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Comparative cost analysis of autologous peripheral blood progenitor cell and bone marrow transplantation in pediatric patients with malignancies

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Background and Objectives. This study was conducted in order to compare and analyze clinical and economic outcomes of autologous transplantation using bone marrow or peripheral blood as the source of hematopoietic progenitor cells in pediatric patients with malignancies.

Design and Methods. We collected clinical information and resource utilization from 131 consecutive autologous transplantations (102 peripheral blood progenitor cell (PBPC) and 29 bone marrow (BM) transplants) at a single institution between January 1989 and December 1998 in children with a variety of malignancies. Multivariable linear regression was used to evaluate the associations between pre-transplantation variables, post-infusion events and overall costs. A cost-effectiveness analysis of transplantation for acute lymphoblastic leukemia (ALL) and acute myeloblastic leukemia (AML) patients was also performed.

Results. Hematopoietic recovery was faster in the PBPCT group (days to neutrophil and platelet engraftment: 9 and 13, respectively, versus 14 and 21 for BMT, $p<0.0001$).There were less transfusion, antibiotic and parenteral nutrition requirements and hospital stay was shorter (median 17 days; range 8-38) in the PBPCT group than in the BMT one (median 28 days; range 11-65) ($p<0.0001$) resulting in a median lower overall cost for PBPCT (US$ 7895) compared to BMT (US$ 11820)($p<0.0001$). Major determinants of overall costs for both groups were total body irradiation (TBI)-based conditioning regimen, days of hospitalization and number of transfused platelets. In PBPCT patients, a graft containing $\geq 5\times10^6$/kg $CD34^+$ cells decreased the total cost of transplantation by 27%. Cost-effectiveness was higher for PBPCT than BMT for pediatric AML patients ($p<0.0001$) whereas in ALL patients the cost-effectiveness of the two transplant strategies was not significantly different.

Interpretations and Conclusions. We conclude that, compared to BMT, autologous PBPCT in children is associated not only with clinical benefits but also economic advantages.

Key words: PBPC transplantation, cost analysis, children

Over the past few years, peripheral blood progenitor cell transplantation (PBPCT) has become an alternative to bone marrow transplantation (BMT) following high dose chemotherapy in the treatment of hematologic malignancies and solid tumors.

PBPCT has clinical advantages over BMT, including easier collection, faster hematopoietic recovery with fewer transfusion requirements, shorter courses of antibiotics and earlier discharge from hospital.[1] This led to lower overall costs of autologous transplantation for multiple myeloma and lymphoma patients.[2,3] Lowering costs while preserving clinical outcomes should be a goal for clinicians involved in hematopoietic transplantation.

In the last five years, several studies have included comparative analyses using PBPCT or BMT. Most of these studies were cost minimization rather than cost effectiveness analyses and included small sample sizes of adult patients.[2-7] However, there are few reports regarding this issue in pediatric patients.[8,9] We retrospectively analyzed and compared outcomes and costs of bone marrow and peripheral blood as the source of stem cells in 124

children who underwent autologous transplantation at a single institution. Like others in adults,[2,3,10] we conclude that PBPCT in children is associated not only with clinical benefits but also economic advantages over BMT.

Design and Methods

Patients

From January 1989 to December 1998, 124 pediatric patients underwent 131 autologous transplantations for several hematologic malignancies and solid tumors. In 5 patients two procedures were performed and one patient was autografted three times. The patients' characteristics are shown in Table 1. PBPC were used in 102 transplants and BM in 29 cases. There was no difference in median age and weight of the patients in the two groups. The proportion of patients having each of the diagnoses is not balanced between the groups as the study was not randomized. Informed consent was obtained in all cases.

Mobilization and collection

BM harvesting was performed under general anesthesia using standard techniques in 29 patients. Mononuclear cells (MNC) were determined, but $CD34^+$ count was not available.

Until 1998, PBPC were mobilized with granulocyte colony-stimulating factor (G-CSF) alone (Neupogen®, Amgen, Thousand Oaks, California, USA) once a day, at a dose of 12 µg/kg/day, subcutaneously (s.c.) for 4 consecutive days before starting apheresis. During 1998 we used G-CSF at the same dose with granulocyte-macrophage colony-stimulating factor (GM-CSF) (Leucomax®, Novartis Pharma, Basel, Switzerland) s.c. at 5 µg/kg/day as an approach to enhance the number of $CD34^+$ cells collected in each apheresis. PBPC collections were done using a Cobe Spectra cell separator (Cobe, Lakewood, CO, USA) through a central venous catheter. Details of apheresis procedures have been previously reported.[11,12]

Each apheresis product was analyzed for $CD34^+$ cell content assessed by flow cytometry using an Epics Elite flow cytometer (Coulter Corporation, Hialeah, Florida, USA).[12] The final product containing dimethylsulphoxide was frozen and stored in liquid nitrogen at –196°C until infusion.

