Donor blood-count changes during and after plateletpheresis

Comparison of two cell-separator techniques[1]

Susan M. Bator, M.D.
Gerald A. Hoeltge, M.D.

Thirty-two platelet donors at the Cleveland Clinic Foundation were monitored for white blood cell count, leukocyte differential, red blood cell count, and platelet count before, during, and after the collection of platelets. Counts were performed at 15-minute intervals during plateletpheresis using the Fenwal CS 3000 cell separator and at the beginning of each draw cycle using the Haemonetics V50 cell separator. Red blood cell concentration declined significantly ($p < 0.05$). Leukocyte counts decreased initially($p < 0.05$), followed by a secondary rise, and reached a plateau below the initial value. Platelet counts declined steadily with a net loss comparable to the platelet yield. Platelet collection efficiencies on the two machines were not significantly different.

Index terms: Blood component removal • Blood donors • Blood platelets

Cleve Clin J Med 54:411–416, Sep/Oct 1987

Apheresis is the removal of whole blood from an individual, the separation of that blood into its components, retention of one or more components, and return of the remaining constituents to the individual. The terms plateletpheresis, leukapheresis, and plasmapheresis refer to the selective removal of platelets, white blood cells, and plasma, respectively. Apheresis has been demonstrated to be an effective form of treatment in various diseases and may be used to obtain appropriate blood components for infusion into patients with a deficiency of that blood constituent.

Centrifugation and membrane filtration have been used as separation methods. Discontinuous- and continuous-flow systems are currently the most commonly used techniques.

[1] Division of Laboratory Medicine (S.M.B.) and Department of Blood Banking, (G.A.H.), Cleveland Clinic Foundation. Submitted for publication Nov 1986; accepted Jan 1987.

See also the editorial by Warkentin (pp 381–383).

0891-1150/87/05/0411/06/$2.50/0

Table 1. Age and sex of platelet donors

Haemonetics V50		Fenwal CS 3000	
Males (yr)	Females (yr)	Males (yr)	Females (yr)
26	29	24	22
26	32	26	24
27		34	26
30		41	28
30		44	30
36		48	30
41		52	47
48			50
50			54
52			
52			
56			
60			
?			

A discontinuous-flow system requires one venipuncture site, using a low-gauge needle. A small volume of whole blood is removed from the donor, blood flow stops, the whole blood is separated into its components via the centrifuge, and undesired components are returned to the donor. The process is repeated. A continuous-flow system requires two venipunctures, a draw line, and a return line, and uses higher-gauge needles. Removal of blood from the donor, separation of whole blood into its components, and infusion of undesired components are continuous throughout the procedure. A "surge pump" collection system, which is a modified centrifugational device, has been used experimentally in plateletpheresis.[1,2] Flat- and hollow-fiber filtration devices are promising for the removal of specific plasma components, however, these techniques are not yet routinely used for component preparation.

Risks associated with apheresis include hypovolemia, citrate reactions, blood loss, red cell hemolysis, air embolism, hepatitis, and depletion of plasma constituents.[3] Complications are more frequent during therapeutic apheresis than during component preparation, due to the morbid condition of the patient. The study of dynamic changes in cellular and solute concentrations during apheresis is straightforward in healthy blood donors. Such studies are important to maximize the safety of the apheresis process.

Increasing demand for platelet transfusion implies the need to recruit greater numbers of donors,[4] and ensuring the safety of the donors is a crucial factor in recruitment. Although most blood components are returned to the donor in plateletpheresis, blood cell count studies are of interest to demonstrate donor safety. The present study measures alterations in donor blood cell counts during plateletpheresis using a continuous-flow system and a discontinuous-flow system.

