Allogeneic peripheral blood and bone marrow stem cell transplantation for chronic myelogenous leukemia: a single center study from Iran

Haematologica 2007; 88:(5)e67-e68

Stem cell transplantation (SCT) is the only known cure for chronic myelogenous leukemia (CML). Peripheral blood stem cells (PBSC) have increasingly been used for allogeneic SCT during recent years.[1] Despite the ease of collection, rapid engraftment and similar incidence of acute GVHD (a-GVHD) with PBSC transplantation, there are still concerns about chronic GVHD (c-GVHD), relapse and survival.[2-5] We describe our experience of 62 consecutive CML patients, who received a sibling allogeneic SCT in our center between August 1991 and February 2002. The diagnosis and disease stage were confirmed by hematological and cytogenetic evaluations performed within 15 days before admission for transplantation. The conditioning regimen consisted of cyclophosphamide and busulfan. All patients were given cyclosporin A and methotrexate for GVHD prophylaxis. The main characteristics of the patients, and donors are summarized in Table 1. The median time to neutrophil count greater than $0.5x10^9$/L was 12 days in the PBSC and 19 days in the BM group ($p<0.001$). The median time to platelet count greater than $50x10^9$/L was 15 days in the PBSC and 27.5 days in the BM group ($p<0.001$). a-GVHD occurred at a median interval of 9.5 days (range, 4-75 days) in the PBSC and 12.5 days (range, 6-31 days) in the BM group post-transplant (p=0.14). The cumulative incidence of a-GVHD grades 0-I, II, and III-IV did not differ significantly between the PBSC and BM groups. c-GVHD of all grades developed in 19/31 (61%) and 7/16 (44%) evaluable patients in the PBSC and BM groups respectively (p=0.2). The incidence of major post-transplant complications including pneumonia, idiopathic pneumonitis, veno-occlusive disease, hemorrhagic cystitis and cardiomyopathy was not significantly different between the two groups. As of February 1 2002, 25 patients (64%) of the PBSC group and 10 patients (43%) of the BM group were alive at a median of 15 months (range, 4-49 months) after PBSC transplantation and 84 months (range, 24-127 months) after BM transplantation. The overall survival is shown in Figure 1. *Discussion.* Previous studies compared these two types of SCT in hematologic disorders,[2,6] but few compared them in individual diseases.[5] The PBSC group had a significantly

Table 1. Transplantation details

		PBSC Group (n = 39)	BM Group (n = 23)	P value
Patients and donors characteristics	Male/Female	23/16	13/10	NS
	Median patients age	26.5	30.5	NS
	Median donors age	30	28	NS
	HLA (identical/mismatch)	34/5	19/4	NS
	Median diagnosis-SCT interval in months (range)	17 (7-51)	22 (7-37)	NS
	Chronic/Advanced phase	37/2	22/1	NS
	Median nucleated cell ($x10^8$/kg)	5.56	1.97	.008
Engraftment, hospitalization, and GVHD	Days to (Median)			
	ANC>0.5 x 10^9/L	12	19	< .001
	ANC>1 x 10^9/L	14	23	< .001
	Platelet>20 x 10^9/L	13.5	18	NS (.24)
	Platelet >50 x 10^9/L	15	27.5	< .001
	Days in hospital (Median)	54	59	NS (.16)
	Acute GVHD			
	Grade 0-I	10	4	NS (.43)
	Grade II	8	7	
	Grade III-IV	21	12	
	Chronic GVHD/Patients at risk	19/30	7/16	.2

NS = not significant.
ANC = absolute neutrophil count.

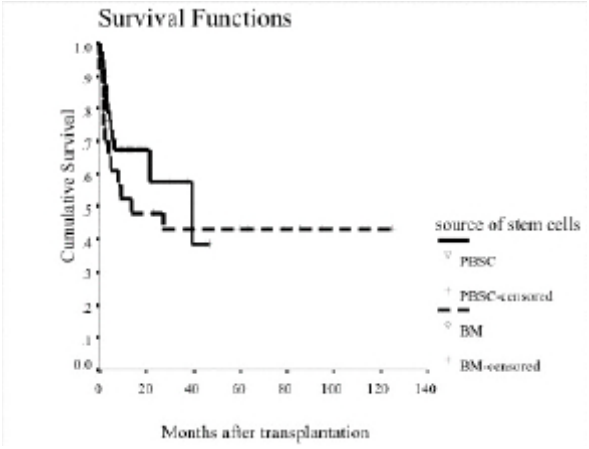

Figure 1. overall survival after SCT

faster neutrophil and platelet engraftment compared to the BM group, which is in agreement with previous studies.[2-4,7,8] Though in our study it was not statistically significant, the earlier engraftment may lead to earlier discharge from hospital (p=0.16). Although much of the morbidity and mortality associated with SCT is due to cytopenias encountered after transplantation,[5] in our experience transplantation-related complications were not significantly different in the PBSC group in spite of a shorter period of cytopenia. One of the greatest concerns with allogeneic PBSC transplantation arises from its high T-cell content which can lead to increased risk and severity of GVHD.[3,7] Although it did not reach statistical significance, in our study, PBSC transplantation was associated with earlier onset of a-GVHD (p=0.14). In both groups the incidence of clinically important a-GVHD (grade II-IV) was similar. These results are consistent with previous studies in various hematological diseases.[2-4,8] Previous studies demonstrated an increased incidence of c-GVHD after PBSC transplantation compared to BM transplantation. Although it is not known why the incidence of c-GVHD is higher after PBSC transplantation than BM transplantation while the incidence of a-GVHD is similar, one hypothesis is that the G-CSF-induced TH1?TH2 polarization and the large number of immunosuppressive monocytes in PBSC grafts may wane within months after SCT.[5,6] Despite a higher incidence of c-GVHD in PBSC recipients, we can not show any significant difference between the two groups. Most previous studies showed that projected actuarial 3-year to 5-year survival rates are around 50-60% with slightly lower probabilities for disease-free survival.[9] One of the limitations in our study comes from the fact that we performed only BM transplantation in the initial years of transplantation in our center and then more PBSC transplantations in recent years, but our transplant-protocols including conditioning, GVHD prophylaxis and management were the same. Consequently, the follow-up of BM transplanted patients has turned out to be much longer than that of PBSC ones considering this fact, although overall survival was not statistically different between the two groups (p= 0.36) it seems that the patients in the PBSC group had a better survival in the first 3 years of follow-up than those in the BM group. It has to be mentioned that in our study no death was reported after the 27th month of the post-transplantation period in the BM group. However, not until that point of time did the PBSC survival curve reach a plateau. This means that the

long-term survival rate of the PBSC group is not necessarily longer than that of the BM group. This study suggests that, as in other hematological malignancies, allogeneic PBSC transplantation performed in the chronic phase of CML is safe and may be associated with a more rapid engraftment than BM transplantation, without increased risk of early complications or clinically important a-GVHD.

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