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Pharmacotherapeutic management of iron deficiency anaemia in patients with chronic kidney disease: A review

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Abstract

Iron deficiency anaemia (IDA) is one of the most prevalent and clinically significant complications of chronic kidney disease (CKD), contributing to increased morbidity, reduced quality of life, and accelerated disease progression. The pathogenesis of IDA in CKD is multifactorial, involving absolute or functional iron deficiency, inflammation-mediated disruptions in iron homeostasis, and diminished erythropoietin production by the diseased kidneys. Elevated hepcidin levels further exacerbate iron sequestration, impairing erythropoiesis. Effective management of IDA in CKD focuses on replenishing iron stores, optimizing haemoglobin levels, enhancing the efficacy of erythropoiesis-stimulating agents (ESAs), minimizing blood transfusions, and improving patient quality of life. Pharmacological interventions include oral and intravenous iron supplementation, ESAs, and novel agents such as hypoxia-inducible factor prolyl hydroxylase inhibitors (HIF-PHIs), ferric pyrophosphate citrate (FPC), and liposomal iron formulations. Emerging therapies targeting hepcidin pathways and erythroferrone analogs offer promising avenues to address treatment limitations, especially ESA resistance and inflammation-associated anaemia. Despite these advances, therapeutic challenges persist, underscoring the need for individualized, multidisciplinary approaches and continued research into innovative therapies for IDA in CKD.

Keywords: Chronic kidney disease; Iron deficiency anaemia; Hepcidin; ESA resistance; Inflammation

1. Introduction

Chronic kidney disease (CKD) is a global public health problem that affects approximately 10–15% of the adult population worldwide. It is characterized by a gradual and irreversible decline in kidney function, ultimately leading to end-stage renal disease (ESRD) in advanced cases. One of the most common and debilitating complications of CKD is anaemia, with iron deficiency anaemia (IDA) being the predominant subtype [1]. The prevalence and severity of IDA increase as kidney function deteriorates, particularly in patients undergoing dialysis.

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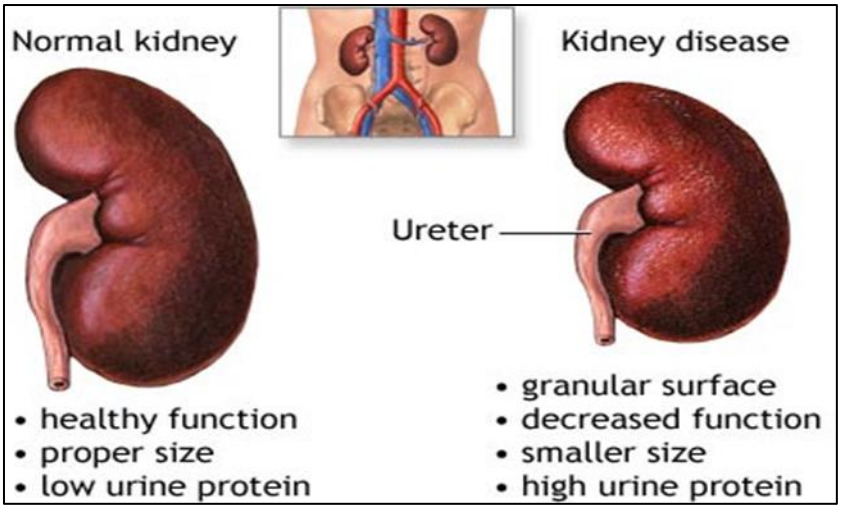

Figure 1 Normal kidney and Chronic Kidney Disease

Iron deficiency in CKD results from a combination of factors, including reduced dietary iron intake, impaired intestinal absorption, chronic blood loss (especially in dialysis patients), and inflammation-mediated disruptions in iron homeostasis. Elevated levels of hepcidin, a key regulator of iron metabolism, play a crucial role in the pathogenesis of iron deficiency in CKD by inhibiting intestinal iron absorption and the release of stored iron from macrophages and hepatocytes. Additionally, CKD is associated with a reduction in erythropoietin (EPO) synthesis by the diseased kidneys, further contributing to the development of anaemia.

