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Acute normovolemic hemodilution

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Abstract Patients and physicians continue to be motivated to find methods to reduce the use of allogeneic blood. Even though donor screening has increased the safety of donated blood products, autologous blood is the most desirable source of red cells during the perioperative period. The methods commonly used to obtain autologous blood during the perioperative period can be initiated prior to the operative procedure (autologous preoperative donation, acute normovolemic hemodilution) or during surgery (cell scavenging). Acute normovolemic hemodilution (ANH) involves a controlled removal of whole blood immediately prior to the operation. The patient's intravascular volume is maintained with solutions that contain non-red cells. The operative procedure is conducted with a normal blood volume, but with a reduced red cell mass. At

the conclusion of the operation, the stored autologous blood is restored to the patient. If operative blood loss is not excessive, the replacement of autologous blood may provide an acceptable red cell mass. In addition to surgical blood loss, some of the key factors in determining how effective acute normovolemic hemodilution will be in limiting allogeneic transfusion are: the patient's initial hematocrit and blood volume; the volume of autologous blood removed prior to the operation; the effectiveness of the hemodilution; and the timing of autologous blood replacement. In contrast to autologous pre-donation, autologous blood removed during acute normovolemic hemodilution is usually stored and re-infused in the operating room.

Keywords Acute normovolemic hemodilution · Surgery · Blood loss

Introduction

Strategies to reduce requirements for transfusion during surgery continue to be a high priority in clinical care. The long-term sequelae of blood transfusion such as latent viral or transfusion-transmitted infectious disease continue to be a source of concern to patients and physicians. Acute normovolemic hemodilution is one of the strategies used to reduce the need for blood transfusion.

The current approach to reducing blood transfusion during major surgery can be broadly divided into methods that decrease operative blood loss and methods that provide autologous red cells. The methods that reduce

blood loss include: deliberate hypotension; the injection of local vasoconstrictive agents at the operative site; and systemic pharmacologic agents for reducing blood loss, such as aprotinin, aminocaproic acid, tranexamic acid and desmopressin. Autologous red cells can be obtained either prior to the operation or during the operation. Autologous preoperative donation via a blood bank or acute normovolemic hemodilution are two techniques that are used prior to the operation to obtain autologous blood. Cell scavenging provides autologous red cells by scavenging blood from the operative field. These strategies may be used in combination during the operation to reduce or eliminate the need for allogeneic transfusion.

Acute normovolemic hemodilution (ANH) reduces red cells lost during the operation by decreasing the patient's red cell mass immediately prior to operation [6, 9, 11, 13]. The first step in ANH is the acute, controlled removal of whole blood. The patient's intravascular volume is maintained with non-red-cell-containing solutions during the phlebotomy. The operative procedure is conducted in a hemodiluted patient. During the operation, fewer red cells (as well as formed elements) are lost because the patient's hematocrit is lower throughout the procedure. The autologous blood is reinfused at the conclusion of the operation. If the volume of red cells stored prior to operation is adequate and the operative blood loss does not result in profound red cell losses, then an acceptable hematocrit may be achieved without the use of allogeneic transfusion. While the amount of surgical blood loss is not appreciably changed by the use of hemodilution, fewer red cells will be lost due to the patient's acute anemia.

Critical red cell mass

One of the key concepts in applying hemodilution is to define a patient's "safe" lower limit for hematocrit [3, 10]. Healthy patients have a considerable usual reserve of red cells. This reserve is the principle reason that the acute removal of blood in the preoperative period is a viable therapeutic option. In ANH, patients experience two sources of red cell loss, the blood loss associated with hemodilution and operative blood loss. For this reason, a relatively profound anemia is expected during the operative procedure. Although the acute anemia associated with hemodilution is considerably different from anemia observed in clinical practice, the lowest safe red cell mass defined for anemic patients can be applied to guide acute normovolemic hemodilution. An abundance of case reports indicate patients can survive with extremely low hematocrits, but these anecdotal case reports are unlikely to provide a consistent "safe" lower limit of hematocrit [15].

