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Optimizing Packed Red Blood Cell Transfusions: Viscosity, Volume, and Time

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A straightforward formula, $V = \left(\frac{H_i \cdot b}{2} - 1\right) \cdot V_i$, which minimizes the product of transfusion time and volume has been derived. V_i represents the initial volume of the packed red blood cells (PRBCs) whereas H_i represents their initial hematocrit. The coefficient b is based upon an approximate exponential representation of viscosity as a function of added volume V and H_i. This formula allows for the minimization of both the volume of diluent, added to a known volume of PRBCs, as well as a minimization of the transfusion time.

Key words: transfusion, viscosity, blood, hemodilution, hypervolemia.

INTRODUCTION

It is common in clinical anesthesia practice to dilute packed red blood cell (PRBC) preparations with normal saline solution prior to transfusion. This results in a decrease in viscosity which expedites the flow rate of the transfusion and consequently decreases transfusion time (de la Roche and Gauchier, 1993).

However, the indiscriminate addition of normal saline solution to PRBCs may excessively increase the transfusion volume. This could consequently increase the transfusion time and may also lead to hemodilution as well as hypervolemia.

Therefore, an ideal amount of diluent, which would limit both transfusion time and volume, would be beneficial. This would be particularly significant in trauma patients requiring rapid as well as massive transfusions.

In addition, this optimization technique would be potentially useful for intraoperative management of blood transfusions for fluid-sensitive patients, such as those with renal failure or congestive heart failure. During surgery, when these patient populations require blood, rapid transfusions, without excessive hydration, would frequently be ideal.

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TRANSFUSION TIME AND VOLUME

An "optimum" amount of diluent can be determined. Initially, the transfusion time can be defined as

$$\text{transfusion time} = \frac{\text{transfusion volume}}{\text{transfusion flow rate}} \quad (1)$$

Using Poisuille's law and assuming laminar flow Eq. (1) can be expressed as

$$\text{transfusion time} = \frac{\text{transfusion volume}}{\left[\frac{\Delta P \pi r^4}{8\mu l}\right]} \quad (2)$$

where ΔP is the difference between the applied pressure to the transfusion bag and venous pressure. The radius of the tubing is r and the tubing length is 1. The viscosity of the packed red blood cells in μ.

Realizing that all the parameters in the denominator of Eq. (2) remain constant except μ, Eq. (2) can be rewritten as

$$\text{transfusion time} = \frac{\text{transfusion volume} \cdot \mu}{K} \quad (3)$$

Therefore, transfusion time is directly proportional to the product of transfusion volume and viscosity:

$$\text{transfusion time} \propto \text{transfusion volume} \cdot \mu \quad (4)$$

Consequently, minimizing this product would result in minimal transfusion time.

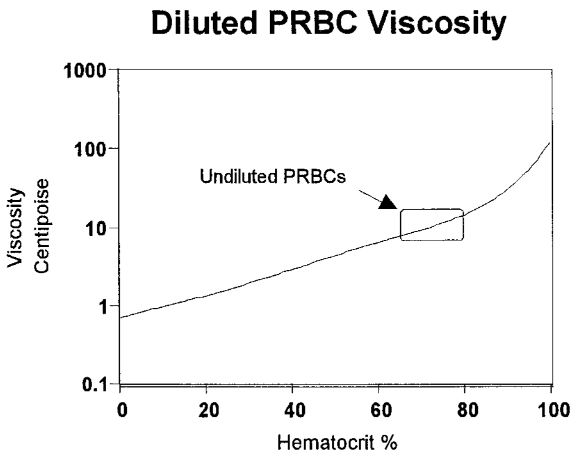

Figure 1. Packed red blood cell viscosity is approximately an exponential function of hematocrit (Chen *et al.*, 1966).