IDA in CKD is not merely a laboratory abnormality but is associated with substantial clinical consequences, including fatigue, reduced exercise tolerance, impaired cognitive function, and diminished quality of life. More critically, it increases the risk of cardiovascular disease, accelerates CKD progression, and is linked with higher rates of hospitalization and mortality[2]. As such, effective & timely management of IDA in CKD is a cornerstone of comprehensive patient care.

2. Pathophysiology of IDA in CKD

Iron deficiency in chronic kidney disease (CKD) may be absolute, resulting from inadequate dietary intake, chronic blood loss, or impaired gastrointestinal absorption. Alternatively, it may be functional, wherein iron stores are sufficient but unavailable for erythropoiesis due to inflammation-induced overproduction of hepcidin. Hepcidin, a peptide hormone produced by the liver, plays a central role in iron homeostasis by inhibiting both intestinal iron absorption and the release of iron from macrophages. In CKD, persistent inflammation and reduced renal clearance contribute to elevated hepcidin levels, thereby worsening iron-restricted erythropoiesis.

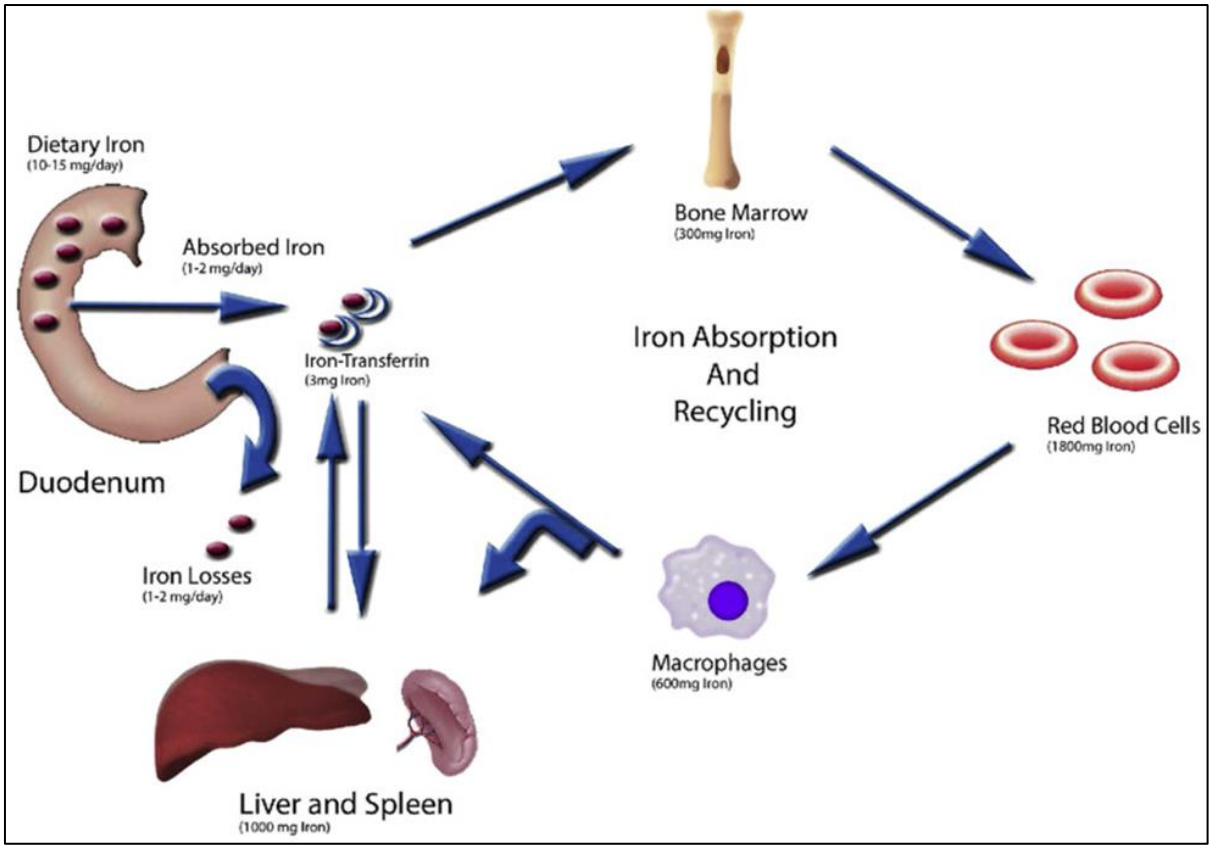

Figure 2 Systemic iron trafficking

Dietary iron is primarily absorbed in the duodenum by enterocytes. Once absorbed, it binds to transferrin, the primary iron-transport protein in the plasma. Transferrin-bound iron is then delivered to the bone marrow for erythropoiesis or to the liver and spleen for storage[3]. Iron is also recycled through the phagocytosis of senescent red blood cells by macrophages, which release iron back into the plasma pool for reuse.

3. Goals of pharmacotherapy in the management of IDA in CKD

Effective pharmacotherapeutic management of iron deficiency anaemia in patients with chronic kidney disease (CKD) is essential to prevent the progression of anaemia-related complications and improve overall clinical outcomes. The treatment goals are multifaceted and aim to address both the underlying iron deficiency and its systemic consequences.

The following are the primary objectives of pharmacotherapy in this context:

3.1. Replenishing Iron Stores

One of the primary goals of pharmacological intervention in CKD-related anaemia is to restore depleted iron reserves in the body. In patients with chronic kidney disease, iron deficiency may be absolute, characterized by a true reduction in total body iron, or functional, where iron is present but sequestered and not readily available for erythropoiesis despite normal or elevated stores[4].

