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NAAC Mission Statement

The National Anemia Action Council, Inc. (NAAC) is dedicated to raising the awareness of health care professionals and the public regarding the prevalence, symptoms, consequences, and undertreatment of anemia.

Anemia Watch Vision

In support of NAAC's mission, the vision of AnemiaWatch is to provide an objective educational resource to health care professionals, and act as a quarterly information liaison in relation to anemia.

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Anemia News

Erythropoietin studies show dramatic improvement in heart failure¹

In a review of different studies on the diverse effects of erythropoietin (EPO) on the cardiovascular system, the authors found descriptions of dramatic improvement in the course of heart failure. EPO receptors are found on cardiac muscle as well as other tissues. New controlled clinical trials on large and diverse groups of patients are warranted.

Ischemic myocardial injury leads to immediate death of some cells and delayed death in others. Animal studies suggest that EPO has an antiapoptotic action that might be responsible rather than the usual hemopoietic function that has been well studied. The effect on cardiac muscle is salvage of cardiomyocytes in acute coronary syndromes that limits the size of a myocardial infarction and improvement of functional recovery.

In this study of heart failure, EPO was used after maximal standard medication had failed. The result was the correction of anemia (Hb<12g/dL), 91.9% reduction in hospital admissions, 5.5% increase in ejection fraction while controls decreased 5.4%, and improvement of NYHA classification in 42.1% of patients. The EPO group demonstrated no deaths versus 4 deaths of 16 patients in the untreated group.

Another study used 5000 U EPO subcutaneously 3 times a week for 3 months with an increase to 10,000 U, along with ferrous gluconate and folate, on the same schedule if the Hb increment was less than 1g/dL in 4 weeks. Those with heart failure treated with EPO had an increase in peak oxygen consumption and exercise duration in a 6-minute walk. There were no thrombotic events or hypertension in the EPO group.

More support for extended dosing using epoetin beta in hemodialysis patients²

A multi-center, prospective, open-label, parallel, randomized control trial (N=203) compared weekly dosing versus every other week dosing of epoetin beta. The observation period of 32 weeks was divided into an 8-week baseline phase after which the patients were randomized on a 1:1 ration into two groups, weekly (group 1w) and every other week (group 2w). A 12-week run-in period followed before a 12-week assessment period ended the study.

Inclusion criteria for adult patients required them to be stable on 6 months hemodialysis with adequate iron stores and treatment with weekly SC epoetin beta in the prior 2 weeks. Exclusion criteria included cardiac failure, hepatic disease, inflammation, other causes for anemia and 5% variation in dry body weight in the last 6 months.

Patients in group 1w continued on their prior treatment dosing. Those in group 2w switched to every other week at the same cumulative dose. Efficacy and safety parameters were evaluated at the end of the study period.

During the assessment period, mean hemoglobin was 11.38 g/dL in group 1w and 11.4 g/dL in group 2w (95% CI). Mean cumulative epoetin beta doses per week were also similar, 71 UI/kg in group 1w and 67.8 UI/kg in group 2w (95% CI). Differences in mean Hb levels and epoetin doses from baseline to assessment were also similar in both arms. There were no significant differences in safety issues between the groups. There were no thrombotic events during the trial.

Anemia News, continued on next page

Web Site Resources for Health Professionals, Patients, and Media

We invite you to visit our web site at WWW.ANEMIA.ORG site for valuable resources, such as a Health Professional Slide Library, Reference Library, Anemia Watch archive, Monograph, categorized answers to Ask the Expert (expert to expert) questions, Patient Education Sheets, and much more.

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Anemia News, continued from cover

First large study of epoetin alfa in children with cancer for anemia, quality of life³

In a large, 16 week, randomized, placebo controlled study (N=222), epoetin alfa (EPO) was given to children with non-myeloid malignancies receiving myelosuppressive chemotherapy. The hypothesis was that by improving anemia, health-related quality of life (HRQOL) issues would also improve

Twenty-seven sites were involved studying anemic children 5- 18 yrs of age with newly diagnosed non-myeloid malignancies excluding brain tumors. Age appropriate HRQOL tests were administered at regular intervals and scores from all domains added to give a total score. The primary endpoint was the comparison of mean change in hemoglobin (Hb) from baseline to final visit.

