Original Research Paper

Volume-8 | Issue-6 | June-2018 | PRINT ISSN No 2249-555X

Biochemistry

ANAEMIA IN CHRONIC RENAL FAILURE PATIENTS: NEED TO UNDERSTAND THE MECHANISM TO DEVELOP NEW THERAPIES

Dr. Shefali Mehta	Post graduate student Department of Biochemistry Geetanjali Medical College and HospitalUdaipur, Rajasthan-313001
Dr. Ashish Sharma*	Professor and Head Department of Biochemistry Geetanjali Medical College and Hospital Udaipur, Rajasthan-313001 *Corresponding Author
Dr K.L Mali	Professor Department of Biochemistry Geetanjali Medical College and Hospital Udaipur, Rajasthan-313001

KEYWORDS :

Introduction:

Chronic Kidney Disease (CKD) is a worldwide public health problem. Indeed, the incidence and prevalence of CKD have increased in recent years in both developed, and developing countries, Chronic kidney disease (CKD) is rapidly assuming epidemic proportions globally.[1] In India too, there is a significant burden of CKD although exact figures vary.[2] This has been attributed to the increasing prevalence of diabetes, hypertension and ischemic heart disease. Less than 10% of end-stage renal disease patients have access to any kind of renal replacement therapy.[3,4] Progression of CKD is associated with a range of serious complications, including increased chance of cardiovascular diseases, anemia, hyperlipidemia and metabolic bone disease. CKD patients need to be assessed for the presence of these complications and receive optimal treatment to reduce the morbidity and mortality.[5] Stauffer et al reported that anemia was twice as prevalent in people with CKD (15.4%) as in the general population (7.6%). The prevalence of anemia also increased with stage of CKD, from 8.4% at stage 1 to 53.4% at stage 5. [6] Moreover the direct healthcare costs are higher in CKD patients with anemia than in those without anaemia.[7]

Early diagnosis of the iron deficiency, anaemia and other factors should be measured so that further damage and complications of the kidney may be prevented.

Anaemia in CKD

Anemia is a common feature of CKD, which is associated with poor outcomes. Anemia leads to poor quality of life and increased complications such as cardiovascular diseases, increased hospitalizations, cognitive impairment, and increased mortality. [8] In 1836, Richard Bright for the first time described the association of chronic kidney disease and anemia, when he observed pallor in the development of Brigit's disease.[9] NKF/KDOQI guideline (2006) defines anemia in Chronic Kidney Disease when the hemoglobin level is < 13.5 g/dl in adult males and 12.0g/dl in adult females, but adult male > 70 years old anemia is defined when hemoglobin < 12.0 g/dl.[8] Iron deficiency has been considered as important cause of anemia in CKD patients and these patients manifest iron deficiency as "absolute" or "functional" iron deficiency in end-stage renal disease. In CKD patients iron stores (absolute) are depleted as a result of decreased intake due to malnutrition, decreased appetite associated with uremia and increased loss through chronic GIT bleeding due to blood vessel fragility associated with uremia, platelet dysfunction related to uremia, chronic blood retention in the dialysis circuit.[10] Functional iron deficiency occurs when there is a need for a greater amount of iron to support hemoglobin synthesis than can be released from the iron store. In CKD there is an impaired release of stored iron from macrophages and hepatocytes to transferring Iron, a transitional metal, can serve as a carrier for oxygen and electrons and as a catalyst for oxygenation, hydroxylation, and other critical metabolic processes, in part because of its ability to cycle reversibly and readily between the ferrous and ferric oxidation states. The ease with which iron is oxidized and reduced reversibly is essential for its metabolic functions. However, this property makes iron potentially hazardous by enabling it to participate in the generation of powerful oxidant species such as hydroxyl radical and/or reactive iron-oxygen complexes such as ferryl or perferryl ion as iron can participate in the formation of ROM,(reactive oxygen metabolites) so body uses transport proteins such as transferrin and storage proteins such as ferritin and minimizing the size of the intracellular iron pool.[11]

Nankivell BJ et al. in 1992 suggested that ischemic or toxic insults to the kidney increase the intracellular release of labile iron (also known as catalytic iron) that result in oxidative damage.[12] More recently, a specific iron-dependent type of regulated cell death due to lipid peroxide accumulation, termed ferroptosis, has been identified and is implicated the pathogenesis of renal ischemia-reperfusion injury. Further studies are needed to better understand the role of iron in the pathogenesis of kidney disease and the potentially harmful or beneficial effects of intravenous iron administration on kidney disease.[12,13,14,15]