Replenishing iron stores provides the necessary substrate for effective red blood cell production, especially in patients receiving erythropoiesis-stimulating agents (ESAs). This can be accomplished through either oral or intravenous iron supplementation, depending on the severity of the deficiency, the stage of CKD, and individual patient characteristics.

3.2. Increasing Haemoglobin (Hb) Levels

A key therapeutic goal is to raise haemoglobin concentrations to alleviate the clinical manifestations of anaemia, such as fatigue, dyspnoea, and reduced exercise tolerance. Maintaining haemoglobin within the target range, typically 10–12 g/dL as per KDIGO guidelines, is associated with improved functional status and reduced cardiovascular risk. However, care must be taken to avoid overcorrection, which may increase the risk of thromboembolic events and hypertension.

3.3. Enhancing the Efficacy of Erythropoiesis-Stimulating Agents (ESAs)

In patients requiring ESAs to stimulate red blood cell production, adequate iron availability is crucial for optimal response. Iron deficiency, particularly functional iron deficiency, can impair the effectiveness of ESAs, necessitating higher doses and potentially exposing patients to increased adverse effects [5]. Iron supplementation enhances ESA responsiveness, allowing for lower ESA dosages, better cost-effectiveness, and improved safety profiles.

3.4. Minimizing the Need for Blood Transfusions

Blood transfusions are generally reserved for severe or symptomatic anaemia that does not respond to pharmacological therapy. However, transfusions carry risks such as alloimmunization, iron overload, infection transmission, and sensitization, which can complicate future kidney transplantation[6]. By effectively managing iron deficiency and anaemia with pharmacotherapy, the reliance on transfusions can be significantly reduced, thus improving long-term outcomes.

3.5. Improving Symptoms and Quality of Life

Anaemia in CKD patients is often associated with a range of debilitating symptoms, including chronic fatigue, reduced cognitive function, impaired physical performance, and decreased overall quality of life. By correcting iron deficiency and restoring hemoglobin to target levels, pharmacotherapy plays a vital role in alleviating these symptoms. Improved anaemia management is linked with better patient-reported outcomes, increased activity levels, and enhanced emotional well-being.

4. Pharmacological interventions

4.1. Iron Supplementation

Iron supplementation remains the cornerstone of IDA management in CKD. The choice between oral and intravenous (IV) iron depends largely on the severity of anaemia, patient tolerability, iron indices (ferritin and transferrin saturation [TSAT]), and whether the patient is on dialysis.