Conditioning regimen and supportive care

In general, ALL patients were conditioned with TBI + cyclophosphamide and AML patients with busulphan and cyclophosphamide. For patients with neuroblastoma or Ewing's sarcoma the preparatory regimen consisted of busulphan and melphalan.[13] Several myeloablative regimens were used for the remaining patients, according to their diagnosis and research protocols.

The transplants were carried out in reverse-barrier isolation. Cotrimoxazole was given for *Pneumocystis carinii* prophylaxis at a dose of 8 mg/kg/day and ondansetron was given as an antiemetic. If the regimen included busulfan, clonazepam was used as prophylaxis against seizures. On day 0, collected cells were infused. All patients in the PBPCT group received G-CSF post-infusion (10 µg/kg/day) beginning on day +1 until neutrophil engraftment.

Platelets were transfused if the platelet counts decreased below 20×10^9/L or in cases of bleeding and red blood cells were given to maintain a hemoglobin (Hb) > 8 g/dL. Blood products were irradiated before using. Febrile neutropenia was treated

Table 1. Patients' characteristics.

	PBPCT	*BMT*	*p*
No. of patients	95	29	
Age (years)			
Median	8	8	ns
Range	1-21	2-15	
Weight (kg)			
Median	27	33	ns
Range	9-94	12-60	
Sex			
Male	59	21	
Female	36	8	ns
Diagnosis			
a) Hematologic malignancies			
ALL	13	13	0.01
AML	13	5	
NHL	11	2	
HD	4	0	
b) Solid tumors			
CNST	20	0	
NB	14	2	
ES	11	3	
RB	11	3	
WT	2	1	
PNET	3	0	
Disease status at transplant			
First remission	47	10	ns
Second remission	22	15	
Partial remission or relapse	26	4	

Abbreviations: ALL, acute lymphoblastic leukemia; AML, acute myeloblastic leukemia; NHL, non- Hodgkin's lymphoma; HD, Hodgkin's disease; CNST, central nervous system tumors; NB, neuroblastoma; ES, Ewing's sarcoma; RB, rhabdomyoblastoma; WT, Wilms' tumor; PNET, primitive neuroectodermal tumor.

with a combination of a third generation cephalosporin and amikacin. Empirical treatment with vancomycin and amphotericin B was added after 3 to 5 days and 5 to 7 days, respectively, for persistent fever despite the use of broad spectrum antibiotics. Patients unable to maintain an adequate oral calorie intake were fed with parenteral nutrition.[14] Complete blood counts and basic blood chemistry tests were performed daily. Cultures were obtained if fever appeared. Discharge criteria included neutrophil engraftment, adequate oral intake and control of medical problems.

Definition of parameters and clinical variables analyzed

The day of infusion was designated as day 0. Neutrophil engraftment was defined as the first of 3 consecutive days with an absolute neutrophil count (ANC) > 0.5×10^9/L. Platelet engraftment was defined as the first of three consecutive days with a platelet count > 20×10^9/L without transfusion support. The duration of hospital stay was defined as the number of days from infusion to discharge date from hospital. Toxic mortality was defined as any cause of death other than relapse or progressive disease. Pre-transplantation variables included in clinical outcome and cost analysis were: age, sex, preparatory regimen used, disease status at transplantation, source of hematopoietic cells and number of $CD34^+$ cells infused. Based on our previous engraftment kinetics studies,[11] we analyzed the clinical and economic impact of the number of $CD34^+$ cells infused using a cut-off value for $CD34^+$ cells of $\geq5\times10^6$/kg in PBPCT group.

Economic assesment

All data were collected retrospectively by one observer from admission into transplantation unit until discharge. Data concerning stem cell collection were also included. Direct medical costs were estimated for all patients. The analysis was performed from a hospital viewpoint. Monetary values for 1999 Spanish prices were used for all components. The exchange rate used was: 1 US $ =170 pesetas. Resources used identified for each patient included: stem cell collection, hospitalization, pharmacy, blood products, laboratory tests and radiological procedures. Table 2 shows the unit prices (US$) of medical resources for a standard pediatric patient weighing 30 kg.

