Erythropoietin-Associated Hypertension: What Role for Blood Viscosity Changes?

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Dear Sir,

Erythropoietin, by correcting anemia, is a major advance in the management of patients undergoing hemodialysis (HD) [1–3]. Continued benefits maintained for up to 24 months without loss in efficacy have ameliorated the quality of life of dialyzed patients [4]. However, worsening or occurrence of hypertension are potential risks for erythropoietin (r-EPO)-treated patients frequently reported in literature [1–3]. Enhanced blood viscosity due to correction of anemia with inadequate adaptation of vascular resistance or cardiac output have recently been evoked, as risk factors for developing hypertension and left ventricular hypertrophy [5]. This could be a major concern in a uremic population already exposed to a high rate of cardiovascular morbidity and mortality [6].

Since data on blood viscosity changes during r-EPO therapy are still lacking in the literature, we are encouraged in presenting the results of a study evaluating this parameter in 13 patients who have received r-EPO for 1 year or longer. r-EPO was administered intravenously at the end of hemodialysis session. Individual r-EPO requirements were determined: (1) by administering r-EPO with stepwise dose increments (24 IU/kg, 3 times weekly) every 14 days according to hemoglobin (Hb) increases and (2) by adapting the weekly dose to maintain Hb levels around 11 g/dl (maintenance dose 349 IU/kg/week; range 36–768). Dynamic blood viscosity was measured at 37°C using a coaxial cylinder viscometer (Contraves AG, Rheomat 15, Zürich-S) at increasing shear rates (28–1,400 s⁻¹).

The results are presented in table 1. r-EPO corrected anemia in all patients and improved their well-being with a very low incidence of side effects. Mean Hb levels increased from 7.08 ± 0.35 to 11.2 ± 0.35 g/dl with r-EPO and stabilized at the upper value. The average dry body weight remained unchanged at 55 ± 1 kg. The supine predialysis mean arterial pressure (MAP) did not change significantly (90 ± 4.9 vs. 90 ± 3.3 mmHg) but antihypertensive drugs had to be prescribed in 3 patients. As shown in table 1 and in figure 1, a 0.33 increase in blood viscosity was observed at all shear rates.

In conclusion, hypertension developed only in 3 patients (0.23) receiving r-EPO, whereas increased dynamic blood viscosity was constantly associated with rising Hb levels. These observations suggest that increased blood viscosity per se is not a major determinant of hypertension in r-EPO-treated patients. Our data underscore the importance of previous hypertension as a predictive factor or arterial pressure elevation in patients submitted to r-EPO therapy. Hypertension associated with hematocrit increases induced by r-EPO is presumably multifactorial.

Viscosity at shear rates from 28 to 1,355 s⁻¹.

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431

With r-EPO

Hb = 11.2 ± 0.45 g/dl

Before r-EPO

Hb = 7.08 ± 0.45 g/dl

Fig. 1. Viscosity in relation to shear rates before and with r-EPO treatment.

> 2

o

Shear rate, s

200

-1

600

1,200

1,400

Among other possibilities, the potential role of r-EPO and renin substrate interactions should be explored, taking into account the structural and immunological relationship between these two peptides [7–9].

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