Interpretation of erythropoietin levels in patients with various degrees of renal anemia

To the Editor: In interesting paper, Fehr et al [1] showed relative erythropoietin deficiency in patients with GFR <40 mL/min, and concluded that it was the sequence of either altered set point for hormone production or due to renal tissue damage. On the other hand, Machiguchi et al’s paper [2] and our preliminary study led to extend Fehr’s explanation. Machiguchi et al [2] have shown that in patients with IgA nephropathy and relatively preserved renal function (sCr 0.5-2.5 mg/dL), urinary excretion of N-acetyl-β-D-glucosaminidase (NAG) inversely correlated with serum erythropoietin concentration. According to these results, our recent study by Sulikowska et al [3] showed that functional status of renal vasculature, estimated as dopamine-induced glomerular filtration response (DIR), strongly correlated with NAG excretion. Furthermore, our preliminary study conducted in 30 untreated IgA patients, with GFR 109 ± 27.5 mL/min, showed that DIR correlated with changes of serum erythropoietin concentration during dopamine infusion (serum erythropoietin, before dopamine mean: 10.9, range: from 1.3 to 10.4; after dopamine mean: 9.2, range: from 1.8 to 29.1 U/L) and 24-hour proteinuria (<10.9, range: from 1.3 to 10.4; after dopamine mean: 9.2, range: from 1.8 to 29.1 U/L). These results suggest that serum erythropoietin concentration come into view as a marker of functional status of tubulointerstitial compartment in patients with various degrees of renal damage.

Regarding these data, we have commenced the study to examine whether serum erythropoietin could be used as a marker to predict the progression of renal disease.

Beata Sulikowska, Grazyna Odrowaz-Sypniewska, and Jacek Manitius
Bydgoszcz, Poland

Correspondence to Jacek Manitius, Department of Nephrology, Hypertension and Internal Medicine, Medical University, Sklodowskie-Curie 9,85-094 Bydgoszcz, Poland.
E-mail: nerka@nerka.mtl.pl

REFERENCES


Reply from the Authors

We would like to thank Sulikowska et al for their comments to our study [1]. We were not aware of the cited study performed in patients with IgA nephropathy and moderate renal insufficiency, which showed that urinary N-acetyl-β-D-glucosaminidase (NAG) excretion inversely correlated with serum erythropoietin levels [2]. Together with their own data also obtained in patients with IgA nephropathy, the authors suggest that serum erythropoietin may be a marker for the functional status of the tubulointerstitial compartment in patients with various degrees of renal damage.

Although this hypothesis is intriguing and worth to pursue further, there are “caveats.” First, NAG is commonly used as a marker for tubular damage. Sulikowska et al mention that NAG excretion in their patients positively correlated with proteinuria, and that the latter may be responsible for tubular dysfunction, as described earlier [3]. However, in order to prove the tubular origin of NAG, they should formally exclude the possibility of glomerular filtration of NAG in the context of nonselective glomerular proteinuria. They would have to demonstrate the absence of immunoglobulins in the urine, which have about the same molecular weight as NAG, and measure other tubular markers (as α1-microglobulin).

Second, the findings in patients with IgA nephropathy may not be generalizable for all patients with renal insufficiency. The same is true for our own findings, which were obtained in a population with mainly diabetic, hypertensive, and vascular renal disease. The well-known example of polycystic kidney disease reminds us that the diagnosis of primary kidney disease may indeed play an important role for the interpretation of erythropoietin levels. In these patients, erythropoietin secretion is markedly preserved, despite advanced renal insufficiency, and some of these patients may even remain independent of erythropoietin while on dialysis [4]. Therefore, one should look closely at the main trigger of erythropoietin secretion in each of these diseases, namely, the partial pressure of oxygen in the renal medulla.

Thomas Fehr
Boston, Massachusetts
Opportunity and cost of sevelamer in dialysis patients

To the Editor: Manns et al [1] have recently pointed out the high cost of replacing by sevelamer, the calcic phosphate-binder, and the higher prevalence of patients who would necessitate sevelamer according to K/DOQI guidelines in America than in Canada, and in hemodialysis patients (66% vs. 54%) than in peritoneal dialysis patients (60% vs. 38% in U.S. and Canadian patients, respectively). These differences suggest us that it may be due to higher prevalence of patients (60% vs. 38% in U.S. and Canadian patients, respectively). These differences suggest us that it may be due to higher prevalence of patients with ESRD and an analysis of its potential economic impact in Canada and the United States. Kidney Int 66:1239–1247, 2004

Unfortunately, the authors were unable to include the Calcium Acetate Renagel Evaluation (CARE) study in their pharmacoconomics analysis because it was published after their cut-off date [2]. Likewise, results of the CARE study were not available during the development of the current K/DOQI clinical practice guidelines for Bone Metabolism and Disease in Chronic Kidney Disease [3].

Given the enormous financial burden of caring for the ever-increasing dialysis population, it is imperative that two criteria be met before expanding Medicare benefits to cover the cost of sevelamer: (1) sevelamer must be shown to be at least as effective as calcium acetate in achieving K/DOQI guidelines for serum phosphorus and Ca × P product; and (2) sevelamer should have documented beneficial effects on the rates of hospitalization and mortality. Unfortunately, sevelamer has not been shown to meet either of these two criteria. In the CARE study, calcium acetate was clearly more efficacious than sevelamer as a phosphate binder [2]. Because uncontrolled hyperphosphatemia is associated with a number of clinical consequences [4], use of more effective phosphate binders may, in fact, be associated with lower overall health care cost. Finally, because the alleged link between calcium loading from use of calcium-based phosphate binders and cardiovascular calcification has not been substantiated in well-designed controlled trials, the argument for the

Economic impact of sevelamer in patients with ESRD

To the Editor: We read with interest the excellent and timely article by Manns et al on the economic impact of the use of sevelamer in ESRD patients [1]. Unfortunately, the authors were unable to include the Calcium Acetate Renagel Evaluation (CARE) study in their pharmacoconomics analysis because it was published after their cut-off date [2]. Likewise, results of the CARE study were not available during the development of the current K/DOQI clinical practice guidelines for Bone Metabolism and Disease in Chronic Kidney Disease [3].

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