A prospective, randomized, sequential, crossover trial of large-volume versus normal-volume leukapheresis procedures: effect on progenitor cells and engraftment

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BACKGROUND: The influence of leukapheresis size on the number of harvested peripheral blood progenitor cells is still unclear. A prospective randomized crossover trial was thus performed, to evaluate the effect of large-volume leukapheresis (LVL) versus normal-volume leukapheresis (NVL) on progenitor cells and engraftment in 26 patients with breast cancer and 15 patients with non-Hodgkin's lymphoma who were eligible for peripheral blood progenitor cell transplantation.

STUDY DESIGN AND METHODS: Patients were randomly assigned to undergo either LVL on Day 1 and on Day 2 or vice versa. The number of progenitor cells was evaluated in the harvest and before and after leukapheresis in the peripheral blood.

RESULTS: The number of harvested CD34+ cells (4.8×10^6 vs. 3.4×10^6/kg body weight, $p<0.001$) and colony-forming units–granulocyte-macrophage (3.1×10^5 vs. 2.4×10^5/kg body weight, $p = 0.0026$) was significantly higher for LVL procedures than for NVL procedures. The median extraction efficacy, defined as the difference between the yield in the harvest and the decrease in the total number of CD34+ cells in peripheral blood during leukapheresis, was significantly ($p<0.0001$) higher for LVL than for NVL (2.6×10^8 and 8×10^7, respectively). In patients with breast cancer, the median amount of CD34+ cells in the harvest and the median extraction efficacy were higher for LVL than for NVL ($p<0.0001$). This was not found for patients with non-Hodgkin's lymphoma.

CONCLUSION: LVL results in a higher yield of CD34+ cells and colony-forming units–granulocyte-macrophage than NVL, but only in patients with breast cancer and with high numbers of CD34+ cells in the peripheral blood before leukapheresis.

Peripheral blood progenitor cell (PBPC) transplantation has become a widely accepted therapeutic option for patients with chemotherapy-sensitive malignancies. The transfusion of PBPCs offers several advantages over bone marrow transplantation. Collection of PBPCs can be performed without general anesthesia, engraftment is faster, and supportive care and costs are reduced. PBPCs are harvested by leukapheresis after mobilization with chemotherapy and/or granulocyte–colony-stimulating factor (G–CSF) or granulocyte-macrophage–CSF (GM–CSF).[1-5]

The number of progenitor cells in the harvest is usually quantified by immunophenotyping for CD34+ cells[6] and/or by evaluating the proliferative potential through measurement of colony-forming units–granulocyte-macrophage (CFU–GM).[7-10] Several studies have been able to demonstrate a good correlation between the number of CD34+ cells in the harvest and the number of CFU–GM.[6,11]

Until now, the minimal number of transplanted PBPCs required for safe and sustained engraftment remains to be

ABBREVIATIONS: BC = breast cancer; BW = body weight; CFU–GM = colony-forming units–granulocyte-macrophage; DexaBEAM = dexamethasone, carmustine, melphalan, etoposide, and cytarabine; G–CSF = granulocyte–colony-stimulating factor; GM–CSF = granulocyte-macrophage–CSF; HDCT = high-dose chemotherapy; LVL = large-volume leukapheresis; NHL = non-Hodgkin's lymphoma; NVL = normal-volume leukapheresis; PBPC(s) = peripheral blood progenitor cell(s).

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determined. Thus, recommendations[12-14] for transplantation dosages range from 1.0×10^6 CD34+ cells per kg of body weight (BW) to more than 5.0×10^6 CD34+ cells per kg of BW in some centers and from 1.0×10^5 CFU–GM per kg of BW to more than 5.0×10^5 CFU–GM per kg of BW in other centers. Recent data suggest that patients being given more than 15×10^6 CD34+ cells per kg of BW may benefit with regard to hematopoietic recovery.[15]

