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Letter to the Editor

Continuing Erythropoietin During Peripheral Blood Stem Cell Collection in Myeloma: Can It Reduce Toxicity of Autologous Transplants?

Erythropoietin (EPO) regulates the growth and production of red blood cells (RBCs) [1,2] and has pleomorphic effects on apoptosis and the regulation of vascular integrity [3]. Randomized, placebo-controlled trials have demonstrated the benefits of recombinant human EPO (rHuEPO) to increase Hb levels, reduce transfusion requirements, and improve quality of life in anemic cancer patients undergoing chemotherapy [1,4,5]. Interestingly, rHuEPO also may provide a survival benefit for patients with multiple myeloma (MM) through beneficial changes in immune function [1,6]. Furthermore, rHuEPO can increase the number of circulating vascular progenitors and may play a role in the repair of ischemic tissue injury, such as myocardial infarction and stroke [3]. Anemia before allogeneic hematopoietic stem cell transplantation (HSCT) has been associated with increased transfusion requirements and increased treatment-related mortality (TRM) [7]. More recently, we have found that anemia on the day of peripheral blood progenitor cell (PBPC) collection influences graft content of vascular progenitors and is associated with increased toxicity after autologous HSCT [8]. Herein we provide new insight on the possible effect of concomitant rHuEPO therapy during the mobilization of PBPCs in patients with MM undergoing autologous HSCT.

Once the study was approved by our Institutional Ethics Review Board, informed consent was obtained from all patients for analysis of medical information. A total of 124 participating patients underwent autologous HSCT to treat MM between August 1994 and February 2006 at our hospital. The mean age of the patients was 58 years (range, 33-69 years), and all patients had symptomatic disease requiring systemic chemotherapy (see Table 1). Seven patients received rHuEPO during pretransplantation chemotherapy cycles and throughout the period of mobilization and collection of autologous PBPCs, 5 patients received rHuEPO at some point during pretransplantation chemotherapy but not during the PBPC mobilization period, and 112 patients did not receive rHuEPO at any time before transplantation. Data were extracted from patient medical records, and transplantation-specific outcomes were retrieved from The Ottawa Hospital Blood & Marrow Transplant Program clinical database.

Patients who received rHuEPO during the PBPC mobilization phase had a lower Hb level at diagnosis compared with patients who did not receive rHuEPO (92 g/L vs 108 g/L; $P = .04$) (see Table 2). However, on the date of the first PBPC collection, the hemoglobin (Hb) levels in both groups were notably similar (110 vs 107 g/L; $P = .54$) with a significantly higher relative increase in Hb in patients receiving rHuEPO (20% increase vs no change in patients who did not receive EPO; $P < .05$). We suggest that EPO may have contributed to the substantial increase in Hb levels at PBPC collection. Interestingly, the clinical toxicity after HSCT was similar in both groups. Moreover, there was an observed trend toward decreased transfusion of packed red blood cells (PRBCs) in the group who received rHuEPO (2.6 vs 3.2 units; $P = .41$).

We recognize that multiple factors may have influenced the decision to administer rHuEPO in the small subset of patients analyzed in this cohort. Furthermore, it remains unclear how anemia at diagnosis is related to Hb levels at PBPC collection. In fact, a subset of patients with Hb < 100 g/L at diagnosis and who never received rHuEPO had similar Hb values at diagnosis as the group of patients who received rHuEPO (85.4 vs 92.6 g/L; $P = .11$). Comparing these 2 groups demonstrated no significant difference in Hb values at PBPC

Table 1. *Cohort characteristics*

Patient characteristics (n = 124)	
Age at transplantation, years, mean (range)	58 (33-69)
Sex, female/male (%)	53/71 (43/57)
Salmon and Durie stage, n (%)	
I	27 (22)
II	18 (15)
III	72 (58)
Unknown	7 (6)
Graft $CD34^+ \times 10^6$ cells/kg, mean	7.3 ± 4.8
Days to absolute neutrophil count recovery, mean	15.6 ± 33.4
Days to platelet recovery, mean	15.5 ± 15.2
Total length of stay, days, mean	21.0 ± 9.3
Patients requiring intensive care, n (%)	3 (2.4%)
Transplantation-related mortality at day 100, n (%)	1 (0.8%)

All means are ± 1 standard deviation.

Table 2. *Comparison of patients who did and did not receive EPO during PBPC collection*

	EPO patients	Non-EPO patients	*P* value
N	**7**	**112**	
Total length of stay, days, mean	**22.0 ± 6.7**	**20.7 ± 8.9**	**.63**
Patients with any organ toxicity, n (%)	**6 (86)**	**87 (78)**	**.95**
Patients with high organ toxicity, n (%)	**3 (43)**	**49 (44)**	**.99**
Mean Hb at diagnosis, g/L	**92.6 ± 9.2**	**108.8 ± 20.9**	**.002**
Mean Hb on day of collection, g/L	**110.1 ± 11.5**	**107.2 ± 12.8**	**.54**
Mean Hb before transplantation, g/L	**110.6 ± 15.6**	**110.4 ± 14.4**	**.98**
Mean PRBC units transfused	**2.6 ± 1.9**	**3.2 ± 2.8**	**.41**

NS indicates not significant.
High organ toxicity is ≥ 2 cumulative grades in all organs by the Seattle criteria.
All means were compared using Student's *t*-test, and proportions were compared used χ^2 analysis.

collection and no observed difference in toxicity after HSCT. The potential influence of concomitant medications, performance status, and other factors could not be further assessed in our retrospective analysis.

A study by Hunault-Berger et al. [9], in which rHuEPO was administered with chemotherapy cycles before autologous transplantation in a cohort of anemic patients with MM, found that these patients required fewer PRBC transfusions compared with patients who were not given rHuEPO. In addition, rhuEPO-treated patients had reduced lengths of hospital stay. In their study, however, patients did not receive rHuEPO during the mobilization of PBPCs. Several studies addressing the addition of rHuEPO to the mobilization of PBPCs have not assessed toxicity patterns after transplantation. We hypothesize that continuing rHuEPO during the mobilization and collection of PBPCs may influence the graft content of vascular progenitors, and we have observed that reinfusion of grafts enriched for vascular progenitors is associated with reduced transplantation-related toxicity [10].

Our results suggest that rhuEPO may be a useful adjunct to increase the regenerative capacity of hematopoietic stem cell grafts and may play a role in preventing toxic organ injury after HSCT.

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