American Journal of Transplantation 2003; 3: 771–772
Blackwell Munksgaard

ISSN 1600-6135

Editorial

Anemia After Kidney Transplantation – Is the Incidence Increasing?

Donald E. Hricik[a,b,*]

[a]*University Hospital of Cleveland, Medicine/Nephrology, Cleveland, OH, USA*
[b]*Case Western Reserve University, Medicine, Cleveland, OH, USA*
**Corresponding author: Donald E. Hricik, deh5@po.cwru.edu*

Received 16 February 2003, accepted for publication 3 March 2003

Introduction

Prior to the availability of recombinant erythropoietin, virtually all kidney transplant recipients exhibited some degree of anemia in the early post-transplant period, primarily as the consequence of operative blood loss and postoperative phlebotomies superimposed on a pre-existing state of hypoerthyropoiesis characteristic of renal failure. Restoration of endogenous erythropoietin secretion by the renal allograft, now known to occur within hours to days after transplantation (1), generally led to correction of anemia within a period of 3–8 months (2), at least in patients with well-functioning grafts. Interestingly, widespread use of recombinant erythropoietin in patients awaiting kidney transplantation has not entirely eliminated the problem of early post-transplant anemia (less than 6 months after transplantation). Recent longitudinal studies in adults (3) and children (4) indicate that the prevalence of anemia at the time of renal transplantation ranges between 41% and 67%, respectively. In addition to perioperative blood losses, other factors contributing to early post-transplant anemia include iron deficiency, the persistent effort of uremic toxins, and the negative effects of immunosuppression on erythropoiesis.

More concerning than the well-recognized problem of *early* post-transplant anemia are recent reports suggesting a relatively high prevalence of *late* post-transplant anemia occurring more than 6 months after transplantation. Cross-sectional studies suggest a prevalence of late post-transplant anemia ranging between 14% and 23.3% in adults (5,6), with much higher rates in children (4). A recent longitudinal analysis performed at two centers showed that 30% of adult renal transplant recipients were anemic at some time during a follow-up period of 5 years and that the prevalence of anemia increased over time (2). In all of these studies, analyses of factors contributing to late post-transplant anemia indicated, not surprisingly, that impaired renal allograft function is the variable most strongly associated with late post-transplant anemia. Iron deficiency, immunosuppressive therapy, and decreased red blood cell survival were cited as contributing factors.

In this issue of *American Journal of Transplantation*, Vanrenterghem et al. present the results of a large multicenter survey of more than 4000 kidney transplant recipients from 16 European countries, performed in an effort to further clarify the prevalence, causes, and current practices for the management of post-transplant anemia (7). Among cohorts of patients transplanted between 6 months and 5 years earlier, the overall prevalence of anemia was 38.6%. This large study confirmed a strong association between hemoglobin concentration and allograft function. Novel findings from the analysis include an association, independent of allograft function, between late post-transplant anemia and the use of angiotensin inhibitors (either angiotensin converting enzyme inhibitors or angiotensin II receptor antagonists), use of either mycophenolate mofetil or azathioprine for immunosuppression, and advanced donor age. Even among the patients categorized as having severe anemia, the use of erythropoietin was surprisingly uncommon. On the other hand, although this survey was not designed to test the hypothesis that exogenous erythropoietin can correct post-transplant anemia, it is concerning that hemoglobin concentrations of the patients treated with erythropoietin were actually lower than those of patients not treated. The latter observation suggests the possibility of resistance to exogenous erythropoietin in some of the transplant recipients.

Because the incidence of post-transplant anemia depends on its definition, it is difficult to compare the results of this study to previous studies that have used slightly different definitions. However, the relatively high prevalence of post-transplant anemia reported by Vanrenterghem et al. is intuitively believable, given recent trends toward increased usage of angiotensin inhibitors for their putative renoprotective effects in transplant recipients, increased use of older donors, and an increased reliance on myelosuppressive immunosuppressants such as mycophenolate mofetil. The use of the potentially myelosuppressive mTOR inhibitors, not represented in the cohort of patients studied by Vanrenterghem et al., may contribute even

further to erythropoietin resistance and post-transplant anemia.

In dialysis patients, anemia can cause profound adverse effects including impaired cognition, reduced exercise capacity, left ventricular hypertrophy, and reduced quality of life. There is no reason to believe that these associations do not apply to kidney transplant recipients as well. Additional studies are warranted to further define the causes, consequences, and appropriate management of anemia after kidney transplantation. Optimizing renal allograft function is an obvious goal that may help to minimize anemia. Although it is logical to presume that more aggressive use of exogenous erythropoietin is warranted to correct post-transplant anemia, the cost of treatment with erythropoietin needs to be considered in future analyses that weigh the benefits and risks of renal transplantation. Finally, additional studies are needed to determine whether some patients are resistant to erythropoietin as the result of myelosuppressive immunosuppression, chronic inflammation within the allograft, or other factors.

References

1. Sun CH, Ward HJ, Paul WL, Koyle MA, Yanagawa N, Lee DBN. Serum erythropoietin levels after renal transplantation. N Engl J Med 1989; 321: 151–157.
2. Kahng K, Kang C, Kwak J. Changes in hemoglobin levels after renal transplantation. Transplant Proc 1998; 30: 3023–3024.
3. Yorgin PD, Scandling JD, Belson A, Sanchez J, Alexander SR, Andreoni KA. Late post-transplant anemia in adult renal transplant recipients. An unrecognized problem? Am J Transplant 2002; 2: 429–435.
4. Yorgin PD, Belson A, Sanchez J et al. Unexpectedly high prevalence of posttransplant anemia in pediatric and young adult renal transplant recipients. Am J Kidney Dis 2002; 40: 1306–1318.
5. Miles AM, Markell MS, Daskalakis P et al. Anemia following renal transplantation. Erythropoietin response and iron deficiency. Clin Transplant 1997; 11: 313–315.
6. Saito S, Fujiwara T, Sakagami K, Matsuno T, Tanaka N. Anemia following renal transplantation. Transplant Proc 1998; 30: 3025–3026.
7. Vanrenterghem Y, Ponticelli C, Morales JM et al. Prevalence and management of anemia in renal transplant recipients: a European study. Am J Transplant 2003; 3: 835–845.