

THE THERAPEUTIC ROLE OF ERYTHROPOIETIN IN ANEMIA: FROM ERYTHROPOIESIS TO CLINICAL PRACTICE

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ABSTRACT

Anemia is a common hematological disorder marked by a drop in red blood cell mass or hemoglobin concentration, which reduces the amount of oxygen that reaches bodily tissues. It continues to be an important worldwide health issue that primarily affects children of young age and women of reproductive stage of life. Numerous factors, such as poor erythropoiesis, persistent infections, inflammatory disorders, and nutritional deficits, contribute to the syndrome. A glycoprotein hormone called erythropoietin (EPO) is secreted by the kidneys and a significant regulator of erythropoiesis. For maintaining sufficient amounts of red blood cells, EPO promotes the growth, development, and survival of red blood cell precursor cells in the bone marrow. The pathophysiology of many types of anemia, including chronic renal disease, inflammatory disorders, chemotherapy-induced anemia, and viral diseases like HIV, is greatly influenced by changes in erythropoietin production or activity. By increasing red blood cell production and lowering reliance on blood transfusions, the formation of recombinant erythropoietin and erythropoiesis-stimulating agents (ESAs) has revolutionized the treatment of anemia. However, as excessive erythropoiesis stimulation might result in consequences such hypertension, cardiovascular risks and thromboembolic events. Biosimilar ESAs and innovative therapy approach like hypoxia-inducible factor prolyl hydroxylase inhibitors, which stimulate endogenous erythropoietin production in a physiologically regulated way, are examples of recent therapeutic advancements. This review provide insight into the global burden of anemia, the mechanisms underlying erythropoiesis and erythropoietin regulation, the link between iron metabolism and RCBs production, and the therapeutic function of erythropoietin and its analogs. It also highlights emerging treatment approaches aimed at improving the safety and effectiveness of anemia management.

Keywords: Erythropoietin, Anemia, Erythropoiesis, Erythrocytes, EPO Therapy

INTRODUCTION

Anemia is the most prevalent hematological disease globally. As stated by World Health Organization (WHO), anemia is a disorder in which RBCs count decreases, which as a result reduces the oxygen-carrying capacity and affects

bodily functions. It is also referred as decreased level of hemoglobin in the blood or mass of erythrocytes and hematocrit. Level of hemoglobin differs according to age and gender, so if these values fall below the developed reference range the condition is diagnosed as anemia (Karagül Yıldız

et al., 2021). Anemia is a worldwide health problem with increasing death rates and occurs most frequently in women of reproductive age about 33% of them are affected, and children below the age of 5. Anemia is divided into different types depending on its origin. Like in nutritional anemia, iron deficiency is considered to be the major cause along with the insufficiency of nutritional elements like folate, vitamin B12, vitamin A, riboflavin, and magnesium. Diseases like HIV, TB, malaria, and hookworm also make the person anemic (Hussien et al., 2023; Turawa et al., 2021). Based on the size of erythrocytes, anemia is divided into three types: microcytic, normocytic and macrocytic anemia (Bhadra & Deb, 2020).

The formation of erythrocytes by the process of cell division and differentiation is called erythropoiesis. Hematopoietic stem cells divide in bone marrow into a series of progenitor cells. First, they form an erythroid burst-forming unit-erythroid (BFU-E) and colony-forming unit-erythroid (CFU-E). They further undergo division and proerythroblast is the very first stage that is distinguishable. Then basophilic, polychromatic, orthochromatic, reticulocyte, and then erythrocytes are formed. Red blood cells are small, hemoglobin-filled, biconcave, enucleated cells in humans and other mammals (Ganz et al., 2023). Mature red blood cells are released into the blood circulation via the barrier of bone marrow. In disease conditions erythrocytes are formed in the liver and spleen as a result of which, reticulated red blood cells containing nucleus appears in the blood however, the process of RBCs maturation is modulated in the genome, but there are some factors that affects the process (Wiciński et al., 2020).

There is an important glycoprotein hormone named erythropoietin secreted by the kidney involved in the regulation of erythropoiesis. Its main function is to deliver enough oxygen to tissues and organs. When there is less oxygen availability either due to hypoxia or decreased hemoglobin level the kidneys detect it and react by increasing the EPO production. The crucial aspect of this regulation is the hypoxia-inducible factor pathway, where HIF is balanced by a low level of

oxygen, resulting EPO transcription and expression. Erythropoietin acts on those target tissues where erythroid progenitor cells and hematopoietic stem cells are located, especially in bone marrow. Erythropoietin attaches to the receptors present on the surface of these cells and a series of intracellular signaling events started. This process is essential for the growth, maturation, and viability of erythroid progenitor cells (Obeagu et al., 2024; Wu et al., 2022).

There is a relationship between iron homeostasis and erythropoiesis. The production of EPO is highly regulated by iron and its regulatory proteins. As iron is important for erythropoiesis in order to produce hemoglobin likewise the process of erythropoiesis speed up iron absorption by producing erythroid hormone called erythroferrone this hormone inhibits the expression of hepcidin. In liver and erythroid cells iron sensor called transferrin receptor is present that regulate the sensitivity of EPO and show connection between hepcidin and erythropoiesis. EPO sensitivity enhanced during EPO reduction in iron deficiency due to the removal of transferrin receptor from cell surface. Anemia occurs due to the imbalance between erythropoiesis and iron and hepcidin in case of lack of iron (Camaschella et al., 2022).

