Staff officers as blood suppliers: Effects of repeated donations and autologous reinfusions of untransfused units

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BACKGROUND:	Limited blood inventory and resupply chains in combat settings can result in preventable deaths from traumatic hemorrhage. One way of mitigating this could be to establish donor pools where blood is collected in advance of high-risk missions and then reinfused back to the donor if not needed to treat casualties.
METHODS:	Four hundred fifty milliliters plus 56 mL of blood was collected, rested for 2 hours in room temperature, and stored at 4°C. The blood was reinfused 22 to 24 hours after donation and the donor observed for adverse reactions. Samples were collected before and 20 minutes after each donation for hematology, immunoglobulin G, ferritin, C-reactive protein, total protein, lactate dehydrogenase, bilirubin, haptoglobin, and activated partial thromboplastin time.
RESULTS:	Nine participants went through a total of 36 donation and reinfusion procedures. Four donors participated in five rounds, two in four rounds, two in three rounds, and one in two rounds. A significant drop was seen in hemoglobin (14.6 ± 0.9 to 13.9 ± 0.9) and ferritin (179 ± 70 to 149 ± 78) from before the first donation to after the last reinfusion ($p < 0.05$). Other parameters were unaffected.
CONCLUSION:	This small pilot study suggests that repeated donations and reinfusions may be both feasible and safe. Blood collected in this way should be labeled with the donor's full name and social security number (or similar) and the identity visually verified by the donor immediately before both donation and reinfusion. To further reduce risk, this form of donation should be restricted to scenarios where there is no other option for making blood available. (*J Trauma Acute Care Surg.* 2018;84: S89–S92. Copyright © 2018 Wolters Kluwer Health, Inc. All rights reserved.)
LEVEL OF EVIDENCE:	Therapeutic/Care management study, level V.
KEY WORDS:	Whole blood donation; autologous reinfusion; traumatic hemorrhage; battlefield deaths and blood supply.

Data from the wars in Afghanistan and Iraq clearly shows that the potentially preventable battlefield deaths are by far caused by hemorrhage.[1] Thus, the ability to provide blood imminently to the injured soldier has become a major task for the military medical community. When logistical constraints prevent the ability to provide blood products and especially platelets for immediate transfusion, this urgent need may be solved by developing preplanned donor pools among the combatants as a last resort for making blood available. This policy is however hampered by the situation—blood donation during battle may be extremely difficult. Even more, ABO blood group issues cause severe risks as incompatibility may lead to fatal transfusion reactions.

A system ensuring that predonated and tested units of whole blood (WB) group O low-titer anti-A and anti-B (low-titer O WB) is transported with the soldiers seems to be an attractive alternative.[2] If the soldiers can be supplied from a field hospital, a safe and robust delivery of blood is possible. For Special Forces, often operating in austere settings in smaller isolated groups, this may not be an option. Additionally, far forward surgical teams operating with a "small footprint" often experience exhausted blood inventory. The need for blood is high, but the ability to get supply through normal logistical pathways may be compromised.

A number of special operation forces have implemented WB protocols including the use of cold stored predonated low-titer O WB transported to the point of injury in Golden Hour boxes (Pelican BioThermal, Plymouth, MN). We recommend using temperature loggers with automatic PDF report and embedded data with USB connectivity to ensure that the product has not exceeded temperature limits before reinfusion.

In addition, these protocols include "buddy transfusion" as a last resort.[3–5] This means that a fellow combatant donates a unit of WB for immediate transfusion to a casualty with life-threatening hemorrhage. As these procedures are not without risk of failure and often have to be carried out by personnel with limited health care provider experience, training becomes an important part of the implementation of the protocols. Donation and autologous reinfusion is trained under strictly controlled supervision, but questions remain whether this is a safe training procedure.

Thus, we wanted to test the potential strategy where staff officers donate blood repeatedly and get the blood reinfused after 24 hours of storage at 4°C. If successful, this could ensure blood availability for both prehospital and in-hospital use in high-risk preplanned missions without compromising the safety of, in this case, the limited pool of blood donors.