Materials and methods

Thirty-two healthy donors at The Cleveland Clinic Foundation were studied with respect to red blood cell count, white blood cell count, platelet count, and leukocyte differential before plateletpheresis, at regular intervals during the collection, and following the termination of the procedure. The age and sex of donors are recorded in *Table 1*. A minimum of 3×10^{11} platelets per unit was obtained from each donor.[5] Continuous-flow plateletpheresis using the Fenwal CS 3000 cell separator (Fenwal Laboratories, Inc., Deerfield, IL) ($n = 16$) and discontinuous-flow plateletpheresis using the Haemonetics V50 cell separator (Haemonetics Corp., Braintree, MA) ($n = 16$) were compared. Samples from the Fenwal CS 3000 group were collected at the beginning of the procedure and at 15-minute intervals thereafter, with the final sample collection just before termination of the donation. Samples from the Haemonetics V50 group were collected at the beginning of each draw cycle and at the end of the procedure. Blood samples were collected via a Y connector placed just above the point of addition of adenosine-citrate-dextrose solution. A total of 2 to 3 mL of blood was collected per specimen.

The means of the platelet count, red blood cell count, total white blood cell count, and percentages of granulocytes and lymphocytes were calculated per time interval or draw cycle for each group. The data gathered on the Haemonetics V50 and Fenwal CS 3000 were compared, matching draw cycle and interval for each of the five variables. An unpaired two-tailed t test was used to compare the data. The limit of statistical significance was set at $p \leq 0.003$ obtained by the Bonferroni method, a multiple comparison procedure.[6]

The early and overall variations in the cell counts were measured for each of the five variables using the previously calculated means. The early changes within groups for each machine were calculated using the differences noted between the first and second or first and third

Table 2. RBC, WBC, and platelet counts (mean ± SD) for Fenwal CS-3000

Volume (mL) (Time, min)	RBC($\times 10^{12}$/L)	WBC($\times 10^{9}$/L)	Granulocyte (%)	Lymphocyte (%)	Platelets ($\times 10^{9}$/L)
0 (0)	4.67 ± .34	7.03 ± 2.30	62 ± 7	32 ± 6	290 ± 88
650 (15)	4.47 ± .29	6.27 ± 2.19	67 ± 7	29 ± 6	263 ± 76
1300 (30)	4.52 ± .32	6.22 ± 1.92	66 ± 4	27 ± 6	242 ± 63
1950 (45)	4.50 ± .36	6.38 ± 2.13	67 ± 6	27 ± 6	235 ± 68
2600 (60)	4.46 ± .31	6.42 ± 2.11	69 ± 6	26 ± 6	220 ± 66
3250 (75)	4.45 ± .32	6.66 ± 2.06	68 ± 8	27 ± 7	206 ± 54
3900 (90)	4.49 ± .37	6.74 ± 2.23	66 ± 6	27 ± 6	201 ± 54
4550 (105)	4.42 ± .49	6.83 ± 2.45	66 ± 7	28 ± 7	191 ± 48

Table 3. RBC, WBC, and platelet counts (mean ± SD) for Haemonetics V50

Volume (mL) (Cycle)	RBC($\times 10^{12}$/L)	WBC($\times 10^{9}$/L)	Granulocyte (%)	Lymphocyte (%)	Platelets ($\times 10^{9}$/L)
0 (1)	4.82 ± .37	6.47 ± 1.47	64 ± 12	30 ± 12	287 ± 65
450 (2)	4.64 ± .38	5.79 ± 1.34	64 ± 10	30 ± 12	262 ± 64
900 (3)	4.77 ± .35	5.76 ± 1.33	66 ± 13	28 ± 12	251 ± 65
1350 (4)	4.63 ± .49	5.81 ± 1.34	67 ± 10	27 ± 11	241 ± 59
1800 (5)	4.75 ± .38	6.06 ± 1.12	64 ± 12	28 ± 12	242 ± 57
2250 (6)	4.66 ± .43	5.95 ± 1.25	66 ± 12	28 ± 12	224 ± 49
2700 (7)	4.62 ± .29	5.97 ± 0.87	67 ± 10	26 ± 9	231 ± 46
3150 (8)	4.62 ± .43	6.11 ± 1.06	70 ± 10	24 ± 8	233 ± 61

specimens. The initial change utilized the first and third specimens if the difference between the second and third specimens was greater than that between the first and second specimens. The early variations were calculated to determine if significant changes in blood count occurred early or late in the donation process. The predonation-postdonation difference was also calculated within each group.

