Dear Sir,

The role of angiotensin-converting enzyme inhibitors (ACEI) in inducing anemia has been reported in people with normal renal function [1], in patients with chronic renal failure on hemodialysis [2] and in kidney transplant patients [3, 4]. Several mechanisms of ACEI-induced anemia have been hypothesized. ACEI may decrease angiotensin II, which stimulates erythropoietin production. They may decrease renal tissue hypoxia due to their property for increasing renal blood flow. Or, by decreasing renin levels, they may diminish one likely precursor of erythropoietin [2, 5].

The association between renal anemia and ACEI in patients at the predialysis stage has not been well discussed. Therefore, we carried out a retrospective analysis of 39 predialysis patients checking their medical records during the follow-up period at our outpatient clinic. Among patients in whom regular renal replacement therapy had been initiated from 1984 to 1993 at Kawasaki Medical School Hospital, 39 Japanese patients (23 males) were entered into the study with the following restrictive criteria: (1) age 30-65; (2) followed up by us from when serum creatinine level had been less than 2.0 mg/dl to the initiation of renal replacement therapy; (3) never showed microcytic hypochromic anemia during the period; (4) had no malignancies, liver cirrhosis, or collagen diseases, (5) no anabolic steroid, recombinant human erythropoietin (rhEpo) or transfusion was given during the period. Patients with diabetic nephropathy and polycystic kidney disease were excluded from the study. Twenty of them had chronic glomerulonephritis or nephrosclerosis diagnosed by renal biopsy.

When their serum creatinine level increased to over 3.0 mg/dl (phase A) and over 7.0 mg/dl (phase B), the patients were divided into three groups according to the medication they were taking for hypertension: group 1 (no antihypertensive agents was prescribed); group 2 (ACEI was prescribed for at least over 2 months), and group 3 (other antihypertensive agent(s) was prescribed, such as calcium antagonists, α- and β-blockers).

Most of the prescribed ACEI were captopril or enalapril. Patients in whom ACEI was prescribed in combination with other agents were put into group 2.

As shown in figure 1, the hematocrit level of group 2 at phase B was significantly lower than in group 1, while no difference was found at phase A (unpaired t test). There was no difference in
white blood cell count, platelet count and reticulocyte count between the three groups at both phases. There was no correlation between the prescribed dose of ACEI and the hematocrit in group 2 at both phases. These findings suggested that ACEI can worsen renal anemia in predialysis patients, especially at advanced stage. Because it was a retrospective analysis, we do not have any conclusion regarding the relationship between erythropoietin, renin or angiotensin II and ACEI-induced anemia. However, we can speculate similar mechanisms of the anemia discussed above to explain our results.

Recently, rhEpo has been introduced for the management of renal anemia in predialysis patients. Antihypertensive treatment with ACEI can interfere with the effect of rhEpo in these patients.

Fig. 1. Hematocrit of three groups in stage A or B.

References


Effects of ACE Inhibitor on Renal Anemia  Nephron 1996;73:336-337

in Predialysis Patients