The key function of EPO is to promote the erythropoiesis, which ensures the constant supply of erythrocytes. Because EPO is highly sensitive towards hypoxia, this makes it critical for body's defense system, especially in conditions where oxygen is low. In conditions like respiratory disorder, anemia, and high altitude, the high rate of EPO influences the production of red blood cells so there would be enough oxygen in the blood. The rate of erythropoietin decreases as its stimulus declines when the level of oxygen is maintained. This negative feedback mechanism promises that erythropoiesis is regulated properly according to the oxygen requirements of the body (Obeagu et al., 2024). It is believed that, in infants suffering from hypoxic-ischemic encephalopathy, EPO has neuroprotective affects (Wu et al., 2022). Anemia occurs frequently alongside chronic kidney disease and is linked with possible burden due to reduced patient well-being increase use of

healthcare resources (Hanna et al., 2021). The person having advanced chronic kidney disease particularly those undergoing dialysis there is significant reduction in erythropoietin synthesis and kidney mass. To overcome this deficiency, therapy like use of recombinant human EPO, and iron supplements are used. Erythropoietin stimulating agent, Epoetin alfa can be found under different brand names like Eprex, Procrit and Epogen. Its administration must be complied to a cautious timed schedule because its brief biological activity period depending on its half-life to have balanced hemoglobin level.

The use of ESA is under safety concerns especially its function in the patients that have decreased EPO production. Administration procedures and resistance gauges have been investigated to analyze the safe effects of ESAs in dialysis patients and the disease conditions arising from decreased or increased EPO production also identified. These insights have been helpful in the formation novel therapeutic agents and refining the safe use of ESAs especially in control of blood cancers. Biosimilar products become more affordable as the ESAs patent have expired. These biosimilar are very closely resemble to those ESAs with respect to their analytical structure, pharmacokinetic characteristics and therapeutic efficiency. The development of these biosimilar medicines is approved by European Medicines Agency with specific guidelines that are updated on regular

terms. Hypoxia inducible factors prolyl hydroxylase inhibitor and gene base therapies are emerging therapeutic strategies that regulate body's natural EPO production. The oral medications are highly efficient that enhance erythropoietin levels by physiologically controlled way for example Roxadustat and Daprodustat (Creangă et al., 2025).

The aim of this review is to describe the prevalence and burden of anemia, to explain the process of erythropoiesis and erythropoietin role in red blood cell production, examine the relation between anemia and iron deficiency, proper usage of ESAs and the emerging therapeutic agents to overcome anemia.

Erythropoietin

A glycoprotein hormone called erythropoietin (EPO) is highly significant to regulate erythropoiesis that is the production of (RBCs) in the body. In some cases, such as anemia where the quantity of RBCs is inadequate the application of the EPO therapy has been a widespread practice in the quest to stimulate the formation of red blood cells. This review will discuss the erythropoietin physiology and regulation and its roles in the treatment of various types of anemia with particular attention to its use in chronic kidney disease (CKD), cancer and other blood anemia (Bhushan ET AL., 2025).

