Erythropoietin Production in Hypertensive Patients with and without Renal Artery Stenosis

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Dear Sir,

The major production site of erythropoietin (EPO) is the inner cortex of the kidney. Its production depends on oxygen concentration, as detected by oxygen sensors [1-3]. Hemoglobin levels and hence oxygen delivery and, possibly, iron stores are involved as well [4]. As oxygen delivery to the kidneys may be affected in patients with hypertension, particularly renovascular hypertension, Nowicki et al. [5] investigated whether EPO production, as measured by serum EPO levels, differs between various forms of hypertension and healthy controls. In addition, they examined to what extent EPO production is affected by stimulation of the renin-angiotensin-aldosterone system (RAAS) by sodium restriction and upright body position. No significant differences were observed in EPO production between the various forms of hypertension and healthy subjects, whereas RAAS stimulation did not alter serum EPO levels. Others have found that angiotensin II enhances EPO production [6] and that, in rats, EPO production was higher due to renal ischemia induced by renal artery stenosis (RAS) [7]. Thus the role of RAS in the regulation of EPO production remains uncertain.

In order to examine whether EPO production is higher in patients with renovascular hypertension on the site of stenosis and to what extent it is influenced by oxygen concentration we studied 27 consecutive hypertensive patients scheduled for selective renal angiography. These patients were selected

Table 1. Demographic data and arterial levels of hematocrit, oxygen saturation, EPO, creatinine and renin in patients with and without RAS

higher in the RAS patients. Renin was significantly higher in RAS patients. There were 2 patients with right-sided RAS (stenosis both 40%), 1 with left-sided RAS (35%) and 4 with bilateral RAS [median stenosis right side 43% (15-75); median left side 48% (10-90)]. Table 2 shows that correlations existed between LRV EPO levels and LRV renin levels as well as stenosis percentage in the left renal artery. Similar, but not significant correlations concerning

these parameters were observed in the right kidney. EPO levels in RRV and LRV correlated with each other. We did not observe a correlation between arteriovenous differences in EPO, ox- because of treatment-resistant hypertension or lateralization on radionuclide radiography. The patients were divided into a group with RAS (n = 7) and a group without, referred to as essential hypertension (n = 20). After cannulation, plasma samples were obtained from a renal artery, the right renal vein (RRV) and the left renal vein (LRV). The hematocrit was determined in arterial blood. EPO (by radioimmunoassay; Boehring, Mannheim, Germany), oxygen saturation and renin were measured in arterial blood, the RRV and LRV. The demographic data are shown in table 1. EPO and creatinine levels were slightly

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xygen saturation and renin (not shown). Arterial EPO levels correlated negatively with hematocrit and oxygen saturation.

Serum EPO levels correlated with hematocrit and arterial oxygen saturation, as is usually found in healthy subjects as well as patients with anemia or hypoxemia. The presence of a correlation between EPO levels in renal veins and percentage of stenosis and renin levels found in this preliminary study may suggest some influence of the RAAS on EPO production. These observations are in agreement with the stimulating effects of angiotensin II (enhanced by renin) on EPO production, found by others [6]. Nowicki et al. [5] did not find a clear correlation between RAAS activation, by sodium depletion, and EPO production. It must be realized, however, that serum EPO levels do not necessarily reflect EPO production. Moreover, it may be assumed that, in the case of one-sided RAS, ipsilateral increased EPO production may be compensatorily reduced in the contralateral kidney. We did not find clear differences in EPO levels between both renal veins, and correlations were poor in the RRV, which may be explained by the fact that 4 of 7 patients had bilateral RAS and the degree of stenosis was moderate in most patients.

Erythrocytosis is not a common finding in patients with RAS; however, the use of ACE inhibitors in renal transplant recipients was associated with a slight hemoglobin decrease [8]. Thus, the in vivo consequences of altered EPO production by RAAS (in)activation are far from clear. Further study is required to establish the role of the RAAS as a regulator of EPO production.

Parameters correlated

EPO (ART) – renin (ART) EPO (RRV) – renin (RRV) EPO (LRV) – renin (LRV) EPO (ART) – 02SAT (ART) EPO (ART) – Ht (ART) EPO (RRV) – STEN% (right) EPO (LRV) – STEN% (left)

Table 2. Correlations of arterial and venous EPO levels with renin levels, percentage of stenosis and oxygen saturation in patients with RAS

ART = Arterial; SAT = saturation; Ht = hematocrit; STEN% = percentage of stenosis. A p value < 0.05 was considered significant.

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