Platelet yield was measured for each of the 32 donations. The total blood volume processed was measured for each donor in the Fenwal CS 3000 group. In the Haemonetics V50 group, a calculated value was recorded for the total blood volume processed, using 500 mL as the blood volume per pass. The actual blood volume processed was calculated by subtracting the volume of anticoagulant added from the total blood volume processed. The platelet collection efficiencies were calculated and the mean values for both the continuous-flow and the discontinuous-flow donation groups were obtained. Platelet collection efficiencies were obtained by the following equation:

$$\% \text{ efficiency} = \frac{\text{platelet yield}}{\text{original platelet count} \times \text{liters processed}} \times 100$$

Paired two-tailed t-test analyses were used to test for differences in initial and overall changes for each blood component, and to test for a difference between machines for collection efficiencies. Differences were considered statistically significant for each of these analyses if the p value was ≤ 0.05.

Results

Of the 16 donations using the Fenwal CS 3000, 13 lasted the complete 105 minutes. Of the remaining three, two lasted 90 minutes and one was terminated at 75 minutes. Samples at 15, 45, and 60 minutes clotted in one case and counts were unattainable. The 30-minute sample differential was unavailable for one donor.

The results for the Fenwal CS 3000 group are shown in *Table 2*. Utilizing cycle 8 or the 105-minute sample as a final collection point, the red blood cell count mean decreased from 4.67 × 10^{12}/L to 4.42 × 10^{12}/L; the platelet count mean decreased from 290 × 10^{9}/L to 191 × 10^{9}/L; and the white blood cell count mean initially decreased from 7.0 × 10^{9}/L in the first sample to 6.2 × 10^{9}/L in the third sample, which then returned to 6.8 × 10^{9}/L. During the procedure, the lymphocyte percentage declined by 3.8% from 31.6% to 27.8%, and there was a corresponding 4.3% increase in granulocytes from 62.1% to 66.4%. The platelet yields ranged from

Table 4. Average platelet count, RBC count, WBC count, and differential results for both groups matched by draw cycle and time interval*

	Platelet Count		WBC Count		RBC Count		Lymphocyte %		Granulocyte %	
Cycle	T	p	T	p	T	p	T	p	T	p
1	0.1096	.91	0.7609	.45	−1.2051	.24	0.4745	.64	−0.4069	.69
2	0.0440	.97	0.6857	.50	−1.4068	.17	−0.2498	.80	0.7727	.45
3	−0.3610	.72	0.7118	.48	−2.0461	.05	−0.2716	.79	0.1733	.86
4	−0.2412	.81	0.8159	.42	−8.448	.41	−0.1247	.90	0.1981	.84
5	−0.9681	.34	0.5919	.56	−2.3049	.03	−0.5217	.61	1.3594	.19
6	−0.9535	.35	1.0858	.29	−1.5511	.13	−0.2787	.78	0.5114	.61
7	−1.4087	.17	1.1220	.28	−0.9540	.38	0.1410	.89	−0.2821	.78
8	−1.7100	.10	0.6768	.51	−0.9600	.35	1.1886	.25	−0.8221	.42

* At the 5% level, p-value = 0.05/(2-tail comparison)/(8 comparisons) = (0.05/2)/8 = 0.003.
No statistically significant differences were found between machines for any of the variables.

3.16×10^{11} to 8.59×10^{11} platelets. The actual blood volume processed was 4,550 to 4,650 mL in 15 cases; one procedure yielded 3,150 mL and 3.55×10^{11} platelets. The platelet collection efficiencies ranged from 33% to 55%.

Of the 16 collections using the Haemonetics V50, seven had a duration of five passes, two had a duration of six passes, and seven lasted seven passes. Results on the fifth draw sample for one donor were unavailable. Samples clotted on draws three and four in another case. The third draw cycle differential was not assessed in one donor.

