The effect of whole-blood donor adverse events on blood donor return rates

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BACKGROUND: Some blood donation–related adverse events (AEs) can negatively impact the blood donor return rate (BDRR) and decrease donor retention.

STUDY DESIGN AND METHODS: One-thousand randomly selected whole-blood donors were interviewed 3 weeks after a 525-mL index whole-blood donation for seven AEs. The number of return visits and duration of follow-up were recorded for each of the 1000 donors. A negative binomial regression analysis was used to determine the contribution of the four most common AEs to the BDRR, and interactions between these AEs were also evaluated.

RESULTS: The four most common AEs were bruise alone (15.1%), sore arm "alone" (7.0%), fatigue "alone" (5.1%), and donor reaction "alone" (4.2%), where "alone" is defined to also include donors who had a bruise but no other AE. The estimated BDRR for donations without AEs was 1.32 visits per year. The estimated BDRRs for the four most common AEs were: bruise alone, 1.32 visits per year; sore arm alone, 1.30 visits per year (2% reduction in BDRR); fatigue alone, 1.06 visits per year (20% reduction in BDRR); and donor reaction alone, 0.87 visits per year (34% reduction in BDRR). The BDRR for donor reaction, fatigue, and sore arm together was 0.20 visits per year (85% reduction in BDRR).

CONCLUSION: Donor reaction had the most negative impact on the BDRR. There appears to be a synergistic effect between donor reaction, fatigue, and sore arm. Theoretically, amelioration of some AEs has the potential to improve BDRRs.

Six recent studies have shown that high-school and general donors who sustain a donor reaction are less likely to return.[1-7] Four studies were based on donor observation at the collection site,[1,4,5,7] and two studies observed and interviewed donors.[2,3,6,8] Two studies used regression analysis.[6,7] In an abstract,[2] we described the effect of donor reactions and other adverse events (AEs)—such as bruise, sore arm, and fatigue—on blood donor return rates (BDRRs), but we did not use regression analysis. We recently applied binomial regression analysis to our data, and we can now more accurately explain our data and its significance.

MATERIALS AND METHODS

Blood donation setting, phlebotomy, and postdonation interview

Blood donors were collected in a metropolitan blood center that collects approximately 210,000 to 225,000 whole-blood units per year. Blood donors who met donor acceptability criteria were placed in a supine position, and 525 mL of blood, including samples for testing, were collected from an antecubital vein with a 16-gauge needle. One-thousand whole-blood donors were randomly selected from the period of April 17, 2001, through April 2, 2002, and were interviewed 3 weeks after the donation for seven AEs.[8] Donors were asked an open-ended question

ABBREVIATIONS: AE(s) = adverse event(s); BDRR(s) = blood donor return rate(s).

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about potential adverse systemic events during or after blood donation, and this was followed by a specific question for each of 3 systemic AEs (donor reaction, fatigue and nausea and/or vomiting unrelated to a donor reaction). A donor reaction was defined as the presence of any of the following symptoms or signs during or shortly after whole-blood donation: dizziness, diaphoresis (sweating), pallor, sudden weakness, hypotension, bradycardia, and syncope (faint). Approximately 97 percent of the donor reactions were nonsyncopal reactions. Similarly, an open-ended question was asked about potential arm problems, and this was followed by a specific question for each of 4 arm-related AEs (bruise, hematoma, nerve injury, and pain). Additional follow-up questions were asked as needed. Blood donor AEs and demographic data such as age, sex, race, self-reported weight, and blood donation status (first-time vs. repeat donor) were recorded. Demographic data were also collected on 211,900 general blood donors collected in 2001, and a comparison between the 1000 interviewed donors and the 211,900 general blood donors was done.

We then obtained follow-up data through January 26, 2003, on blood donor return visits. A visit could either be a blood donation or a deferral. The follow-up period ranged from 9 to 21 months. The BDRRs were annualized (i.e., expressed as returns per year). We focused on the four most common AEs and combinations of AEs.

Statistical analysis

We evaluated the BDRR data for each AE and also for combinations of AEs. The BDRR data were analyzed with a negative binomial regression analysis because the data had too much variability to fit the usual Poisson regression model. The estimated BDRR is expressed as e^R, and the number of times a donor returns is the BDRR multiplied by the follow-up period in years. For the baseline regression coefficient for donations without AEs, R is denoted by R_b. For AEs, the R is written as $R_b - R_c$, which is the baseline regression coefficient (R_b) minus the regression coefficient unique to each AE or combination of AEs (R_c). The p value indicates the extent of the evidence (or lack thereof) that an AE had an effect on the BDRR or that a combination of AEs exhibited a synergistic effect on the BDRR, that is, a larger effect than would have been expected based on the effects of the individual AEs alone. The p values are one-sided and based on likelihood ratio statistics for a type 3 analysis (The SAS System, Version 8, GENMOD procedure, SAS Institute, Cary, NC). Demographic data were not included in the statistical analysis but were treated separately as univariables.