The yield of CD34+ cells obtained by leukapheresis is significantly influenced by the extent[13,16] and duration[17] of prior chemotherapy, therapy with stem cell-toxic drugs such as carmustine or melphalan, and extensive radiotherapy.[18] In some uncontrolled studies, an influence of the leukapheresis size on the number of PBPCs in the harvest was observed. Large-volume leukapheresis (LVL) is defined either by processing a minimum of 15 L of peripheral blood[19-21] or by processing more than three times the total peripheral blood volume.[22] LVL can cause an additional intrapheresis recruitment of PBPCs.[21-23] It has been suggested that it might be possible to harvest sufficient numbers of PBPCs for transplantation by one LVL only.[24,25] In 50 percent of previously treated patients it has been possible to harvest more than 1.0×10^6 CD34+ cells per kg of BW in a single LVL procedure.[26] However, these favorable results could not be confirmed in all investigations. Recently, it was suggested that the recruitment of PBPCs during LVL does not occur in small children at all,[27] and that in older children the effect might be less pronounced than it is in adults. In addition, patient tolerance may limit the clinical use of LVL.[26]

We therefore performed a prospective, randomized, sequential crossover trial in patients with breast cancer (BC) or non-Hodgkin's lymphoma (NHL) to evaluate the effect of LVL compared with normal-volume leukapheresis (NVL) on the absolute number of harvested CD34+ cells and on the extraction efficacy, defined as the difference between the yield in the harvest and the decrease in the total number of CD34+ cells in peripheral blood during leukapheresis.

MATERIALS AND METHODS

Study design

All patients admitted for PBPC mobilization and harvest between September 1995 and June 1997 were evaluated for inclusion in the study, which had been approved by the Institutional Ethical Review Board of the Medical Faculty of the University of Göttingen (Göttingen, Germany). After giving informed consent, patients in each patient group, that is, BC and NHL, were randomly allocated by sealed-envelope technique to undergo either LVL in which 4.5 ± 15 percent of the total peripheral blood volume was processed and an NVL in which 2.5 ± 15 percent of the total peripheral blood volume was processed on the consecutive day, or vice versa (an NVL followed by an LVL). The main evaluation criteria of the study were the comparison of the number of CD34+ cells per harvest and the extraction efficacy for CD34+ cells in LVL and NVL. Extraction efficacy was defined as the number of CD34+ cells per leukapheresis – (the number of CD34+ cells in the peripheral blood before leukapheresis – the number of CD34+ cells in the peripheral blood after leukapheresis).

Furthermore, the number of CFU–GM was measured after cryopreservation for all leukapheresis samples.

Inclusion criteria

Patients ≤60 years with high-risk BC or NHL were included in the protocol. Inclusion criteria for patients with BC were ≥10 positive lymph nodes, positivity in all examined lymph nodes at first diagnosis, or local regional relapse within 2 years after first diagnosis and initially positive lymph nodes. Inclusion criteria for patients with NHL were large-cell lymphoma with persistent disease after standard chemotherapy or at relapse or low-grade NHL stage III/IV and progressive disease. All patients with chemotherapy-sensitive disease were eligible. Patients' characteristics are described in Table 1. Eligibility requirements included mobilization with chemotherapy and G–CSF (5-10 µg/kg/BW/day, given subcutaneously). G–CSF was administered 3 to 10 hours before leukapheresis.

TABLE 1. Patient characteristics

	BC (n = 26)	NHL (n = 15)
Median age (range)	49 (36-59)	51 (20–57)
Sex (male/female)	0/26	7/8
Median number of chemotherapy cycles before leukapheresis (range)	2 (1-7)	7* (3-9)
Prior chemotherapy	VIPE† (n = 12) VIPE and EC§ (n = 4) EC (n = 7) CMF** (n = 3)	PmM‡ (n = 3) MCP‖ (n = 2) CHOEP¶(n = 4) COP/CHOP†† + DexaBEAM‡‡ (n = 5) CVP§§ (n = 1)

* p<0.00001.
† Etoposide, ifosfamide, cisplatinum, and epirubicin.
‡ Prednimustine and mitoxantrone.
§ Epirubicin and cyclophosphamide.
‖ Mitoxantrone, chlorambucil, and prednisone.
¶ Cyclophosphamide, adriamycin, vincristine, etoposide, and prednisone.
** Cyclophosphamide, methotrexate, and fluorouracil.
†† Cyclophosphamide, adriamycin, vincristine, and prednisone.
‡‡ Dexamethasone, carmustine, etoposide, cytarabine, and melphalan.
§§ Cyclophosphamide, vincristine, and prednisone.