Unit prices of hospitalization were obtained from the hospital's accounting system. Costs for pharmaceutical products were based on wholesale price lists applied in our pharmacy department in 1999.

The calculation of costs for blood products was based on the official tariff as published in the *State Official Journal* on 17 February, 1999.

Cost effectiveness analyses were performed in ALL and AML patients. Sensitivity analyses were performed by varying the most significant parameters according to our results: platelet units transfused and duration of hospitalization.

Table 2. Unit prices.

Resource	*Unit prices (US$)*
Stem cell collection	
Mobilization	93
Harvest	1,071
Apheresis	946
Cryopreservation	365
Hospitalization:	
Hematologic care unit (day)	172
Intensive care unit (day)	209
Blood products:	
Platelet transfusions (unit)	236
Red blood cell transfusions (unit)	67
Pharmacy	
Growth factors (day)	31
Conditioning (with TBI / without TBI)	1,403/161
Antibiotics (day)	35
Parenteral nutrition (day)	37
Morphine (day)	1
Inotropics (day)	1
Laboratory investigations	
Blood count (unit)	7
Culture (unit)	1
Radiologic procedures	
X-ray (unit)	9
CT (unit)	189

Abbreviations: TBI, total body irradiation; CT, computer tomography.

Statistical analysis

Data are expressed as median and range. Statistical significance was determined using Student's test when samples were normally distributed and a non-parametric test (Mann-Whitney-Wilcoxon) when samples were not normally distributed. Results were considered significant if the p value was < 0.05.

Correlations were determined by linear regression. A multiple regression model was employed in the multivariant analysis to correlate the dependent variable with significant independent variables from the univariant analysis. To calculate cost-effectiveness we divided the mean total cost

Table 3. Engraftment kinetics.

	PBPCT		BMT	p
No. of CD34+ cells	≥ 5×10⁶/ Kg	< 5×10⁶/Kg	NA	
No. of patients	n = 37	n = 65	n = 29	
Days to neutrophil recovery: median (range)	9 (7-10)	10 (7-16)	14 (9-60)	0.0001
Days to platelet recovery: median (range)				
> 20×10⁹/L	12 (8-33)	14 (7-91)	21 (10-54)	0.0001
> 50×10⁹/L	17 (10-90)	30 (10-270)	37 (12-97)	0.0001
>100×10⁹/L	37 (12-323)	53 (17-288)	55 (21-140)	0.0001

Abbreviations: NA, not available.

Table 4. Resource utilization.

	PBPCT		BMT	p
No. of CD34+	*≥ 5×10⁶/kg*	*<5×10⁶/kg*	*NA*	
No. of patients	n = 37	n = 65	n = 29	
Growth factors median (range)	10 (7-11)	11 (8-18)	0	0.0001
Transfusions median (range)				
Red cells	2 (0-13)	2 (0-16)	4 (1-14)	<0.2,* <0.0001°
Platelets	3 (0-29)	4 (0-33)	8 (1-24)	<0.1,* <0.001°
Antibiotics median (range)	7 (0-23)	10 (0-33)	14 (4-54)	<0.005,* <0.0001°
Parenteral nutrition median (range)	15 (0-30)	17 (0-41)	20 (5-48)	ns,* <0.008°
Inotropic drugs median (range)	0 (0-19)	0 (0-33)	1 (0-49)	ns
Morphine median (range)	0 (0-16)	0 (0-16)	0 (0-18)	ns
Biochemistry tests median (range)	22 (18-37)	24 (15-44)	34 (18-70)	<0.09,* <0.0001°
Blood cultures median (range)	3 (0-24)	3 (0-19)	9 (1-42)	ns,* < 0.0001°
X-ray median (range)	1 (0-12)	1 (0-8)	2 (0-15)	ns
CT median (range)	0 (0-8)	0 (0-4)	0 (0-3)	ns

*Abbreviations: NA, not available; CT, computer tomography; *p value between PBPCT groups; °p value between PBPCT and BMT.*

by the number of saved life years calculated by the Kaplan-Meier method with PBPCT and BMT. We then compared the results to determine the cost per life year gained by PBPCT in relation to BMT.

