

투석환자의 빈혈관리 - 심평원 적정성 평가 지표 중심

고대안산병원 인공신장실

한 현 선

투석환자의 빈혈

- 원인인자
적혈구 생성인자(erythropoietin, EPO) 감소.
EPO 합성은 신장의 배설기능이 감소됨에 따라 줄어듦.
- 1.1.3 Diagnosis of anemia:
In the opinion of the Work Group, diagnosis of anemia should be made and further evaluation should be undertaken at the following Hb concentrations:
• <13.5 g/dL in adult males.
• <12.0 g/dL in adult females.

- EPO 투여 시 반응 저하 이유

Functional iron deficiency

- EPO 사용으로 인해 철분 요구량이 증가하면서 철분부족 초래
- Ferritin이 정상이거나 높아도 transferrin 포화도가 낮음

혈액투석 적정성평가 지표

지표명	산출식
Hb 10g/dl 미만인 환자비율	$\frac{\text{Hb} < 10\text{g/dl인 환자수}}{\text{조혈제를 투여 받은 환자수}} \times 100$
철 저장능 증속률	$\frac{\text{철 저장능을 충족한 환자수}}{\text{빈혈이거나 조혈제를 투여 받은 적이 있는 환자수}} \times 100$
철분제 투여율	$\frac{\text{주사용 철분제를 투여 받은 환자수}}{\text{빈혈이거나 조혈제를 투여 받은 적이 있는 환자 중 철 저장능이 떨어진 환자수}} \times 100$

NKF KDOQI Guidelines

- USING ESAs

3.1.1 Frequency of Hb monitoring:

- 3.1.1.1 In the opinion of the Work Group, the frequency of Hb monitoring in patients treated with ESAs should be at least monthly.

3.1.2 ESA dosing:

- 3.1.2.1 In the opinion of the Work Group, the initial ESA dose and ESA dose adjustments should be determined by the patient's Hb level, the target Hb level, the observed rate of increase in Hb level, and clinical circumstances.
- 3.1.2.2 In the opinion of the Work Group, ESA doses should be decreased, but not necessarily withheld, when a downward adjustment of Hb level is needed.

- 3.1.2.3 In the opinion of the Work Group, scheduled ESA doses that have been missed should be replaced at the earliest possible opportunity.
- 3.1.2.4 In the opinion of the Work Group, ESA administration in ESA-dependent patients should continue during hospitalization.
- 3.1.2.5 In the opinion of the Work Group, hypertension, vascular access occlusion, inadequate dialysis, history of seizures, or compromised nutritional status are not contraindications to ESA therapy.

3.1.3 Route of administration:

- 3.1.3.1 In the opinion of the Work Group, the route of ESA administration should be determined by the CKD stage, treatment setting, efficacy, safety, and class of ESA used.
- 3.1.3.2 In the opinion of the Work Group, convenience favors subcutaneous (SC) administration in non-HD-CKD patients.
- 3.1.3.3 In the opinion of the Work Group, convenience favors intravenous (IV) administration in HD-CKD patients.

■ USING IRON AGENTS

3.2.1 Frequency of iron status tests:

In the opinion of the Work Group, iron status tests should be performed as follows:

- 3.2.1.1 Every month during initial ESA treatment.
- 3.2.1.2 At least every 3 months during stable ESA treatment or in patients with HD-CKD not treated with an ESA.

3.2.3 Targets of iron therapy:

In the opinion of the Work Group, sufficient iron should be administered to generally maintain the following indices of iron status during ESA treatment:

- 3.2.3.1 HD-CKD:
Serum ferritin >200 ng/mL AND TSAT >20%, or CHr >29 pg/cell.
- 3.2.3.2 ND-CKD and PD-CKD:
Serum ferritin >100 ng/mL AND TSAT >20%.

• 3.2.4 Upper level of ferritin:

In the opinion of the Work Group, there is insufficient evidence to recommend routine administration of IV iron if serum ferritin level is greater than 500 ng/mL. When ferritin level is greater than 500ng/mL, decisions regarding IV iron administration should weigh ESA responsiveness, Hb and TSAT level, and the patient's clinical status.