Exclusion criteria

Exclusion criteria were refractoriness to platelet transfusion, disorders of blood coagulation, heparin-induced thrombocytopenia, disease manifestation in the central nervous system, fever ≥38.5°C within 48 hours before leukapheresis, dilatative cardiomyopathy, symptomatic ischemic heart disease, heart attack within 6 months before leukapheresis, chronic lung disease with hypoxemia, severe drug-resistant hypertension, severe nonadjustable diabetes, epileptic seizures, impairment of renal function with serum creatinine >2.0 mg per dL, elevation of liver enzymes >3 times the normal value and/or a bilirubin value >2.0 mg per dL, clinical symptoms of impaired cerebral blood circulation, severe psychiatric disease, and previous bone marrow or PBPC transplantation.

Patients and study population

During the study period, a total of 100 patients underwent PBPC mobilization and harvest. Of these patients, 58 met the inclusion criteria regarding diagnosis and mobilization regimen. Forty-five patients gave informed consent and were randomly assigned. Of these patients, 4 had to be excluded from study evaluation. One patient had no mobilizable PBPCs, 1 patient did not meet the inclusion criteria, and 2 did not undergo a leukapheresis of appropriate size, because of technical errors (Fig. 1). In 2 of the 41 remaining patients, CD34+ cell counts after leukapheresis were not performed. Twenty-six patients had BC and 15 patients had NHL. Twenty-two patients with BC were treated in an adjuvant setting because of high-risk disease; the other 4 patients were eligible for high-dose chemotherapy (HDCT) because of high-risk locoregional relapse. Seven patients of the NHL group had stage IV follicular lymphoma and were included in an ongoing randomized trial comparing the effect of HDCT to that of conventional chemotherapy. One additional patient with follicular lymphoma presented with relapse after conventional chemotherapy. Three patients with diffuse large-cell lymphoma and persistent disease after standard chemotherapy and two with a chemotherapy-sensitive relapse were included. One patient had mantle cell lymphoma and one presented with a malignant lymphoma of mucosa-associated lymphoid tissue.

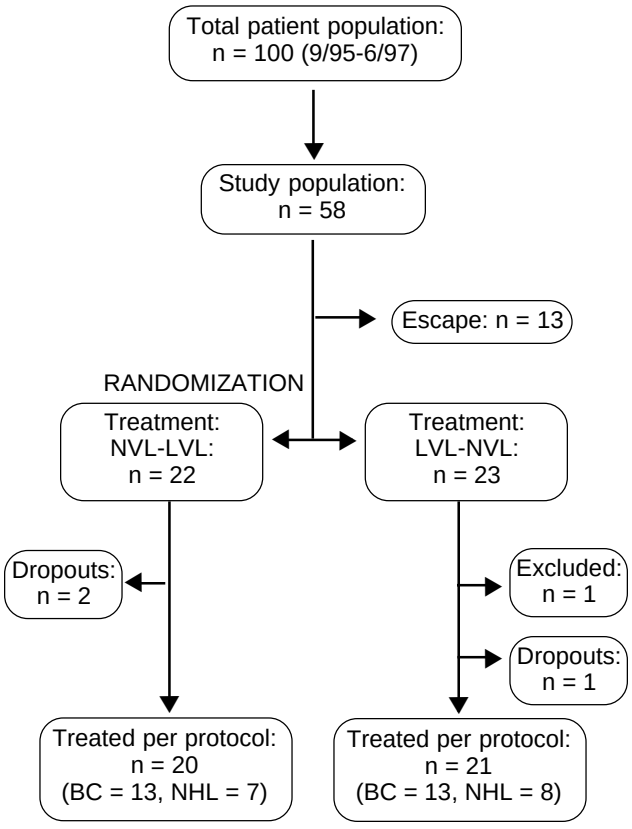

Fig. 1. Summary of patients and study population.

