietin deficiency:** associated with delayed graft function, or chronic graft dysfunction and renal insufficiency.
* **Bone marrow suppression:** Medications (i.e. azathioprine, mycophenolate mofetil, mycophenolic acid, sirolimus, thymoglobulin, and less commonly ACE inhibitors).
* **Infections** (Parvovirus, many viral syndromes and septic episodes)
* **Malignancies:** PTLD, leukemia, etc.
* **Acute or chronic blood loss** (i.e., perioperative, gastrointestinal, return of menstrual cycles, etc.)
* **Hemolysis** (i.e. hemolytic uremic syndrome, prosthetic valves, thrombotic thrombocytopenia purpura, DIC, G6PD deficiency, and medications like sulfonamides, isoniazid, and dapsone)
* **Iron Deficiency**
* **Vitamin B12 and Folate Deficiency**
* **Chronic inflammatory conditions**

**PROTOCOL:**

A comprehensive approach to the diagnosis and management of anemia is beyond the scope of these guidelines, but an initial assessment may include:

**History & Physical:**

Medication review
Complete blood count to assess for other cytopenias

Chemistry to assess for CKD
Stool guaiac
Serum iron, TIBC, TSAT, ferritin and reticulocyte count
Vitamin B12 and Folate levels

LDH and Haptoglobin

Viral Studies

**General guidelines:**

1. Diagnose anemia when Hgb < 13 g/dL in males and Hgb < 12 g/dL in females.
2. Consider ESA therapy if Hgb <10 g/dL – Individualized decision based on rate of fall of Hgb, risk of needing a transfusion and the risks related to ESA therapy and presence of symptoms attributable to anemia.
3. Monitor iron stores every 8-12 weeks and maintain TSAT >30%.
4. Hemoglobin should be monitored initially q2 weeks, later monthly and q3months in maintenance phase-
5. ESA should not be used to maintain Hgb > 11.5 g/dL and should be held temporarily if hemoglobin >13 g/dL.
6. Patients are considered hyporesponsive to ESA if they have not had a response in three months and should be referred to hematology if iron stores are adequate.
7. Monitor for thrombotic complications during ESA therapy.
8. Transfuse only when there is acute severe hemorrhage or unstable coronary artery disease.

**Management of Specific Conditions:**

**Iron deficiency** (see NKF K/DOQI Guidelines, 2012)

In patients with chronic kidney disease, iron deficiency exists if ferritin <500 ng/ml and serum transferrin saturation (TSAT) <30%

*Treatment:*

Oral iron should be used in patients with normal kidney function

If patient is intolerant to oral iron, or non-responsive to oral replacement, intravenous iron may be given: (need to rule out active infection)

* **Iron Sucrose** (Venofer ®) total dose of 1000mg given as increments of 200-300mg IV x 3-4 doses over 2 week period
* **Sodium Ferric** **Gluconate** (Ferrlecit ®) total dose of 1000mg given as increments of 125-250mg IV x 4-8 doses over 2-3 week period

*Follow up:*

Assess Iron stores at 3 month intervals

Assess Iron stores more frequently when initiating or increasing erythropoietin-stimulating agent (ESA) dose, when there is blood loss or when monitoring response after a course of IV iron, and in other circumstances where iron stores may become depleted

**Relative erythropoietin deficiency**

For adult CKD non-dialysis patients with Hgb concentration <10.0 g/dl, erythropoietin-stimulating agent (ESA) therapy should be initiated

Need iron stores within 3 months *prior* to ESA initiation

Monitor hemoglobin every 2 weeks after initiation of ESA therapy:

* Target Hemoglobin 10-11.5 g/dL.
* Discontinue ESA therapy when HgB above 10 g/dL.
* On day of ESA administration, obtain HgB level prior to dose for review unless most recent HgB value is within 14 days and also *after* ESA therapy.

