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A Comprehensive Review on Anemia of Chronic Kidney Disease

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A B S T R A C T

Anemia is a common complication among patients with chronic kidney disease (CKD) and is associated with various factors such as gender, age, body mass index, CKD stage, comorbidity condition, proteinuria, and hypocalcemia. In CKD anemia occurs due to progressive reduction of endogenous erythropoietin levels, iron deficiency, iron-restricted erythropoiesis due to hepcidin. Additionally, CKD restricts erythropoietin production. Other factors include uremic-induced inhibitors of erythropoiesis and reduced red blood cell lifespan. Anemia of CKD is associated with reduced quality of life, increased morbidity and mortality and increased healthcare costs. Understanding the mechanisms and appropriate management of anemia of CKD is crucial for improving patient outcomes and quality of life.

Keywords: Anemia, Chronic Kidney Disease, erythropoietin, erythropoiesis-stimulating agents (ESA's).

1. Introduction

Hemoglobin levels below 12.0 g/dL in non-pregnant women and below 13.0 g/dL in men are considered anemic. In chronic kidney disease (CKD), anemia occurs due to inadequate erythropoietin production by the kidneys and/or dysregulated iron homeostasis[1].

Kidney failure causes numerous changes in the body that destabilize the homeostasis. One of them is erythropoiesis with anemia being the most common complication of kidney disease[2]. It is associated with a decreased quality of life, a worse renal survival increased morbidity and mortality rates[3] and higher healthcare costs[4].

The incidence and prevalence of anemia in chronic kidney disease patients are more significant and its prevalence is associated with renal function. The stages of CKD are also associated with anemia. Patients with CKD stage have more severe anemia[5].

2. FACTORS ASSOCIATED WITH ANEMIA AMONG CKD PATIENTS[6]

- Gender
- Stage of CKD
- Age
- Body Mass Index
- Comorbidity conditions
- Proteinuria
- Hypocalcemia

3. PATHOPHYSIOLOGY

In chronic kidney disease, anemia occurs due to progressive reduction of endogenous erythropoietin production by peritubular interstitial cells of kidney and relative iron deficiency2, 3. Iron and erythropoietin (EPO) plays a crucial role in red blood cell production in the bone marrow. Hepcidin, a liver hormone controls dietary iron absorption and regulates iron availability. In CKD patients, the hepcidin levels are highly elevated due to reduced renal clearance which leads to iron restricted erythropoiesis. CKD also restricts EPO production7. As kidney failure progresses, the erythropoietin (EPO) deficiency becomes more pronounced1. EPO deficiency starts early in the course of CKD but when the GFR rate decreases below 30 mL/min/1.73 m2 it becomes more severe2. Compared to similar anemic patients who has normal kidney function, the levels of EPO are inappropriately low7. Apart from EPO deficiency, circulating uremic-induced inhibitors of erythropoiesis and decreased lifespan of red blood cells also contribute to anemia.

4. SYMPTOMS AND IMPACT OF ANEMIA IN CKD PATIENTS[1, 8, 9]

- Tiredness
- Shortness of breath
- Difficulty in sleeping
- Decreased mental agility
- Gastrointestinal symptoms
- Feeling distressed
- Lack of motivation
- Headache
- Reduced exercise tolerance
- Respiratory distress
- Tachycardia
- Chest pain

The CKD patients with anemia, there is an increased risk of mortality and decreased quality of life.

5. DIAGNOSTIC EVALUATION[1, 10]

Hemoglobin levels < 13.0 g/dL in men and <12.0 g/dL in women is considered as anemia according to WHO and bone marrow examination is considered as the "gold standard" in determination of anemia in CKD patients. Additionally, several other investigations are also done to evaluate anemia in CKD patients such as hematocrit levels, reticulocyte count, serum ferritin levels, TSAT (Transferritin saturation), hepcidin levels, TIBC (Total Iron Binding Capacity), vitamin B12.

6. MANAGEMENT[9, 11]

The management of CKD anemia includes:

- ESAs (short and long acting),
- Oral and intravenous (IV) iron formulations, and
- Red blood cell transfusions when not possible to avoid.

Treatment of anemia of chronic renal disease is directed toward improving renal function (when possible) and increasing red blood cell production. Therefore, erythropoiesis-stimulating agents (ESAs), together with iron supplementation, is the treatment of choice in anemia of CKD.

Recombinant human erythropoietin and darbepoetin alpha are the two ESAs generally used in managing anemia in CKD. They are fairly similar in efficacy and side effect profile, except for the longer half-life of darbepoetin alpha, thus allowing for less frequent dosing.

As per KIDGO guidelines, in patients with CKD who are not on dialysis, ESAs are typically considered when hemoglobin level drops below 10 g/dl. In these patients, erythropoietin (50 to 100 units/kg IV or SC) is usually given every 1 to 2 weeks, and darbepoetin alpha dosing is every 2 to 4 weeks.

In patients on dialysis, ESAs are usually avoided unless the hemoglobin level is between 9 and 10 g/dL. In this subset, erythropoietin is given with every dialysis, i.e., three times a week, whereas darbepoetin alpha is dosed once weekly.

KIDGO recommends target transferrin saturation between 20 to 30% and ferritin level 100 to 500 ng/mL in patients with CKD who are not on dialysis. In patients with ESRD on dialysis receiving intravenous iron, goal transferrin saturation of 30 to 50% and ferritin higher than 200 ng/mL.

7. CONCLUSION

Anemia is a common and significant complication of chronic kidney disease (CKD). It is primarily caused by inadequate production of erythropoietin (EPO) by kidneys and dysregulated iron homeostasis. The severity of anemia is associated with the stage of CKD and various factors such as gender, age, body mass index (BMI) and comorbidity conditions. Anemia in CKD patients leads to range of symptoms, decreased quality of life and increased morbidity and mortality rates. The management of anemia in CKD includes the use of erythropoiesis-stimulating agents (ESA's), iron supplementation and red blood cell transfusion, when necessary.

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