Mobilization and leukapheresis

All patients underwent mobilization with chemotherapy and G–CSF. In 18 patients with BC, the mobilization regimen given consisted of epirubicin at 50 mg per m^2, ifosfamide at 4000 mg per m^2, cisplatinum at 50 mg per m^2, and etoposide at 500 mg per m^2 . The other 8 patients with BC underwent mobilization with epirubicin at 90 mg per m^2 and cyclophosphamide at 600 mg per m^2. In 13 patients with NHL, mobilization was performed by the administration of dexamethasone at 3 × 8 mg on Days 1 through 10, carmustine at 60 mg per m^2 on Day 2, melphalan at 20 mg per m^2 on Day 3, etoposide at 75 to 150 mg per m^2 on Days 4 through 7, and cytarabin at 2 × 100 mg per m^2 on Days 4 through 7 (DexaBEAM). High-dose cyclophosphamide (4 g/m^2) as single-agent mobilization was given to 2 patients with NHL.

On the second day after the end of chemotherapy, subcutaneous administration of G–CSF at a dose of 5 to 10 µg per kg of BW per day was started and continued until the last day of leukapheresis. Leukapheresis procedures were begun when the white cell count exceeded 1×10^9 per L. Leukapheresis procedures were performed on a cell separator (Spectra, COBE Laboratories, Heimstetten, Germany) via a central venous catheter. In NVL procedures, ACD-A (Fresenius, Bad Homburg, Germany) alone was used as the anticoagulant. Two patients received heparin during NVL because of an operator error. In all LVL procedures, 6 International Units (IU) of heparin (Hoffmann-La Roche, Grenzach-Wyhlen, Germany) per 1 mL of ACD-A was used as additional anticoagulant.[28] The leukapheresis values are described in Table 2. The targeted transplantation dose was a minimum of 1×10^6 CD34+ cells per kg of BW[11,14,29] and the same dose was used as a "back-up."[30]

TABLE 2. Leukapheresis values (data are given as median and range)

	LVL	NVL	Statistics
Number of times peripheral blood volume was processed	4.6 (4.01-5.03)	2.5 (2.2-2.8)	$p<10^{-6}$
Processed total peripheral blood volume (mL)	19,589 (15,425-27,329)	10,282 (8,332-14,811)	$p<10^{-6}$
Flow rate (mL/min)	100 (80-140)	70 (50-90)	$p<10^{-6}$
Citrate ratio (ACD-A/blood)	1/22 (20-22)	1/14 (12-22)	$p<10^{-6}$
Infused citrate (mL)	937 (735-1,301)	791 (456-1,139)	$p<10^{-6}$
Infused citrate (mL/kg BW/min)	0.065 (0.052-0.082)	0.069 (0.053-0.118)	$p = 0.012$
Duration (min)	204 (181-235)	168 (107-205)	$p<10^{-6}$

Laboratory methods

A whole-blood count was performed routinely by use of an electronic counter (NE 1500, TOA Sysmex, Kobe, Japan) according to standard methods. Immunophenotyping for CD34+ cells and the evaluation of colony growth were performed as previously described.[11] The numbers of CD34+ cells before leukapheresis and in the leukapheresis component were evaluated in all 82 harvest procedures. In 3 apheresis procedures, the number of CD34+ cells after leukapheresis was not determined (NVL: n = 1, LVL: n = 2).

Transplantation

Patients with BC received HDCT consisting of mitoxantrone at 10 mg per m^2, cyclophosphamide at 1500 mg per m^2, and thiotepa at 150 mg per m^2 on 4 consecutive days, as a conditioning regimen. Patients with low-grade NHL underwent conditioning with total body irradiation (12 Gy) and high-dose cyclophosphamide (60 mg/kg BW). In patients with high-grade NHL, carmustine at 300 mg per m^2 and melphalan at 150 mg per m^2 on Day 5 before transplantation and etoposide at 100 mg per m^2 and cytarabin at 200 mg per m^2 on Days 5 to 2 before transplantation were given. Beginning on the day of PBPC transfusion, all patients received G–CSF subcutaneously at a daily dose of 5 µg per kg of BW until a white cell count above 1000 per µL was determined on 3 consecutive days. After mobilization and progenitor cell harvest, two patients with NHL and two with BC were not eligible for HDCT and PBPC transplantation because of progressive disease. One patient underwent transplantation twice, and thus a total of 38 PBPC transplantations were performed in 37 patients. One patient with NHL underwent transplantation with autologous bone marrow and PBPCs, because neither the bone marrow cells nor the PBPCs were sufficient for transplantation as a single source of progenitor cells.

