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Photograph by Daniel Wester

HEMATOLOGIC ABNORMALITIES

Anemia in CKD

A normocytic, normochromic anemia is observed as early as stage 3 CKD and is almost universal by stage 4.

The primary cause is insufficient production of EPO by the diseased kidneys.

TABLE 305-3

Causes of Anemia in CKD

Relative deficiency of erythropoietin

Diminished red blood cell survival

Bleeding diathesis

Iron deficiency due to poor dietary absorption and gastrointestinal blood loss

Hyperparathyroidism/bone marrow fibrosis

Chronic inflammation

Folate or vitamin B_{12} deficiency

Hemoglobinopathy

Comorbid conditions: hypo-/hyperthyroidism, pregnancy, HIV-associated disease, autoimmune disease, immunosuppressive drugs

The anemia of CKD is associated with a number of adverse pathophysiologic consequences, including:

1-decreased tissue oxygen delivery and utilization,

2-increased cardiac output,

3-ventricular dilation,

4-ventricular hypertrophy.

Clinical manifestations include:

- fatigue
- diminished exercise tolerance,
- angina
- heart failure
- decreased cognition and mental acuity
- impaired host defense against infection.

TREATMENT

Anemia

The availability of recombinant human ESA has been one of the most significant advances in the care of renal patients since the introduction of dialysis and renal transplantation.

Its routine use has obviated the need for regular blood transfusions in severely anemic CKD patients, thus dramatically reducing the incidence of transfusion-associated infections and iron overload.

Frequent blood transfusions in dialysis patients also lead to the development of alloantibodies that can sensitize the patient to donor kidney antigens and make renal transplantation more problematic.

Adequate bone marrow iron stores should be available before treatment with ESA is initiated.

Iron supplementation is usually essential to ensure an optimal response to ESA in patients with CKD because the demand for iron by the marrow frequently exceeds the amount of iron that is immediately available for erythropoiesis (measured by percent transferrin saturation), as well as the amount in iron stores (measured by serum ferritin).

For the CKD patient not yet on dialysis or the patient treated with peritoneal dialysis,

oral iron supplementation should be attempted.

If there is GI intolerance or poor GI absorption,

the patient may have to undergo IV iron infusion.

- آزمایش تحمل آهن: Iron Tolerance Test
- دوقرص آهن با معده خالی به بیمارداده میشود وآهن بیماربه صورت سریال تا۲-۳ساعت بعد چک می شود.

- نرمال:حداقل۱۰۰میکروگرم دردسی لیترآهن افزایش یابد.

For patients on hemodialysis,

IV iron can be administered during dialysis,

keeping in mind that iron therapy(IV) can increase the susceptibility to:

1-bacterial infections,

2-the adverse effects of free serum iron are still under investigation.

- دوروش شجهت استفاده از آهن تزریقی وجوددارد:
- ۱)تجویزدوزتوتال آهن موردنیازجهت اصلاح وایجاد حداقل ۵۰۰میلی گرم ذخیره آهن با فرمول زیر:
- Body weight*2/3*(15-patient,s hb)+500mg or1000mg
- ۲)تجویز دوزهای کم ومکرر آهن تزریقی به مدت طولانی که اغلب دردیالیزاستفاده می شود

- آنافیلاکسی درتزریق وریدی هر داروی حاوی آهن ممکن است رخ دهد.

- فاکتورهای مرتبط باواکنش آنافیلاکتیک :
- -سابقه آلرژی های متعدد
- -سابقه واکنش آلرژیک به فرآورده های حاوی آهن

- علایم جنرالیزه زیرممکن است تاچندروزپس ازتزریق دوززیاد آهن ایجاد شود ولی سبب ممنوع شدن استفاده مجدد نمی شوند:
- -آرترالژی
- -راش پوستی
- -تب خفیف

- اگربیماربه دوزبالایی ازآهن نیازداشته باشد(بیش از ۱۰۰mg)این فرآورده بایددرسرم%DW5یا%NS0.9رقیق شود ودرطی ۶۰تا۹۰دقیقه تزریق گردد.

- درصورت ایجادعلایم زیربایدتزریق قطع گردد:
- -دردقفسه سینه
- -ویزینگ
- -هیپوتانسیون
- -سایرعلایم سیستمیک

In addition to iron, an adequate supply of other major substrates and cofactors for red cell production must be ensured, including vitamin B12 and folate.

- فراورده های دارویی موجوددرایران:

۱)اریتروپوئتین Eprex=Epogen

Amp:1000u/ml-2000u/ml-4000u/ml-10000u/ml

20000u/ml

دوز:50-150u/kgسه باردرهفته به صورت وریدی

۲)Feric oxide=Venofer

Amp:20mg/ml

(تا 200mgدرهرتزریق)

۳)آهن خوراکی:-Ferrus sulfate-ferrus foarate-Fefol

Ferfolic-Ferrofort-Easyiron

۴)اسید فولیک:قرص ۱و۵میلی گرمی

Anemia resistant to recommended doses of ESA in the face of adequate iron stores may be due to some combination of the following:

1-acute or chronic inflammation,

2-inadequate dialysis,

3-severe hyperparathyroidism,

4-chronic blood loss or hemolysis,

5-chronic infection,

6-malignancy.

Randomized, controlled trials of ESA in CKD have failed to show an improvement in cardiovascular outcomes with this therapy.

Indeed, there has been an indication that the use of ESA in CKD may be associated with:

- an increased risk of stroke in those with type 2 diabetes,
- an increase in thromboembolic events,
- perhaps a faster progression of renal decline.

Therefore, any benefit in terms of improvement of anemic symptoms needs to be balanced against the potential cardiovascular risk.

Although further studies are needed, it is quite clear that complete normalization of the hemoglobin concentration has not been demonstrated to be of incremental benefit to CKD patients.

Current practice is to target a hemoglobin concentration of 100–115 g/L.

Abnormal Hemostasis:

Patients with later stages of CKD may have:

- a prolonged bleeding time,
- decreased activity of platelet factor III,
- abnormal platelet aggregation and adhesiveness,
- impaired prothrombin consumption.

Clinical manifestations include:

- prolonged bleeding from surgical incisions,
- an increased tendency to bleeding and bruising,
- Menorrhagia,
-GI bleeding.

Interestingly, CKD patients also have a greater susceptibility to thromboembolism, especially if they have renal disease that includes nephrotic-range proteinuria.

The latter condition results in hypoalbuminemia and renal loss of anticoagulant factors, which can lead to a thrombophilic state.

TREATMENT

Abnormal Hemostasis

Abnormal bleeding time and coagulopathy in patients with renal failure may be reversed temporarily with:

- desmopressin (DDAVP),
- cryoprecipitate,
- IV conjugated estrogens,
- blood transfusions,
- ESA therapy.

Optimal dialysis will usually correct a prolonged bleeding time.

Given the coexistence of bleeding disorders and a propensity to thrombosis that is unique in the CKD patient,decisions about anticoagulation that have a favorable risk-benefit profile in the general population may not be applicable to the patient with advanced CKD.

One example is warfarin anticoagulation for atrial fibrillation; the decision to anticoagulate should be made on an individual basis in the CKD patient because there appears to be a greater risk of bleeding complications.

Certain anticoagulants, such as fractionated low-molecular-weight heparin, may need to be avoided or doseadjusted in these patients, with monitoring of factor Xa activity where available.