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Stem cell transplantation

CD34+ cell dose predicts costs after autologous peripheral blood stem cell transplantation for breast cancer

We assessed the effect of CD34+ cell dose on costs in breast cancer patients undergoing autologous peripheral blood stem cell (PBSC) transplantation. Mean hospitalization costs were 26,992.9±9582.9 for patients receiving a CD34+ cell dose <5×10⁶ cells/kg versus 22,339.4± 5471.1 for those receiving >5×10⁶ CD34+ cells/kg (p=0.0065).

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Several studies have evaluated the use of high-dose chemotherapy followed by autologous hematopoietic cell transplantation (HCT) in primary high-risk or metastatic breast cancer.[1-3] Similarly, the association between CD34+ cell dose and hematopoietic recovery has been previously examined.[4] However, although the impact of CD34+ cell dose on costs has been previously assessed in other malignancies,[5,6] such a study has never been published in breast cancer patients. To assess this question, 55 women with high-risk primary or metastatic breast cancer transplanted with autologous PBSC after a standard Stamp V regimen were included. The protocol was approved by the Ethics Committee at the University of Liège. Patients receiving a CD34+ cell dose of less than 5×10⁶ cells/kg were included in group 1 (n=13) and those receiving a CD34+ cell dose 5×10⁶ cells/kg in group 2 (n=42). Progenitor cells were mobilized with an intensified

Table 1. Patients' characteristics and clinical parameters.

	Group 1	*Group 2*	*p value*
Age (years)	47±7	45±8	NS
Weight (kg)	66±10	67±13	NS
Body surface area (m^2)	1.7±0.1	1.7±0.1	NS
ECOG performance status : N(%)			NS
0	5 (38)	17 (40)	
1	8 (62)	25 (60)	
Disease: N (%)			NS
Adjuvant	7 (54)	23 (55)	
Metastatic	6 (46)	19 (45)	
Prior radiation therapy : N (%)			NS
Yes	4 (31)	13 (31)	
No	9 (69)	29 (69)	
Number of previous lines of chemotherapy	1.5±0.5	1.4±0.7	NS
Graft composition			
NC (×10⁸/kg)	3.9±2.1	9.2±31.5	NS
CD34+ cells ×10⁶/kg)	2.6±1.1	12.6±9.5	<0.0001
CFU-GM (×10⁴/kg)	42.9±28.8	159.4±112.3	<0.0001
BFU-E (×10⁴/kg)	62.7±41.5	295.7±245.2	<0.0001
CFU-Mix (×10⁴/kg)	4.6±4.1	26.7±19.1	<0.0001
Median time (days) to achieve :			
Neutrophil count > 0.5×10⁹/L	10	9	<0.001
Neutrophil count > 1.0×10⁹/L	10	9	<0.001
Platelet count > 20×10⁹/L	12	9	<0.001
Platelet count > 100×10⁹/L	49	14	<0.001
Reticulocytes > 1%	13	11	<0.001
Median time to last RBC transfusion	10	7	0.003
Median time to last platelet transfusion	9	8	0.029
Median time to hospital discharge	14	12	0.049
Days of G-CSF administration	14±3	10±1	<0.001
Number of platelets transfusions	5±6	3±4	0.0516 (NS)
Number of RBC transfusions	6±6	2±2	0.0027
Number of days of hospitalization	17±8	13±5	0.0098

Mean±standard deviation unless otherwise specified.

Table 2. Transplantation costs (euros).

	Group 1 (Mean±SD)	*Group 2 (Mean±SD)*	*p value*
Pharmaceutical costs			
Chemotherapy	1,371.7±397.2	1,578.9±454.9	NS
Antibiotics	2,475.2±1261.2	2,155.0±780.2	NS
G-CSF	1,782.2±543.5	1,380.7±298.1	0.0073
Others	2,302.5±1859.3	1,676.3±961.0	NS
Sub-total	7,998.7±2,888.6	6,848.5±1,462.3	NS
Blood products			
Transfusions	2,705.6±2,117.7	1,828.9±2028.6	0.0559 (NS)
PBSC	2,688.8±1,157.7	1,541.8±348.5	<0.0001
Sub-total	5,440.1±2,723.8	3,399.3±2,075.9	0.0038
Medical fees			
Clinical biology	931.5±558.2	714.8±225.9	0.0734 (NS)
Imaging	321.7±462.4	214.1±160.2	0.0833 (NS)
Transplant fee	2677.0+0.0	2677.0±0.0	NS
Others	1914.6±1988.4	1370.1±905.9	NS
Sub-total	5,969.9±2,957.1	5,224.7±1,363.7	NS
Hospitalization	7,256.1±2,351.5	6,295.5±1,623.7	0.0090
Total costs	26,992.9±9,582.9	22,339.4±5,471.1	0.0065