In patients undergoing harvest in complete remission, the bag containing the maximum number of PBPCs and the smallest volume was chosen for transfusion. In patients with partial remission or initial bone marrow involvement, PBPCs were collected again after further cycles of chemotherapy. Bags of PBPCs harvested as late as possible during treatment but still containing a sufficient number of PBPCs were chosen for transplant.

Statistics

The study was designed to detect a difference of 50 percent in the CD34+ cell yield between NVL and LVL. On the basis of an expected number of 3×10^6 CD34+ cells per kg of BW in an NVL, a difference of 50 percent between NVL and LVL, and a variance of 3×10^6, we calculated that, for statistical significance ($p<0.05$ and $1 - \beta = 0.80$), at least 41 patients should be enrolled in the study.

Unless otherwise stated, data values are described as median and ranges. The data were analyzed by the nonparametric paired-rank test[31] or by the distribution-free Mann-Whitney test. Calculations were performed with a software program (Statistical Analysis System, version 6.12, SAS Institute, Cary, NC). Results were considered to be significantly different when the p value was below 0.05.

RESULTS

Yield of CD34+ cells and extraction efficacy

The median number of CD34+ cells was significantly higher in LVL than in NVL (Table 3 and Fig. 2). In five patients with BC and seven with NHL, the NVL component contained more CD34+ cells than did the LVL component. In all but three of these patients, the NVL was scheduled on Day 2. In addition, the number of CD34+ cells per µL of peripheral blood before leukapheresis was significantly higher in these 12 patients ($p<0.01$) before NVL than before LVL. With all 82 procedures considered, the median number of CD34+ cells per µL of peripheral blood was not different before NVL and LVL (57/µL and 50/µL, respectively, $p = 0.38$). There was a significant decrease in CD34+ cells per µL of peripheral blood after both NVL and LVL ($p = 0.01$ and $p = 0.009$, respectively), but the median postapheresis values did not differ between NVL and LVL (35 vs. 29 CD34+ cells/µL, $p = 0.09$). We determined the difference(s) between the preapheresis/postapheresis values for CD34+ cells per kg of BW in NVL and LVL; the values were similar. But the median extraction efficacy was significantly higher ($p<0.0001$) for LVL than for NVL (Table 3). In relation to BW, the median values were 3.5×10^6 CD34+ cells per kg of BW for LVL and 1.1×10^6 CD34+ cells per kg of BW for NVL ($p<0.0001$). As this value was greater than zero for both procedures, NVL as well as LVL seems to lead to a recruitment of PBPCs.

TABLE 3. Data for LVL and NVL procedures compared for all samples and separately for different diagnoses*

	Total		BC		NHL	
	NVL	LVL	NVL	LVL	NVL	LVL
CD34+ cells per kg of BW ($\times 10^6$)	3.4 (0.3-12.9)	4.8† (0.2-15.5)	3.8 (0.3-8.5)	6.1‡ (0.8-15.5)	2.5 (0.3-12.9)	3.1 (0.2-8.5)
Extraction efficacy for CD34+ cells ($\times 10^8$)	0.8 (–3.3-12.0)	2.6† (–0.3-16.6)	0.8 (–3.3-5.1)	3.2† (0.4-16.6)	1.2 (–0.2-12.0)	1.4 (–0.3-4.8)
Extraction efficacy per kg of BW ($\times 10^6$)	1.1 (–3.2-15.4)	3.5†† (–0.3-27.2)	1.1 (–3.2-8.3)	5.0† (0.5-27.2)	1.7 (–0.4-15.4)	2.1 (–0.3-6.5)

* Data given as median (range).
† $p<0.001$.
‡ $p<0.0001$.