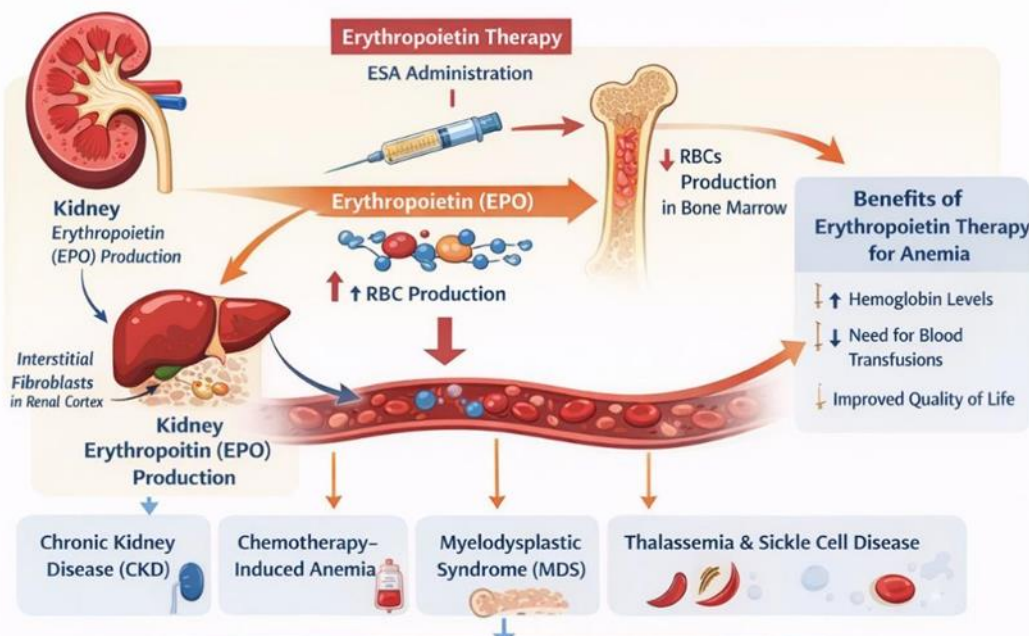


Figure 2: The role of Erythropoietin therapy in treatment of Anemia

Erythropoietin Physiology

The manufacture of erythropoietin occurs mostly in the kidney and in the kidney through special cells called interstitial fibroblasts owing to insufficient oxygen (hypoxia). These are the cells which are located in the renal cortex and are vital as regards to detecting the fluctuations in the supply of oxygen. In case the kidneys realize that oxygen supply is limited they trigger the up-regulation of EPO production. The liver also produces erythropoietin, but in much less amounts compared to the amount produced by the kidneys unless it is in the case of fetal development or pathologies (Jabbar ET AL., 2025).

The erythropoietin production is closely regulated by oxygen in blood. This is done via hypoxia - inducible factor (HIF) pathway. When in normoxic conditions, the HIF transcription factor is oxalated by prolyl hydroxylases (PHDs), and flagellated. However, in a hypoxic condition, the blockade of these PHDs occurs and this leads to stabilization of HIF and subsequent transcription of EPO gene. It is the process that enables the production of the erythropoietin to respond to the low oxygen concentration (Carollo et al., 2025).

Having been produced, erythropoietin binds to some receptors called erythropoietin receptors (EPORs) on the erythroid precursors of the bone

marrow. The communication between EPO and EPORs activates intracellular signaling cascades among them JAK-STAT pathway. This sub-series of signals improves the survival, growth and development of erythroid precursors that lead to increased synthesis of mature RBCs. The systolic erythrocytes turnover and normal erythropoiesis require the availability of erythropoietin, thus (Corwin et al., 2025). A condition in which there is reduction in the number of RBCs or the rate of hemoglobin in the blood which equates to the reduced oxygen supply to the tissues is called anemia. The other causes of anemia are chronic kidney disease, cancer treatment among other blood disorders. In this case, erythropoietin has become an extension and continuation of treatment to cure anemia.

Erythropoietin in Chronic Renal Disease (CKD)

A chronic kidney disease (CKD) is one of the most key causes of anemia and worries a big number of people on the international scale. CKD causes kidney dysfunction that inhibits the potential of the kidneys to synthesize erythropoietin. Through this, there is insufficient stimulation of erythropoiesis and hence anemia. Erythropoiesis-stimulating (ESA) Recombinant erythropoietin (400mg bimodally) is the most common agent of ESA in the management of anemic CKD patients.

Such agents are useful in the correction of the anemia by enhancing the generation of RBCs to make sure that the patients are able to lead a better life. ESAs have also been effective in dialysis patients with CKD who have had a decrease in the rate of blood transfusion (Corwin et al., 2025). Nevertheless, therapy with erythropoietin is to be controlled. Overdose or inappropriate dosage can lead to high hemoglobin level that brings about such complications as high blood pressure, clotting, and heart attacks. In turn, ESA therapy must be founded on the needs of each patient and frequency hemoglobin intake to be made in order to sustain safe and effective dosage (Yin & Noguchi, 2025).

Erythropoietin in Carcinogenic Therapy

The hematopoiesis is suppressed using chemotherapy drugs and therefore cancer patients who are undergoing chemotherapy tend to develop anemia. This is the most prevalent form of anemia that is known as chemotherapy-induced anemia (CIA) and is acquired by cancer patients resulting in fatigue, level of life decrease, and frequent blood transfusion. Recombinant erythropoietin was also indicated to be useful in the management of CIA which encourages the formation of erythrocytes and reduction in the rate of blood transfusion (Yin & Noguchi, 2025). The use of erythropoietin on cancer patients also finds applications to manage the implications of anemia that includes fatigue and weakness that among other things are to deal with the well-being of patients of cancer. Nevertheless, the use of

erythropoietin as a tumor therapy is quite problematic. Some studies have raised concerns that the erythropoietin treatment may encourage the growth of tumors or that the effect of certain treatment interventions used in cancer is impeded by the erythropoietin treatment. In this regard, there is a necessity to weigh the potential benefits and side effects of EPO therapy in cancer patients, and these patients should be adequately selected on this matter and closely monitored (Toniolo et al., 2014).

Blood disorders like thalassemia, sickle cell disease and myelodysplastic syndrome (MDS) had been treated using erythropoietin therapy in order to manage anemia. In patients with MDS, erythropoietin has also been used to promote the production of RBCs therefore reducing the frequency of blood transfusion. However, erythropoietin is not always effective in terms of its response to MDS and does not always respond to the treatment of every patient (Fenaux et al., 2016).

Application of erythropoietin therapy has been used in the case of thalassemia, which is a hereditary blood disorder linked with low production of hemoglobin. Thalassemic patients normally require frequent transfusion of blood over their lives, and erythropoietin has been reported to reduce the same in some cases (Oliviero et al., 2012). This is also applicable to the sickle cell disease which has shown good success with the application of erythropoietin treatment that has enhanced the production of the cells and reduced the impact of anemia.

