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Anaemia of renal failure. Anaemia and chronic kidney disease. Anaemia of chronic renal failure.

In this subset, erythropoietin is given with every dialysis, i.e., three times a week, whereas darbepoetin alfa is dosed to once a week. Generally, the peak rise in RBCs in response to ESAs occurs at 8 to 12 weeks. Eur J Heart Fail. Anemia and renal insufficiency are independent risk factors for death among patients with congestive heart failure admitted to community hospitals: a population-based study. 2007 Nov;41(11):1761-9. Ferric gluconate is highly efficacious in anemic hemodialysis patients with high serum ferritin and low transferrin saturation: results of the Dialysis Patients' Response to IV Iron with Elevated Ferritin (DRIVE) Study. J Am Med Dir Assoc. Erythropoiesis-stimulating agents, together with iron supplementation, constitute the treatment of choice for anemia of chronic renal disease. 2001;16 Suppl 3:3-13. Objectives: Explain the pathophysiology of anemia of chronic renal disease. Common symptoms include:Dyspnea (shortness of breath)FatigueGeneralized weaknessHeadachesDecreased concentrationDizzinessReduced exercise tolerance.Commonly observable signs include:Skin and conjunctival pallorRespiratory distressTachycardiaChest pain (mostly with severe anemia)Heart failure (usually with chronic severe anemia)Common workup required to diagnose the condition include,CBC with differentialPeripheral smearIron indices (iron, ferritin, TIBC, transferrin saturation)Iron, vitamin B, and folate levels (included in initial workup to rule out other reversible causes of anemia)Thyroid function tests (rule out alternate etiology of hypoproliferative normocytic anemia).Normocytic normochromic anemia and peripheral reticulocytopenia are observable on CBC with a peripheral smear. Unfortunately, due to high serum ferritin levels secondary to chronic inflammation in CKD, serum iron indices are not accurately indicative of the degree of iron deficiency in dialysis patients, thus raising the standard cutoffs of iron responsiveness.[8][9] The Dialysis Patients' Response to IV Iron With Elevated Ferritin (DRIVE) study demonstrated that intravenous iron is beneficial in dialysis patients even in the setting of ferritin as high as 1200 ng/mL if the transferrin saturation is less than 30%. [10] Measuring serum erythropoietin levels are discouraged in CKD, and is not usable as an indicator of a renal source of the anemia, because, in kidney disease, there is 'relative erythropoietin deficiency,' that is, an inappropriate rise in erythropoietin levels for the severity of anemia. [11][12] Bone marrow may show erythroid hypoplasia, which correlates to the reports of resistance of bone marrow to erythropoietin. Treatment directs toward improving renal function (when possible) and measures aimed at increasing red blood cells production. ESAs, together with iron supplementation, is the treatment of choice in anemia of CKD. Treatment of anemia in CKD has come a long way. Clin Nephrol. 2015 Nov;17(11):1201-7. In these patients, erythropoietin (50 to 100 units/kg IV or SC) is usually given every 1 to 2 weeks, and darbepoetin alfa dosing is every 2 to 4 weeks. In patients who are on dialysis, ESAs are usually avoided unless the hemoglobin level is between 9 and 10 g/dL. 2017 Dec;10(Suppl 1):i16-i24. 1986 Nov 22;2(8517):1175-8. Nephron. Long-term cardiorespiratory effects of amelioration of renal anaemia by erythropoietin. They are fairly similar in efficacy and side effect profile, except for the longer half-life of darbepoetin alfa, thus allowing for less frequent dosing. [19][20] 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, but is individualized depending on various factors, including symptoms related to anemia, dependence on transfusions, the rate of drop in hemoglobin concentration, and response to iron therapy. It has been shown to promote faster progression of left ventricular hypertrophy, peripheral oxygen demand and worsening of cardiac outcomes. Erythropoiesis and erythropoietin in patients with chronic renal failure treated with hemodialysis and testosterone. [PMC free article: PMC2902279] [PubMed: 18596733] 23. Besarab A, Bolton WK, Browne JK, Egrie JC, Nissenson AR, Okamoto DM, Schwab SJ, Goodkin DA. To enhance responsiveness to erythropoietin, iron supplements are recommended. Anemia of renal disease is an independent risk factor for death. 