4.1.1. Oral Iron Therapy

Oral iron is often the first-line therapy for non-dialysis CKD (ND-CKD) patients with mild-to-moderate anaemia. It is inexpensive, easy to administer, and generally safe. Common formulations include ferrous sulfate, ferrous gluconate, and ferrous fumarate. Newer oral agents like ferric maltol and sucrosomial iron offer better tolerability and improved bioavailability. Limitations of oral iron includes poor gastrointestinal absorption (especially in the presence of inflammation), Gastrointestinal side effects (nausea, constipation, abdominal discomfort), Reduced efficacy in advanced CKD or those with ongoing inflammation. Oral iron is generally recommended when TSAT is <20% and serum ferritin is <100 ng/mL in non-dialysis CKD patients[7].

Intravenous Iron Therapy IV iron is preferred in: Patients on haemodialysis (HD), Those with severe anaemia, Individuals intolerant to oral iron, Situations where rapid iron repletion is required. Common IV iron formulations includes Iron sucrose, Ferric gluconate, Ferric carboxymaltose, Iron dextran, Ferumoxytol. IV iron allows for quicker replenishment of iron stores and improved erythropoietic response. However, it must be used cautiously due to risks of hypersensitivity reactions, iron overload, and oxidative stress. Monitoring during IV iron therapy is essential and should include regular checks of serum ferritin and TSAT. According to KDIGO guidelines, IV iron is appropriate when TSAT is <30% and ferritin is <500 ng/mL.

4.2. Erythropoiesis-Stimulating Agents (ESAs)

ESAs stimulate red blood cell production by mimicking endogenous erythropoietin, which is typically deficient in CKD patients. ESAs are often used in conjunction with iron therapy to achieve and maintain target Hb levels. Common ESAs includes Epoetin alfa and beta (short-acting), Darbepoetin alfa (long-acting), Methoxy polyethylene glycol-epoetin beta (very long-acting) and Indications are Persistent anaemia (Hb <10 g/dL) despite iron supplementation, Symptomatic anaemia impacting quality of life and the Dosing Strategy aims to maintain Hb between 10–12 g/dL. [8]. Rapid increases in Hb or levels exceeding 13 g/dL are associated with adverse outcomes, including cardiovascular events and hypertension. Risks associated with ESAs: are Thromboembolism, Hypertension, Pure red cell aplasia (rare), Increased risk of stroke or cancer progression (controversial). Therefore, ESA therapy must be individualized and carefully monitored.

4.3. Hypoxia-Inducible Factor Prolyl Hydroxylase Inhibitors (HIF-PHIs)

HIF-PHIs are a novel class of oral agents used in the treatment of anaemia associated with CKD. These agents function by stabilizing HIFs, which in turn stimulate the production of endogenous erythropoietin. Additionally, HIF-PHIs improve iron metabolism by reducing hepcidin levels and enhancing both iron absorption and mobilization[33]. Notable examples of HIF-PHIs include roxadustat, daprodustat, and vadadustat, enarodustat.

Their key advantages include oral administration, improved iron utilization, effectiveness in patients who are resistant to ESAs, and potential cardiovascular safety benefits in certain populations. However, limitations remain, as these drugs are still under evaluation in long-term clinical trials, and they may pose risks such as hyperkalemia and gastrointestinal disturbances[9].Despite these concerns, HIF-PHIs represent a promising alternative to traditional ESA therapy, particularly in non-dialysis CKD patients and those with ESA hypo responsiveness.

4.4. Monitoring and Individualization of Therapy

Regular monitoring is essential to ensure both the safety and effectiveness of pharmacotherapy in managing iron deficiency anaemia in CKD. Key parameters that should be routinely assessed include haemoglobin levels, which should be monitored every 1–2 months, and iron indices such as serum ferritin and transferrin saturation (TSAT), which should be evaluated every 1–3 months. To prevent iron overload and potential toxicity, excessive iron supplementation must be avoided.