The transfusion volume is simply the sum of the initial volume of the PRBC preparation, V_i, and the volume of the diluent, V:

$$\text{transfusion volume} = \mathrm{V_i} + V \quad (5)$$

TRANSFUSION VISCOSITY

The viscosity of diluted PRBCs is an exponential function of their hematocrit (Chen *et al.*, 1966; Eckmann *et al.*, 2000) as shown in Fig. 1. This relationship can be represented as (see Appendix A)

$$\mu(H) = e^{(\alpha_0+\alpha_1 H+\alpha_2 H^2+\alpha_3 H^3+\alpha_4 H^4+\alpha_5 H^5)} \quad (6)$$

The hematocrit of the PRBCs will decrease as the volume of the diluent, V, is added. The viscosity of these diluted PRBCs will then be

$$\mu(V) = e^{\left(\alpha_0+\alpha_1\left(\frac{H_i\cdot \mathrm{V_i}}{[\mathrm{V_i}+V]}\right)+\alpha_2\left(\frac{H_i\cdot \mathrm{V_i}}{[\mathrm{V_i}+V]}\right)^2+\alpha_3\left(\frac{H_i\cdot \mathrm{V_i}}{[\mathrm{V_i}+V]}\right)^3 + \alpha_4\left(\frac{H_i\cdot \mathrm{V_i}}{[\mathrm{V_i}+V]}\right)^4+\alpha_5\left(\frac{H_i\cdot \mathrm{V_i}}{[\mathrm{V_i}+V]}\right)^5\right)} \quad (7)$$

where H_i is the initial hematocrit of the undiluted PRBCs.

For calculation purposes, $\mu(H)$ can be approximated using a simple exponential function which is specific for the nature of the diluent, temperature, as well as the estimated shear rate (see Appendix A and Appendix B):

$$\mu(H) = ae^{bH} \quad (8a)$$

In addition, this approximate viscosity can then be defined as a function of the volume of the diluent:

$$\mu(V) = ae^{b\frac{H_i\cdot \mathrm{V_i}}{[\mathrm{V_i}+V]}} \quad (8b)$$

Therefore, the initial undiluted volume of PRBCs would have a viscosity of $\mu(0) = ae^{bH_i}$ and an initial transfusion time which would be proportional to the product of $\mathrm{V_i}$ and $\mu(0)$.

Relative transfusion time can then be defined as

$$\text{relative transfusion time} = \frac{\text{transfusion volume}\cdot\mu(V)}{\mathrm{V_i}\cdot\mu(0)} = \frac{(\mathrm{V_i}+V)\cdot\mu(V)}{\mathrm{V_i}\cdot\mu(0)} \quad (9)$$

The numerator of Eq. (9) represents the final transfusion volume and final viscosity, after dilution, with a known volume V. Figure 2 illustrates how relative transfusion time decreases, then increases, as a function of added volume.

MINIMIZING ONLY TRANSFUSION TIME

By minimizing Eq. (4), a volume of diluent can be found which would result in a minimum transfusion time. Equations (8) and (5) are substituted into Eq. (4):

$$\text{transfusion time} \propto (\mathrm{V_i}+V)\cdot ae^{b\left[\frac{H_i\cdot \mathrm{V_i}}{(\mathrm{V_i}+V)}\right]} \quad (10)$$

By determining when $\frac{d[\text{transfusion time}]}{dV} = 0$ then a volume, V, can be determined which would minimize

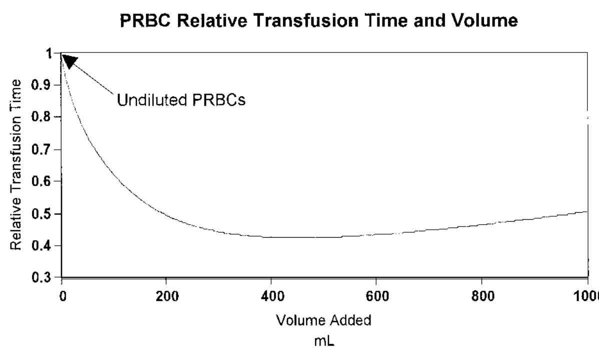

Figure 2. Relative transfusion time decreases markedly with the initial addition of volume. Note that this parabolic-like function approaches a minimum, with approximately 500 mL of added volume, and then increases.