Suggested initial doses are:

* **FIRST LINE: Erythropoietin, Epoetin alfa (Procrit ®, Retacrit®, or Epogen ®)**
	+ 50-100 units/kg once or every 1-2 weeks
	+ 10,000 to 20,000 units every 2 weeks

Adjust **erythropoietin, epoetin alfa** dose every 4 weeks

* If hemoglobin does not increase >1 g/dL after any 4-week period: increase dose by 25%
* If hemoglobin increases > 1 g/dL in any 2-week period or > 2 g/dL in any 4-week period: decrease dose by 25-50% or consider holding therapy
* If hemoglobin is increasing and approaching upper target threshold of 10 g/dL: decrease dose by 25%
* If hemoglobin increase > than 2.5-3 g/dL in any 2-week period, dose should be held or reduced by 50%

If adequate response not achieved over 12 weeks, further increases are unlikely to be of benefit

* **If patient has failed above therapy at 2-3 months, SECOND LINE: Darbepoetin (Aranesp ®)** initial dosing outlined below, conversion from epoetin alfa in table further below:
	+ 0.45 ug/kg qwk or 0.75 ug/kg every 2 weeks
	+ 40-60 mcg sq weekly or every 2 weeks with monitoring of hemoglobin levels every 2 weeks

Adjust **darbepoetin** dose every 2 weeks

* If hemoglobin does not increase > 1 g/dL, increase dose by 25%
* If hemoglobin increases > 1 g/dL in any 2-week period: decrease dose by ≥ 25%
* If hemoglobin increase > than 2.5-3 g/dL in any 2-week period, dose should be held or reduced by 50%
* If adequate response not achieved over 12 weeks, further increases are unlikely to be of benefit

**DOSE CONVERSION TABLE BETWEEN ESA AGENTS**

| **Weekly Epoetin Alfa Dose (units/week)** | **Weekly Darbepoetin Alfa Dosage** |
| --- | --- |
| **Age ≥18 years (mcg/week)** |
| **Note**: Due to the longer serum half-life of darbepoetin alfa, when converting from epoetin alfa, administer darbepoetin alfa once weekly if the patient was receiving epoetin alfa 2 to 3 times weekly and administer darbepoetin alfa once every 2 weeks if the patient was receiving epoetin alfa once weekly. |
| <1,500 | 6.25 |
| 1,500 to 2,499 | 6.25 |
| 2,500 to 4,999 | 12.5 |
| 5,000 to 10,999 | 25 |
| 11,000 to 17,999 | 40 |
| 18,000 to 33,999 | 60 |
| 34,000 to 89,999 | 100 |
| ≥90,000 | 200 |

Recommendation by K/DOQI guidelines to use ESA therapy with great caution, if at all, in CKD patients with active malignancy, a history of stroke, or a history of malignancy

For adult CKD non-dialysis patients with Hgb concentration ≥10.0 g/dl, ESA therapy should not be initiated

Guidelines for the management of anemia in patients with chronic kidney disease have been published by the National Kidney Foundation (NKF K/DOQI Anemia Guidelines, 2006, updated in 2012) which can be accessed through the NKF website.

**Megaloblastic Anemia: (Folate Deficiency)**

*Treatment:*

Start Folic Acid 1mg daily up to a maximum of 5mg daily until hematologic correction

**Pernicious Anemia: (B12 Deficiency)**

*Treatment:*

Vitamin B12 will be repleted either via parenteral or oral supplementation

**RELATED POLICIES / PROCEDURES:**

Kidney and Pancreas Post-transplant Management of Care

**DEFINITIONS:**

N/A

**REFERENCES AND SOURCES OF EVIDENCE:**

1. Kidney Disease: Improving Global Outcomes (KDIGO) Anemia Work Group. KDIGO Clinical Practice Guideline for Anemia in Chronic Kidney Disease. Kidney inter., Suppl. 2012; 2: 279–335
2. Medical Care of the Kidney Transplant Recipient after the First Posttransplant Year. Djamali et al. Clin J Am Soc Nephrol 1: 623-640, 2006
3. National Kidney Foundation: KDOQI Clinical Practice Guidelines and Clinical Practice Recommendations for Anemia in Chronic Kidney Disease. Am J Kidney Dis 47:S1-S145, 2006 (suppl 3).
4. Aranesp (darbepoetin alfa) [product monograph]. Mississauga, Ontario, Canada: Amgen Canada Inc; May 2018.

**KEY WORDS:**

Anemia, kidney transplant, pancreas transplant