BLOOD CONSERVATION AND TRANSFUSION ALTERNATIVES

A mathematical model of cell salvage compared and combined with normovolemic hemodilution

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BACKGROUND: Mathematical models have been used to describe the factors that affect cell salvage (CS) and normovolemic hemodilution (ANH). Here, the CS and ANH models were used to compare these two techniques alone or in combination with each other.

STUDY DESIGN AND METHODS: Variables used for a hypothetical patient included an estimated blood volume of 5000 mL, a presurgery hematocrit (Hct) of 45 percent, and a transfusion trigger of 21 percent. The model accounts for both the effect of decreasing the Hct due to blood loss and the effect of increasing Hct due to the readministration of blood in an isovolemic patient. The efficacy of CS and ANH is defined to be the maximum allowable blood loss for a fixed blood volume and a fixed transfusion trigger.

RESULTS: Comparison of CS with ANH showed that 3 units of ANH was comparable to CS when CS recovery rates ranged from 19 to 24 percent. For a patient with a blood volume of 5000 mL and a starting Hct of 40 percent, 3 units of ANH would allow for 3972 mL of blood to be lost before crossing a 21-percent transfusion trigger, whereas CS with a 125-mL bowl would allow for 7611 mL.

CONCLUSION: When comparing ANH to CS, this mathematical model would suggest that CS has the potential to offer significantly greater red blood cell avoidance than does ANH; however, the combination of ANH with CS may offer allogeneic avoidance superior to either technique alone.

Multiple models of acute normovolemic hemodilution (ANH) have been previously described.[1-4] A mathematical model of cell salvage (CS) has also been developed.[5] In the cell salvage model, it was determined that the efficiency of recovering red blood cells (RBCs) and returning them to the patient was critical in CS's ability to avoid allogeneic transfusion. The efficiency is dependent on many factors, which might include the degree of RBC hemolysis during suction and the loss of RBCs to surgical drapes and sponges. In the CS model, data from actual cases were matched to the developed model to determine the average efficiency of the system. This efficiency was 57 percent, but had 20-percent variability between the highest and lowest efficiencies. This efficiency rate means that 57 percent of the RBCs shed are collected, washed, and returned to the patient. Because some cases had lower efficiencies, the question was posed as to what level of

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ABBREVIATIONS: ANH = acute normovolemic hemodilution; CS = cell salvage; MABL = maximum allowable blood loss.

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Financial support for this study came from internal funding from the Department of General Anesthesiology and the Cleveland Clinic.

Lay reader statement: In this study, a previously developed mathematical model of cell salvage was combined and compared with an existing model of normovolemic hemodilution. From the model, it appears that maximal transfusion avoidance would be achieved by combining both techniques.

Received for publication February 10, 2004; revision received May 29, 2004, and accepted June 1, 2004.

TRANSFUSION 2004;44:1412-1416.

efficiency do normovolemic hemodilution and CS reach equivalence. In this study, the CS mathematical model was compared with an existing model for ANH. Though mathematical modeling generally deals with the ideal, it was anticipated that this model would add additional insight into the optimal strategies for approaching blood conservation management.

MATERIALS AND METHODS

Mathematical modeling: assumptions

To develop a sensible model that is comparable to the existing ANH and CS models and one that does not have too much complexity, we retained the same assumptions that have been made by other researchers. These assumptions are that 1) the patients remain isovolemic; 2) blood is instantaneously administered; 3) the elapsed time is not directly modeled but can be assumed to be incorporated into the time of blood loss, the duration of CS recovery, and the duration of readministration; 4) the recovery rate is constant; 5) allogeneic transfusion occurred at a hematocrit (Hct) of 21 percent; 6) volume of ANH bag is 450 mL; and, finally, 7) the Latham bowl Hct (H_B) is assumed to be 60 percent. This last assumption was derived by review of our CS database, which showed that the Medtronic Sequestra (Minneapolis, MN) produced blood with a Hct of 57.6 ± 7.3 percent (n = 1034 bowls).