The safe lower limit of hematocrit continues to be debated, yet an appreciation of the factors that define the lower limit of safety for red cell mass is an important consideration in implementing a hemodilution program. Critical red cell mass is the lower limit of hemoglobin associated with effective oxygen delivery. When cardiorespiratory compensatory mechanisms can no longer maintain effective oxygen delivery, a critical red cell mass exists. Anaerobic metabolism and/or tissue ischemia will occur when the red cell mass remains below this critical level. The critical red cell mass is reached first in tissue groups such as the myocardium and central nervous system, because a greater proportion of oxygen extraction occurs in the coronary or cerebral circulation under normal circumstances. The myocardium is particularly sensitive to decreased oxygen availability, because systemic compensatory responses to reduced red cell mass increase cardiac

output. This higher cardiac output leads to increased myocardial work and heightened myocardial oxygen requirements. The increased cardiac energy expenditure puts additional demands on myocardial oxygen reserve at a time when oxygen supply is limited due to anemia. At hematocrits less than 20%, myocardial metabolism may be compromised by the decreased supply and heightened oxygen demand. Subendocardial ischemia and myocardial infarction can occur in healthy patients with normal coronary arteries when hematocrits are less than 15%. These changes are often manifested by EKG changes with ST segment elevation. In the liver and kidneys, centrilobular hepatic necrosis and acute renal failure may occur when hematocrits are sustained at hematocrit levels less than 15%.

Hemodilution to relatively low hematocrits may be better tolerated, because the period of anemia is brief and oxygen requirements are reduced by anesthesia. For this reason, hematocrit values of less than 20% are often recorded in a hemodiluted patient during the intraoperative period. If blood loss is replaced with crystalloid and replacement is withheld until a hematocrit of 20% is observed, then more than one-half of a patient's blood volume could be removed by a combination of hemodilution and operative blood loss prior to replacing red cells.

Factors determining efficacy of hemodilution:

1. Red cell mass. Patients with greater red cell masses can donate more blood. Red cell mass is based on hematocrit and blood volume
 - a) Initial hematocrit: Patient's with higher hematocrits are able to provide more red cells for storage prior to the operation. The patient's beginning hematocrit and blood volume are key factors in estimating the amount of blood that should be removed prior to surgery
 - b) Blood volume. Blood volume increases with weight. The "ideal" 70-kg male has approximately a 5-l blood volume. Females have a slightly lower blood volume on a weight basis. For example, a 55-kg, adolescent female's blood volume would be approximately 3,500 ml ($55 \text{ kg} \times 60\text{--}65 \text{ ml/kg}$)
2. Magnitude of hemodilution. When lower hematocrits are achieved following hemodilution, less red cell loss will occur as a result of surgical blood loss. For this reason, the more blood removed prior to the operation the greater potential efficacy in reducing red cell losses. However, at the same time, this hemodilution leads to more profound hemodynamic consequences. If more blood is removed, the operative hematocrit will be lower, and, consequently, fewer red cells will be lost during surgical dissection. For example, a profound hemodilution (four units of whole blood in a 70-kg healthy patient) requires the administration of large volumes of non-red-cell-containing solutions to main-

Table 1 Theoretical hematocrit changes expected prior to, during and following operation in three groups of patients. The patients are assumed to be 70 kg with a starting hematocrit of 40%. Patients'

experience 1,500 ml of blood loss during the operation and another 500 ml of blood loss in the post-operative period

Treatment groups	Pre- Op	Hemodilution (withdrawal)	Postoperative (1,500 ml blood loss)	Hemodilution (replace)	500 ml postoperative blood loss
No treatment	40%	—	30%		26%
Hemodiluted (2 units)	40%	32%	24%	32%	30%
Autologous (2 units)	36%*	—	26%		32%*

*Autologous donors have lower hematocrit prior to surgery. Timing of blood replacement for autologous donors is in the period following operation (after intraoperative and postoperative blood loss)

tain normovolemia. A more moderate degree of hemodilution (two units) may be more safely used, but may not be as effective in reducing red cell losses. This balance between the magnitude of hemodilution employed and theoretic red cell losses can be calculated by predicting changes in red cell mass with different levels of hemodilution (Table 1) [4, 8]

If a 70-kg patient with a hematocrit of 40% has four units of blood removed prior to operation, the operation begins after normovolemia is reestablished in a patient who has a hematocrit approximately 25%. If the operative blood loss is 1,500 ml, then intraoperative hematocrit reaches a nadir of less than 20%. Following replacement of the four units of stored blood, hematocrit is restored to a hematocrit of 34%. If the same patient had only two units stored, then hematocrit following operative blood loss of 1,500 milliliters would reach a lower limit of approximately 24%. Following replacement of the two units, then hematocrit would be restored to 31%. In contrast, if no hemodilution were used during the procedure, then the hematocrit following operative blood loss would be approximately 28%