• 3.2.6 Hypersensitivity reactions:

In the opinion of the Work Group, resuscitative medication and personnel trained to evaluate and resuscitate anaphylaxis should be available whenever a dose of iron dextran is administered

▪ **Evaluating and Correcting Persistent Failure To Reach or Maintain Intended Hb**

- 3.5.1 Hyporesponse to ESA and iron therapy:
In the opinion of the Work Group, the patient with anemia and CKD should undergo evaluation for specific causes of hyporesponse whenever the Hb level is inappropriately low for the ESA dose administered. Such conditions include, but are not limited to:
- A significant increase in the ESA dose requirement to maintain a certain Hb level or a significant decrease in Hb level at a constant ESA dose.
 - A failure to increase the Hb level to greater than 11 g/dL despite an ESA dose equivalent to epoetin greater than 500 IU/kg/wk.

▪ **3.5.2 Evaluation for PRCA:**

In the opinion of the Work Group, evaluation for antibody-mediated PRCA should be undertaken when a patient receiving ESA therapy for more than 4 weeks develops each of the following:

- Sudden rapid decrease in Hb level at the rate of 0.5 to 1.0 g/dL/wk, or requirement of red blood cell transfusions at the rate of approximately 1 to 2 per week, AND
- Normal platelet and white blood cell counts, AND
- Absolute reticulocyte count less than 10,000/ μ L.

2012 KDIGO guideline

▪ **Use of Iron Agents for Anemia Treatment**

2.1.1: When prescribing iron therapy, balance the potential benefits of avoiding or minimizing blood transfusions, ESA therapy, and anemia-related symptoms against the risk of harm in individual patients (e.g., anaphylactoid and other acute reactions, unknown long-term risks). *(Not Graded)*

• 2.1.2: For adult CKD patients with anemia not on iron or ESA therapy we suggest a trial of IV iron (or in CKD ND patients alternatively a 1-3 month trial of oral iron therapy) if (2C):

- an increase in Hb concentration without starting ESA treatment is desired, AND
- TSAT is 30% and ferritin is 500 ng/ml (500 g/l)

• 2.1.3: For adult CKD patients on ESA therapy who are not receiving iron supplementation, we suggest a trial of IV iron (or in CKD ND patients alternatively a 1-3 month trial of oral iron therapy) if (2C):

- an increase in Hb concentration OR a decrease in ESA dose is desired, AND
- TSAT is 30% and ferritin is 500 ng/ml (500 g/l)

• 2.1.5: Guide subsequent iron administration in CKD patients based on Hb responses to recent iron therapy, as well as ongoing blood losses, iron status test (TSAT and ferritin), Hb concentration, ESA responsiveness and ESA dose in ESA treated patients, trends in each parameter, and the patient's clinical status. *(Not Graded)*

▪ **IRON STATUS EVALUATION**

- 2.2.1: Evaluate iron status (TSAT and ferritin) at least every 3 months during ESA therapy, including the decision to start or continue iron therapy (*Not Graded*)
- 2.2.2: Test iron status (TSAT and ferritin) more frequently when initiating or increasing ESA dose, when there is blood loss, when monitoring response after a course of IV iron, and in other circumstances where iron stores may become depleted (*Not Graded*)

▪ **CAUTIONS REGARDING IRON THERAPY**

- 2.3: When the initial dose of IV iron dextran is administered, we recommend (1B) and when the initial dose of IV non-dextran iron is administered, we suggest (2C) that patients be monitored for 60 minutes after the infusion, and that resuscitative facilities (including medications) and personnel trained to evaluate and treat serious adverse reactions be available.
- 2.4: Avoid administering IV iron to patients with active systemic infections. (*Not Graded*)

▪ **Initiating and Maintaining ESA Therapy**

- 3.3: We recommend using ESA therapy with great caution, if at all, in CKD patients with active malignancy—in particular when cure is the anticipated outcome—(1B), a history of stroke (1B), or a history of malignancy (2C).
- 3.4.3: For adult CKD 5D patients, we suggest that ESA therapy be used to avoid having the Hb concentration fall below 9.0 g/dl (90 g/l) by starting ESA therapy when the hemoglobin is between 9.0-10.0 g/dl (90-100 g/l). (2B)