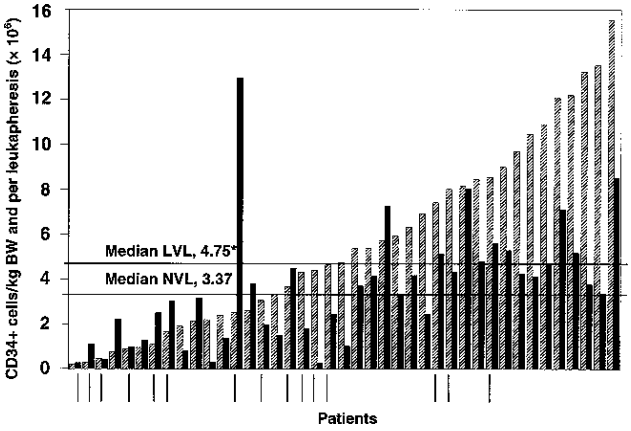

Fig. 2. Number of CD34+ cells per kg of BW and per leukapheresis in the 41 NVL (□) and LVL (▨) procedures. Data pairs are ranked by the number of CD34+ cells per kg of BW in the LVL component. * significantly different with $p<0.001$. | indicates patients with NHL.

Influence of diagnosis on the yield of CD34+ cells

In the 26 patients with BC, the median amount of CD34+ cells per kg of BW was significantly higher ($p<0.0001$) in LVL than in NVL, whereas in the 15 patients with NHL, there was no significant difference for the two procedures (Table 3). The median number of CD34+ cells per µL in peripheral blood before leukapheresis did not differ for either group of patients or either procedure. But patients with BC had significantly higher ($p = 0.012$ and $p = 0.028$, respectively) median numbers of CD34+ cells per µL in peripheral blood before leukapheresis than patients with NHL had (LVL: 61 vs. 24; NVL: 64 vs. 23). Moreover, in patients with BC, the median extraction efficacy was significantly higher ($p<0.0001$) for LVL than for NVL, whereas, in patients with NHL, there was no difference ($p = 0.24$) between the two procedures (see Table 3).

Number of CFU–GM after cryopreservation

The median number of CFU–GM per kg of BW in each sample of cryopreserved leukapheresis component was higher ($p = 0.0026$) for LVL than for NVL (3.1×10^5 and 2.4×10^5, respectively). Considering this value for the two patient groups separately, in patients with BC, the median number of CFU–GM per kg of BW after cryopreservation was significantly higher in the patients undergoing LVL than in those undergoing NVL (3.5 vs. 2.4×10^5, $p = 0.0047$), whereas in the patients with NHL there was no difference between LVL and NVL (2.7 and 2.1×10^5, $p = 0.35$).

Transplantation

With Day 1 and Day 2 leukapheresis procedures taken together, one transplantation dose and a back-up dose were collected in all patients with BC, but in only 11 of the 15 patients with NHL ($p = 0.026$, chi-square test with Yates's correction). In 36 patients, 37 transplantations with PBPCs alone were performed. One patient with BC underwent transplantation twice. One other patient received both autologous bone marrow and autologous PBPCs. In PBPC transplantation, patients received a median of 2.7×10^6 CD34+ cells per kg of BW (range, 1.0-7.8 $\times 10^6$) and a median of 2.0×10^5 CFU–GM per kg of BW after cryopreservation (range, 0.7-10.4 $\times 10^5$). One patient with BC died on Day 34 after transplantation, because of respiratory failure due to fungal pneumonia with *Candida albicans*. After a median of 10 days (range, 9-16), all other patients had a WBC count >1,000 per µL in peripheral blood. A platelet count >20,000 per µL without transfusion support was reached after a median of 12 days (8-70) after transplant.

Twenty-five transplantations were performed in 24 patients with grafts from study leukapheresis procedures alone. In 23 transplantations, the graft of one leukapheresis component was sufficient in PBPC content. Seventeen patients, 14 with BC and 3 with NHL, received a graft from an LVL. Only 1 of these patients with BC needed a total harvest; the other 16 received only one-half of the leukapheresis component. Of the 6 patients being given grafts from an

NVL, only 3 with BC had sufficient numbers of PBPCs in one-half of the collection; the others, 2 with BC and 1 with NHL, received a total harvest. Two patients with NHL received the LVL and the NVL graft.

