Effective Health Care

Biomarkers to Guide Treatment for Iron-Deficiency Anemia in Renal Dialysis Patients Nomination Summary Document

Results of Topic Selection Process & Next Steps

- Biomarkers to guide treatment for iron-deficiency anemia in renal dialysis patients will go forward for refinement as a systematic review. The scope of this topic, including populations, interventions, comparators, and outcomes, will be further developed in the refinement phase.

- When key questions have been drafted, they will be posted on the AHRQ Web site and open for public comment. To sign up for notification when this and other Effective Health Care (EHC) Program topics are posted for public comment, please go to http://effectivehealthcare.ahrq.gov/index.cfm/join-the-email-list1/.

Topic Description

Nominator: Health care professional association

Nomination Summary: The nominator is interested in a systematic review to define the markers that provide the best assessment of iron metabolic status and give optimal results in guiding iron replacement therapy in hemodialysis patients by reducing morbidity and mortality related to the complications of anemia.

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Population(s): Hemodialysis patients, with specific focus on the subgroups of hemodialysis patients treated with erythropoiesis stimulating agents (ESA), or with ESA resistance, malnutrition-inflammation complex syndrome, or other co-morbid conditions such as liver disease or malignancies.

Intervention(s): Content of hemoglobin in reticulocytes and percentage of hypochromic red blood cells. When data are available, evaluation of other novel markers will include erythrocyte zinc protoporphyrin, soluble transferrin receptor, hepcidin, and superconducting quantum interference devices.

Comparator(s): Serum iron, transferrin saturation (TSAT), iron binding capacity, and ferritin.

Outcome(s): Analytic validity and standardization; biological variability; intermediate outcomes including 1) more consistent maintenance of hemoglobin or hematocrit within desired range, 2) decreased use of ESA for maintenance of hemoglobin or hematocrit within the desired range, and 3) most effective interval of testing at the lowest cost; patient-centered outcomes related to optimal treatment of ESA or iron therapy including 1) reduced mortality, 2) reduced morbidity, 3) reduced adverse events, and 4) improved quality-of-life.

Key Questions from Nominator:

1. What are the benefits and associated costs of using hematologic measures such as percentage of hypochromic erythrocytes or reticulocyte hemoglobin content in relation to other measures of iron metabolic status to assess iron deficiency in patients with chronic kidney disease (CKD)?
2. What are the benefits and associated costs of using hematologic measures such as percentage of hypochromic erythrocytes or reticulocyte hemoglobin content in relation to other measures of iron metabolic status for guiding iron replacement therapy in CKD dialysis patients receiving erythropoietin?
3. What are the impacts of the biological variation or analytical variation for laboratory markers of iron status on their reliability in guiding iron replacement therapy?
4. What impact would standardization of these marker tests have on the effectiveness of iron replacement therapy?
5. What laboratory markers or marker combinations are associated with optimal outcomes (maintenance of hemoglobin or hematocrit within the desired range with minimal doses of recombinant erythropoietin) when used in following iron supplementation in the target population?
6. What is the most effective interval in which to measure markers of iron metabolic status to achieve optimal outcomes at the lowest cost?

Considerations

- The topic meets all EHC Program selection criteria. (For more information, see http://effectivehealthcare.ahrq.gov/index.cfm/submit-a-suggestion-for-research/how-are-research-topics-chosen/.)

- Anemia in patients with end-stage renal disease (ESRD) is a risk factor for increased mortality, morbidity, hospitalization, and medical costs. Fatigue, poorer quality of life, and cognitive impairment have also been associated with anemia in these patients. The most frequent cause of anemia in patients with ESRD is erythropoietin deficiency (which can be treated with erythropoietin-stimulating agents (ESAs)), and the second most frequent cause is iron deficiency. Currently, the main impact of anemia in the ESRD population is among incident hemodialysis patients and among prevalent hemodialysis patients who are under responsive to ESAs.

- The two traditional tests used to assess serum iron status are TSAT and serum ferritin. Although both tests are easy to perform, there are some limitations to using these traditional laboratory indicators of iron status. The alternative markers of iron deficiency include content of hemoglobin in reticulocytes and percentage of hypochromic red blood cells. In addition, many new alternative markers for iron status are under investigation.

- In current clinical guidelines, there is no consensus on which combination of iron biomarkers is required, how frequently to test iron-deficiency anemia, and what targets of iron therapy should be achieved, indicating considerable clinical uncertainty. A review in this area could help to inform guideline creation and influence clinical practice decisions.