2001 Nov;12(11):2465-2473. Proc Natl Acad Sci U S A. Erythropoietic response of dialyzed patients to testosterone administration. Clin Kidney J. [PubMed: 11402085] 21. Winearls CG, Oliver DO, Pippard MJ, Reid C, Downing MR, Cotes PM. 2007 Mar;18(3):975-84. [PubMed: 17267740] 11. Radtke HW, Clausner A, Erbes PM, Scheuermann EH, Schoeppe W, Koch KM. Hemoglobin cycling in hemodialysis patients treated with recombinant human erythropoietin. The role of iron status markers in predicting response to intravenous iron in haemodialysis patients on maintenance erythropoietin. An interdisciplinary team approach will maximize positive outcomes and minimize adverse events. 1979 Oct;5(4):677-84. [PMC free article: PMC41725] [PubMed: 7539919] 16. Agarwal AK, NDT Plus. Development and characterization of novel erythropoiesis stimulating protein (NESP). Secondary analysis of the CHOIR trial epoetin-alpha dose and achieved hemoglobin outcomes. [PMC free article: PMC2638549] [PubMed: 19461859] 20. Egrie JC, Browne JK, Nephrol Nurs J. Ann Intern Med. [PubMed: 17486947] 18. Maddux FW, Shetty S, del Aguila MA, Nelson MA, Murray BM. Results of a combined phase I and II clinical trial. 1970 Jun;72(6):913-8. 2007 Mar-Apr;34(2):167-73. 182. These trials, including CHOIR, NHCT and TREAT trials demonstrated higher mortality, thrombosis, adverse cerebrovascular and cardiovascular events due to higher levels of ESAs when used for target hemoglobin greater than 11 g/dL. [22][23][24] These events are likely related to the effect of ESAs on vascular remodeling and causing vasoconstriction. [25] CHOIR trial also showed that patients requiring higher levels of ESAs to achieve target hemoglobin had worse outcomes. [22] The discovery of stated side effects of ESAs, when used to target high normal hemoglobin levels, raised questions about the benefits of ESAs beside avoidance of transfusions, which has led to growing interest in looking for alternative etiologies and thus, management for anemia of CKD. Patients with CKD have increased risk of iron deficiency, due to impaired dietary iron absorption, chronic bleeding due to platelet dysfunction from uremia, frequent phlebotomy, and blood trapping in the dialysis apparatus. This deficiency, in addition to depletion of the circulating iron pool by stimulation of erythropoiesis by ESAs, makes iron supplementation the core of treatment of anemia in CKD. 2008 Sep;74(6):791-8. Inhibition of prolyl hydroxylases increases erythropoietin production in ESRD. 1998 Aug 27;339(9):584-90. Finally, there is no level of erythropoietin that can be considered adequate for defining renal anemia. Epidemiology of anemia associate with chronic renal disease among adults in the United States: results from the Third National Health and Nutrition Examination Survey. J Am Soc Nephrol. Lancet. As the GFR worsens, the anemia gets more severe. Anemia in chronic renal disease is a multifactorial condition, the widely accepted etiology being decreased renal production of erythropoietin, the hormone that is responsible for the stimulation of red blood cells production. [PubMed: 17098634] 7. Hsu CY, McCulloch CE, Curhan GC. Serum erythropoietin concentration in chronic renal failure: relationship to degree of anemia and excretory renal function. [PubMed: 11427634] 9. Mittman N, Sreedhara R, Mushnick R, Chattopadhyay J, Zelmanovic D, Vaseghi M, Avram MM. 2006 Nov;7(9 Suppl):S7-S12; quiz S17-21. Due to decreased absorption of oral iron, intravenous iron is preferable in hemodialysis patients. [26][27] 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. 