RESULTS

Table 1 shows that 83 percent of the interviewed donors were repeat donors, 86 percent were Caucasian, and 55 percent were female. A comparison of the 1000 interviewed donors with the 211,900 general donors from the same period shows that the two populations were roughly equivalent, except that there were more women in the interviewed population (55% vs. 45%). The interviewed donors were divided into subgroups based on sex, donation status (first-time vs. repeat donor), and race, and the subgroups were compared. Men were heavier than women and were more likely to be repeat donors. Repeat donors were older and heavier than first-time donors; African American donors had a higher percentage of females and first-time donors than Caucasian donors and they were slightly heavier than Caucasian donors.

Table 2 shows that 64 percent of the donors had no AEs; the remaining 36 percent of the donors had one or more AEs. We focused on the four most common AEs, which were bruise alone (15.1%), sore arm “alone” (7.0%), fatigue “alone” (5.1%), and donor reaction “alone” (4.2%), where “alone” (in quotes) is defined as donors with no AEs or donors who also had a bruise, but no other AEs. This definition was adopted because bruise was found to have no effect on the BDRR, either alone or in combination

TABLE 1. Demographics of the general donor population, interviewed donors, and interviewed donor subgroups

Donors	Number	Women (%)	First-time donors (%)	Caucasian (%)	African American (%)	Median age (years)	<30 years (%)	Age: 17 years (%)	Median weight (lb)	Weight < 130 lb (%)
2001 blood center donor population	211,900	45.4	19.2	89.9	6.0	41	27.2	6.4	*	*
Interviewed donors	1,000	55.3	16.5	86.2	6.8	41	26.9	7.4	170	8.5
Men	447	NA†	12.5	87.2	4.0	42	23.7	5.4	190	0.7
Women	553	NA	19.7	85.4	9.0	41	29.5	9.0	150	14.8
Repeat	835	53.2	NA	88.5	6.1	43	19.4	1.7	175	5.5
First-time	165	66.1	NA	74.5	10.3	22	64.8	36.4	145	23.6
African American	68	73.5	25.0	NA	NA	39	32.4	7.4	177.5	1.5
Caucasian	862	54.8	14.3	NA	NA	42	25.8	6.6	170	8.5

* Not readily available.
† NA = not applicable.

TABLE 2. Effect of whole-blood donation AEs on BDRRs

AE(s)*	Incidence (%)†	R_b or R_c‡	R value§	p Value‖	BDRR/year (returns/ year)	Percent reduction relative to baseline	Percent reduction in full donor population relative to baseline¶
Baseline (No AEs)	63.8	0.281	0.281		1.32	0	0
Bruise alone	15.1	0.000**	0.281	0.83[7]	1.32	0	0
Sore arm "alone"††	7.0	0.019	0.262	0.061	1.30	2	0.14
Fatigue "alone"††	5.1	0.223	0.058	0.002	1.06	20	1.02
Donor reaction "alone"††	4.2	0.418	–0.137	0.002	0.87	34	1.43
Donor reaction and sore arm††	0.8	0.437**	–0.156	0.88**‡‡	0.86	35	0.28
Sore arm and fatigue††	0.5	1.051	–0.770	0.070‡‡	0.46	65	0.33
Donor reaction and fatigue††	1.3	1.080	–0.799	0.17‡‡	0.45	66	0.86
Donor reaction + fatigue + sore arm††	0.7	1.908**	–1.627	0.012**‡‡	0.20	85	0.60
Subtotal							*4.66*
All rare AEs							1.23§§
Total (including the rare AEs)							*5.89*‖‖