transfusion time:

$$\frac{d\,[\text{transfusion time}]}{dV} = \frac{d}{dV}\left[(\mathrm{V_i} + V)\cdot ae^{b\left[\frac{H_i\cdot \mathrm{V_i}}{(\mathrm{V_i}+V)}\right]}\right] = 0 \tag{11}$$

Evaluating the derivative of Eq. 11 yields

$$\frac{d}{dV}\left[(\mathrm{V_i} + V)\cdot ae^{b\left[\frac{H_i\cdot \mathrm{V_i}}{(\mathrm{V_i}+V)}\right]}\right] = \left[a\cdot \exp\left[H_i\cdot \mathrm{V_i}\cdot \frac{b}{(\mathrm{V_i}+V)}\right] - \frac{1}{(\mathrm{V_i}+V)}\cdot a\cdot H_i\cdot \mathrm{V_i}\cdot b\cdot \exp\left[H_i\cdot \mathrm{V_i}\cdot\frac{b}{(\mathrm{V_i}+V)}\right]\right] \tag{12}$$

The amount of added volume, where transfusion time is a minimum, can be determined by setting Eq. (12) equal to zero and solving for V:

$$\left[a\cdot \exp\left[H_i\cdot \mathrm{V_i}\cdot \frac{b}{(\mathrm{V_i}+V)}\right] - \frac{1}{(\mathrm{V_i}+V)}\cdot a\cdot H_i\cdot \mathrm{V_i}\cdot b\cdot \times \exp\left[H_i\cdot \mathrm{V_i}\cdot\frac{b}{(\mathrm{V_i}+V)}\right]\right] = 0 \tag{13}$$

The solution to the above is $V = ([H_i \cdot b] - 1)\cdot \mathrm{V_i}$. By substituting typical values (Chaplin, 1969) (see Appendix A) of $H_i = 75\%$ and $b = 0.0438\%^{-1}$ and $\mathrm{V_i} = 250$ mL then $V = 571$ mL. This volume of diluent (V) is excessive by clinical standards. An infusion of this much volume, especially if done to a fluid-sensitive patient, or if repeated for massive transfusions, could easily lead to hemodilution and/or hypervolemia.

It should be noted that the relative transfusion time, for $V = 571$ mL, can be determined by utilizing Eq. (9):

$$\text{relative transfusion time} = \frac{(\mathrm{V_i}+V)\cdot\mu(V)}{\mathrm{V_i}\cdot\mu(0)} = \frac{(250+571)\cdot\mu(571)}{250\cdot\mu(0)} = 0.334$$

Consequently, this much volume of diluent offers a reduction in relative transfusion time of about 66.6%.

MINIMIZING BOTH TRANSFUSION VOLUME AND TIME

The (Transfusion Time · Volume) Product

Clearly, the above solution must be modified to determine both a minimum transfusion time as well as a minimum volume of diluent.

This can be accomplished by minimizing the (transfusion time · volume) product. This product is defined by modifying Eq. (10):

$$(\text{transfusion time}\cdot\text{volume}) \propto (\mathrm{V_i}+V)^2\cdot ae^{b\left[\frac{H_i\cdot \mathrm{V_i}}{(\mathrm{V_i}+V)}\right]} \tag{14}$$

Note that the sum of $(\mathrm{V_i} + V)$ is now raised to the second power. The derivative, with respect to volume, can be determined:

$$\frac{d[\text{transfusion time}\cdot\text{volume}]}{dV} = \frac{d}{dV}\left[(\mathrm{V_i}+V)^2\cdot ae^{b\left[\frac{H_i\cdot \mathrm{V_i}}{(\mathrm{V_i}+V)}\right]}\right] \tag{15}$$