1995 Jun 06;92(12):5510-4. Before the advanced treatment options that are available today, the main treatment option used to be blood transfusions, which came with numerous complications including infections, hemosiderosis, fluid overload, transfusion reactions, etc. It started with the use of androgens in the 1970s to avoid transfusion in patients with CKD. [13][14] After that, in the 1980s, the development of recombinant EPO followed by erythropoiesis-stimulating agents (ESAs) revolutionized the management of anemia in CKD. [15] Although initially instituted to avoid transfusions, they were soon known to have various positive effects, including improved survival and quality of life, improved cardiac function and mortality associated with it. [16] lower hospitalizations, [17] and lower costs. [18] Recombinant human erythropoietin and darbepoetin alfa are the two ESAs generally used in the management of anemia in CKD. Many develop adverse cardiac events that lead to a high mortality rate. 1990 Mar 03;335(8688):489-93. 2010 Dec;21(12):2151-6. [PubMed: 9678430] 27. Markowitz GS, Kahn GA, Feingold RE, Coco M, Lynn RI. Reticulocyte hemoglobin content predicts functional iron deficiency in hemodialysis patients receiving rHuEPO. 2000 Feb 25;292(1-2):149-54. One should target a hemoglobin level of no more than 11.5 g/dL. The management of the anemia of CKD is complex because it is not a simple matter of giving patients more blood transfusions or erythropoietin. [PubMed: 11805181] 8. Tessitore N, Solero GP, Lippi G, Bassi A, Faccini GB, Bedogna V, Gammaro L, Brocco G, Restivo G, Bernich P, Lapo A, Maschio G. Am J Kidney Dis. Decreased erythropoietin has recently linked with downregulation of hypoxia-inducible factor (HIF), a transcription factor that regulates gene expression of erythropoietin. [4][5] Other mechanisms include uremia (leading to RBC deformity responsible for hemolysis), folate and vitamin B12 deficiency, iron deficiency, bleeding due to dysfunctional platelets, and rarely blood loss from hemodialysis. [6] RBC fragmentation by injured renovascular endothelium in selected conditions such as glomerulopathy and malignant hypertension exacerbates the anemia, which explains why anemia can be particularly severe in renal glomerulopathies, including glomerulonephritis, diabetic nephropathy, for the degree of erythrocyte failure. The condition usually starts to develop following a greater than 50 percent loss of the kidney function, typically when the glomerular filtration rate (GFR) decreases to less than 60 mL/min. [7] The severity of anemia tends to worsen as chronic kidney disease (CKD) progresses. [PMC free article: PMC4703474] [PubMed: 26423928] 25. Fishbane S, Berns JS. An evaluation of the effectiveness of oral iron therapy in hemodialysis patients receiving recombinant human erythropoietin. 1997 Dec;30(6):912-22. Effect of human erythropoietin derived from recombinant DNA on the anaemia of patients maintained by chronic haemodialysis. [PubMed: 9718377] 24. Bello NA, Lewis EF, Desai AS, Anand IS, Krum H, McMurray JJ, Olson K, Solomon SD, Swedberg K, van Veldhuisen DJ, Young JB, Pfeffer MA. [PubMed: 11675424] 4. Bernhardt WM, Wiesener MS, Scigalla P, Chou J, Schmieder RE, Günzler V, Eckardt KU. Treatment is directed toward improving renal function, when possible, and increasing red blood cell production. Nephrol Dial Transplant. Outcomes The outcomes for patients with anemia of renal disease are guarded. [PubMed: 16105069] 26. Fudin R, Jaichenko J, Shostak A, Bennett M, Gottoib L. Thus, erythropoietin levels should not regularly be measured in the evaluation of patients with renal anemia. Differential Diagnosis Anal fistulas and fissures Disseminated intravascular coagulation Dysfunctional uterine bleeding Henoch-Schoenlein