The results for the Haemonetics V50 group are shown in *Table 3*. Utilizing cycle 8 (specimen collected after seventh pass) as a final collection point, the red blood cell count mean decreased from 4.83×10^{12}/L to 4.62×10^{12}/L; the platelet count mean decreased from 287×10^9/L to 233×10^9/L; and the white blood cell count mean initially decreased from 6.5×10^9/L in the first sample to 5.8×10^9/L in the third sample. The white blood cell count then increased to 6.1×10^9/L. There was a 6.4% decline in lymphocytes from 30.0% to 23.6%, and a corresponding 6.1% increase in granulocytes from 63.5% to 69.6%, during the procedure. The platelet yield ranged from 2.26×10^{11} to 5.0×10^{11} platelets. The actual blood volume processed ranged from 2,250 mL to 3,150 mL. Platelet collection efficiencies ranged from 23% to 69%.

The complete blood cell counts were similar for the continuous and discontinuous centrifugation techniques. No statistically significant differences between machines were found for any of the five variables (red blood cell count, leukocyte count, platelet count, lymphocyte percentage, and granulocyte percentage matched for draw cycle and 15-minute interval) despite the difference in volumes of blood processed (*Table 4*). *Tables 5* and *6* demonstrate the changes in complete blood count, lymphocyte percentage, and granulocyte percentage in both groups. A small decrease in the red blood cell concentration was noted in both methods, 4% for the V50 and 6% for the CS 3000. There was a steady decline in the platelet count, averaging 20% for the V50 and 34% for the CS 3000. We observed no brief increase in platelet concentration as reported in previous studies.[7,8] In the V50 group, there was an initial 11% decline in the white blood cell count that was followed by an increase to 94% of the initial value. In the CS 3000 group, there was an initial 12% decline in leukocyte count that was followed by a return to 97% of the initial value. The differential change in lymphocyte and granulocyte percentages was proportional, as stated previously. No cell counts dropped below established normal ranges.

Statistically significant differences in age and sex were found when comparing both population groups via the two-tailed *t* test and chi-square analysis, respectively. Due to the larger gauge needles used with the Haemonetics V50, males were more likely to be chosen for this population group. Age was considered a random phenomenon at the time of testing.

Discussion

The long-term effects of plateletpheresis on the blood count are known. Westphal[9] and Ho[10] agree that in this group of donors, lymphocytopenia and thrombocytopenia are occasional complications. Strauss[11] suggested that donors with

prepheresis lymphocyte counts less than 1.2 × 10^9/L be deferred. Koepke et al[12] examined donors who had undergone plateletpheresis weekly with the Haemonetics Model V30 blood processor and found a 20% decrease in circulating lymphocytes, most of which were of the B cell type. In a study of 11 donors who had undergone cytapheresis more than 50 times, Heal et al[13] recognized that despite a drop in lymphocyte count, the ratios of T:B and helper: suppressor cells had been maintained. Glowitz and Slichter[14] examined a large group of donors whose platelets had been collected on alternate days with the Haemonetics V30 and found the platelet concentration to drop to 70% of the predonation level. This effect occurred after six to eight donations and then stabilized with sequential donations.

There are many reports on blood cell counts of the platelet-rich product. Mintz,[15] in a comparison of the Fenwal CS 3000 and the IBM 2997 Dual Stage devices, found more leukocyte contamination (0.46 × 10^9/L) of the CS 3000 platelet-rich product than of the product of the IBM 2997 group (0.09 × 10^9/L). The IBM 2997, Fenwal CS 3000, and Haemonetics V50 platelet-rich products are all characterized by a hematocrit of less than 1% and leukocyte contamination less than 0.5 × 10^9/L.[16,17] Slight differences in platelet collection efficiency have been described for the various licensed devices.[15,18,19]

Multiple studies of the changes in donors' blood counts immediately following the procedure have been reported. Following collection with the Fenwal CS 3000, the hematocrit decreases by 3% to 5%, and the platelet concentration decreases by about 20%.[20–22] The leukocyte concentration may increase by 1% to 2% after the donation procedure.[20,21] Other studies of variations in donors' blood counts immediately following the procedure have been observed for the IBM 2997 Single and Dual Stage channels.[23–26]

Two studies reported blood counts before, during, and after the donation procedure using the Haemonetics V30 for plateletpheresis.[27,28] These studies found a larger early decrease in hematocrit and platelet count followed by a leveling off of the decline. The present study reports predonation and postdonation complete blood counts and differentials, and changes in these values at frequent intervals during the donation process, using two apheresis devices, the Haemonetics V50 and the Fenwal CS 3000.