Setting the right-hand side of Eq. (15) equal to zero and evaluating the derivative,

$$\left[2\cdot(\mathrm{V_i}+V)\cdot a\cdot\exp\left[H_i\cdot \mathrm{V_i}\cdot\frac{b}{(\mathrm{V_i}+V)}\right] - a\cdot H_i\cdot \mathrm{V_i}\cdot b\cdot\exp\left[H_i\cdot \mathrm{V_i}\cdot\frac{b}{(\mathrm{V_i}+V)}\right]\right] = 0 \tag{16}$$

the solution of Eq. (16) is

$$V = \left(\frac{H_i\cdot b}{2} - 1\right)\cdot \mathrm{V_i} \tag{17}$$

Using the same values from the prior example, $H_i = 75\%$, $\mathrm{V_i} = 250$, and $b = 0.0438\%^{-1}$ then, using Eq. (17), $V = 161$ mL.

The solution, which is based upon minimizing the product of transfusion time and volume, is clearly advantageous from a clinical standpoint. This is illustrated by comparing the relative transfusion times for each minimization technique as well as comparing the amount of added volume.

The relative transfusion time can be calculated, as before, using Eq. (9):

$$\text{relative transfusion time} = \frac{(\mathrm{V_i}+V)\cdot\mu(V)}{\mathrm{V_i}\cdot\mu(0)} = \frac{(250+161)\cdot\mu(161)}{250\cdot\mu(0)} = 0.454$$

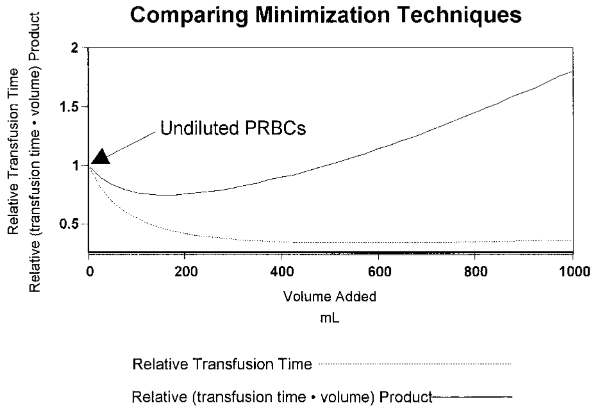

Figure 3. This graph represents a comparison of PRBC dilution based upon relative transfusion time, with the relative (transfusion time · volume) product. Notice that the minimum of the relative (transfusion time· volume) product occurs with approximately 160 mL of added volume. As in Fig. 2, the minimum of the relative transfusion time occurs with an added volume of approximately 500 mL.

Relative (transfusion time · volume) product can similarly be defined:

$$\text{relative (transmsion time} \cdot \text{volume) product} = \frac{(\mathrm{V_i} + V)^2 \cdot \mu(V)}{\mathrm{V_i}^2 \cdot \mu(0)} \tag{18}$$

The benefits of this "co-minimization" technique can be assessed by comparing the values obtained from minimization of only relative transfusion time to those obtained from minimization of the relative (transfusion time · volume) product. This is illustrated in Fig. 3.

With respect to the above examples, the reduction in the added volume of the diluent can be evaluated as $\left[1 - \frac{161}{571}\right] \cdot 100\% \cong 72\%$. Whereas the relative transfusion time is only marginally increased from 0.33 to 0.45.

Therefore, by utilizing this combined minimization technique, an overall benefit in a reduction of transfusion time and volume is achieved.

CONCLUSION

Clearly, using straightforward mathematical techniques, PRBC transfusion can be optimized with respect to both time and volume. Validation of this could readily be done using either nonhuman blood or discarded human blood. Ultimately, banked blood units might be labeled with an appropriate statement regarding dilution management.

Nonetheless, this strategy is advantageous when compared to the all-to-common indiscriminate addition of normal saline to dilute PRBC preparations. However, individual patient management demands may lead to variations in its implementation. Furthermore, fluid-sensitive patients would frequently still require the concomitant use of ancillary volume monitoring techniques. In addition, the use of arterial or venous blood gas monitoring, which is usually accompanied with hematocrit measurement, remains vital. This is particularly important during trauma, vascular, and similar procedures where blood loss can be rapid and dramatic.