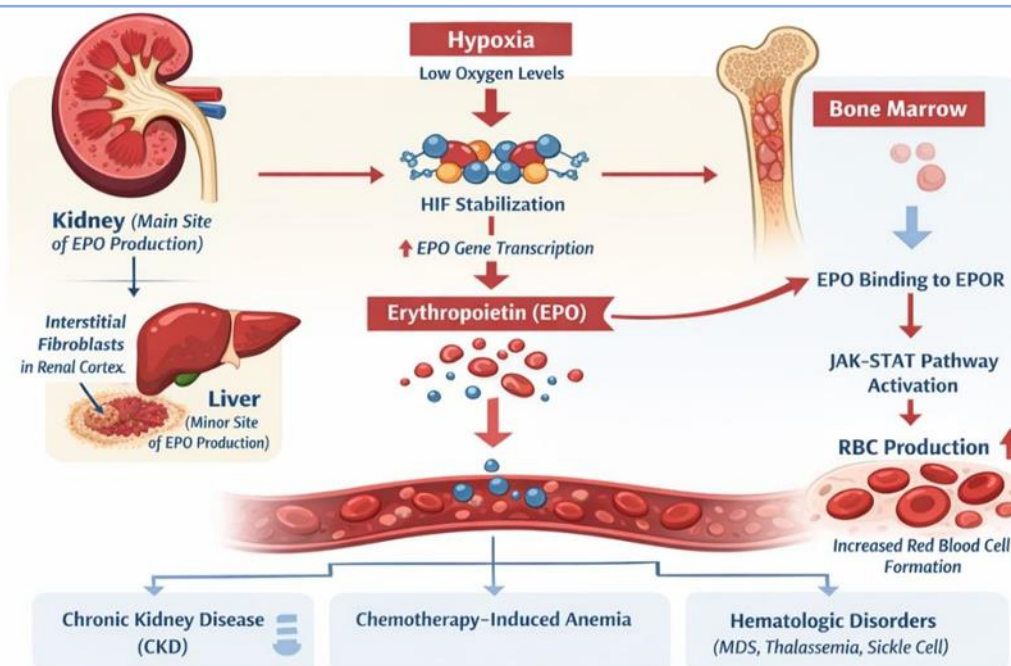


Figure 3: Erythropoietin physiological aspects

Pathophysiology of anemia related to erythropoietin (EPO)

The kidneys make a helper called Erythropoietin or EPO for short. EPO is a kind of hormone that tells the bone marrow to make blood cells. When we do not have oxygen the kidneys release EPO to help make more red blood cells. In some diseases like Chronic Kidney Disease, the kidneys get damaged. The damaged kidneys cannot make EPO. This means the bone marrow does not get the signal to make blood cells. As a result, we have red blood cells and this can cause anemia. Erythropoietin plays a role in this. When the kidneys are damaged, they cannot make EPO. This leads to anemia. A lot of people with severe kidney disease gets anemia. In fact 80 to 90 percent of people, with bad Chronic Kidney Disease get anemia because their kidneys do not make enough Erythropoietin (Bunn, 2013).

The bone marrow has a problem responding to erythropoietin when EPO resistance happens. This is something that people with term diseases and inflammation have to deal with. It is also common in things like Anemia of Chronic Disease. When the body is inflamed it makes cytokines like interleukin-1 and interleukin-6 and tumor necrosis factor-alpha. EPO resistance is a

condition where the bone marrow does not work well with the erythropoietin that's already in the body. These cytokines stop the bone marrow cells that make blood cells from growing. They also get in the way of the EPO receptor signaling in the bone marrow. So even if the EPO levels are normal or high the EPO cannot do its job. Help make more red blood cells, which is called erythropoiesis or the process of making red blood cells and that is because the cytokines interfere with the EPO receptor signaling and the bone marrow cells that make red blood cells the erythroid progenitor cells are not working properly (Ganz & Nemeth, 2015). Inflammation has an impact on the way our body handles iron. This is because of a hormone called hepcidin that the liver produces. When we have much hepcidin it stops our body from absorbing iron from the food we eat. It also prevents iron from being released from the stores in our liver and from cells called macrophages. Iron is really important for making hemoglobin, which's a key part of our red blood cells. So, when this process happens it can lead to a problem where we do not have iron to make red blood cells even if we have enough iron, in our body. This is called iron deficiency. It limits how well a medicine called EPO can help our body make red blood cells. We

often see levels of hepcidin in people who have long term inflammation and kidney disease and this is linked to anemia (Kumar et al., 2021).

