Letter and Reply

Drug-induced erythropoiesis and outcome: should we give up the haemoglobin target approach and return to the ratio between erythropoiesis-stimulating agents and haemoglobin?

Sir,

In a recent paper, the authors expressed concern that further evidence has bolstered the link between erythropoiesis-stimulating agents (ESA) and the risk of stroke, death due to cancer in patients with history of malignancies and thrombosis in patients with chronic kidney diseases randomized to complete anaemia correction. Therefore, we ask if ‘the authors should give up the haemoglobin (Hb) target approach’ [1].

In fact, recent evidence not only demands the lowering of Hb target levels but also underscores that there is also a price to be paid in terms of the ESA dose to reach this target—that is, a poor haematopoietic response and the associated increased risk of death or cardiovascular events. Therefore, the degree of haematopoietic responsiveness—or lack of responsiveness—to treatment, and not Hb values alone, should be taken into account in ESA therapy [2–5].

But how can we measure this ‘lack of responsiveness’ to ESA? Different arbitrary cut-off definitions of responsive quartiles have been used, thus rendering comparisons impossible. ‘Lack of responsiveness’, ‘ESA response coefficient at the individual level’, ‘poor response to ESA dosage’ and ‘ESA dose requirement’ [4, 5] are terms suggested to identify these new criteria for evaluating ESA efficacy/safety with different arbitrary cut-off definitions: the lowest responsive quartile of change in haemoglobin level is < 2 or < 3%, but which one should be used?

We suggest returning to the common and simple reproducible parameter which is the weekly ESA dose/kg divided by Hb as ESA/Hb ratio (Figure 1). ESA/Hb ratio is a simple, numerical and comparable parameter that can be used for statistical evaluation.

In our Regional Audit on Anaemia, weekly ESA dose/kg divided by Hb was used in 3053 uraemic patients (Figure 1). The mean value was 9.0 ± 3.5, and logistic regression analyses allowed the identification of the strongest predictors for ESA resistance, such as transferrin saturation < 30% [odds ratio (OR) 2.87, 95% confidence interval (CI) 1.34–6.31] and C-reactive protein > 12 mg/dL (OR 2.70, 95% CI 1.01–7.14).

The adoption of this ratio could allow for comparable criteria beyond those predicted by Hb alone and could replace the use of Hb values exclusively as a target for ESA treatment.

Conflict of interest statement. None declared.

1. Locatelli F, Del Vecchio L. Erythropoietic response to erythropoiesis-stimulating agents and outcome: should we give up the haemoglobin target approach? Nephrol Dial Transplant 2011; 26: 2069–2071
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