The EPO-treated group had a greater overall increase in Hb (P=.002) and were more likely to be transfusion free after 4 weeks (38.7% v 22.5%: P=.010). The change in Hb in the EPO group was correlated with the increase change in Pediatric Quality of Life Inventory Generic Core Scales (PedsQL-GCS) scores, but this change was not seen in the placebo group. Mean final values for the HRQOL scores were not significantly different for the groups, nor was mean change of Hb at final visit (1.3 g/dL v 1.0:P=.129). Repeat-measures analysis determined the EPO group had significantly greater increases in Hb than placebo overall (P=.002)

Influencing the correlations between groups may have been a low starting dose (600 U/kg per week) since 60% of the EPO group required an increase dose at 3-4 weeks. Hb endpoints increased significantly over placebo after the increased dose. The placebo group also had a higher use of RBC transfusion (75%) and, in a post-hoc analysis, was less likely to have received high-intensity chemotherapy. These factors may have influenced Hb response. Further studies might be more successful.

Every 2 week epoetin alfa dosing shown to be as effective as weekly in chemo patients⁴

In a 12-week, randomized open-label trial, 80,000 U epoetin alfa was given to patients receiving cycled chemotherapy for non-myeloid cancer every 2 weeks (Q2W) and results, safety and efficacy compared to established dosing of 40,000 U epoetin alfa weekly (QW). Sixty-nine centers were involved and screen-

ing excluded pre-erythropoietic treatment, anemia for other reasons, cell or marrow harvest treatments planned and a life expectancy of less than 6 months. Dosing schedules of epoetin alfa for QW patients were adjust as needed. Q2W patients who had a decrease in Hb >1 g/dL were changed to a QW regimen. No dose increase was used in the Q2W group. Safety was assessed and coded by incidence and severity of the adverse event, lab tests, blood pressure and physical exams. Thrombotic events were classified as to clinical relevance and life-threatening severity. Primary efficacy endpoint was the change from baseline in Hb values at the end of the study.

The mean change in Hb for the Q2W group was 1.6 g/dL and the QW group 1.8 g/dL with a CI of 95% for the per protocol population. Both groups achieved Hb improvement of > 1 g/dL per week from week 5 to 12. The hematologic response rate and time to response were similar.

Evaluations of safety judged 10% of adverse events to be related to the study drug. Diarrhea, nausea and fatigue were the most common complaint. Thrombotic events were 8% for each group. One pulmonary embolism occurred in the Q2W group and 4 cerebral vascular accidents occurred in the QW group. Two were fatal.

This extended dosing period would provide convenience to medical staff and patients and coincide with cyclic, does-dense chemotherapy. Discontinuation of the treatment protocol was consistent with other similar studies of epoetin alfa regimen.

ACE inhibitors slow recovery from anemia following cardiac surgery⁵

Forty male patients of the same age, similar physical condition and with normal or slightly decreased left ventricular function and anemia were separated into two groups 9 days post-cardiac surgery. Post-op cardiac patients frequently have anemia. ACE inhibitors are usually used after heart surgery to treat cardiac function problems such as cardiac overload, reduction of graft thrombosis and ventricular dysfunction. The ACE inhibitor groups have been associated with the interference of erythropoietic response. Enalapril maleate, an ACE inhibitor, was given to the test group. Both groups received normal medications used in the post-op period. Hemoglobin (Hb) and red blood cell (RBC) counts were measured and cardiac function monitored.

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The baseline Hb was 10.65 mg/dL (+/- 0.9 mg/dL) with no significant differences between groups. By study day 16, the Hb difference between groups was 1 g/dL (P=0.012). Hb values had significantly increased by day 8 only in the control group. RBC counts followed a similar pattern. Both groups normalized by the day 60, the end of the study, but the ACE inhibitor group had a persistently lower, though not significant, Hb and red cell counts. The ACE inhibitor group showed a lower mean Hb value and delayed improvement (P<0.04). There were no significant differences between groups in other blood chemistries.

Thirteen of the 20 treated patients showed no increase in Hb by day 8 versus 6 in the control group. The Hb decreased in 9 of the treated group by day 8. The control group had 4 with decreased Hb. Eight of the ACE inhibitor group had persistently lower Hb than the baseline values. Only 2 did so in the control.

Prompt erythropoiesis response is crucial but it is counterbalanced by ACE inhibitors which are useful in post-cardiac surgical patients, particularly in the elderly and those with severe ventricular function. No significant functional differences were noted in this normal or slightly decreased cardiac function study group. Specific clinical trials are needed to evaluate clinical impact of anemia on rehabilitation of patients with more severe ventricular dysfunction.