Results

PBPC mobilization, apheresis procedure and bone marrow harvest

In the PBPCT group, G-CSF alone was used in 81 transplants; G-CSF+GM-CSF was given as the mobilization regimen in the remainder. No significant side-effects were observed during mobilization. A median of 1 leukapheresis was performed (range 1-3). The procedure was well tolerated in all cases, even in small children as we have reported elsewhere.[15] The median number of CD34+ cells obtained was 3.05×10⁶/kg (range 0.17-44.4). No significant differences in CD34+ cells collected were found between either groups[16] as previously published by others.[17] Bone marrow harvest was performed without side-effects and yielded a median of 11.35×10⁸/kg mononuclear cells (range 2.34-45.74).

Hematopoietic recovery

Engraftment was significantly faster in the PBPCT group, especially in patients receiving at least 5×10⁶/kg CD34+ cells. No graft failure was observed. Engraftment kinetics are shown in Table 3.

Supportive care

As Table 4 shows, transfusions requirements were less in the PBPCT group because of the faster hematopoietic recovery. Moreover, patients who underwent PBPCT received antibiotics and parenteral nutrition for a significantly shorter period of time. If we consider the $CD34^+$ cell dose, antibiotic requirements were greater for patients receiving fewer than 5×10^6/kg $CD34^+$ cells. No significant differences were found for median number of days of inotropic drugs, morphine requirements, Intensive Care Unit (ICU) stay days and radiological procedures performed between groups. Patients in the PBPCT group were discharged earlier from the transplantation unit (median 17 days, range 8-38 days) than patients receiving BMT (median 28 days, range 11-65 days) ($p< 0.0001$).

In the PBPCT group, there were seven transplant-related deaths (4 of multiorgan failure, 1 of hepatic failure, 1 of sepsis and another of interstitial pneumonia). Four patients who underwent BMT died of infection. There was no statistically significant difference in toxic-related mortality (TRM) between either group (PBPCT 6.8% and BMT 13.7%).

Economic analysis

Economic results are presented in Table 5. The median collection costs were significantly higher in the PBPCT group because it included mobilization costs. Conditioning regimen costs were higher in BMT group. This difference is due to the greater number of patients with acute lymphoblastic leukemia, who underwent TBI as conditioning regimen, in the BMT group. Supportive care and laboratory tests costs were significantly lower in the PBPCT group because of faster engraftment and shorter hospitalization. The costs of radiological procedures were similar in both groups. In the PBPCT group, transfusions and antibiotic costs were less in patients who received $\geq 5\times10^6$/kg $CD34^+$ cells because of more rapid hematopoietic recovery. Collecting $\geq5\times10^6$/kg $CD34^+$ cells decreased the total cost of transplantation by 27%. The distribution of resources was similar in the two groups, except BMT collection that represented 8% of total cost whereas PBPC collection accounted for 18% of the cost in the PBPCT group. Hospitalization represented the major cost factor in both groups. The overall cost of the procedure was significantly less for the PBPCT group (7,895 US$) than for the BMT group (11,820 US$) and represented a saving of 33%. A multiple linear regression on total costs was performed in both groups.

Table 5. Economic analysis.

	PBPCT n = 102		BMT n = 29		p*
	Cost (US$)	%	Cost (US$)	%	
Collection					
Mobilization	272	4	0	0	<0.0001
Apheresis	946	14	0	0	<0.001
Harvest	0	0	1071	8	<0.0001
Hospitalization					
Hematologic care unit	2921	36	4810	42	<0.0001
ICU unit	196	2	296	2.5	ns
Blood products					
Platelets	471	9	967	11	<0.01
Red blood cell	135	3	269	3	ns
Pharmacy					
Growth factors	678	8	0	0	
Conditioning	284	8	619	16	<0.002
Antibiotics	261	4	459	5	<0.006
Parenteral nutrition	622	8	983	9	<0.001
Morphine	0	0.02	0	0.01	ns
Inotropics	0	0.02	0	0.02	ns
Laboratory tests					
Blood counts	146	2	210	2	<0.0001
Cultures	18	0.8	47	0.5%	<0.002
Radiologic procedures					
X-ray	9	0.16	9	0.17	ns
CT	9 0	1	0	0.8	ns
Total	7,895		11,820		<0.0001

*Abbreviations: ICU, intensive care unit; CT, computer tomography; *p value between PBPCT and BMT cost.*

In the PBPCT group, the main determinants of total costs were TBI-based conditioning, platelet units transfused, days of hospital and ICU stay and number of $CD34^+$ cells infused. The model obtained was: *total cost (US$)* = 2987 + 5435 × TBI + 318 × No. ICU stay days + 283 × No. of platelets units transfused + 224 × hospitalization days - 98 × No. $CD34^+$ cells/kg (R2 = 0.7, $p< 0.001$).