Furthermore, therapy should be individualized based on several patient-specific factors, including the stage of CKD (non-dialysis versus dialysis-dependent), the presence of inflammation, the patient's compliance and tolerability to treatment, and any co-existing cardiovascular disease. Tailoring treatment in this manner helps optimize therapeutic outcomes while minimizing associated risks[10].

4.5. Minimizing Blood Transfusions

Pharmacotherapy should aim to reduce the need for red blood cell transfusions, which carry risks such as iron overload, immunologic sensitization (especially in transplant candidates), and infection. Adequate use of iron therapy and ESAs can help avoid transfusions in most cases[32].

4.6. Improving Patient-Centered Outcomes

Beyond numerical targets, effective anaemia management improves fatigue, cognitive function, physical activity, and overall quality of life. Regular reassessment of symptoms, treatment response, and patient preferences is essential in guiding therapy[11].

5. Monitoring and targets

Effective management of IDA in patients with CKD necessitates regular and comprehensive monitoring to guide therapeutic decisions and ensure patient safety. Key parameters include haemoglobin levels, with a recommended target range of 10–11.5 g/dL[12].Maintaining haemoglobin within this range helps alleviate anaemia-related symptoms while avoiding the risks associated with excessive erythropoiesis, such as hypertension and thromboembolic events.

Monitoring of serum ferritin is also critical. The goal is to maintain ferritin levels at ≥100 ng/mL in non-dialysis CKD (ND-CKD) patients and ≥200 ng/mL in those receiving dialysis[13]. These thresholds help ensure sufficient iron stores to support effective erythropoiesis, especially when erythropoiesis-stimulating agents (ESAs) are used.

Transferrin saturation (TSAT), which reflects the availability of iron for erythropoiesis, should be maintained at ≥20%. A TSAT below this threshold suggests inadequate iron delivery to the bone marrow, warranting iron supplementation[14].

Additionally, monitoring inflammatory markers such as C-reactive protein (CRP) is important, as inflammation can impair iron utilization and affect the response to therapy[15].Elevated CRP may indicate functional iron deficiency due to hepcidin-mediated iron sequestration, even in the presence of adequate iron stores.

Ultimately, treatment decisions should be individualized, taking into account the stage of CKD, iron indices, the presence of inflammation, and patient-specific factors such as comorbidities and treatment tolerance. Clinicians must carefully balance the benefits of correcting anaemia against potential risks, particularly the heightened risk of cardiovascular

complications associated with overtreatment. A patient-centered, evidence-based approach to monitoring ensures optimal outcomes and minimizes harm[16].

6. Clinical guidelines

The pharmacotherapeutic management of iron deficiency anaemia (IDA) in patients with chronic kidney disease (CKD) is guided by several international clinical guidelines. These guidelines aim to standardize care while allowing flexibility for individual patient needs. The Kidney Disease: Improving Global Outcomes (KDIGO) guidelines recommend initiating a trial of oral iron supplementation in non-dialysis CKD (ND-CKD) patients[17].For patients undergoing dialysis or those who exhibit intolerance or inadequate response to oral iron, intravenous (IV) iron is preferred due to its superior efficacy in replenishing iron stores and improving haemoglobin levels.

The National Institute for Health and Care Excellence (NICE) in the United Kingdom advocates the use of IV iron in patients with low serum ferritin and transferrin saturation (TSAT), especially those requiring high doses of erythropoiesis-stimulating agents (ESAs) [18].This approach aims to optimize the response to ESAs by ensuring sufficient iron availability for erythropoiesis. Similarly, the Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines support the use of ESAs in conjunction with adequate iron supplementation. They emphasize the importance of individualized haemoglobin targets, rather than a one-size-fits-all approach, to reduce the risk of adverse events such as cardiovascular complications and stroke[19].

7. Challenges in therapy

Despite advancements in treatment options, the management of IDA in CKD patients continues to face several significant challenges. One of the most common issues is non-adherence to oral iron therapy, often due to gastrointestinal side effects such as nausea, constipation, and abdominal discomfort. These adverse effects can significantly reduce patient compliance and limit the effectiveness of treatment[20]. Another concern is the overuse of IV iron, which, while effective, can lead to iron overload and associated complications, including oxidative stress and increased risk of infections. Careful monitoring of iron indices is essential to mitigate these risks.