purpura Inflammatory bowel disease Systemic lupus erythematosus There are many patients with renal failure who will not respond to erythropoietin and this is important as it is an important predictor of adverse cardiac events. [PubMed: 9247776] 28. Macdougall IC. 1968;40:5-37. Multiple trials were done to assess the superiority of target hemoglobin to 'high normal' versus lower range. Anemia of chronic renal disease, also known as anemia of chronic kidney disease (CKD), is a form of normocytic, normochromic, hypoproliferative anemia. Report of a WHO scientific group. Intravenous iron therapy in patients with chronic kidney disease: recent evidence and future directions. Blood. [PubMed: 4763051] 12. Korte W, Cogliatti SB, Jung K, Riesen W. Explain the management of anemia of chronic renal disease. However, in around 10% to 20% of cases, anemia can be resistant to ESAs. Common adverse effects of ESAs include seizures, the progression of hypertension, clotting of dialysis access, the progression of malignancy and higher mortality in cancer patients. [21][15] In all patients with CKD, regardless of the need for dialysis, goal hemoglobin with the use of ESAs is less than 11.5 g/dL. [PubMed: 4975372] 2. McClellan WM, Flanders WD, Langston RD, Jurkowitz C, Presley R. 1997 Jul;48(1):34-40. Access free multiple choice questions on this topic. Use of darbepoetin alfa in the treatment of anaemia of chronic kidney disease: clinical and pharmacoeconomic considerations. [PubMed: 1968526] 17. Perkins R, Olson S, Hansen J, Lee J, Stiles K, Lebrun C. More important anemia of renal failure leads to depression, fatigue, stroke, reduced exercise tolerance and increased rate of re-admissions. Long term treatment with erythropoietin can cause hypertension, vasoconstriction, and seizures. Eat a healthy diet Take iron and multivitamin supplements Pearls and Other Issues Anemia of renal disease is common and is chiefly due to a decrease in erythropoietin production. It is necessary to investigate other treatable causes of anemia in renal failure patients. Anemia of renal disease is associated with adverse cardiac events, heart failure, MI and death. Erythropoietin levels are not indicative of anemia in renal failure patients. [PMC free article: PMC5716151] [PubMed: 25225819] The deficiency in renal production of erythropoietin and the severity of anemia do not always tend to correlate with the severity of renal dysfunction. Anemia is generally defined as hemoglobin of less than 13.0 g/dL in men and less than 12.0 g/dL in premenopausal women. [1] Anemia of chronic kidney disease (CKD) is a form of normocytic normochromic, hypoproliferative anemia. Among other complications of CKD, it is frequently associated with poor outcomes in CKD and increases mortality. [2][3] The disorder starts to develop when the glomerular filtration rate drops to below 60 mg/ml. High levels of CRP predict resistance to erythropoietin in dialysis patients. [PubMed: 17895328] 19. Carrera F, Burnier M. Both these products have serious adverse effects when given chronically. Death, hospitalization, and economic associations among incident hemodialysis patients with hematocrit values of 36 to 39%. [PubMed: 2877323] 22. Szczech LA, Barnhart HX, Inrig JK, Reddan DN, Sapp S, Califf RM, Patel UD, Singh AK. 1987 Jan 08;316(2):73-8. [PubMed: 3537801] 16. Macdougall IC, Lewis NP, Saunders MJ, Cochlin DL, Davies ME, Hutton RD, Fox KA, Coles GA, Williams JD. Explain the interprofessional team strategies for improving coordination and communication to enhance the management of patients with anemia of chronic renal disease. The dialysis nurse should always monitor vital signs and obtain total blood counts to determine the level of anemia. [PMC free article: PMC3014028] [PubMed: 21115615] 5. Wang GL, Jiang BH, Rue EA, Semenza GL. [PubMed: 5455991] 15. Eschbach JW, Egrie JC, Downing MR, Browne JK, Adamson JW. In patients with ESRD on dialysis receiving intravenous iron, goal transferrin saturation of 30 to 50% and ferritin higher than 200 ng/mL. [28] Iron has correlations with a risk of acute toxicity and infection, which should be weighed against the benefits in individual patients. Unlike the general population, high serum ferritin levels are not predictive of hemoglobin responsiveness in renal failure patients. [PubMed: 9398141] 10. Coyne DW, Kapoian T, Suki W, Singh AK, Moran JE, Dahl NV, Rizkala AR, DRIVE Study Group. 