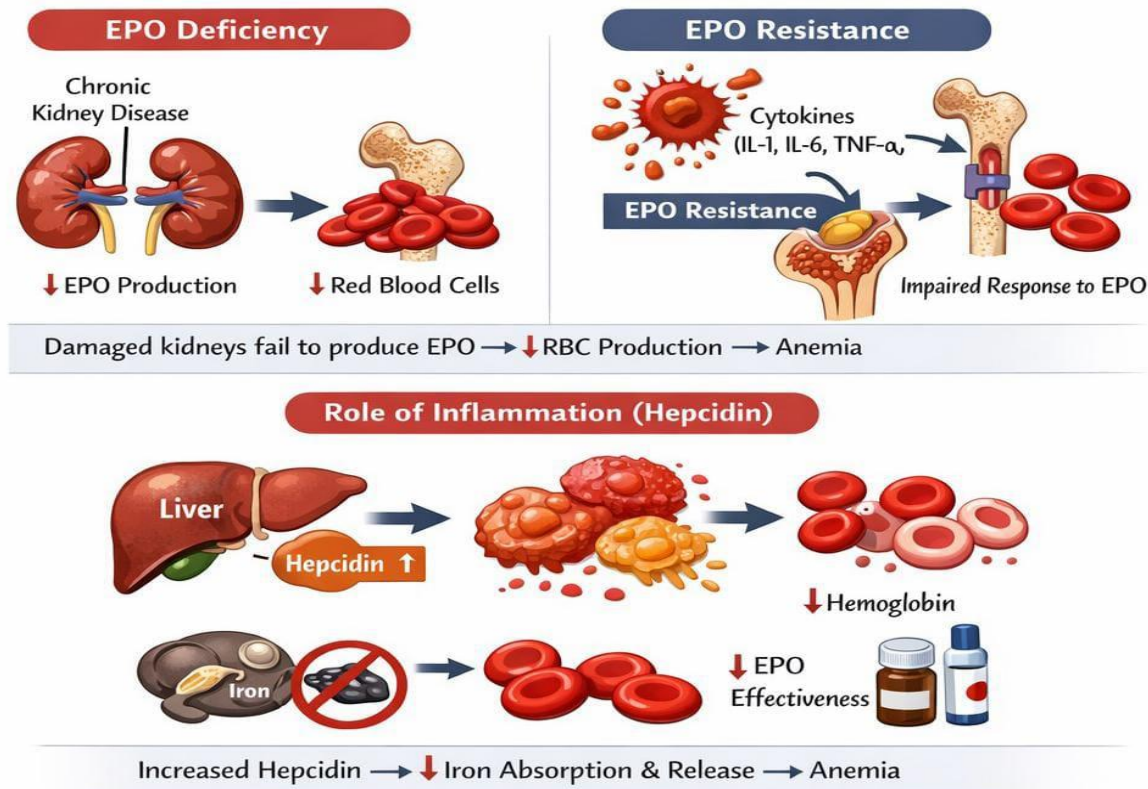


Figure 4: EPO-related mechanisms of anemia

Therapeutic EPO and Its Analogs

Recombinant Human Erythropoietin (rhEPO)

Doctors have done studies that show giving the amount of EPO therapy can help reduce problems that come with very low blood counts like stress on the heart and not enough oxygen getting to the organs. This helps people with blood counts live longer and have better results when their EPO therapy and hemoglobin levels are watched closely. EPO therapy is important for people with anemia because it helps keep them healthy. When people with anemia get the right amount of EPO therapy, they are less likely to have problems like cardiovascular stress and organ hypoxia which is when the organs do not get enough oxygen. This is why EPO therapy is so important for people, with anemia. The medicine rhEPO is mainly used to help people with anemia. This is when you have red blood cells. It helps people with kidney disease, cancer patients who get anemia from

chemotherapy people with HIV who take zidovudine and people with anemia from diseases that cause inflammation. The way rhEPO works is that it attaches to receptors on cells in the bone marrow that make red blood cells. This helps these cells to grow, change and survive. As a result, the levels of hemoglobin in the blood go up. The blood can carry more oxygen. There are a couple of types of rhEPO. These are epoetin alfa and epoetin beta. They work in a way, to the natural erythropoietin that our bodies make (Elliott et al., 2008).

Long-Acting Erythropoiesis-Stimulating Agents (ESAs)

To make treatment work better and be given often special kinds of medicine called long-acting erythropoiesis-stimulating agents (ESAs) have been created. Darbepoetin alfa, Methoxy polyethylene glycol-epoetin beta (CERA), help

make blood cells last longer in the body than the regular epoetin medicine. These ESAs have changes made to their structure or have sugar chains that make them stay in the body longer. This means they can be given weekly or even monthly. This helps patients because they do not have to take medicine often as they would with traditional epoetin. Acting ESAs are often used for patients with chronic kidney disease that are on dialysis and for people with anemia caused by cancer. ESAs help these patients feel better by reducing the need for epoetin injections. Acting ESAs like Darbepoetin alfa and CERA have made treatment easier, for many patients (Macdougall, 2000).

Erythropoietin therapies are usually given through injections because the Erythropoietin hormone would break down if you took it by mouth. You can get Erythropoietin therapies through injection or Intravenous injection. The doctor chooses how to give the Erythropoietin therapies based on the patient's condition, where the patient is being treated and what the doctor thinks is best, for the Erythropoietin therapies (Locatelli et al., 2010). The amount of erythropoietin that a patient needs is figured out by looking at the patient's condition the level of hemoglobin in their blood and how well they are responding to the treatment. Initial dosing, Monitoring, Dose adjustment, Target hemoglobin. The amount of erythropoietin that patients need is different for each person for people with kidney disease that lasts a long-time anemia that is related to cancer or other health problems. Erythropoietin dose requirements are not the same, for every patient because erythropoietin needs can vary a lot from one person to another (Locatelli et al., 2004; AHemii, 2012).