METHODS

This is a single-center cohort study approved by the local ethics committee. The cohort consisted of nine voluntary staff

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TABLE 1. Hemoglobin Concentration (g/dL) of Each Study Participant Before and After Each Donation and Reinfusion

	Participant								
Sample	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**
Before Donation 1	13.8	16.0	14.8	14.7	15.1	15.6	14.0	13.9	13.5
After Donation 1	13.4	15.8	14.0	14.2	14.8	15.1	14.0	14.6	13.2
Before Reinfusion 1	13.2	15.0	13.7	13.9	13.9	15.0	13.6	13.8	12.8
After Reinfusion 1	13.2	15.5	13.7	13.5	14.4	14.8	13.4	13.7	13.2
Before Donation 2	13.8	15.7	13.1	14.1	14.3	14.9	14.0	14.8	13.8
After Donation 2	13.8	15.3	12.9	14.6	14.5	14.4	13.8	14.6	13.7
Before Reinfusion 2	12.3	14.6	12.4	13.2	14.2	13.7	13.5	13.5	13.1
After Reinfusion 2	12.6	14.2	12.7	13.0	14.4	13.8	13.4	13.4	13.2
Before Donation 3	13.1	15.5	13.8	14.3	15.5	15.3		14.2	13.6
After Donation 3	13.3	15.7	14.0	13.9	15.0	15.1		14.1	13.6
Before Reinfusion 3	13.3	14.9	13.2	14.7	15.9	14.1		14.4	12.6
After Reinfusion 3	13.3	15.2	13.3	14.1	15.4	14.7		13.9	12.8
Before Donation 4	13.7	15.9	13.7	14.7		14.8		14.0	
After Donation 4	13.7	16.1	13.3	14.1		14.8		13.8	
Before Reinfusion 4	12.7	15.7	14.0	13.6		14.3		13.8	
After Reinfusion 4	13.2	15.4	14.1	13.8		14.6		13.6	
Before Donation 5	13.5	15.6				14.6		14.1	
After Donation 5	12.9	15.2				14.7		13.9	
Before Reinfusion 5	12.8	14.5				13.4		13.4	
After Reinfusion 5	12.9	15.4				13.7		13.6	

officers who consented to donate WB up to five times during a 5-week period and to get the unit reinfused after 24-hour storage at 4°C. This simulates the period where the blood is available for emergency transfusion during a high-risk mission before it is reinfused to the donor.

Collection

Before donation, blood pressure, pulse, and temperature were recorded. The donation procedure was performed in accordance with the blood bank's standard procedure, except that the WB bags were signed by the donor himself instead of using the standard International Society of Blood Transfusion 128 label. The blood bag was also labeled with ABO and RhD blood group. Four hundred fifty milliliters + 56 mL for sampling was collected in bags containing 63 mL of citrate-phosphate-dextrose. There was no leukocyte filtration of the units. After thorough mixing and 2 hours rest on the bench in room temperature, the WB units were stored unmanipulated in the blood bank at 4°C.

Reinfusion

Twenty-two to 24 hours after donation, the WB units were reinfused to the autologous donors. Before reinfusion, the donor had identified the blood bag as his own. Blood pressure, pulse, and temperature were recorded before and after transfusion. The participants were observed during the transfusion procedure, and stayed for 30 minutes afterward. They were informed in detail about possible transfusion reactions and were told to contact the study coordinators in case any complication should occur.

Sampling

Samples were collected before and 20 minutes after each donation and each reinfusion. The following parameters were analyzed: hemoglobin, mean cellular volume, red cell count, reticulocyte count, white blood cell count and platelet count (Cell-Dyn Sapphire, Abbott Diagnostics, Abbott Park, IL, USA), immunoglobulin G (BN ProSpec, Siemens Healthcare GmbH, Erlangen, Germany), ferritin (Modular E170, Roche Diagnostics GmbH, Mannheim, Germany), C-reactive protein, total protein, lactate dehydrogenase and bilirubin (Modular P800, Roche Diagnostics GmbH), haptoglobin (Cobas Integra 400 plus, Roche Diagnostics GmbH), and activated partial thromboplastin time (STA-R Evolution, Stago S.A.S, Asnières-sur-Seine, Paris, France).

Statistics

IBM SPSS Statistics for Windows, Version 24.0 (IBM Corp, Armonk, NY, USA) was used for statistical analysis. Results were reported as mean ± standard deviation. The change in test parameters from before the first donation (baseline) to after the last reinfusion (last) was analyzed using paired-sample *t*-tests. $p < 0.05$ was considered statistically significant.

RESULTS

The study group consisted of nine male officers, aged 30 to 45 years. Nine participants went through a total of 36 donation and reinfusion procedures. Four donors participated in all five rounds, two participants donated blood and had four reinfusions, two participated three times, and one person participated twice.

Table 1 shows hemoglobin concentrations for each participant before the trial started, before and after each donation, and before and after each reinfusion.