In the BMT group, the main factors were TBI-based conditioning, number of platelet transfusions and hospitalization days. The model that we can use to estimate charges is: total cost (US$) = 3590 + 4516 × TBI + 252 x No. of platelets transfusions + 187 × hospitalization days (R2= 0.85, $p<0.003$).

A sensitivity analysis was performed to assess the impact of possible changes of the main unit cost factors involved in transplantation: platelets units transfused and days of hospitalization. Increasing platelet cost by 20% in the PBPCT group, the median platelet cost would be US$ 979. In the BMT group, decreasing platelet cost by 20% would yield a median cost of US$ 1,118. The differences are statistically significant ($p<0.0001$). If we make the same changes with

days of hospital stay, the median cost in the PBPCT group would be US$ 3,842 whereas in the BMT group it would be US$ 4,379 (p<0.0001). Consequently, the sensitivity analysis showed that economic results were robust and that the overall cost difference between the two groups remained significant despite modification of individual costs.

Cost-effectiveness analysis

AML category. Thirteen patients underwent PBPCT and 5 patients BMT. The disease-free survival (DFS) in the PBPCT group was 74% with a median follow-up of 707 days (range 167-1723). The DFS in the BMT group was 20% (median follow-up 224 days, range 16-2471). This difference in DFS was significant (p<0.01). The incremental cost per life-year gained by a survivor in the BMT group from 1 to 5 years after transplantation was US$ 69,814. PBPCT was more cost effective than BMT in patients diagnosed as having AML (p<0.001).

ALL category. Thirteen patients underwent PBPCT and 13 patients BMT. The DFS in the PBPCT group was 41% with a median follow-up of 564 days (range 76-1,794). The DFS in the BMT group was 7% (median follow up 217 days, range 11-3,319) (p<0.06). The incremental cost per life-year gained by a survivor in the BMT group was US$ 40,047 at the 1st year, US$ 26,828 at the 2nd year, US$ 54,443 at the 3rd year and US$ 137,215 at the 4th and 5th years. PBPCT was more cost-effective than BMT in patients diagnosed as having ALL but the difference was not significant.

Discussion

The first study of stem cell transplantation costs was published in 1989 by Welch and Larson. It reported a cost-effectiveness study comparing costs and outcomes of allogeneic bone marrow transplantation and standard chemotherapy for patients with acute myelogenous leukemia and concluded that transplantation was more cost-effective than chemotherapy.[18]

In the last five years, several studies have included comparative analyses on the use of bone marrow or peripheral blood as the source of progenitor cells. Most of these were cost-minimization rather than cost-effectiveness studies and included small sample sizes.[2-7]

There are few reports of stem cell transplantation costs in pediatric patients. Only a study published by Barosi *et al.*[8] included 8 children in their model for analyzing autologous PBPCT costs. Phillips *et al.*[9] evaluated the impact on survival and resources involved in allogeneic BMT and chemotherapy in children with acute myeloid leukemia, but they did not consider costs.

The study reported here involves a large group of children who underwent autologous transplantation for a variety of malignancies in a single institution. Possible associations between pre-transplantation variables and cost were made. The statistically significant pre-transplantation predictive factors in an univariant analysis were: using a TBI-regimen as conditioning and disease status at transplantation in both groups. However, in a multiple linear regression analysis the only one predicting cost variable was TBI for conditioning. These results differ from those published by Lee *et al.*[19] who did not find any clinical information available before transplantation that accurately predicted inpatient hospitalization costs in a study involving adult patients undergoing allogeneic and autologous transplantation.