* Table assumes absence of all rare AEs through the subtotal, causing the effects of all AEs to be underestimated. This is corrected in the last two lines.
† In this column only, cases with one or more rare AEs are included, so that the incidences sum to 100 percent.
‡ R_b is the baseline value for donations with no AEs and R_c values are for the AEs.
§ R_b for donations with no AEs, $R_b - R_c$ for the AEs.
‖ One-sided for decreases in BDRR.
¶ Obtained via multiplication of incidence and percentage reduction relative to baseline.
** This factor not included in final model. R_c summed from its lower level factors (if any). p Value obtained from augmented model with this factor included.
†† With or without bruise, which does not affect any of the estimates.
‡‡ p Value is for synergy (statistical interaction), i.e., for additional effects that cannot be accounted for by a combination of all preceding lines.
§§ Calculations (not shown) are analogous to what is done in this table for the more common AEs.
‖‖ Assumes that rare and common AEs occur independently. Calculated as 1) %BDRR = 95.28% × 98.77% =94.11% and 2) %Reduction = 100 – %BDRR = 5.89%.

with another AE. We also investigated the effects of combinations of the four common AEs. Three other AEs (hematoma, sensory changes in the arm, and nausea and/or vomiting), which we will refer to as the rare AEs, had incidences of less than 2 percent and will be mentioned only when necessary for quantifying the effects of the more common AEs.

Single AEs

Table 2 shows whether the AE had an effect on the BDRR (p value), the degree of the effect on the BDRR, and the effect on total blood donations. The BDRRs from donations inducing a donor reaction or fatigue were significantly lower than the BDRR from donations with no AEs ($p = 0.002$), the decrease in BDRR from donations inducing a sore arm was almost, but not quite, large enough to be significant ($p = 0.061$), and the BDRR from donations inducing a bruise was not different ($p = 0.83$) from donations with no AEs. A donor reaction had the greatest effect, causing a 34 percent reduction in the BDRR, and fatigue caused a 20 percent reduction in the BDRR.

Combinations of AEs

Sore arm and fatigue caused 2 and 20 percent reductions, respectively, in the BDRR, but together they caused a 65 percent reduction ($p = 0.070$ for synergy), compared to an expected reduction of 22 percent [1 – (0.98)(0.80)] in the absence of synergy. Though the level of synergy did not achieve significance for any pair of AEs, the synergy became significant ($p = 0.012$) when donor reaction, fatigue, and sore arm occurred together. The presence of all three AEs (donor reaction, fatigue, and sore arm) caused an 85 percent reduction in the BDRR. In contrast, by considering the effect of one pair of these AEs and then factoring in the effect of the third one, a 48 to 77 percent reduction (depending on which pair was chosen first) would have been expected in the absence of this three-way synergy.

The incidence rates of the various AEs multiplied by their corresponding reductions in BDRR suggest that donor reaction, fatigue, and sore arm cumulatively could cause about a 4.7 percent reduction in subsequent blood donations in a general blood donor population. When another 1.2 percent (per Table 2, footnotes §§ and ‖‖) is added for the rare AEs (hematoma, sensory changes to the arm, and nausea and/or vomiting), assuming that they occur independently of the common AEs, the total reduction in subsequent blood donations is approximately 5.9 percent. Donor reactions "alone" or in combination with one or more AEs were responsible for 53 percent of the total decrease in subsequent blood donations.

TABLE 3. BDRR by sex and donation status

Variable	Number of donors	Returns	Follow-up period (years)	Annualized BDRR (returns/year)
Sex				
Women	553	689	591	1.17
Men	447	663	470	1.41
Donation status				
First-time donors	165	95	165	0.58
Repeat donors	835	1257	897	1.40

Univariable analysis of demographic factors on BDR

Table 3 shows that women were 17 percent less likely to return to donate than men, and first-time donors were 59 percent less likely to return to donate than repeat donors. The difference between first-time donors and repeat donors was not due to high-school donors because first-time high-school students returned 14 percent more often than first-time, non–high-school donors (data not shown).

DISCUSSION

In this study, a follow-up was done on 1000 interviewed donors for subsequent return visits, and these data were evaluated with a negative binomial regression analysis to estimate the BDRR for the different AEs, either alone or in combinations. The study found that donors with no AEs had the highest BDRR and that a bruise had virtually no effect on the BDRR. Donor reactions "alone" decreased the BDRR by 34 percent and had the most effect of any single factor. Fatigue decreased the BDRR by 20 percent. Donor reactions, fatigue, and sore arm together had the greatest effect, an 85 percent reduction in the BDRR, and synergy was present.