There was a significant drop in hemoglobin and ferritin concentrations from the baseline before the first donation and after the last reinfusion (Table 2). For the other parameters tested, no significant changes were found. In one participant,

TABLE 2. Results of All Test Parameters Before the First Donation and After the Last Reinfusion (Mean ± Standard Deviation)

	Baseline	**Last**
Hemoglobin, g/dL	14.6 ± 0.9	13.9 ± 0.9*
RBC, 10^{12}/L	4.7 ± 0.4	4.5 ± 0.4
MCV, fL	89 ± 3	89 ± 2
WBC, 10^9/L	5 ± 1.6	4.4 ± 0.9
PLT, 10^9/L	222 ± 56	234 ± 58
Reticulocytes, 10^{12}/L)	0.052 ± 0.017	0.055 ± 0.017
Haptoglobin, g/L	1.06 ± 0.37	1.06 ± 0.54
Ferritin, µg/L	179 ± 70	149 ± 78*
CRP, mg/L	3 ± 7	1 ± 2
Bilirubin, umol/L	9 ± 2	10 ± 3
LDH, U/L	148 ± 22	145 ± 26
Total protein, g/L	70 ± 3	69 ± 3
IgG, g/L	10.15 ± 1.48	9.87 ± 1.64
APTT, s	34 ± 4	35 ± 3

*$p < 0.05$.

The two sample points were compared using a paired-sample *t*-test.

APTT, activated partial thromboplastin time; CRP, C-reactive protein; IgG, immunoglobulin G; LDH, lactate dehydrogenase; MCV, mean corpuscular volume; PLT, platelet count; RBC, red blood cells.

the platelet count dropped to 75 × 10^9/L after the second donation and reinfusion round.

During the study, there was no sign of any adverse events judged by neither clinical symptoms nor laboratory testing. One participant developed mild thrombocytopenia during the study period. There was no bleeding associated with this.

DISCUSSION

The main purpose of this pilot study was to investigate if repeated blood donations and reinfusion procedures were safe and doable from a practical point of view. Considering practicalities, the study was performed without other issues than that not all of the nine included participants were available at every scheduled donation time. This may mimic the situation in a military mission situation. At all donation points, a minimum of six WB units were collected.

Concerning safety, no single clinical symptom indicating adverse reactions was identified in any of the participants, both concerning blood donation and blood transfusion (reinfusion). The participants were observed during and after each donation guided by symptoms identified through hemovigilance reports.[6] Similarly, each reinfusion episode was thoroughly monitored by personnel trained to discover adverse effects.[7–9] Additionally, the laboratory testing did not provide any sign of hemolytic episodes and the test battery was intended to discover laboratory indications of hemolysis or any other breakdown of blood cells.[10–13] One participant developed mild thrombocytopenia during the study period. After the study was completed, the platelet count recovered to baseline levels. We think that this decrease in platelet count was related to an intercurrent upper airway infection rather than the reinfusion procedures. This is based on papers describing infection-induced temporary thrombocytopenia. Additional virus testing and direct and indirect platelet antibody tests were not performed.[14–18]

During the study period, the average hemoglobin and ferritin concentrations decreased significantly, even if the data are not adjusted for the number of donations and time between donations. The total volume of blood samples for each donation and reinfusion was 56 mL and, in addition a smaller volume, is always left in the transfusion set and bag, on average 20 mL. The total volume of blood lost during the 5 weeks for the participants who donated five times is 380 mL. This might explain the significant drop in hemoglobin and ferritin. The effect of each donation was as reported in other studies.[19–21] In real-life implementation of a staff member donor base, iron supplementation must be considered, as repeated blood loss is accompanied by loss of iron and risk of iron depletion.[22]

The limitation of this study is clearly linked to the small number of participants. A total number of 36 transfusions do not allow any final conclusions. However, we will advocate that the additional security effort by labeling the WB units with the donor's handwritten name and social security number is important. Both from autologous patient transfusions[23,24] and blood doping,[25,26] we know that severe adverse effects may occur.

CONCLUSION

We have performed a pilot study that shows that repeated donations and reinfusions of short time–stored WB may be feasible and safe. Thus, predonation of WB units may be a viable alternative for soldiers on dangerous operations of limited duration. It should be emphasized that a thorough risk-benefit analysis before initiating the proposed procedure must be carried out. It is the authors' opinion that this is only recommendable in extreme scenarios where no other options for making blood available are present.

AUTHORSHIP

GS and HE designed the study. JS analyzed data. GS JS, HE, and TAH wrote the article.

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DISCLOSURE

The authors declare no conflicts of interest.

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