No other variables such as age, gender, diagnosis and chemotherapy-based regimen used had a significant impact on overall cost. As this was a retrospective study involving an heterogenous patient population, a selection bias may have limited the ability to detect associations between some pre-transplantation variables and overall cost. This may explain why pre-transplantation costs were similar in the PBPCT and BMT groups despite mobilization and collection-related costs being higher in PBPCT patients as reported by others.[2,5]

The use of PBPC as source of hematopoietic rescue following myeloablative therapy was associated with a significant reduction in post-infusion cost. This reduction was mainly due to shorter hospitalization and less supportive care in the PBPCT group. Patients undergoing PBPCT were discharged earlier than patients in the BMT group (median 17 days vs 28 days, respectively), needed fewer transfusions, less antibiotics and less parenteral nutrition, probably as a consequence of faster engraftment kinetics. We are aware that a learning curve effect over time may have had an influence on cost,[19,20] mainly in the PBPCT group because this procedure was used later. However, the cost difference between the two procedures remained significant even after performing a sensitive analysis taking into account the main factors involved in multivariant analysis. Total cost may be strongly influenced by severe clinical complications after infusion.[19] Death after transplantation may increase cost.[19] However, in our study, as TRM was low and not different between groups, no significant cost impact was found in univariate analysis. ICU stay

certainly may be used as surrogate indicator of severe clinical complications after transplant. In fact, in the PBPCT group this variable had a significant influence on costs. This was not found in the BMT group, probably because of the small number of patients.

Resource distribution was similar in both groups except for collection costs that represented 18% of overall costs in the PBPCT group versus 8% in the BMT group. Cost ascribable to hospitalization accounted for 40% in our study whereas it represented 65% in the study reported by Duncan *et al.*[2] These differences in proportional cost distribution may be explained by protocols, institutional characteristics, diseases included, and salaries for medical and paramedical personnel. The low overall cost in our study, compared to that in other reports, is also noteworthy .[2,3,5,6] The reasons for this are: our study included only a pediatric population whose median weight was 30 kg, and only considered direct costs.

The estimated median cost for a PBPCT patient was 33% less than that for a BMT patient. This cost saving was similar to the 30% reduction reported comparing recipients of filgrastim-mobilized progenitor cells vs historical BMT controls.[21] In the PBPCT group we also focused on the number of $CD34^+$ cells infused and its economic impact. Based on our previous studies in engraftment kinetics,[11] a threshold of 5×10^6/kg $CD34^+$ cells was chosen for analysis. Patients grafted with $\geq 5\times10^6$/kg $CD34^+$ cells had a median cost saving of 27% compared to patients grafted below this threshold. This finding is in accordance with results from other studies previously reported in adult patients.[22,23] Thus, efforts on PBPC collection should be adressed to achieving this $CD34^+$ cell target. As leukemia patients represented a homogeneous population in our study, a cost-effectiveness analysis was made. The cost-effectiveness of PBPCT was higher than that of BMT for pediatric leukemia patients. The incremental cost per life-year gained by PBPCT was US$ 69,814 for AML patients. Although in ALL patients PBPCT was more cost effective than BMT the incremental cost per life-year of BMT survivors rose until US$ 137,215 at the 5th year; the difference was not, however, significant.

Although these results must be interpreted cautiously before being extensively generalized having been derived from a small sample of patients, they do have some strengths because the study was performed in only one institution with the same medical and nursing team and using similar therapeutic methods.

Future efforts must be made to improve the cost effectiveness of transplantation by decreasing the cost of the procedure. This can be achieved pre-transplantation, choosing a mobilization regimen that allows optimal apheresis and achieves a target dose of 5×10^6/kg $CD34^+$ cells. Other ways to reduce costs could be to move transplants to an outpatient setting and not use TBI for conditioning whenever possible according to the type of disease.

In regard to the post-infusion phase, parenteral nutrition should be changed to enteral nutrition if clinical status allows and the use of hematopoietic growth factors should be restricted, according to reports previously published.[24]

In summary, we conclude that, compared to BMT, autologous PBPCT in children is associated not only with clinical benefits but also economic advantages.

Contributions and Acknowledgments

MGV and MAD were the main investigators and designed the study. MGV wrote the article and reviewed the literature. LC and RM managed the statistical data. MGV, MAD and LM revised the study critically and all authors approved the revised version. We thank Dr. Félix García for the $CD34^+$ cytometric analyses and the nursing team for their care of the patients.

Disclosures

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Manuscript processing

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Potential implications for clinical practice

In children with malignant disorders efforts should be made in order to collect as higher as possible $CD34^+$ cells for autologous PBPCT[25,26] since high numbers of $CD34^+$ cells infused result in both clinical and economical benefits.

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