Cell salvage

The CS device cycles on and off, accumulating blood until a target Hct (H_B) in the processing bowl is reached. The blood is then readministered to the patient. In each cycle, a fraction of blood is lost that cannot be recovered. The recovery rate (k) ranges between 0 percent to 100 percent. In the previously developed mathematical model,[5] for cycle i the final Hct during CS (H_{Fi}) can be described as a function of lost blood volume during cycle i (V_{Li}) and the initial Hct (H_{0i}) at cycle i.

$$H_{Fi} = H_{0i} \times e^{-V_{Li}/V} \tag{1}$$

The lost blood volume at cycle i (V_{Li}) can be estimated by a fixed recovery rate (k), the initial Hct when the cycle begins (H_{0i}), and the Hct saved in the processing bowl ($H_B \times V_B$). That is,

$$V_{Li} = \frac{1}{k}\left(\frac{H_B \times V_B}{H_{0i}}\right) \tag{2}$$

The initial Hct for cycle i is the sum of the final Hct for cycle (i – 1) and the CSd Hct ($H_B V_B / V$, where V is the patient blood volume before surgery). That is,

$$H_{0i} = H_{F(i-1)} + \frac{V_B}{V} H_B,\ \mathrm{i} \geq 2 \tag{3}$$

ANH

Modeling of ANH has been previously reported.[1-4] Assuming the volume of each ANH bag is V_A, a patient's Hct after removal of m bags of ANH (H_{0m}) can be described as follows:

$$H_{0m} = H_0 \times e^{-m(V_A/V)} \tag{4}$$

and the Hct in the i^{th} ANH bag is

$$H_{Ai} = \frac{V}{V_A} \times H_0 \times e^{-(i-1)(V_A/V)} \times (1 - e^{-(V_A/V)}) \tag{5}$$

When m bags of ANH blood are removed before surgery, a patient's final Hct (H_F) after surgery with V_L units surgical blood loss, before the readministration of ANH blood, is

$$H_F = H_{0m} \times e^{-V_L/V} \tag{6}$$

Readministering the i^{th} bag of ANH blood after surgery, the Hct becomes

$$H_{Fi} = H_F + \frac{V_A}{V} H_{Ai} \tag{7}$$

Generalizing Equation 7 to describe the time course of Hct when adding each bag of ANH blood, we have

$$H_{Fj} = H_{Fi} + \frac{V_A}{V} H_{Aj} \tag{8}$$

where $j > i$.

Combining CS with ANH

Using these previous models, we can combine CS with ANH, assuming that m bags of ANH blood are taken before surgery and that CS is used during the surgery. The final Hct before the readministration of ANH blood, following Equations 1, 2, and 3, can be described as:

$$H_{Fi} = H_{0i} \times e^{-V_{Li}/V} \tag{9}$$

where V_{Li} is

$$\frac{1}{k}\left(\frac{H_B \times V_B}{H_{0i}}\right) \tag{10}$$

and

$$H_{0i} = H_{F(i-1)} + \frac{V_B}{V} H_B,\ \mathrm{i} \geq 2 \tag{11}$$

$$H_{01} = H_{0m} = H_0 \times e^{-m(V_A/V)} \tag{12}$$

Note: H_0 is the initial Hct before ANH.

When the Hct reaches the critical point on the j^{th} CS cycle, the i^{th} ANH bag is added. Hence, Equation 11 becomes

$$H_{0j} = H_{F(j-1)} + \frac{V_B}{V} H_B + \frac{V_A}{V} H_{Ai},\ \mathrm{i} \geq 2. \tag{13}$$

RESULTS

Using the equations described in the methods, calculations were made to determine the maximum allowable blood loss (MABL) that a hypothetical patient could sustain before needing a transfusion, assuming a blood volume of 5000 mL (V), an initial Hct of 0.45 (H_0), and a transfusion trigger or critical Hct of 0.21 (H_c). Without blood conservation techniques, this hypothetical patient would be able to tolerate a MABL of 3810 mL before crossing the critical Hct.

