Anemia is a common complication of HIV infection. Erythropoietin (Procrit, Epogen) can correct anemia. When given to patients with HIV infection, erythropoietin ameliorates anemia and improves quality of life. Given these three facts, one wonders why an effective drug such as erythropoietin is not used appropriately in patients with HIV infections.

As pointed out by Aboulafia, mild to moderate degrees of anemia occur in virtually all patients with HIV disease. The severity of anemia, in the absence of drug therapy, is directly related to the severity of the underlying immune deficiency. Depending on the patient population studied, up to 30% of patients with CD4 counts in excess of 200 cells/mm$^3$ can have a hemoglobin below 115 g/dL. Four placebo-controlled, double-blind studies have evaluated recombinant erythropoietin for the treatment of severe anemia associated with zidovudine (Retrovir) therapy.[1] In patients receiving erythropoietin doses ranging from 100 to 200 IU/kg three times a week, an increase in hemoglobin level of nearly 2 g/dL was observed over a 12-week period relative to the placebo group. This dramatic increase in erythropoiesis was associated with significant improvements in quality of life, which included increases in energy level, work capacity, and overall self-reported quality of life. These significant quality-of-life improvements were substantiated in the large observational data set of over 2,000 patients treated with erythropoeitin on its investigational new drug (IND) treatment study. In this data set, patients attaining any increase in hemoglobin had an incremental improvement in their self-reported energy level, work capacity, and overall quality of life. There was a relationship between the magnitude of the increase in hemoglobin and the patients' ability to do work. Together with the placebo-controlled studies, these data clearly demonstrate that erythropoeitin is an active, effective agent in ameliorating anemia and its attendant impact on quality of life.

Anemia—Uncommon or Ignored in Patients With HIV?

Despite the unequivocal evidence of the benefit of erythropoeitin therapy, the use of this agent has remained relatively constant or declined over the last several years. Clinicians often point out that anemia is a less serious complication of HIV therapy or that it is less common. However, in a recent placebo-controlled study of ritonavir in patients with advanced-stage HIV disease,[1] the mean entry hemoglobin for both study groups was less than 11 g/dL. This is not different from the baseline hemoglobin observed in 1987 in untreated individuals with a similar CD4 count. In a soon-to-be published retrospective study of HIV patients by the Apache Group, the incidence of severe anemia (less than 11 g/dL) has fallen to 9% but the prevalence is still approaching 22%. In the recent Centers for Disease Control spectrum of disease survey, severe anemia (40 g/dL) was observed in 19% of all HIV infected patients. Thus, it appears that anemia is somewhat less common, and largely ignored.

There is no doubt that there has been a substantive improvement in the overall treatment of HIV disease during the last few years. The introduction of three- and four-drug regimens results in suppression of HIV often to undetectable levels, with an overall improvement in quality of life and immune function. Despite this improvement, fatigue remains a common complaint of patients with HIV infection.

What's Important to Patients Is Not What's Important to Physicians

At the most recent International AIDS Meeting in Vancouver, surveys of patients with HIV demonstrated that fatigue was the single most common complaint of patients receiving combination
therapy. Nearly 70% of patients identified fatigue as the most disconcerting symptom that they experience on a daily basis. At the same conference, HIV-treating physicians ranked fatigue as one of the least significant consequences of HIV infection. Thus, there is a discrepancy between what is important to patients and what is important to physicians.

Given the unequivocal benefit of erythropoietin in improving hemoglobin, as well as work capacity, energy level, and quality of life, one wonders why erythropoietin is not used more commonly. Aboulafia notes that a rigorous cost-benefit analysis of erythropoietin has been applied to HIV-associated anemia. He adds that at the usual dose of erythropoietin, treatment can cost nearly $5,000 for 4 months. He also notes that unless a patients requires 4 units of transfused blood per month, erythropoietin is a more expensive therapeutic option.

This prevailing attitude that erythropoietin must always offset transfusions clearly underlies the problem that patients with fatigue and mild degrees of anemia face. Well-trained specialists in HIV disease, even hematologists, dismiss the substantial impact on quality of life that mild and moderate degrees of anemia can have. As pointed out in the surveys of patients and physicians, there is an obvious discordance between what is important to the patient (fatigue) and what is important to the physician (anemia, need for transfusion). Patients are clearly telling us that even mild to moderate degrees of anemia adversely affect their quality of life. Yet physicians are saying that this is an insignificant degree of anemia and not worth the expense of erythropoietin therapy.

This dichotomy between issues that concern patients and physicians is common and not restricted to the use of erythropoietin for HIV infection. There is no doubt that if erythropoietin were less expensive, physicians would utilize the drug more frequently to treat milder forms of anemia. Many managed-care organizations have strict guidelines regarding the use of erythropoietin and restrict its use to patients with more severe degrees of anemia. Paradoxically, this is the group that is least likely to respond to erythropoietin. Moreover, this group is also least likely to be able to take advantage of the quality-of-life improvements obtained through erythropoietin use. Thus, because of economic concerns, the patients who are least likely to derive an overall benefit in functional status are the ones who are given the drug.

Clearly, this situation is an unintended consequence of the design of the clinical trials conducted to demonstrate the efficacy of erythropoietin. These clinical trials were conducted only in patients with severe anemia (less than 10 g/dL). Nonetheless, it has had a direct, negative impact on the quality of life of many thousands of patients with HIV.

**Clinical Trials Needed**

Clinical studies demonstrating the impact of erythropoietin on the work capacity and functioning of patients with mild degrees of anemia (11 to 12.5 g/dL of hemoglobin) are clearly needed. Patients with mild to moderate anemia will undoubtedly respond to erythropoietin, and the drug will have a great impact on their energy level, work capacity, and overall quality of life. This group is also the most likely to be currently employed, and the improvements in work capacity are likely to directly affect their employers' bottom line. However, without these clinical studies, physicians will continue to ignore what is one of the most common, if not the most common, complaint of patients with HIV infection.

**References:**


**Source URL:**

http://www.diagnosticimaging.com/review-article/use-hematopoietic-hormones-bone-marrow-defects-aids-0

**Links:**

[1] http://www.diagnosticimaging.com/review-article