2002 Feb;13(2):504-510. 1970 Sep;73(3):403-7. Increased risk of stroke with darbepoetin alfa in anaemic heart failure patients with diabetes and chronic kidney disease. Correction of the anemia of end-stage renal disease with recombinant human erythropoietin. Mild renal dysfunction is sufficient to induce erythropoietin deficiency in patients with unexplained anaemia. Two factors that lead to unresponsiveness include iron deficiency and inflammation. The pharmacists should educate the patient about the importance of iron supplements because without iron, many patients develop resistance to erythropoietin. Further, anemia of renal disease is also associated with adverse cardiac outcomes and hence the patient's cardiopulmonary status has to be monitored for life. Finally, the involvement of a nutritionist is essential for avoidance and/or treatment of the deficiency of vitamins that can exacerbate the anemia of kidney disease. [PubMed: 12089390] 3. Collins AJ, Li S, Peter WS, Ebben J, Roberts T, Ma JZ, Manning W. Ann Pharmacother. 2005 Sep;68(3):1337-43. It is frequently associated with poor outcomes in chronic kidney disease and confers an increased mortality risk. World Health Organ Tech Rep Ser. Finally, chronic use of erythropoietin has been associated with severe hypertension, stroke and heart failure. Effect of erythropoiesis-stimulating agents on healthcare utilization, costs, and outcomes in chronic kidney disease. One should never assume that anemia of renal disease is solely due to lack of erythropoietin, it may be due to poor nutrition or chronic illness- so a thorough workup is essential to determine the cause. To manage patients on dialysis with anemia requires an integrated approach by an interprofessional team consisting of the nephrologist, PCP including the nurse practitioner, physician assistant, physician, nursing, pharmacy, and occasionally also a hematologist may be necessary to help achieve the best possible outcomes. Practical approach to the diagnosis and treatment of anemia associated with CKD in elderly. [PubMed: 10686284] 13. DeGowin RL, Lavender AR, Forland M, Charleston D, Gottschalk A. 2001 Jul;16(7):1416-23. Hypoxia-inducible factor 1 is a basic-helix-loop-helix-PAS heterodimer regulated by cellular O2 tension. At least 90% of patients who end up on dialysis will eventually develop anemia of chronic disease. Clinical presentation of anemia of renal disease is not different from that of anemia due to other causes. [PubMed: 5448750] 14. Richardson JR, Weinstein MB. Correction of uremic iron deficiency anemia in hemodialyzed patients: a prospective study. This activity reviews the evaluation and management of the anemia of chronic renal disease and highlights the role of the interprofessional team in the care of individuals affected by this condition. Impact of an anemia clinic on emergency room visits and hospitalizations in patients with anemia of CKD pre-dialysis. The anemia is rare when the GFR is above 80 ng/ml. 1998;79(3):299-305. Kidney Int. Explain how to diagnose anemia of chronic renal disease. The effects of normal as compared with low hematocrit values in patients with cardiac disease who are receiving hemodialysis and epoetin. Clin Chim Acta. [Level 5] Review Questions 1. Nutritional anaemias. N Engl J Med. Too much iron from blood transfusions also affects outcomes. 2009 Jan;2(Suppl 1):49-117. 2002 Jul;13(7):1928-36.

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