All costs were those actually billed to the patient. Some unit prices (in euro) are indicated here: one day of hospitalization in an intensive hematological care room: 357.84; platelet transfusion: 376.97; red blood cell transfusion: 40.46; G-CSF 300 μg:98.35; PBSC collection: 743.68.

FEC regimen[4] and collection of PBSC was carried out as previously described.[7] The number of CD34$^+$ cells was determined as previously reported.[8] All patients were treated with 5 μg/kg/day filgrastim from day +1 until the granulocyte count was $\geq 10^9$/L for three consecutive days or 10^{10}/L for one day. We analyzed all direct costs involved in the initial hospitalization. This included the fee charged for the PBSC products previously collected but not the costs of ambulatory care after discharge. Costs were collected from charges appearing on the patients' hospitalization bills. Total costs were divided into pharmaceutical products (including costs related to chemotherapy, antibiotics, granulocyte colony-stimulating factors and others medications), blood products (including PBSC, red blood cells and platelets), medical fees (including clinical biology, imaging and other fees) and hospitalization costs including room and board. Statistical analyses were carried out with Graphpad Prism (Graphpad Software, San Diego, CA, USA) and SAS (SAS Institute, Cary, NC, USA). Wilcoxon's rank tests were used to compare variables in the two groups. χ^2 tests or Fisher's exact tests, as appropriate, where used to compare the incidence of various events in the two groups. Correlations between parameters were calculated using the Spearman's R correlation coefficient. The speed of engraftment, probability of experiencing infection as well as survival and transplant-related mortality (TRM) were studied by life-table analyses and Wilcoxon's rank tests were used for comparisons between groups.

The two groups were well balanced (Table 1). The speed of engraftment was significantly faster in group 2 and this translated into a shorter duration of hospitalization (Table 1). The number of CD34$^+$ cells transplanted was strongly correlated with the time to achieve 0.5×10^9 neutrophils/L (r=-0.6, $p<0.0001$), 100×10^9 platelets/L (r=-0.7, $p<0.0001$), as well as with the day of hospital discharge (r=-0.5, $p=0.0356$). The 1-year incidence of TRM was 16% in group 1 versus 0% in group 2 ($p=0.009$). Infectious complications tended to be more frequent in group 1 than in group 2 (62% vs 31%, $p=0.06$) with an odds ratio of 2.6 (1.0-6.9). With a median follow-up of 5.3 years, overall survival was 45% in group 1 versus 60% in group 2 ($p=0.06$) and the probability of relapse was identical in the two groups. Mean total transplantation costs were 4654 higher in group 1 than in group 2 ($p=0.0065$) (Table 2). The excess costs in group 1 were mainly due to PBSC products (+ 1147), filgrastim use (+ 401) and hospital room and board (+ 961). Finally, total costs showed a significant inverse correlation with the CD34$^+$ cell dose (r=-0.3, $p=0.0395$).

Few studies have investigated the impact of CD34$^+$ cell dose on costs. One report on patients with a variety malignancies showed a $9000 increase of costs ($41,516 vs $32,382) in patients receiving fewer than 5×10^6 CD34$^+$ cells/kg.[5] Limat *et al.* reported that a high CD34$^+$ cell count resulted in a total cost saving of around $4000 ($29,600 vs $33,810) in patients transplanted for non-Hodgkin's lymphoma (NHL).[6] Similarly, Stockerl-Goldstein *et al.* reported major additional costs for NHL patients receiving fewer than 5×10^6 CD34$^+$ cells/kg ($140,264 vs $80,833).[9] Finally, Vincent *et al.* evidenced that a graft containing $\geq5\times10^6$/kg CD34$^+$ cells decreased the total cost of transplantation by 27% ($7,895 vs $11820) in pediatric patients with various malignancies.[10] Our study in breast cancer patients concur with these data by showing that a high CD34$^+$ cell dose reduces the cost of an autologous PBSC transplant procedure by around 4500 in breast cancer patients.

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