Anemia Management: European Guidelines

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Anemia is a critical field in nephrology and its management can influence patient outcome. Clinical practice varies worldwide. In 1997 'Clinical practice guidelines for the treatment of anemia of chronic renal failure' as part of the US National Kidney Foundation-Dialysis Quality Outcomes Initiative were published, some of which were not appropriate for clinical use in Europe. European Best Practice Guidelines are recommended by a Working group, chaired by J. S. Cameron, which included representatives of ERA/EDTA and national nephrology societies, who revised a draft document of an advisory board which reviewed all the publications taken into account the NFK-DOQI and 200 relevant publications from January 1996 to December 1998. Best practice guidelines are evidence-based as a result of systematic review of the available literature and of unpublished data.

The quality of evidence has been graded according to US Dept of Health and Social Services in three categories : A) at least one prospective randomized controlled trial, B) good but uncontrolled open studies C) opinion of consensus groups. Guidelines recommend strategies of management and levels of attainment.

The 18 EBPG assess 6 topics : 1) Evaluation of anemia : should be considered in CRF pts when Hb < 12 g/dl in adult males or < 11 g/dl in pre-menopausal women. Onset of erythropoietin (EPO) therapy : when Hb is consistenly below 11 g/dl. 2) Target Hb : 85% of CRF pts should have Hb > 11 g/dl (mean for the total patient population will be 12,5 g/dl) Variations in target Hb according to co-morbidity. 3) Iron handling : sufficient iron is needed to achieve and maintain Hb target. Administration of iron to attain in all patients : serum ferritin ≥ 100 μg/l, hypochromic red cells < 10% (TSAT > 20%). Optimal levels of iron : serum ferritin 200-500 μg/l, hypochromic red cells < 2,5% (TSAT 30-40%). Intravenous (iv) iron administration will be required in all HD pts. 4) Management of anemia : starting dose of EPO is 50-150 iu/kg/wk sc. Target increase of Hb is 1-2 g/dl per month. Hb levels should be checked regularly every 1-2 weeks in correction phase or every 4-6 weeks in maintenance phase. 5) Inadequate response to EPO treatment : resistance or hyporesponsiveness to EPO is defined the need for EPO > 300 iu/kg/wk. Absolute or functional iron deficiency is the common cause of incomplete response. Other conditions should be evaluated (chronic blood loss, infection / inflamation, hyperparathyroidism, aluminum toxicity, haemoglobinopathies, folate or B_{12} deficiency, malignancy, malnutrition, haemolysis, inadequate dialysis). 6) Possible adverse events of EPO treatment : blood pressure levels may increase. Dry-weight and ultrafiltration should be reconsidered before initiation or increase of anti-hypertensive therapy.

European Survey on Anemia Management (ESAM) is an observational study contacted between September 1998 and April 1999 to test the implementation of the EBPG in 14 European countries.

The main results showed that EPO therapy started at the onset or after dialysis therapy had been initiated. Hb levels in patients who started EPO are significantly lower than recommended (mean Hb 8,7 g/dl). HD patients with diabetic nephropathy or polycystic kidney disease started EPO therapy having higher Hb levels. The 'stated' target Hb for the majority of patients was set higher than the recommended, while the target Hb was not adjusted for co-morbidity or primary renal diseases. Hb level > 11 g/dl the last month of assessment was achieved in only 54% of all patients, far away of the recommended level of 85%.

Median EPO dose the 3rd month of the study was within the suggested limits of EBPG (109,1 iu/kg/wk). IV prescription of EPO was slightly preferable than subcutaneous (s) in HD patients. Two thirds of the patients were scheduled to receive iv EPO thrice per week. A quarter of patients who treated with EPO sc were scheduled for one shot per week.

Regarding to iron handling, throughout the study a larger percentage of HD than PD patients suffered from absolute iron deficiency. Iron status in correction phase of anemia was assessed less frequently than recommended by EBPG. Supplementation of iron was not prescribed in 12% and 14% of HD and PD patients respectively during the study. HD patients with sufficient iron stores reached higher Hb level taking lower EPO dose.

Almost 70% of EPO resistant patients (n = 393) as defined by EBPG had Hb < 11 g/dl. Therapy with angiotensin inhibitor did not seem to influence EPO requirements.

In conclusion the results of ESAM showed that EPO therapy in dialysis patients started rather late at lower than the recommended Hb level. Subsequent treatment was inadequate to achieve the therapeutic Hb target in the majority of patients and this was due to undertreatment with EPO and particular iron supplementation.

References

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