▪ **ESA MAINTENANCE THERAPY**

- 3.5.1: In general, we suggest that ESAs not be used to maintain Hb concentration above 11.5 g/dl (115 g/l) in adult patients with CKD. (2C)
- 3.5.2: Individualization of therapy will be necessary as some patients may have improvements in quality of life at Hb concentration above 11.5 g/dl (115 g/l) and will be prepared to accept the risks. (*Not Graded*)
- 3.6: In all adult patients, we recommend that ESAs not be used to intentionally increase the Hb concentration above 13 g/dl (130 g/l). (1A)

▪ **Evaluating and Correcting Persistent Failure to Reach or Maintain Intended Hemoglobin Concentration: Frequency of Monitoring**

- 3.12.1: During the initiation phase of ESA therapy, measure Hb concentration at least monthly. (*Not Graded*)
- 3.12.3: For CKD 5D patients, during the maintenance phase of ESA therapy measure Hb concentration at least monthly. (*Not Graded*)

▪ **Evaluating and Correcting Persistent Failure to Reach or Maintain Intended Hemoglobin Concentration : Initial ESA Hyporesponsiveness**

- 3.13.1: Classify patients as having ESA hyporesponsiveness if they have no increase in Hb concentration from baseline after the first month of ESA treatment on appropriate weight-based dosing. (*Not Graded*)
- 3.13.2: In patients with ESA hyporesponsiveness, we suggest avoiding repeated escalations in ESA dose beyond double the initial weight-based dose. (2D)

Management of hemoglobin cycling

- Gentler ESA dose changes and wider Hb target range
- Evaluation of iron deficiency
- Reduction protocol vs. discontinuation protocol in pts with Hb>13g/dL
- Frequent monitoring of Hb levels
- Evaluation of poor responder for correction of anemia

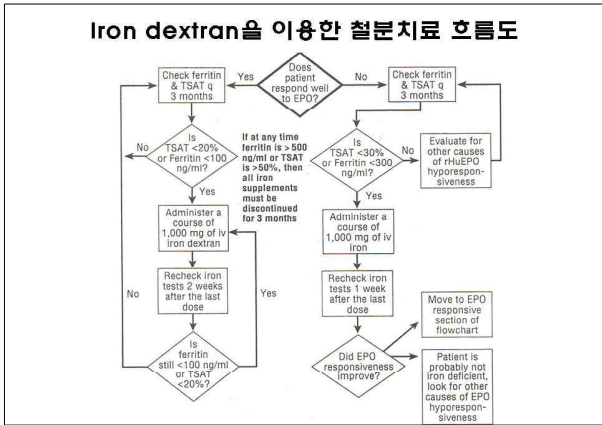
EPO 투여용량

- 초기용량
Hb 또는 Hct을 서서히 증가시켜 2~4개월 후 목표치에 도달하게 하는 용량 설정
- 피하주사 : 80~120U/Kg, 주2~3회
- 정맥주사 : 120~180U/Kg, 주3회
- 첫 투여 또는 용량 증가 후
 - 2~4주동안 Hct이 2% 미만으로 증가하면 EPO 용량 50% 증가
 - 4주동안 Hb이 3g/dL(Hct 8%) 이상 증가했거나 목표치에 도달했다면 EPO 용량 25% 감소

- EPO에 대한 반응과 용량 조절
목표 Hb 또는 Hct 수치에 도달하면 반응 속도에 따라 EPO 용량 조절
- 4주에 8% 이상 증가한 경우 EPO 중단하고 1~2주 후에 원래 용량의 75% 다시 투여하거나 원래 용량을 횡수를 줄여 다시 투여
- 4주에 증가속도가 8% 미만이면 EPO 중단하지 말고 용량을 줄여 계속 사용



- Darbepoetin α
- EPO와 같은 작용을 하여 적혈구의 생성 자극
- EPO보다 분자량이 크고 혈청 반감기가 약 3배로 늘어나 인체에서 작용하는 능력이 커져 투여 횡수를 줄일 수 있게 개발됨 (상품명: aranesp, nesp..)



Reference

- John T. Daugirdas, Peter G. Blake, Todd S. Ing(2001). Handbook of Dialysis. Lippincott Williams & Wilkins.
- 안재영, Laurence Chan(2004). 투석 환자용 가족, 치료팀을 위한 투석 생활. 일조각.
- 김문실 외(2006). 혈액투석 간호. 군자출판사.
- <http://www.kidney.org>
- <http://hdcn.com/crf/anemia>