ESA resistance, particularly in patients with chronic inflammation or co-morbid conditions, presents another therapeutic obstacle. Inflammatory states can suppress the bone marrow response to ESAs and hinder iron utilization, complicating anaemia management. In such cases, higher doses of ESAs may be required, which in turn increases the risk of adverse effects. Additionally, the limited availability and high cost of hypoxia-inducible factor prolyl hydroxylase inhibitors (HIF-PHIs) in certain healthcare settings restrict their widespread use, despite their promising benefits in improving iron metabolism and reducing ESA dependency[21].To address these challenges, patient education and multidisciplinary management involving nephrologists, nurses, dietitians, and pharmacists are essential. Educating patients about the importance of adherence, dietary considerations, and the risks and benefits of various treatments can empower them to participate actively in their care. A collaborative, individualized approach remains the key to optimizing outcomes in the management of IDA in CKD[22].

8. Novel therapies in iron deficiency anaemia in patients with CKD

In recent years, research into iron deficiency anaemia (IDA) in chronic kidney disease (CKD) has led to the development of several novel therapies aimed at overcoming limitations associated with traditional treatments such as oral iron, intravenous (IV) iron, and erythropoiesis-stimulating agents (ESAs). These new approaches target both iron metabolism and erythropoiesis regulation, offering more effective, convenient, and potentially safer options for patients with CKD[23].

8.1. Hypoxia-Inducible Factor Prolyl Hydroxylase Inhibitors (HIF-PHIs)

Mechanism of Action: HIF-PHIs work by stabilizing hypoxia-inducible factors (HIFs), which promote the endogenous production of erythropoietin and enhance iron metabolism. They reduce hepcidin levels, thereby improving iron absorption and mobilization from body stores[24]. Examples: Roxadustat, Daprodustat, Vadadustat, Enarodustat

8.1.1. Advantages

- Oral administration offers improved patient convenience and adherence.
- Effective in patients with ESA resistance or inflammation-related anaemia.
- Enhance iron utilization and reduce the need for IV iron.

8.1.2. Limitations:

- Long-term safety and cardiovascular outcomes are still under investigation.
- May cause side effects such as hyperkalemia, elevated liver enzymes, and gastrointestinal symptoms.

HIF-PHIs are particularly promising in non-dialysis CKD patients and in those with inadequate response or intolerance to ESAs[25].

8.2. Ferric Pyrophosphate Citrate (FPC)

- Mechanism of Action: FPC is a water-soluble iron salt designed for continuous iron delivery. It bypasses the reticuloendothelial system and delivers iron directly to transferrin, reducing the risk of iron sequestration and overload[26].
- Route: Administered via dialysate during haemodialysis or as an IV infusion.

8.2.1. Benefits:

- Lower risk of oxidative stress and inflammation compared to traditional IV iron.
- No need for separate iron infusions during dialysis sessions.
- Provides steady, low-dose iron replenishment.

8.2.2. Limitations:

- Currently limited to use in dialysis-dependent CKD patients.
- Requires specialized delivery systems[27].

8.3. Liposomal Iron Formulations

- Mechanism of Action: Liposomal iron encapsulates iron in a phospholipid bilayer, improving gastrointestinal tolerance and bioavailability[28].

8.3.1. Advantages:

- Better GI tolerability compared to conventional oral iron salts.
- Reduced gastrointestinal side effects such as constipation, nausea, and metallic taste.
- Enhanced iron absorption and lower risk of mucosal irritation.

8.3.2. Limitations:

- Higher cost than standard oral iron supplements.
- Limited availability in some regions[29].

8.4. Hepcidin Antagonists and Modulators (Under Investigation)

Hepcidin plays a key role in iron regulation and is often elevated in CKD due to chronic inflammation. Novel agents targeting the hepcidin pathway aim to improve iron availability by:

- Reducing hepcidin production
- Blocking hepcidin activity
- Inhibiting pathways like IL-6 that induce hepcidin synthesis[30].