DISCUSSION

We analyzed in a prospective controlled study the efficacy of LVL in 41 patients with BC or NHL. When all procedures were considered, the median number of CD34+ cells and the median extraction efficacy were significantly higher in LVL than in NVL. In both LVL and NVL, the median extraction efficacy was greater than zero, which suggests that additional PBPCs must have been recruited into the peripheral blood during leukapheresis, as also reported by others.[21,23] The number of "recruited" CD34+ cells per kg of BW is in the magnitude of 1 (NVL) to 3.5 (LVL) times that in a transplantation dose. Our observation that the extraction efficacy of LVL differed in patients with BC and those with NHL may help to explain conflicting data in the literature. In children, the processing of more blood volumes does not necessarily lead to increased recruitment of PBPCs.[27] Factors such as the percentage of CD34+ cells in bone marrow before mobilization therapy[32] may have an influence on the extraction efficacy during leukapheresis. The phenomenon of hematopoietic progenitor cell mobilization is poorly understood. Stem and progenitor cells are released from the bone marrow into the peripheral blood, where they can be harvested by leukapheresis. Upon return, these mobilized progenitor cells migrate into the bone marrow and reconstitute hematopoiesis. At least from a kinetic point of view, a transient, rapid increase, such as that after physical exercise or the administration of adrenocorticotropic hormone,[33] endotoxin,[34] dextran sulfate, or antibodies against the cell adhesion molecule VLA-4,[26] can be distinguished from a delayed, sustained increase that can be observed, for example, after the administration of G–CSF.

These observations and the data obtained in our study could be explained by a dynamic equilibrium of progenitor cells in peripheral blood and bone marrow, caused by continuous mobilization and homing of PBPCs. Preliminary data (Humpe A, manuscript in preparation) suggest that the decrease in CD34+ cell numbers in peripheral blood during leukapheresis and the increase in the numbers in the collection bag can be well described by a cell-kinetic model consisting of the three distributional compartments: bone marrow, peripheral blood, and extracorporeal volume. With the help of such a model, a better prediction of the yield of CD34+ cells on the basis of values such as number of CD34+ cells, total peripheral blood volume, flow rate, and duration of leukapheresis may be possible in the future.

During LVL, patients received significant amounts of heparin. In vitro experiments were able to show that homing and transmigration of PBPCs are also dependent on PECAM-1 (CD31), a heparin-binding adhesion molecule.[35,36] Thus, it may be that heparin interacts with the microenvironment of PBPCs. The interaction of PECAM-1 with glycosaminoglycans may be influenced by the administration of heparin during leukapheresis, leading to increased PBPC numbers in the peripheral blood. In addition, the influence of previous chemotherapy on the expression of such molecules and the interaction with heparin has not yet been determined.

The difference in extraction efficacy between the BC and NHL patient groups could be an explanation for the different correlation coefficients between preapheresis numbers of CD34+ cells per µL in peripheral blood and the CD34+ cell yield in the harvest.[37,38] The leukapheresis size, the obviously varied extent of recruitment of PBPCs during the harvest, and the different extraction efficacies may influence the relationship between preleukapheresis numbers of CD34+ cells and the yield in the PBPC harvest.

Nevertheless, some data showed that sufficient amounts of PBPCs for transplantation can be harvested by a single LVL in most pediatric patients after mobilization with G–CSF alone[39] and in adult patients with NHL, Hodgkin's disease, or acute lymphoblastic leukemia after mobilization with chemotherapy and G–CSF.[24] In our study, 14.6 percent and 24.4 percent of the patients failed to achieve 1 and 2×10^6, respectively, CD34+ cells per kg of BW with an LVL. These figures were lower when only the patients with BC were considered. With both leukapheresis procedures taken together, none of the patients with BC failed to achieve 2×10^6 CD34+ cells per kg of BW, but, in the NHL group, 26.7 percent of the patients still did not achieve a transplantation dose and a back-up dose. An explanation might be the different mobilization regimens and the differences in previous chemotherapy between our study patients and the reported data. Recently published data[18] showed that prior exposure to chemotherapy, especially to DexaBEAM, or prior radiotherapy has a significant influence on the yield of PBPCs.

Apart from the harvest of a transplantation dose and an additional dose as back-up, the aim of a leukapheresis could be to harvest maximum numbers of CD34+ cells. Recent data[15] suggest that hematopoietic toxicity, platelet transfusion support, and quality of life may be positively influenced by the return of more than 15×10^6 CD34+ cells per kg of BW after HDCT.

Our data suggest that patients with BC and with high numbers of CD34+ cells in the peripheral blood before leukapheresis obviously profit from a substantial recruitment of PBPCs during an LVL, whereas other patients do not. It would be highly desirable to identify the latter patients before leukapheresis.

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