CS versus ANH

Utilizing the equations for ANH and CS, a comparison between the two techniques was performed. Table 1 shows the recovery rate (k) at which the CS would be equivalent to multiple units of ANH blood. It is obvious that even with 5 units of ANH, the CS and ANH reached equivalence only at low CS recovery rates (27-29%). For example, under the common practice of removing three bags of ANH blood, the MABL would be 4803 mL. CS would achieve this degree of MABL when approximately a 20-percent recovery rate is achieved. Table 2 shows how starting Hct influences the MABL when three bags of ANH blood are harvested, or CS is used with a RBC recovery rate of 57 percent. Table 3 details how blood volume influences the MABL when three bags of ANH blood are harvested or CS is used with a RBC recovery rate of 57 percent.

Combining CS with ANH

The combination of CS and ANH offered better blood avoidance when compared to either technique alone. At a CS efficiency of 20 percent (MABL = 4803 mL), CS is equivalent to that of ANH with presurgical removal of three ANH bags. At these levels, each blood conservation technique alone extends the patient approximately 993 mL beyond what the patient would be able to tolerate without any blood conservation techniques. With these variables, the combination of CS and ANH reached a MABL of 5389 mL, a gain of 1579 mL when compared with no blood conservation method. Thus, by combining the two techniques, additive efficacy is achieved. By increasing the CS recovery rate from 20 percent to 60 percent, a greater increase in extending the utility of each technique was seen. Fig. 1 shows the MABL for the combined technique of 3 units of ANH and 0.57 recovery rate of CS, utilizing a 225-mL Latham bowl. The MABL for 3 units of ANH by itself is 4803 mL, whereas the MABL for CS at a recovery rate of 0.57 is 9266 mL. Combining the ANH and CS drives the MABL to 10,829 mL, which is 1563 mL greater than using the CS technique alone or 6026 greater than using the ANH technique alone.

TABLE 1. The recovery rate at which the MABL reached the equivalence between CS and ANH*

ANH bags	MABL (mL)	Recovery rate (k) with 125-mL Latham bowl (%)	Recovery rate (k) with 225-mL Latham bowl (%)
1	4207	10-14	10-16
2	4536	15-18	17-23
3	4803	19-22	24
4	5012	23-26	24-29
5	5168	27-29	24-29

* The following variables were used: volume of ANH bag is 450 mL; the estimated blood volume, $V = 5000$ mL; presurgery Hct, $H_{01} = 0.45$; critical HCT = 0.21; the targeted Hct in the Latham bowl, $H_B = 0.60$.

TABLE 2. Comparing ANH and CS on MABL (mL) with various starting Hct levels*

Starting Hct	ANH	CS (125 Latham bowl)	CS (225-mL Latham bowl)
0.45	4803	8809	9022
0.40	3972	7611	7369
0.35	3057	5874	5516
0.30	2035	3884	3391

* The following variables were used: three bags of ANH blood for ANH method; volume of ANH bag is 450 mL; the estimated blood volume, $V = 5000$ mL; critical Hct = 0.21; the targeted Hct in the Latham bowl, $H_B = 0.60$; the recovery rate for CS method, $k = 0.57$.

TABLE 3. Comparing ANH and CS on MABL (mL) with various blood volumes*

Estimated blood volume (mL)	ANH	CS (125-mL Latham bowl)	CS (225-mL Latham bowl)
4000	3932	7,120	6,872
4500	4372	7,963	8,245
5000	4803	8,809	9,022
5500	5226	10,000	9,798
6000	5643	10,846	10,575
6500	6055	11,690	11,970
7000	6464	12,535	12,744
7500	6870	13,380	13,522
8000	7272	14,583	14,297

* The following variables were used: three bags of ANH blood for ANH method; volume of ANH bag is 450 mL; presurgery Hct, $H_{01} = 0.45$; critical Hct = 0.21; the targeted Hct in the Latham bowl, $H_B = 0.60$; the recovery rate for CS method, $k = 0.57$.