High-density lipoprotein levels may be increased with long term erythropoietin treatment⁶

Patients with chronic kidney disease (CKD) have a high incidence of cardiovascular disease that may be associated with serum lipid profile changes. Decrease in serum high-density lipoprotein cholesterol (HDL-C) and an increase in other lipid parameters contribute to atherogenic cardiovascular disease. Long-term treatment with erythropoietin may be cardioprotective.

A previous study demonstrated that long-term erythropoietin (EPO) treatment slowed progression of CKD. This nested substudy looked at the influence long-term EPO treatment had on HDL-C in comparison with other lipid changes.

Eighty-eight patients (38 women and 50 men) with non-diabetes related, pre-dialysis CKD were divided into 2 groups. Group 1 was treated with EPO. Group 2 was untreated. The groups were followed for 12 months. Details for eligibility were reported in the previously published randomized study.

The treated patients achieved a significant increase in Hematocrit (Hct) to 30.8%-38% (P<0.001). The Hct in the untreated group was unaltered. Significantly, 12 months after initiation of EPO, group 1 achieved a HDL-C level of 55.9 mg/dL (+/- 8.1mg/dL: P<0.001). There was also a decrease in the atherogenic LDL-C/HDL-C ratio (P=0.0001).

Patient/consumer News

Brisk Walking May Assist in Maintaining Hemoglobin Levels in Women with Breast Cancer Undergoing Radiation Therapy⁷

A team of researchers recently studied 20 women with breast cancer between the ages of 35 and 65 during 7 weeks of radiation therapy, and randomized the patients to 2 treatment groups: 1) One group walked for 20 to 45 minutes 3 to 5 times per week at 50-70% of maximum heart rates; 2) One group did placebo stretching activities 3 to 5 days per week. After measuring serum blood analyses and peak aerobic capacities, it was determined patients participating in moderate intensity aerobic exercise appeared to maintain erythrocyte levels during radiation treatment, whereas patients in the placebo stretching group experienced a decline in erythrocyte levels during the study. The peak VO(2) increased in the exercise group by 6.3% (P = .001) and decreased by 4.6% (P = .083) in the placebo group. In addition, hematocrit levels increased in the exercise group from 12.3 to 12.4 g/dL, compared to a decrease in the placebo group (12.25 to 11.77 g/dL: between group difference P = .009). The researchers concluded, "These findings suggest a safe, economical method to improve fitness and maintain erythrocytes in women during radiation treatment of breast cancer".

Use of multi-nutrient Sprinkles with iron improves hemoglobin indices in children⁸

In a clustered, randomized trial, SprinklesTM containing 12.5, 20, and 30 mg of ferrous fumarate, a similar product with 20 mg of ferric pyrophosphate and 12.5 mg of liquid ferrous sulfate drops were given to 133 Ghanian children aged 6 to 18 mos. Hemoglobin (Hb) indices and serum transferrin were increased and IDA prevalence decreased over an 8 week treatment program, regardless of product used.

The children were considered anemic if Hb was <10.0 g/dl and transferrin receptor concentration was > 8.5 mg/L. Screening for malaria and inflammatory causes for Hb concentrations was done. Hb and serum ferritin were measured at 3 and 8 weeks.

Baseline Hb was in the range of 8.7-9.1 g/dl. At week 8, the range was 10.2-11.0 g/dl (95% CI). Ferritin showed a similar increase. Prevalence of IDA decreased from a baseline of 50-70% across groups to 22-36% with a risk reduction of 28-46%. The difference between groups was not significant. The study suggests that all forms of iron are well absorbed in iron-deficient children even in doses as low as 12.5 mg. Ferrous sulfate drops had low adherence and high side effects such as staining of the teeth.

Patient/consumer News, continued on next page



Ask the Expert

NAAC welcomes clinical questions from health care professionals related to anemia management. Answers will be provided by physicians who are medical experts in the field of anemia. All relevant clinical questions will be posted on the Ask the Expert section of the web site if appropriate, at times via e-mail, and selected questions will be published in Anemia Watch. Please e-mail anemia-related clinical questions to Asktheexpert@anemia.org.

Question 1. What is the prevalence of anemia in females? Do you have different percentiles for different age group? Thank you.

Question 1 NAAC Expert Response: The most recent data on prevalence of anemia community dwelling men and women were those published by Guralnik et al in Blood, 2004, as part of the analysis of the NHANES III study. Anemia was more prevalent in women until age 50, similar in women and men until age 65, and thereafter higher in men. These findings are based on the WHO definition of anemia, however, that definition may be too restrictive for post-menopausal women. Recent studies suggest that women should be considered anemic for Hb < 13 g/dL rather than 12 g/dL.