The donor's platelet count decreased proportionately with the platelet yield in both collection systems. The results of this study differ slightly from the results of Rock et al[17] by demonstrating a greater decline in leukocyte count during plateletpheresis. Even though the difference between the predonation and postdonation leukocyte counts was less than 5 × 10^8/L, during plateletpheresis the leukocyte count decreased by 8.0 × 10^8/L (CS 3000) and 7.0 × 10^8/L (V50). This suggests self-limited margination of the white blood cells in response to plateletpheresis. Red blood cell loss was minimal for both centrifugation systems, but slightly greater in the CS 3000 group. This finding, as well as the greater decline in platelets with the CS 3000, can be explained by the larger total blood volume processed. The platelet collection efficiencies between the two machines were comparable.

Blood counts, including venous platelet concentration, red cell concentration, and white cell concentration, change predictably during the course of the procedure. At no time is an unphysiologic state measurable. Donor safety is ensured throughout the course of these procedures.

Table 5. Change from initial to final values for both groups

	Haemonetics V50		CS 3000	
	T	p-value	T	p-value
Platelet count	8.69	.0001*	7.29	.0001*
WBC count	4.03	.0017*	2.54	.0238*
RBC count	3.69	.0022*	3.99	.0012*
Lymphocyte %	2.43	.0282*	3.29	.0050*
Granulocyte %	−1.93	.0729	−3.02	.0087*

* p-value <0.05.

Table 6. Initial change for both groups

	Haemonetics V50		CS 3000	
	T	p-value	T	p-value
Platelet count	8.12	.0001*	7.13	.0001*
WBC count	4.85	.0004*	8.77	.0001*
RBC count	2.24	.0405*	4.36	.0006*
Lymphocyte %	0.74	.4682	1.87	.0815
Granulocyte %	−1.47	.1614	−2.29	.0367*

* p-value <0.05.

Acknowlegments

The authors are grateful for the technical assistance of Bruce Millward of the Department of Blood Banking and Christine I. Skibinski, M.S., of the Department of Biostatistics and Epidemiology.