DISCUSSION

The previously developed mathematical model of CS[5] highlighted several variables that alter CS's ability to avoid transfusion. These factors included 1) the patient's start-

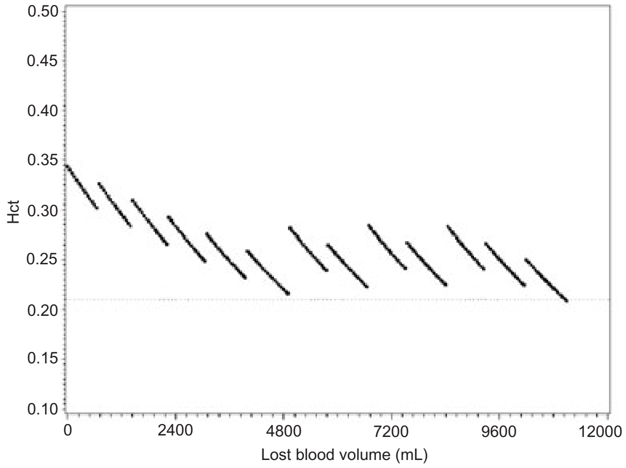

Fig. 1. Combination of ANH and CS: This figure shows the extent of blood loss that might be tolerated in a patient whose presurgical Hct starts at 45 percent, who is allowed to lose blood until a transfusion trigger of 21 percent is reached, who has a blood volume of 5000 mL, who has had 3 units (450 mL per unit) of ANH harvested, and who has 57 percent of their RBCs recovered into the CS system. What is seen in the figure is that CS starts after the harvesting of the 3 units of blood so that the starting Hct is 34 percent. The saw-tooth pattern shows the blood loss occuring until adequate blood loss has occurred to result in CS processing. The blood is readministered but does not ever reach the prior starting point because of the loss of some RBCs to hemolysis and failed collection. This is the efficacy of the system. The figure shows the Hct steadily dropping until the transfusion trigger is crossed, at which point the unit of harvested blood is then readministered. Blood loss continues until the 2nd and 3rd units are administered.

ing Hct (*H*); 2) the patient's blood volume, (*V*); (3) the size of the Latham bowl (V_B); and 4) the efficiency of RBC salvage *k* (i.e., the RBC recovery rate). Similarly, the patient's starting Hct and blood volume influence ANH's ability to avoid transfusion. This study compares how these factors vary the MABL when the techniques are used alone or in combination with each other under varying conditions.

Cell salvage efficiency relates to how well lost RBCs are captured and returned to the patient. Factors that may influence the efficiency of RBC recovery include sponge rinsing,[6,7] anticoagulant variation,[8] and regulated suction.[9] To see how varying CS efficiency would compare to varying degrees of ANH blood removal, the MABL of CS and ANH were calculated in a hypothetical patient as shown in Table 1. The MABL that the patient could tolerate without blood conservation methods would be 3810 mL. Application of ANH to this patient would gain 397 mL, 726 mL, and 993 mL in MABL for 1, 2, and 3 units of hemodilution, respectively. When the other conditions of the model are kept constant, CS with RBC efficiency rates ranging from 10 to 22 percent would gain the same degree of MABL as 1 to 3 units of ANH. In the previously published CS model, the efficiency rate (*k*) was estimated to be 57 percent with a 95-percent confidence interval of 51 to 63 percent. Thus, if moderate levels of CS efficiency can be assured, it would appear that the CS offers a higher likelihood of blood avoidance than does ANH.