Recommendations on Erythropoietin use in Treatment of Anemia

Even though erythropoietin has proven to be an effective drug used to treat most forms of anemia, its use should be taken into consideration. In order to utilize its therapeutic effect to its maximum and minimize the degree of risks the following recommendations are provided:

Hemoglobin checkups are of great importance in the course of erythropoietin therapy use. Over transfusion of anemia can be accompanied by certain complications such as, increased viscosity of blood, high blood pressure and thrombosis. The level of hemoglobin should therefore be closely monitored to ensure that it is kept to optimal level. The target hemoglobin levels can depend on the medical condition of the patient and the treatment can be modified (Macdougall et al., 2016).

The erythropoietin therapy should be administered in patients with chronic kidney disease, chemotherapy, and other blood-related disorders. However, careful choice of patients should be made. Not all anemic patients are eligible erythropoietin therapy. The patients who do not manage their blood pressure or those with some forms of cancer might not be the best candidates as an example. The choice of a patient, based on the underlying cause of anemia, and one-on-one risk factors, is critical to the success of the treatment (Locatelli et al., 2004).

Threats of using erythropoietin therapy include the development of hypertension, thromboembolisms, and also in a small number of cancer patients, tumor growth. In this way, medical personnel are advised to assess the risks of taking erythropoietin therapy and then proceed with the treatment. Close monitoring of blood pressure levels, hemoglobin level, and overall state of a patient should help reduce these risks. Additionally, the erythropoietin treatment of the patients presenting with adverse reactions, such as high blood pressure or uncontrolled polycythemia, is to be changed or discontinued (Toniolo et al., 2014).

Erythropoietin is an important hormone of the erythropoiesis regulation, and its use as an aid to treatment in chronic kidney disease, cancer and other patients with blood disorders has revolutionized the treatment of the anemia. The recombinant EPO and erythropoiesis-stimulating agents (ESAs) have made significant improvement to the quality of life of the patients as they remove the impacts of blood transfusion and reduce fatigue and weakness among other symptoms related to anemia. However, there should be a

strict observation in erythropoietin therapy to ensure that the potential complications of the therapy such as high blood pressure, thromboembolic and cancer cell growth are avoided. When patients have been selected and risk mitigation measures followed and observed, erythropoietin may provide an effective solution in the process of anemia treatment. (Fenau et al., 2016).

Role of Erythropoietin in Different Type of Anemia

A glycoprotein hormone called erythropoietin that is specifically synthesized in the kidneys when levels in the blood decreases. Its main role is to trigger the bone marrow for the production red blood cells by acting on erythroid progenitor cells. EPO promotes survival, proliferation, and differentiation of these cells, thereby helping to maintain sufficient hemoglobin levels and proper oxygen carrying capacity in the bloodstream (Badura et al., 2024).