References

1. Hogge DE, Schiffer CA. Collection of platelets depleted of red and white cells with the "surge pump" adaptation of a blood cell separator. Transfusion 1983; **23:**177–181.
2. Schoendorfer DW, Hansen LE, Kenney DM. The surge technique: a method to increase purity of platelet concentrates obtained by centrifugal apheresis. Transfusion 1983; **23:**182–189.
3. Cohen RJ. Apheresis in hematologic and oncologic disease. Hospital Practice Oct 1983; **18:**199–205.
4. Hester JP. Donor symptomatology and safety in blood cell separation procedures. [In] Vogler WR, ed. Cytapheresis and Plasma Exchange: Clinical Indications. New York, Alan R. Liss, Inc., 1982, pp 115–124.
5. Standard B4.430, Standards for Blood Banks and Transfusion Services. 12th edition. American Association of Blood Banks, Arlington VA, 1987.
6. Kleinbaum D, Kupper L. Applied Regression Analysis and other Multivariable Methods. North Scituate, MA, Duxbury Press, 1978, pp 264–266.
7. Lee EJ, Schiffer CA. Evidence for rapid mobilization of platelets from the spleen during intensive plateletpheresis. Am J Hematol 1985; **19:**161–165.
8. Eriksson KA, Sigvaldason A, Lindholm A, Safai-Kutti S, Kutti J. Platelet activation in response to phlebotomy: an experimental study of healthy blood donors. Acta Med Scand 1982; **212:**121–123.
9. Westphal RG. Health risks to cytapheresis donors. Clin Haematol 1984; **13:**289–301.
10. Ho W. Multiple pheresis-effect of donor. [In] Mielke HC Jr, ed. Apheresis: Development, Applications, and Collection Procedures. New York, Alan R. Liss, Inc., 1981, pp 91–99.
11. Strauss RG. Apheresis donor safety–changes in humoral and cellular immunity. J Clin Apheresis 1984; **2:**68–80.
12. Koepke JA, Parks WM, Goeken JA, Klee GG, Strauss RG. The safety of weekly plateletpheresis: effect on the donors' lymphocyte population. Transfusion 1981; **21:**59–62.
13. Heal JM, Horan PK, Schmitt TC, Bailey G, Nusbacher J. Long-term follow-up of donors cytapheresed more than 50 times. Vox Sang 1983; **45:**14–24.
14. Glowitz RJ, Slichter SJ. Frequent multiunit plateletpheresis from single donors: effects on donors' blood and the platelet yield. Transfusion 1980; **20:**199–205.
15. Mintz PD. Comparison of plateletapheresis with two continuous-flow cell separators using the identical donors. Transfusion 1985; **25:**330–333.
16. Rock G. Centrifugal apheresis techniques. [In] Nosé Y, Malchesky PS, Smith JW, Krakauer RS, eds, Plasmapheresis. New York, Raven Press, 1983, pp 75–79.
17. Rock G, Herzig R, Mc Combie N, Lazarus HM, Tittley P. Automated platelet production during plasmapheresis. Transfusion 1983; **23:**290–293.
18. Kalmin ND, Grindon AJ. Comparison of two continuous-flow cell separators. Transfusion 1983; **23:**197–200.
19. Rock G, Blanchette V, McCombie N, Tittley P. Comparative function of centrifugal apheresis devices. Vox Sang 1985; **48:**136–142.
20. Katz AJ, Genco PV, Blumberg N, Snyder EL, Camp B, Morse EE. Platelet collection and transfusion using the Fenwal CS-3000 cell separator. Transfusion 1981; **21:**560–563.
21. Buchholz DH, Porten JH, Menitove JE, et al. Description and use of the CS-3000 blood cell separator for single-donor platelet collection. Transfusion 1983; **23:**190–196.
22. Kurtz SR, McMican A, Carciero R, et al. Plateletpheresis experience with the Haemonetics blood processor 30, the IBM blood processor 2997, and the Fenwal CS-3000 blood processor. Vox Sang 1981; **41:**212–218.
23. Hester JP, Kellogg RM, McCredie KB, Freireich EJ. Cross cellular contamination in plateletpheresis, leukapheresis and plasma exchange. [In] Mielke HC Jr, ed. Apheresis: Development, Applications, and Collection Procedures. New York, Alan R. Liss, Inc., 1981, pp 109–121.
24. Langley JW, Spiva D, Hendren D, Orrell J. Effective cell support by repeat plateletpheresis of related donors on the IBM 2997 cell separator. Am J Clin Pathol 1981; **76:**148–154.
25. Hester JP, Kellogg RM, Mulzet AP, Freireich EJ. Continuous-flow techniques for platelet concentrate collection: a step toward standardization and yield predictability. J Clin Apheresis 1985; **2:**224–230.
26. Bond R, Wood L, Jacobs P, Kernoff LM. Platelet collection using the IBM 2997 cell separator. J Clin Apheresis 1985; **2:**258–261.
27. Lasky LC, Lin A, Kahn RA, McCullough J. Donor platelet response and product quality assurance in plateletpheresis. Transfusion 1981; **21:**247–260.
28. Rosenkvist J, Holsøe E, Freiesleben E, Sørensen H. A critical review of platelet yield by Haemonetics 30. Scand J Haemtol 1980; **25:**165–170.

Gerald A. Hoeltge, M.D.
Chairman of Department of Blood Banking
Cleveland Clinic Foundation
9500 Euclid Avenue
Cleveland, OH 44106