

Complete normalization of hemoglobin levels in patients with advanced renal failure does not reduce cardiovascular events

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It is well proven that complete correction of anemia associated with advanced renal failure with erythropoetin leads to improved quality of life. However, in stage 5 (end-stage) chronic renal failure (CRF), complete correction of anemia does not increase survival. The effect of complete correction of anemia on survival and on the rate of cardiovascular events in stage 3 and 4 CRF was not well established.

The CREATE study evaluated if cardiovascular events would be reduced by complete normalization of hemoglobin (Hb) level, as compared with mild anemia, in stage 3 and 4 CRF. 603 patients were included in the study. All patients had mild anemia at randomization (Hb level between 11 and 12.5 g/dl). Patients were randomized in two groups of treatment. In Group 1 treatment with erythropoetin was administered from randomization in order to completely normalize the Hb level (target between 13 and 15 g/dl). In Group 2 a mild

level of anemia was allowed (Hb = 10.5 – 11.5 g/dl) and erythropoetin was administered only if Hb level fell below 10.5 g/dl. The primary objective of the study was a composite index of sudden death, myocardial infarction, acute heart failure, stroke, angina pectoris, peripheral vascular disease and severe cardiac arrhythmias. After a follow up of 3 years, there were no differences between the two groups for the incidence of the primary objective. Quality of life was significantly improved in Group 1 (complete correction of anemia). However, hypertension and headache were significantly more frequent in the same group.

In conclusion, complete correction of anemia in patients with advanced, stage 3 and 4 CRF does not reduce the rate of adverse cardiovascular events. Treatment with erythropoetin can be delayed even if mild anemia is present.

Comment on the paper:

Wang TJ, Gona G, Larson MG et al – Multiple Biomarkers for the Prediction of First Major Cardiovascular Events and Death. *N Engl J Med* 2006; 355:2631-2639