Although relative EPO deficiency may contribute to the anemia of CKD, [16] it is not the sole cause. Moreover, anemia of CKD is resistant to erythropoiesis-stimulating agents (ESAs) in approximately 10%–20% of patients. [8] It can be due to the reason that supraphysiologic doses of ESAs, especially at very high doses or in patients who are resistant to treatment, have off-target effects in other tissues. These findings have recommenced the interest in understanding the molecular mechanisms of anemia in CKD, so that the new therapies could be developed, which target the underlying pathophysiology of low hemoglobin [17]

To conclude it can be said that anemia of CKD is a multifactorial process due to relative EPO deficiency, disordered iron homeostasis uremic-induced inhibitors of erythropoiesis and shortened erythrocyte survival. Current research suggests that hepcidin excess is the main contributor to the disordered iron homeostasis and anemia of CKD by impairing dietary iron absorption and iron mobilization from body stores.[17] It is prerequisite to improve our understanding of the molecular mechanisms responsible for anemia of CKD, so that newly developed pharmacologic agents more closely target the underlying pathogenic mechanisms of this disease to improve efficacy and reduce treatment-related adverse effects.

REFERENCES

1. Collins A J, Foley R N, Chavers B, Gilbertson D, Herzog C, Johansen K, et al. 'United States Renal Data System 2011 Annual Data Report: Atlas of chronic kidney disease and end-stage renal disease in the United States. (e1-420).Am J Kidney Dis. 2012; 59
2. Rajapurkar M M, John G T, Kirpalani A L, Abraham G, Agarwal S K, Almeida A F, et al. What do we know about chronic kidney disease in India: First report of the Indian CKD registry. BMC Nephrol. 2012; 13:10.
3. Agarwal S K, Dash S C, Irshad M, Raju S, Singh R, Pandey R M: Prevalence of chronic renal failure in adults in Delhi, India. Nephrol Dial Transplant, 2005; 20:1638-1642
4. Kher V. End-stage renal disease in developing countries. Kidney Int. 2002; 62:350–62.
5. Thomas R, Kanso A, Sedor JR. Chronic kidney disease and its complications. Primary care: Clinics in office practice. 2008 Jun 1;35(2):329-44.
6. Stauffer ME, Fan T. Prevalence of anemia in chronic kidney disease in the United States. PloS one. 2014 Jan 2;9(1):e84943.
7. Van Nooten FE, Green J, Brown R, Finkelstein FO, Wish J (2010) Burden of illness for patients with non-dialysis chronic kidney disease and anemia in the United States: review of the literature. J Med Econ 13: 241–256
8. KDOQI National Kidney Foundation : KDOQI Clinical Practice Guidelines and Clinical Practice Recommendations for Anemia in Chronic Kidney Disease. Am J Kidney Dis 47[Suppl 3]: S11–S145, 2006
9. Remuzzi G, Weening JJ. Albuminuria as early test for vascular disease. The Lancet. 2005 Feb 18;365(9459):556-7.
10. Besarab A, Coyne DW. Iron supplementation to treat anemia in patients with chronic

kidney disease. Nature Reviews Nephrology. 2010 Dec;6(12):699
11. Halliwell B, Gutteridge J M C: Role of free radicals and catalytic metal ions in human disease: an overview. Meth- ods Enzymol 1990; 186:1–85.
12. Araujo M, Welch W J: Oxidative stress and nitric oxide in J Am Soc Nephrol 2007; 18:16–28.
13. Wilcox C S: Oxidative stress and nitric oxide deficiency in the kidney: A critical link to hypertension? Am J Physiol Regul Integr Comp Physiol 2005; 289:913–935.
14. Thomas M C, Burns W C, Cooper M D: Tubular changes in early diabetic nephropathy. Adv Chronic Kidney Dis 2005; 12:177–186.
15. Kawamura T, Yoshioka T, Bills T, Fogo A, Ichikawa I: Glucocorticoid activates glomerular antioxidant enzymes and protects glomeruli from oxidant injuries. Kidney Int, 1991; 40:291–301.
16. Besarab A, Ayyoub F: Anemia in renal disease. In: Diseases of the Kidney and Urinary Tract, edited by Schrier RW, editor. , 8th Ed., Philadelphia, Lippincott Williams and Wilkins, 2007, pp 2406–2430
17. Babitt JL, Lin HY. Mechanisms of anemia in CKD. Journal of the American Society of Nephrology. 2012 Aug 30:ASN-2011111078