Introduction

Anemia is a severe complication of chronic kidney disease (CKD) that is seen in more than 80 % of patients with impaired renal function ***(Melnikova ; 2006).*** Although there are many mechanisms involved in the pathogenesis of renal anemia, the primary cause is inadequate production of erythropoietin by the damaged kidneys.

Erythropoietin is produced in the peritubular cells of the kidney and is the major hormone involved in the synthesis of red blood cells (Erythropoiesis). When erythropoietin levels are low, an inadequate number of oxygen-carrying red blood cells are produced. Anemia decreases oxygen supply all over the body and causes decreased exercise capacity, cognitive impairment, and diminished quality of life ***(Melnikova ; 2006).***

Anemia has also been implicated in the development of congestive heart failure and left ventricular hypertrophy ***(Rao and Pereira ; 2006)***. If left untreated, anemia may cause death ***(Melnikova ; 2006).***

By 1990 , recombinant human erythropoietin (epoetin) was licensed in the United States and Europe for the treatment of anemia associated with chronic renal failure, including patients on dialysis ***(Macdougall ; 2006) .***

Epoetin is administered by subcutaneous or intravenous injection 1 to 3 times weekly. Darbepoetin alfa, a second-generation erythropoiesis stimulating agent, can be administered once weekly or once every other week ***(Macdougall and Eckardt ; 2006).***

Though treatment with recombinant erythropoietin (EPO) has improved the management of anemia in chronic kidney disease (CKD), anemia persists as a significant problem in the disease**(Obrador GT,et al;2002)**.

Several issues in the management of renal anemia remain unresolved and controversial.Clarifying these issues could improve renal anemia management, enhancing patient outcomes. Furthermore, how anemia is managed in CKD has major economic implications. Resolving these controversies and thus providing more efficacious management of renal anemia might reduce morbidity and mortality**(USRDS 2004).**

The ‘‘clinically ideal’’ threshold Hb for the initiation of erythropoietic agents in early COD has still not been established. This uncertainty is reflected in the differences in the recommended threshold Hb for the initiation of treatment **(Working Party for European Best Practice Guidelines;1999).**

The effect of EPO on the rate of progression of CKD in humans is a matter of controversy. Anemia has been shown to increase the risk for progression to ESRD, and Hb is an independent risk factor for cod progression in patients with type 2 diabetes**(Kuriyama S,1997)**

IV iron therapy is vigorously advocated for renal anemia management. Is there a long-term risk to this policy, and have we inappropriately abandoned caution in the use of IV iron? Is it possible that the K/DOQI anemia management guidelines of the NKF are being misapplied by clinicians uncritically administering IV iron to patients with low Hb without excluding other causes of EPO hyporesponse? **(National Kidney Foundation.2001).**

Although recent guidelines on anemia management in ESRD advocate the use of IV iron, they omit mention of the effect of dialysis adequacy on the response to EPO. Reduced marrow inhibition by post dialysis sera, less severe anemia with more frequent or longer dialysis sessions, and better response to EPO in well-dialyzed patients all suggest that nitrogenous inhibitors are extracted by dialysis **(National Kidney Foundation.2001).**

Whether Hb should be normalized in patients with ESRD remains a hotly debated issue. But it is not widely known that the current Hb target for those with subnormal levels of 11– 12 g/dL essentially is the result of a historical accident. the Food and Drug Administration (FDA) decided to ‘‘mandate’’ these subnormal Hb values during the drug approval process, ostensibly because of safety concerns. The Health Care Finance Administration, principally concerned about cost issues, latched onto these FDA-mandated lower Hb targets, and the nephrology community uncritically accepted thesesubnormal targets in subsequent guidelines**(Furuland H,et al;2003).**

In patients with ESRD, acute bacterial infection often results in a precipitous drop in Hct, possibly from red blood cell hemolysis. In addition, infection stimulates the production of IFN-gamma andTNF-alpha, which directly inhibit erythropoiesis locally in the bone marrow and block the transfer of iron from reticuloendothelial cells to the marrow sites. Infection may also exacerbate anemia by decreasing red blood cell survival, and the production of endogenous erythropoietin .Under these circumstances, it is unlikely that that the ‘‘marrow’’ block can be overridden by increasing the dose of EPO during an active infection. Although it seems reasonable to continue EPO therapy during an active infection, it is unlikely that additional benefit will accrue by increasing the dose of EPO **(Bar-Or D,2004).**