The effect of an AE on subsequent return donations is a function of the incidence rate of the AE multiplied by the corresponding reduction in BDRR. The three major AEs collectively should decrease subsequent return donations by approximately 4.7 percent, and this would increase to 5.9 percent with consideration of the rare AEs. This rate applies to the general donor population. It would be expected to be higher in first-time, Caucasian high-school donors because of the higher donor reaction rate in this group, assuming that the rates of other AEs are the same as in the general blood donor population. The donor reaction rate in a high-school population has been reported to be in the 8 to 11 percent range,[9,10] although it was slightly higher (12%) in a recent 2004 study of 4340 donors in our center.[11] Based on the same calculations made in Table 2, the decrease in subsequent blood donations in high-school students might be as high as 6.4 percent if the donor reaction rate was 12 percent, and this would increase to 7.6 percent with inclusion of the rare AEs.

Donor reactions are fully or partially responsible for 53 percent of the decrease in return rates in the general donor population and possibly an even higher percentage in high-school students, which makes donor reaction the best target for change. Several methods to decrease donor reactions are reviewed in Table 4. Attention paid to the donors and keeping their minds occupied are probably two of the most important factors to decrease donor reaction rates,[12-14] but it is difficult to measure these activities. A small study, which gave 500 mL of water to 83 college donors, found that water decreased donor reactions as measured by a donor survey and the blood collection staff's actions relative to reactions.[15] In Fall 2004, we completed a randomized trial in 4340 high-school donors in which 16 ounces of water was given to every other high-school student after the donor was accepted for whole-blood donation.[11] A second study of 4733 high-school donors was completed in Fall 2005. The results of the two studies were similar. In aggregate, there was a 21 percent reduction in the donor reaction rate in students who drank 16 ounces of water in comparison to students who did not drink water. Men had a greater donor reaction rate reduction than women, 28% vs. 14%. We also evaluated donor reaction rates in 7274 first-time, Caucasian high-school donors and developed a model to determine donor reaction rates for other collection volumes.[16] The model suggested that a collection volume reduction from 500 to 400 mL could decrease the donor reaction rate by 28 percent in first-time, Caucasian high-school students. In another study of 605 college students, Ditto et al.[17] showed that prophylactic muscle tension reduced the donor reaction rate in women by more than 50%, but there was no effect in men. There may be a prophylactic role for muscle tension in high-risk women, if its use does not discourage future blood donations. In sum, having high-school students drink 16 ounce of water, collection of 400 mL of blood instead of 500 mL of blood, and the use of prophylactic muscle tension in women have the potential to significantly decrease donor reactions in high-school students.

This study was limited to studying the effects of AEs on BDRRs and did not include the effects of demographic factors. Clearly our data showed that men and repeat donors are more likely to return to donate blood.

In summary, this study shows that the blood donors' physical experience affects their BDRR. Donor reaction, as a single factor, had the most negative impact on the BDRR, but certain combinations of events had an even greater negative impact. In contrast, a bruise had no effect. Efforts to decrease donor reactions and fatigue, in theory, have the potential to increase blood donor retention in general and particularly in high-school students.

TABLE 4. Methods to decrease donor reaction rates

Method	Feasibility (1+ to 4+)*	Comments	References
1. Paying attention to donors and keeping their minds occupied	4+	Difficult to measure.	
2. Predonation drinking of water	4+	28 and 14% reduction in male and female high-school donor reaction rates, respectively, in study of 9073 high-school students. Positive benefit in another study.[15]	Newman et al.,[11] Hanson and France,[15] Jordan et al.,[18] Scott et al.,[19] Schroeder et al.,[20] Lu et al.[21]
a. Predonation drinking of salt-containing fluids	4+	More expensive than water. No studies done.	
b. Predonation drinking of coffee	3+	Some success in first-time female donors.[22] Possibility of more unsuccessful donations due to venoconstriction.	Sauer and France[22]
3. Lower collection volume from 500 to 400 mL	3+	Potentially 28% reduction in donor reaction rate in first-time, Caucasian high-school students.	Newman et al.[16]
4. Muscle tension	2+	Potential for 50%-60% reduction of donor reactions in college-aged women but no benefit for college-aged men. Difficulty with doing the muscle tension might decrease donor satisfaction with the donation process.	Ditto et al.[17]
5. Isovolemic collection with an apheresis machine	1+	Cost, labor, and slower process are deterrents. No studies for single RBC units.	
6. Medication—β-blockers	0+	All medications have potential side effects, precluding their use.[23]	
7. Epidemiologic changes—i.e., increase the minimum weight or age limit	0+	Would severely decrease the donor pool.	Newman et al.[23]

* 4+ = very feasible; 1+ = lowest level of feasibility; 0+ = not feasible.

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