Examples under research:

- Anti-hepcidin antibodies
- IL-6 inhibitors (e.g., ziltivekimab)
- TMPRSS6 agonists to suppress hepcidin

These therapies are still in clinical trial phases but hold significant promise for addressing functional iron deficiency in CKD patients.

8.5. Transferrin Modulators and Erythroferrone Analogs (Emerging Research)

Erythroferrone, a hormone released by erythroblasts, suppresses hepcidin production in response to erythropoietic demand. Therapeutic analogs or strategies to enhance erythroferrone action may aid in increasing iron availability and supporting erythropoiesis, particularly in ESA-resistant anaemia[31].This area of research is still experimental but reflects the growing interest in fine-tuning iron regulation beyond conventional therapies.

9. Conclusion

IDA is a common and serious complication of CKD, driven by reduced erythropoietin production, inflammation, and impaired iron metabolism. Effective management requires replenishing iron stores, optimizing haemoglobin levels, and minimizing transfusion needs. Standard treatments include oral and intravenous iron supplements and ESAs, though limitations such as poor absorption, gastrointestinal side effects, and ESA resistance persist. Recent innovations—like HIF-PHIs, ferric pyrophosphate citrate, and liposomal iron—offer improved efficacy and tolerability, particularly for patients unresponsive to traditional therapies. Emerging therapies targeting hepcidin and iron-regulatory pathways show promise in overcoming functional iron deficiency. Clinical guidelines advocate for individualized, closely monitored treatment plans, with regular assessment of haemoglobin, ferritin, and transferrin saturation. A patient-centered, multidisciplinary approach is essential to achieving optimal outcomes, enhancing quality of life, and reducing long-term risks associated with anaemia in CKD.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

References

[1] KDIGO Clinical Practice Guideline for Anemia in Chronic Kidney Disease. Kidney Int Suppl. 2012;2(4):279-335.

[2] Babitt JL, Lin HY. Mechanisms of anemia in CKD. J Am Soc Nephrol. 2012;23(10):1631-4.

[3] Perusomula RS, Paturi G, Sarkar A, Theja BV, Raja H, Rohini K. Diabetic nephropathy: pathogenesis, clinical features, and emerging therapeutic strategies. Int J Multidiscip Res. 2025;7(4):8.

[4] Macdougall IC, Bircher AJ, Eckardt KU, et al. Iron management in chronic kidney disease: conclusions from a KDIGO Controversies Conference. Kidney Int. 2016;89(1):28-39.

[5] Locatelli F, Bárány P, Covic A, et al. Kidney Disease: Improving Global Outcomes guidelines on anaemia management in chronic kidney disease: a European Renal Best Practice position statement. Nephrol Dial Transplant. 2013;28(6):1346-59.

[6] KDOQI Clinical Practice Guideline and Clinical Practice Recommendations for Anemia in CKD. Am J Kidney Dis. 2006;47(5 Suppl 3):S11-145.

[7] Coyne DW. Iron indices: what do they really mean? Kidney Int Suppl. 2006;69:S4-8.

[8] Fishbane S, Pollack S, Feldman HI, et al. Iron indices in chronic kidney disease: usefulness in diagnosis and treatment. Am J Kidney Dis. 2009;54(4):861-74.

[9] Chen N, Hao C, Liu BC, et al. Roxadustat for anemia in patients with kidney disease not receiving dialysis. N Engl J Med. 2019;381(11):1001-10.

[10] Chertow GM, Pergola PE, Farag YMK, et al. Vadadustat in non-dialysis-dependent CKD. N Engl J Med. 2021;384(17):1589-600.

[11] Barratt J, Andric B, Tataradze A, et al. Roxadustat for the treatment of anemia in chronic kidney disease patients not on dialysis: a Phase 3, randomized, double-blind, placebo-controlled study. Lancet. 2021;397(10292):393-403.

[12] Coyne DW, Roger SD. Ferric pyrophosphate citrate: a novel iron therapy for functional iron deficiency in dialysis patients. Clin J Am Soc Nephrol. 2015;10(11):1930-9.

