Clinical and economic evaluation of using granulocyte colony-stimulating factor after autologous peripheral blood progenitor cell transplantation in children

We evaluated the clinical and economic impact of using granulocyte colony-stimulating factor (G-CSF) post-infusion in 129 children receiving autologous peripheral blood progenitor cell transplant (PBPCT) (96 with G-CSF, 33 with no G-CSF). Neutrophil engraftment was faster in the G-CSF group (9 days vs 11 days, p<0.0007), whereas platelet engraftment (> 50¥109/L) was delayed (25 days vs 15 days, p<0.005). Patients receiving G-CSF needed more platelet transfusions and the overall cost of their care was increased by 26%.

From December 1993 to December 2000, 129 children with hematologic malignancies and solid tumors underwent 133 autologous PBPCT, because 4 patients underwent two procedures. Two groups of patients were defined: those who were given G-CSF (n=96) and those who were not given G-CSF (n=33). The patients' clinical characteristics are shown in Table 1. The conditioning regimens used were grouped as follows: total body irradiation (TBI)-based or chemotherapy-based. Peripheral blood progenitor cells were collected by apheresis as we previously reported elsewhere.[1]

Post-infusion G-CSF was given at a dose of 10 μg/kg/day i.v. from day +1 until an absolute neutrophil count greater than 0.5×10^9/L was reached and maintained for three days.

Costs were calculated in US dollars. Differences in costs were investigated for the post-infusion period because costs prior to the PBPCT were similar in both groups. Supportive care requirements were analyzed in the two groups. Unit prices of medical resources for pediatric patients have been previously reported.[2] Statistical significance was determined using Student's test when samples were normally distributed and the Mann-Whitney U test when they were not. Engraftment probability was estimated by the Kaplan-Meier method. The log-rank test was used for comparisons.

Neutrophil engraftment was reached earlier in patients who received G-CSF (median 9 days, range: 7-44) than in the group not given G-CSF (median 11 days, range: 8-15) ($p< 0.0007$). Platelet engraftment (≥ 20×10^9 platelets / L) was similar in both groups (median 13 days, range: 7-91 vs median 12 days, range: 9-41) (p=ns). However, the time to achieve a platelet count of more than 50×10^9/L was shorter in the group not given G-CSF (median 15 days, range: 12-71) than in patients receiving G-CSF (median 25 days, range: 10-270) ($p<0.005$).

Data about supportive care requirements are shown in Table 1. Platelet requirements were less among the group not given growth factors ($p<0.02$). There were no significant differences between the two groups in antibiotic therapy and duration of hospitalization.

Supportive care costs were similar for the two groups (Table 2), but the use of G-CSF costs a median of 700$ for each patient, increasing the overall cost by 26%.

The main findings of our study are: first, neutrophil engraftment was accelerated in patients who received G-CSF after infusion, as has been previously reported.[3-7] However, platelet recovery was delayed in patients under G-CSF treatment, in accordance with data published by Kawano *et al.*[7] These authors concluded that the use of G-CSF in children undergoing PBPCT should be reconsidered because the marginal benefit of a 1 day earlier recovery of granulocytes could be offset by delayed platelet recovery. Moreover, the faster neutrophil recovery did not lead to clinical benefits such as shorter antibiotic therapy and hospital stay. This can be explained because one of the main discharge hospital factors used to be platelet requirements which are increased in the G-CSF-treated group, and the small

Table 1. Patients' characteristics.

	G-CSF group	No G-CSF	p
No.	96	33	
Age (years)			
Median	8	7	0.8
Range	(1-18)	(1-18)	
Sex: male/female	60/36	23/10	0.4
Diagnosis			
Hematologic malignancies	42	7	
Solid tumors	54	26	0.04
Disease status			
1 CR	50	14	0.11
2 CR	21	4	
> 2 CR	25	15	
Conditioning	10	3	0.8
TBI-based			
chemotherapy-based	89	31	
$CD34^+$ cells/kg			
Median (range)	3 (0.17-44)	6 (1-35)	0.2
$<5\times10^6$	60	15	
$>5\times10^6$	38	17	
Days of antibiotics			
Median	9	7	0.07
Range	(0-33)	(0-36)	
No. of PLT units transfused			
Median	3	2	0.02
Range	(0-39)	(0-11)	
No. of RBC units transfused			
Median	2	2	0.06
Range	(0-17)	(0-4)	
Days in hospital			
Median	17	16	0.2
Range	(9-72)	(6-42)	

CR: complete remission; TBI: total body irradiation; PLT: platelets; RBC: red blood cells.

Table 2. Economic analysis.

Costs (US$)	G-CSF group (Mean±SD)	No G-CSF (Mean±SD)	p
Antibiotics	350±275	355±592	0.1
Platelets	850±1065	635±675	0.3
RBC	275±1080	160±115	0.5
Hospitalization	3315±1180	2900±1032	0.1
G-CSF	700±433	0	0.0001

Abbreviations: SD: standard deviation, RBC: red blood cells.

difference in neutrophil engraftment does not have a clinical impact on supportive care. Our results contrast markedly with those of other studies by Tarella[5] and McQuaker[6] who found a shorter median duration of antibiotic use and a shorter hospital stay in patients treated with G-CSF. These differences could be explained by the small number of patients in these studies (only 20 patients in each group) and the age group (adult patients).

Another significant finding of our study is that G-CSF after autologous PBPCT was associated with a higher overall cost, not only due to the cost of the G-CSF itself (median of 700$ per patient), but also due to an increased resource utilization (mainly platelet transfusions).

Recently, the *American Society of Clinical Oncology* (ASCO)[8] recommended administration of G-CSF as an adjunct to PBPCT to accelerate hematopoietic reconstitution. The ASCO guidelines for using G-CSF in children state that in the absence of conclusive pediatric data, recommendations for adults are applicable to children.

Parsons *et al.*[9] analyze the use of hematopoietic growth factors after transplantation in children and found that up to 32% of indications were at the discretion of the physician. Since there is not a definitive consensus on this issue, these pediatric patients should be included in prospective studies as suggested by Cairo.[10]

We conclude that the administration of hematopoietic growth factors after PBPCT increases overall cost, with no clinical advantages.

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