Factors predicting peripheral blood progenitor cell collection from pediatric donors for allogeneic transplantation

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Background and Objectives. Although several studies have reported on the use of children as donors for peripheral blood progenitor cells (PBPC), no specific characteristics have been identified as predictors of PBPC collection in this population. In this study we analyzed predictive factors for PBPC collection in pediatric donors.

Design and Methods. We retrospectively analyzed factors predicting the yield for a target CD34+ cell dose of ≥4×10^6/kg donor or recipient body weight, in 105 aphereses from 76 healthy pediatric donors (36 boys and 40 girls) included in the Spanish National Donor Registry. Mobilization consisted of granulocyte colony-stimulating factor (G-CSF) in single doses of 10 μg/kg per day subcutaneously for 4 or 5 days. Apheresis started after the fourth dose of G-CSF.

Results. Median age and body weight were 10 years (range 1-18) and 42 kg (range 9-89), respectively. The median number of CD34+ cells/kg recipient body weight was 4.22 (range 0.1-32). On multivariate analysis variables that had a significant negative impact on the CD34+ cell yield, considering the recipient's body weight were the total blood volume processed (regression coefficient (RC): 0.41, 95% CI: 0.21-0.81; p=0.01) and day of apheresis other than first (RC: 0.16, 95% CI: 0.07-0.34; p=0.0001). When considering donor's body weight the variables that positively influenced collection were younger age (RC: 6.79, 95% CI: 1.57-29.25; p=0.01) and large volume leukapheresis (RC: 3.33, 95% CI: 1.13-9.77; p<0.02).

Interpretation and Conclusions. Our data suggest that pediatric donors mobilized by G-CSF may donate sufficient numbers of CD34+ cells for allogeneic transplantation. The variables that influenced the yield were the donor's age, blood volume processed and the first day of the apheresis.

Key words: pediatric donors, children, transplantation, mobilization, apheresis.

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body weight was considered for this study. The independent variables analyzed included donor age and sex, donor and recipient weight, baseline white blood cell (WBC), platelet and hemoglobin counts, maximum WBC count following G-CSF administration and blood volume processed. Non-parametric Mann–Whitney U tests and Fisher’s exact tests were applied for continuous and categorical variables, respectively, in the univariate analysis. For multivariate analysis a stepwise logistic regression model was used. Age was included for this analysis as a continuous variable. Results were considered statistically significant if the $p$ value was <0.05.

## Results

A total of 105 aphereses performed in 76 healthy children (median 1; range 1–3) were included in this study. The median age of the donors was 10 years (range 1–18), with 30 of them (40%) aged less than 10 years. There were 36 boys and 40 girls. Their median body weight was 42 kg (range 9–89). Two apheresis procedures were performed in 26 donors and three in 3 donors. The percentage of donors undergoing only one collection in the LVL group and in the standard leukapheresis group was 82% and 58%, respectively.

Data regarding mobilization side effects have been published in part elsewhere and are in accordance with those reported by others. In all cases, symptoms were mild and managed with minor analgesics. G-CSF did not have to be discontinued in any donor because of toxicity.

The median number of CD34+ cells $\times 10^6$/kg recipient body weight was 4.22 (range 0.1–23.36). In the first apheresis the median number of CD34+ cells $\times 10^6$/kg recipient body weight was 5.55 (range 0.71–23.36), whereas it was 2.37 (range; 0.84–14.86) in the second one and 1.07 (range; 0.1–2.27) in the third ($p=0.0035$).

Sixty-one donors (58%) achieved the CD34+ cell dose of $\geq 4 \times 10^6$/kg donor body weight after only one leukapheresis. We found, on univariate analysis, that the factors affecting CD34+ cell collection, considering donor’s body weight, were: age ($r=0.4$, $p=0.0002$), gender (girls vs boys) (RR: 1.46, 95% CI: 1.04–2.05; $p=0.03$), LVL vs standard leukapheresis (RR: 1.76, 95% CI: 1.12–2.76; $p=0.008$), and first procedure vs subsequent ones (RR: 1.55, 95% CI: 0.98–2.47; $p=0.04$). As greater blood volumes were processed in younger donors than older ones, we also considered the CD34+ cells per kg of donor body weight and per liter of blood volume processed in the procedure and found better collections from younger donors (Table 2). In multi-

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### Table 1. Apheresis characteristics (n=105).