APPENDIX A

An Exponential Model of Red Cell Viscosity

An empirical model of red cell viscosity has been developed which shows an exponential relationship between their viscosity $\mu(H)$ and their hematocrit H (Chen *et al.*, 1966):

$$\mu(H) = e^{(\alpha_0 + \alpha_1 H + \alpha_2 H^2 + \alpha_3 H^3 + \alpha_4 H^4 + \alpha_5 H^5)} \tag{1A}$$

Table 1A illustrates the associated coefficients which are specific for a particular shear rate of 52 s^{-1}, as well as normal body temperature, and a crystalloid diluent.

Using the coefficients from Table lA, Eq. (1A) can be approximated with a simple exponential

Table 1A. These Coefficients are Specific for an Associated Shear Rate of 52 s^{-1}, a Temperature of 37° C, and Ringer's Lactate as a Diluent (Chen *et al.*, 1966)

α_0	α_1	α_2	α_3	α_4	α_5
-3.76×10^{-1}	3.763×10^{-2}	-0.645×10^{-3}	3.802×10^{-5}	-4.073×10^{-7}	1.369×10^{-9}

Note. Ringer's Lactate and normal saline are both similar crystalloids.

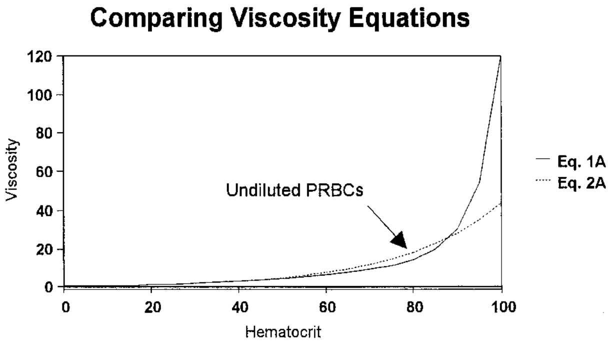

Figure 1A. A comparison between Eqs. (1A) and (2A) which model PRBC viscosity as a function of their hematocrit.

function:

$$\mu(H) = ae^{bH} \tag{2A}$$

With values of $a = 0.549$ cp and $b = 0.0438\%^{-1}$, Eq. (2A) has an R^2 correlation of 0.968 with Eq. (1A). Both Eqs. (1A) and (2A) are graphically represented in Fig. 1A.

APPENDIX B

Shear Rate

Shear rate, dv/dr, is defined as the change in velocity with respect to radius. This formula can be readily derived by first examining the radial velocity profile:

$$V = \frac{\Delta P(R^2 - r^2)}{4\mu l} \tag{3A}$$

where $0 \le r \le R$. dv/dr is then evaluated at $r = R$:

$$\frac{dv}{dr}\Big|_{r=R} = \frac{\Delta PR}{2\mu l} \tag{4A}$$

Recalling Poisuille's law:

$$Q = \frac{\Delta P\pi R^4}{8\mu l} \tag{5A}$$

Substituting Eq. (3A) into Eq. (2A) yields shear rate at $r = R$:

$$\frac{dv}{dr} = \frac{4Q}{\pi R^3} \tag{6A}$$

Substituting mean velocity $\bar{V} = Q/A$ where $A = \pi R^2$ then:

$$\frac{dv}{dr} = \frac{4\bar{v}}{R} \tag{7A}$$

Therefore, shear rate has dimensions of s^{-1}. Using Eq. (6A), and an approximate flow rate of 1.3 mL/s, through a large-bore IV catheter with a radius of 0.3 cm, an estimate of the shear rate would be $\frac{4\cdot(1.3)}{\pi\cdot 0.3^3} = 61.3\ s^{-1}$.

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