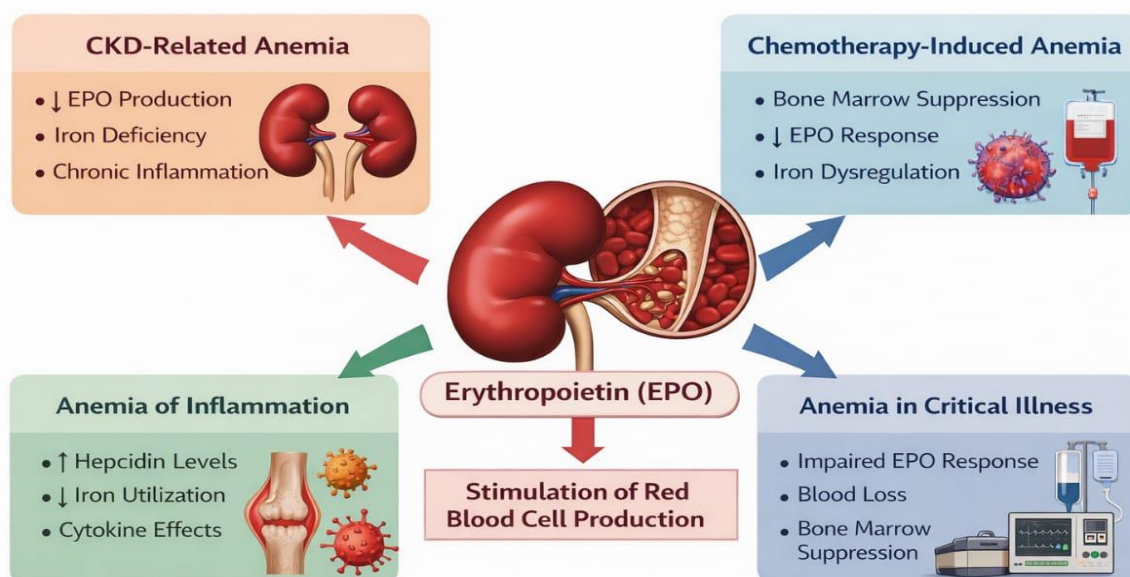


Figure 5: EPO role in different types of anemia

Anemia of Chronic Kidney Disease

Anemia associated with chronic kidney disease is one of the most frequent and significant complications observed in individuals with reduced kidney function, especially when the estimated glomerular filtration rate (eGFR) declines below 30ml/min/1.73m. The major underlying cause of CKD-related anemia is a deficiency of erythropoietin, (EPO) as damage renal tissue fails is unable to produce adequate amount of this hormone. Erythropoietin is essential for stimulating erythroid progenitor cells in the bone marrow and promoting the formation of red blood cell (Badura et al., 2024). Beyond erythropoietin deficiency, abnormalities in iron metabolism and persistent inflammation also play

role significantly in the development of anemia. During chronic inflammatory conditions, increased levels of hepcidin restrict iron release from body stores and decrease its absorption from the intestine. This reduction in available iron further disrupts hemoglobin production and red blood cell formation (Badura et al., 2024). Clinically, anemia in chronic kidney disease (CKD) patients often present with symptoms such as fatigue, reduced exercise capacity, and a declines overall quality of life. It is also linked with serious cardiovascular complications, including left ventricular hypertrophy and a higher risk of mortality (Badura et al., 2024). The treatment of CKD related anemia generally includes the use of agents that stimulate erythropoiesis compensate

for the deficiency of erythropoietin, along with iron supplementation to provide sufficient iron for affective red blood cell production (Badura et al., 2024).

Chemotherapy Induced Anemia

Chemotherapy induced anemia (CIA) is a recurring complication observed in cancer patients undergoing cytotoxic chemotherapy. It happens because anticancer drugs damage rapidly proliferating cells, including hematopoietic stem cells in the bone marrow that produces red blood cells. This inhibition of erythropoiesis results in decreased hemoglobin levels and a reduced the capacity of blood to carry enough oxygen (Bohlius et al., 2019). Another significant factor contributing to anemia induced by chemotherapy is the disturbance of erythropoietin production and iron metabolism. Chemotherapy and tumor associated inflammation can increase the release of inflammatory cytokines, which suppress erythropoietin activity and reduced the responsiveness of the bone marrow to this hormone. Consequently, red blood cell production becomes less effective, ultimately leading to the developing anemia (Ludwig et al., 2013). Clinically, chemotherapy induced anemia may lead to symptoms such as lethargy, weakness, dizziness, and dyspnea, which can greatly reduce the well-being of cancer patients. Treatment approaches generally include transfusions of red blood cells, iron supplementation, and the usage of agents that stimulate erythropoiesis such as recombinant erythropoietin to increase hemoglobin levels and alleviate symptoms associated with anemia (Bohlius et al., 2019).

Anemia in Inflammatory Disorders

Anemia linked to with inflammatory disorders, commonly known as anemia of inflammation or chronic diseased anemia, is a prevalent complication observed in patients with chronic infections, autoimmune diseases, cancer, or other persistent inflammatory conditions. This form of anemia is marked by decreased production of red blood cell and inefficient utilization of iron, even though the body may have normal or elevated iron stores. Inflammatory mediators play a central role

in altering erythropoiesis and iron metabolism, which ultimately leads to decreased hemoglobin levels (Weiss & Goodnough, 2005).

One of the key mechanisms involved in inflammatory anemia is the increased formation of hepcidin, a liver derived hormone that regulates iron metabolism. During inflammation, cytokines such as interleukin-6 stimulate hepcidin synthesis, which blocks iron absorption in intestine and prevents the release of iron from macrophages and liver stores. Consequently, iron becomes less available for the hemoglobin production in the bone marrow, resulting in functional iron deficiency and reduced red blood cell formation (Weiss & Ganz, 2019).

Inflammatory cytokines also directly suppress erythropoietin production and reduce the responsiveness erythroid precursor cells in the bone marrow to EPO stimulation. This leads to decreased red blood cell formation and contributes significantly to the development of anemia in chronic inflammatory diseases. In addition, inflammation may lessen the lifespan of circulating erythrocytes, further worsening anemia (Weiss & Ganz, 2019).

Clinically, anemia in inflammatory disorders is usually mild to moderate and presents with symptoms such as lethargy, weakness, and decreased physical performance. Management focuses primarily on treating the underlying inflammatory conditions, along with supportive therapies such as iron supplementation or erythropoiesis stimulating agents in selected cases to improve hemoglobin levels (Weiss & Ganz, 2019).

Anemia in HIV and Critical Disorders

Anemia is a widespread hematological disorder in individuals infected with human immunodeficiency virus (HIV) and is linked with disease worsening and increased morbidity. In HIV patients the development of anemia is multifactorial and may result from chronic inflammation, nutrient deficiencies, opportunistic infections, bone marrow suppression, and the side effects of antiretroviral or antimicrobial therapies. HIV infections can directly affect the bone marrow microenvironment, impairing

hematopoiesis and reducing the production of red blood cells (Belperio & Rhew, 2004).