CS equivalence to ANH occupies a range of *k* values. The CS model is built upon a full Latham bowl. The range that is reported in Table 1 relates to blood loss that occurs before complete filling of the Latham bowl. While working in complete bowl cycles, the process stops at the end of the last whole cycle before the critical Hct is reached. While the patient continues to lose blood, the critical Hct is reached. The next cycle is not performed because the lost blood volume between the last whole cycle and the critical Hct is inadequate to fill up the Latham bowl. The total blood loss at this point is defined as MABL. As long as the MABL is the same and the final Hct in the CS procedure is above 0.21, we consider the two methods to be equivalent. Therefore, a range of *k* values will produce the equivalence. For example, with 2 units of ANH, the MABL is 4536 mL and the final Hct is 0.21004. For CS, a range of recovery rates will satisfy this condition. A 15-percent recovery rate will result in a MABL of 4536 and final Hct of 0.21290. A 16-percent recovery rate will result in a MABL of 4536 and final Hct of 0.21161. In Tables 2 and 3, MABL was calculated for CS and 3 units of ANH with varying starting Hct and initial blood volume. For CS, the recovery rate was held constant at 57 percent.

Some concern has arisen regarding the extent of hemodilution that is required to achieve maximal benefit from ANH. Concern also arises when performing hemodilution on patients with coronary artery disease. Advocates of ANH suggest that maximal benefit of ANH is achieved by harvesting up to 5 units before the start of the surgical procedure.[3,10] This degree of hemodilution becomes costly and requires considerable time. Furthermore, extensive hemodilution has led to questions as to how far a patient's Hct can be lowered before impairing a patient's ability to deliver oxygen to their microcirculation.[11,12] By combining limited ANH with CS, the risks of ANH can be minimized or avoided. ANH also provides an added benefit in that whole blood is being collected. This whole blood provides a source of plasma and platelets.[13-15] By limiting ANH harvesting to a volume that is adequate to correct any coagulation defect and utilizing CS for extension of RBC avoidance, the best of both techniques may be obtainable.

In a study by Torella et al.,[16] ANH was better than no technique in infrarenal aortic aneurysm repair. The addition of CS provided limited benefit in that only a small amount of CS blood was collected in the majority of cases; however, they concluded that the combination of the two techniques may render cross-matching obsolete and that the two techniques together offered high degrees of assurance that allogeneic transfusion would not be needed. This mathematical model would support this conclusion in that the blood avoidance capabilities of both techniques combined are significant and that only under rare circumstances would blood loss exceed the capacity of both techniques combined.

This mathematical analysis suggests that CS offers significantly greater ability to avoid allogeneic transfusion then would that of ANH. A separate issue regarding these strategies relates to the cost of applying the techniques. Intuitively, one would think that ANH, with a cost of approximately $16.00 per donor bag, would easily be more cost favorable when compared to the $85.00 disposable cost of CS. (Costs are for supplies purchased by the Cleveland Clinic Foundation.) Comparing costs between the strategies is not as simple as this comparison would suggest. For instance, blood loss is frequently unpredictable, making the application of multiunit ANH unnecessary in some cases. Thus, calculating the cost of ANH needs to account for the cost of application of ANH that was not needed. Likewise, CS may not be needed in some circumstances. Unlike ANH, CS can be staged dependent upon blood loss expectation. For cases where blood loss is uncertain, a collection reservoir and a suction line can be used. If blood loss occurs, then the expenditure is made for the Latham bowl and tubing to process the lost blood. The cost of CS is also complicated by the fact that the cost varies depending upon the number of units produced. To adequately compare these strategies, sound accounting principles would need to be applied. This analysis is beyond the scope of this paper. Multiple factors need to be considered when deciding the optimal strategy for blood conservation. Two key factors are how much blood is anticipated to be lost during a specific procedure and how cost effective each strategy might be in providing allogeneic avoidance. In many circumstances, it is difficult to predict possible blood loss or the range of potential blood loss. We suggest that application of both techniques offers the best of both techniques and potentiates the possibility for all patients to avoid allogeneic transfusion. If one technique is to be applied, CS offers greater ability than does ANH in avoiding allogeneic transfusion.

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