Question 2. Clinical scenario: Elderly 83-year-old female in residential care with a history of:

- . Breast Cancer and metastases in bone
- . Dementia
- . Diverticulum
- . anti-inflammatory pain relief
- . Hemoglobin 6

Possible causes of severe anemia are:

- . Bone involvement
- . Drug therapy
- . Bleeding from unknown origin

Family and patient adamant that no more intervention (i.e., blood) wanted. They are questioning me on how low a Hb can go, how long it can take and the end of life situation.

Question 2 NAAC Expert Response: Heart attacks may be seen in patients with normal coronary arteries for hemoglobin levels between 5 and 6 g/dL. While sympathizing with the family's decisions, one might consider offering blood transfusion or a trial of erythropoietin and iron in order to prevent an uncomfortable death.

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CME Announcements

NAAC Presented a Free 1 Day CME Symposium: Crossroads of Anemia and Aging on November 15, 2006 in Dallas, TX

The meeting, held the day before the Gerontological Society of America Annual Meeting brought together NAAC experts and members from the medical community to educate health professionals on the importance for appropriate anemia management, and to standardize clinical pathways for anemia detection, workup, management, and therapeutic modalities.

COURSE TOPICS INCLUDED:

- The mechanisms of anemia in older people
- The long term consequences of anemia in older people
- The link of aging, chronic inflammation and anemia
- The link of aging and myelodysplasia

For requests regarding information on future meetings, please write to info@anemia.org

NAAC Clinical Trial of Interest

NAAC is interested in all valid anemia research. Anemia Watch will highlight clinical trials of interest to NAAC. The following information is posted at the public domain: www.clinicaltrials.gov

Iron Supplementation Among Low-Income Postpartum Women
This study is currently recruiting patients.
Verified by Centers for Disease Control and Prevention September 2005

Sponsored by: Centers for Disease Control and Prevention
Information provided by: Centers for Disease Control and Prevention
ClinicalTrials.gov Identifier: NCT00207610

Purpose

Anemia is common among low-income women after they have given birth. Anemia, or low hemoglobin in the blood cells, is usually caused by not having enough iron. Blood cells usually carry oxygen to other parts of the body. Without enough hemoglobin, the ability of blood cells to carry oxygen is decreased. Memory and work may be impaired. The purpose of this study is to evaluate three methods of giving iron to prevent anemia among low-income women after they have given birth.

| Condition | Intervention | Phase |
|-----------|--|-----------|
| Anemia | Behavior: Daily iron supplements of 65 mg a day for 3 months Behavior: Universal anemia screening and treatment Behavior: Selective anemia screening and treatment | Phase III |

MedlinePlus related topics: Anemia

Genetics Home Reference related topics: Anemia

Study Type: Interventional

Study Design: Prevention, Randomized, Open Label, Active Control, Parallel Assignment, Efficacy Study

Official Title: Phase 3 Study of the Prevention of Postpartum Anemia by Three Different Strategies

Further study details as provided by Centers for Disease Control and Prevention:

Primary Outcomes: Anemia at 6 months postpartum

Expected Total Enrollment: 3000

Study start: June 2003; Expected completion: September 2006

Last follow-up: March 2006; Data entry closure: June 2006

Currently the Centers for Disease Control and Prevention recommendations to prevent iron deficiency advocate selective screening and treatment of anemia at about 6 weeks postpartum. However, among some groups, such as low income women, data suggest that anemia and iron deficiency are common. This study aims to evaluate the effectiveness of three strategies to prevent iron deficiency among low income postpartum women in Mississippi.

Comparisons: Clinics will be randomized to one of three strategies: 1) Selective anemia screening and treatment of anemic women, 2) universal anemia screening and treatment of anemic women, or 3) universal iron supplementation of 65 mg a day for three months.

Eligibility

Ages Eligible for Study: 3 Years and above, Genders Eligible for Study: Female

Accepts Healthy Volunteers

Criteria

Inclusion Criteria: postpartum girls and women, 2-6 weeks after birth

age 13 years or more

WIC certified

Exclusion Criteria: sickle cell anemia

Hemoglobin < 7 g/dL

Location and Contact Information

Please refer to this study by ClinicalTrials.gov identifier NCT00207610

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