Another key factor contributing to anemia in HIV infection is the reduced production and effectiveness of erythropoietin. Persistent immune activation and release of inflammatory cytokines such as tumor necrosis factor (TNF) and interleukin-1 (IL-1) can inhibit erythropoiesis and lower the sensitivity of erythroid progenitor cells to erythropoietin stimulation. Furthermore, opportunistic infections and nutritional deficiencies including iron fate, folate, or vitamin B12 deficiency also contribute a role in the development of anemia among individuals infected with HIV (Belperio & Rhew, 2004).

Anemia is very common among patients with critical illness, especially, those admitted to intensive care units (ICUs). It can develop quickly during severe illness as a result of multiple factors, including systemic inflammation, blood loss due to frequent laboratory testing, decreased production of erythropoietin, and a reduced potential of the bone marrow to produce RBCs effectively. During severe illness, inflammatory cytokines disrupt normal iron metabolism and inhibit erythropoiesis, which results in reduced production of red blood cell (Corwin, Gettinger, & Pearl, 2004).

Moreover, patients with critical illness often show an insufficient erythropoietin response compared with the severity of their anemia, further contributing to decreased red blood cells formation. This reduced hormonal response, along with shorter lifespan of red blood cell and functional iron deficiency, have a great role in the onset and persistence of anemia in critically ill patients (Corwin et al., 2004).

Clinical Benefits of EPO Therapy

Reduced Blood Transfusions

The treatment with human erythropoietin really helps people with anemia because of kidney disease or chronic illness. It does this by helping the body make red blood cells, which is called erythropoiesis. When people get this erythropoietin treatment it increases the amount of hemoglobin in their blood. That helps get more oxygen to the tissues in their body. The

erythropoietin treatment is very good at decreasing the requirement of transfusing blood in patients with anemia due, to kidney disease or chronic illness (Wish, 2021).

Improved Hemoglobin rates and Quality of Life

EPO treatment helps increase hemoglobin rate. For patients with Chronic Kidney Disease (CKD) their hemoglobin levels usually go up from about 7 to 8 grams per deciliter to around 10 to 11 grams per deciliter. This increase, in hemoglobin helps reduce tiredness. As a result, patients can be more active physically. Their overall being and life quality also improve because of EPO therapy (Biggar & Kim, 2017; Block et al., 2004)

Improved Survival Outcomes

Doctors have done research that shows taking the amount of EPO medicine can help people with very low red blood cell counts. This EPO therapy can reduce problems like stress on the heart and organs not getting oxygen. When people take EPO therapy and their red blood cell counts are well managed, they are more likely to survive and get better. This is because EPO therapy helps to make sure the body gets the oxygen it needs. EPO therapy is very important for people, with anemia (Tonelli et al., 2008).

Adverse Effects and Limitations of EPO Therapy Hypertension

Erythropoietin therapy can cause a lot of problems. One of the issues, with erythropoietin therapy is that it can cause high blood pressure. When you take erythropoietin therapy it helps make red blood cells. This can make your blood thicker which is not good. The thick blood can make it harder for your heart to pump blood so your blood pressure goes up. Because of these doctors need to keep an eye on your blood pressure when you are getting erythropoietin therapy. They have to check your blood pressure a lot to make sure it does not get too high. Erythropoietin therapy and high blood pressure are closely linked so your doctor will watch your blood pressure carefully during erythropoietin therapy (Bohlius et al., 2009).

Thromboembolism

The EPO therapy may cause problems with clotting of blood, which also includes deep vein thrombosis, pulmonary embolism and stroke. This happens because the blood gets thicker when there is much hemoglobin in it. The hematocrit and blood viscosity go up. That is a problem when the hemoglobin levels are higher than they should be. Hematocrit and blood viscosity are really important. When hemoglobin levels rise above what is recommended it can cause issues (Bennett et al., 2008).

Conclusion

Anemia is a common health problem that has a big effect on people's health and quality of life. Erythropoietin is very important for regulating erythropoiesis because it helps red blood cells grow, live, and differentiated in the bone marrow. Changes in the production and biological activity of erythropoietin are closely related to different types of anemia, such as anemia that happens with chronic kidney disease, chemotherapy, inflammation, or serious infections. The creation of recombinant erythropoietin and agents that stimulate erythropoiesis has made treating anemia much better. These treatments help raise the level of hemoglobin, boost the production of RBCs, and lower the need for frequent blood transfusions. This all leads to better health outcomes and a better quality of life for patients. Erythropoietin therapy does have some clinical benefits, but it needs to be watched closely because too much stimulation of erythropoiesis can lead to problems like high blood pressure, thromboembolic events, and possible heart problems. Recent improvements in treatment methods, such as bio similar ESAs and hypoxia-inducible factor prolyl hydroxylase inhibitors, open up new possibilities for better managing anemia by increasing the EPO natural formation in a way that is more in line with how the body normally works. These new methods could make treatments more effective while reducing the negative effects that come with traditional treatments. Erythropoietin is still an important part of understanding and treating anemia. Ongoing research into molecular mechanisms,

better dosing strategies, and new therapeutic approaches will help make erythropoietin treatments safer and more effective. This will ultimately lead to better management of anemia in a wide range of clinical settings.

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