<table>
<thead>
<tr>
<th>Age group</th>
<th>0-4</th>
<th>5-9</th>
<th>10-14</th>
<th>15-18</th>
<th>$p$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Number of aphereses)</td>
<td>(18)</td>
<td>(28)</td>
<td>(26)</td>
<td>(33)</td>
<td></td>
</tr>
<tr>
<td>Donor age median (range)</td>
<td>3 (1-4)</td>
<td>7 (5-9)</td>
<td>12 (10-14)</td>
<td>17 (15-18)</td>
<td></td>
</tr>
<tr>
<td>Donor weight median (range)</td>
<td>13.5 (9-18)</td>
<td>30 (19-50)</td>
<td>45.5 (29-84)</td>
<td>60 (42-89)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Recipient weight median (range)</td>
<td>22 (14-47)</td>
<td>49 (9-85)</td>
<td>50 (7-71)</td>
<td>66 (22-95)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Blood volume processed (mL/Kg) median (range)</td>
<td>303 (117-513)</td>
<td>214 (100-588)</td>
<td>202 (85-391)</td>
<td>125 (113-275)</td>
<td>0.0001</td>
</tr>
<tr>
<td>% of large volume leukapheresis</td>
<td>77.7</td>
<td>62.5</td>
<td>73.3</td>
<td>30</td>
<td>0.01</td>
</tr>
<tr>
<td>Day of apheresis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First</td>
<td>15</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Second</td>
<td>3</td>
<td>8</td>
<td>6</td>
<td>9</td>
<td>0.7</td>
</tr>
<tr>
<td>Third</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>CD34+ cells $\times 10^6$/Kg recipient body weight median (range)</td>
<td>5.2 (1.48-22.5)</td>
<td>4.22 (1.03-16.05)</td>
<td>5.18 (1.07-23.36)</td>
<td>4.35 (0.1-17)</td>
<td>0.6</td>
</tr>
<tr>
<td>CD34+ cells $\times 10^6$/Kg donor body weight median (range)</td>
<td>8.5 (2.8-50.9)</td>
<td>7.2 (2.4-41.8)</td>
<td>3.95 (1.7-14.2)</td>
<td>3.4 (1.1-15.7)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Pre-apheresis WBC count ($\times 10^9$/L) median (range)</td>
<td>36.6 (21.6-56.7)</td>
<td>42.6 (25.6-68.5)</td>
<td>44.4 (11.2-23.8)</td>
<td>38.1 (21.6-74.9)</td>
<td>0.8</td>
</tr>
</tbody>
</table>
variate analysis only younger age (RC: 6.79, 95% CI: 1.57-29.25; \( p < 0.01 \)) and large volume leukapheresis (RC: 3.33, 95% CI: 1.13-9.77; \( p < 0.02 \)) were found to be significant predictors of yield (Table 3).

When considering the recipient body weight, 57 leukapheresis procedures achieved the target dose (\( \geq 4 \times 10^6 \)/Kg recipient body weight) after the first procedure (54.3%). Only 11 of the 76 donors could not finally produce the target number of CD34+ cells (14.5%). However, all patients underwent hematopoietic transplantation. Univariate analysis of the factors predicting the achievement of a CD34+ cell target of \( \geq 4 \times 10^6 \)/Kg recipient body weight showed that the variables that had a positive influence were: volume processed expressed as mL/kg donor body weight \( (r=0.2; ~ p=0.03) \), large volume leukapheresis \( (RR: 1.55, 95\% \text{ CI}: 1.02-2.37; ~ p=0.03) \), first day of apheresis \( (RR: 1.65, 95\% \text{ CI}: 1.21-2.32; ~ p=0.0003) \) and platelet count at the end of the apheresis procedure \( (r=0.2; ~ p=0.04) \) in that donors with a lower platelet count at the end of apheresis were those who yielded higher numbers of CD34+ cells. In multivariate analysis only the volume processed (standard leukapheresis) and the day of apheresis (other than first) had a negative impact on CD34+ cell yield (Table 4).

Discussion

Although no definitive mobilization regimen has been established, the mobilization regimen employed in this series has been considered safe in adults and children.\(^5\) It allowed us to compare variables related to the apheresis since all donors in the series underwent the same mobilization regimen. Our results show that the use of large volume leukapheresis (LVL) as the method for collecting the PBPC and the first day of collection were the only variables that significantly affected the CD34+ cell yield. However, if we consider the same target with respect to donor body weight, younger age was also a variable that significantly influenced the CD34+ cell yield.

These data suggest that very small children mobilize better than older children do and that they may donate a high number of CD34+ cells for allogeneic transplantation. There are controversial data in the literature regarding the influence of age in CD34+ cell mobilization.\(^6,12,13\) Although previous studies in adult donors have reported a negative impact of age on CD34+ cell mobilization and collection,\(^6,7\) other series have not described the same effect.\(^12,13\) No differences were observed in CD34+ cell mobilization between donors aged below 18 years and adult donors in a previous study reported by our group, although greater age was associated with a more frequent requirement for more than one apheresis.\(^5\) In this pediatric donor series, the largest reported so far, the yield was related to donor’s age when considering donor’s weight. However, a relationship between donor’s age and CD34+ cell yield considering recipient’s body weight was not found (data not shown). This may be explained by significant differences between recipient and donor’s weight, especially in those donors aged less than 5 years: a higher number of donors below this age yielded the CD34+ cell target with only one apheresis, whereas the number of second and third aphereses needed to reach the target cell collection increased for older donors (Table 1).

The other variable that influenced the collection was the volume of blood processed. In this study, LVL was related to better yields when considering either donor or recipient body weight. The relationship between platelet count at the end of apheresis and achievement of the target number of CD34+ cells probably reflects the volume processed and duration of apheresis.\(^11,14\) Regarding secondary
effects of LVL, this procedure has been considered a feasible and safe approach for PBPC collection from children, even very small ones, undergoing autologous PBPC transplantation.11,15–17

In summary, our data suggest that younger age is also a variable to consider among pediatric donors for better collections, and that pediatric donors mobilized by G-CSF may donate sufficient number of CD34+ cells for allogeneic transplantation using a single large volume leukapheresis.

Participating centers
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