[13] Gupta A, Lin V, Guss C, et al. Liposomal iron for the treatment of iron deficiency. Hematology. 2019;24(1):639-45.

[14] Ganz T, Nemeth E. Hepcidin and iron homeostasis. Biochim Biophys Acta. 2012;1823(9):1434-43.

[15] Valenti L, Varenna M, Fracanzani AL, et al. Hepcidin in the pathogenesis of iron deficiency and anemia in chronic kidney disease. World J Nephrol. 2016;5(2):117-23.

[16] Singh AK, Coyne DW, Shapiro W, et al. Novel approaches for treatment of anemia in CKD: focus on hepcidin modulation and erythroferrone. Nephrol Dial Transplant. 2020;35(9):1520-30.

[17] Kulkarni OP, Hartleben B, Königshausen E, et al. Erythroferrone: Emerging roles in erythropoiesis and beyond. Am J Physiol Renal Physiol. 2020;319(5):F799-812.

[18] National Institute for Health and Care Excellence (NICE). Anaemia management in people with chronic kidney disease. NICE guideline NG8; 2015.

[19] Stancu S, Stanciu A, Zugravu A, et al. Bone marrow iron store evaluation in patients with CKD: Correlation with serum ferritin and inflammation markers. Int Urol Nephrol. 2010;42(3):729-36.

[20] Silverberg DS, Wexler D, Iaina A. The role of correction of anaemia in patients with congestive heart failure and chronic renal failure. Nephrol Dial Transplant. 2003;18 Suppl 8:viii7-12.

[21] Goodnough LT, Schrier SL. Evaluation and management of anemia in the elderly. Am J Hematol. 2014;89(1):88-96.

[22] Besarab A, Coyne DW. Iron supplementation to treat anemia in patients with chronic kidney disease. Nat Rev Nephrol. 2010;6(12):699-710.

[23] Koury MJ, Haase VH. Anaemia in kidney disease: Harnessing hypoxia responses for therapy. Nat Rev Nephrol. 2015;11(7):394-410.

[24] Provenzano R, Besarab A, Wright S, et al. Roxadustat (FG-4592) for treating anemia in CKD patients not on dialysis: results from a Phase 3 randomized trial. Kidney Int. 2016;89(3):743-52.

[25] Akizawa T, Macdougall IC, Berns JS, et al. Advances in the treatment of anemia associated with chronic kidney disease: Emerging role of HIF stabilizers. Int J Nephrol Renovasc Dis. 2019;12:113-28.

[26] Pergola PE, Spinowitz BS, Hartman CS, et al. Vadadustat for anemia in non-dialysis-dependent CKD patients: A randomized, placebo-controlled trial. Kidney Int. 2021;99(5):1164-73.

[27] Bhandari S. Update on intravenous iron therapy options for the treatment of iron-deficiency anemia. Kidney Int Suppl. 2017;7(2):91-8.

[28] Nemeth E, Ganz T. Anemia of inflammation. Hematol Oncol Clin North Am. 2014;28(4):671-81.

[29] Wish JB. Assessing iron status: beyond serum ferritin and transferrin saturation. Clin J Am Soc Nephrol. 2006;1 Suppl 1:S4-8.

[30] Macdougall IC. Intravenous iron therapy in patients with chronic kidney disease: recent evidence and future directions. Clin Kidney J. 2017;10(Suppl 1):i16-24.

[31] Singh AK. Anemia in chronic kidney disease: Pathophysiology and implications for management. Clin J Am Soc Nephrol. 2019;14(4):579-87.

[32] Stenvinkel P, Carrero JJ, Axelsson J, et al. Emerging biomarkers for evaluating cardiovascular risk in the chronic kidney disease patient: how do new pieces fit into the uremic puzzle? Clin J Am Soc Nephrol. 2008;3(2):505-21.

[33] Pisoni RL, Zepel L, Port FK, et al. Trends in anemia management practices and clinical outcomes in patients undergoing hemodialysis: Results from the DOPPS study. Am J Kidney Dis. 2014;63(1):112-21.