3. Intraoperative blood loss. The most obvious main determinant of red cell loss is blood loss during the operation
4. Intraoperative management. If normovolemia is not effectively reestablished and maintained following removal of the autologous blood, then the procedure offers no benefit in terms of reducing red cell losses. In the absence of hemodilution, operative blood loss would occur at the higher preoperative hematocrit level. The timing of red cell replacement is another factor that influences the effectiveness of ANH. When the stored blood is replaced after the operative blood loss, then the patient will experience the least red cell losses. From a safety perspective, occasionally, blood removed prior to operation may need to be transfused to treat severe anemia during the operation

Special considerations for hemodilution

From a clinical management perspective, patients experience two sources of blood loss, the blood loss associated

with hemodilution and operative blood loss. For this reason, larger volumes of crystalloid or colloid solutions will be required during the intraoperative period [6, 11, 13]. These changes in intravascular volume may need to be more closely monitored during the procedure to assure intravascular volume is maintained throughout the operation. If the patient is hypovolemic (i.e., hemoconcentrated), more red cells will be lost and hemodilution will be less effective in achieving a higher postoperative hematocrit. Postoperative edema is a frequent consequence of the need to maintain normovolemia with crystalloid and colloid solutions.

Intraoperative hematocrits of less than 20% are often encountered during hemodilution (Table 1). The lower hematocrits observed during the operation may demand additional cardiovascular monitoring. This monitoring provides a means to assess the impact of the lower hematocrit on systemic function. Invasive hemodynamic monitoring also establishes vascular access to frequently measure blood chemistry and pH. Serial hematocrits and arterial blood gases help confirm blood loss estimates, evaluate fluid replacement and provide information about adequacy of oxygen delivery. Persistent tachycardia and electrocardiogram changes suggestive of myocardial ischemia are often the first signs of inadequate oxygen delivery as a result of anemia. The decreased blood viscosity associated with hemodilution often decreases blood pressure. Consequently, profound hemodilution probably should not be combined with other techniques such as deliberate hypotension that also decrease tissue oxygen delivery.

Comparison of hemodilution, autologous donation and red cell scavenging

Autologous pre-donation of blood and intraoperative red cell scavenging are two techniques frequently compared to acute normovolemic hemodilution. These techniques share a common strategy of providing autologous blood source during the perioperative period. A theoretical comparison of autologous donation, ANH and no replacement is provided in Table 1.

Autologous donation was enthusiastically endorsed 20 years ago, but the decreasing risk of allogeneic blood

has led to a reevaluation of this approach to reducing allogeneic blood transfusion. A variety of studies have concluded autologous donation may not be a cost-effective strategy, primarily because of the reduced infectious risk of the current volunteer donor blood pool. The main limitations of autologous donation relate to efficacy, cost-efficiency and patient preference. In surgical patients, the factors that influence the efficacy of autologous donation include: the frequency of patient participation, whether autologous donors avoid allogeneic blood use, and the proportion of autologous blood that is reinfused used during the perioperative period [1, 2, 7, 13].

Autologous donation does offer some advantages to ANH, because the blood donation occurs in the weeks prior to operation. Unlike ANH, autologous donors will not require the larger volumes of crystalloid or colloid intravascular volume replacement to reestablish normovolemia. The delay between collections of autologous blood may effectively replace some of the autologous red cells removed preoperatively, but most autologous donors are unable to effectively restore a pre-donation hematocrit [5, 12]. An additional advantage of pre-deposit autologous blood is that the units can be reinfused at any time during the perioperative period (Table 1). The primary reason that blood replacement is necessary is the postoperative loss of red cells into drains or the surgical wound. Unlike ANH or cell scavenging techniques that are primarily an intra-

operative method to return autologous blood, pre-donated autologous blood can usually be stored until later in the postoperative period. On the other hand, the use of a blood bank exposes autologous donors to the numerous sources of iatrogenic errors that are associated with collecting, labeling, storing and checking a patient's autologous blood. These clerical errors are the most common serious complications associated with the use of a blood bank.

Red cell scavenging from the operative site is also an effective method to preserve red cells [14]. The yield of red cells from blood lost during an operation is dependant on factors such as the amount of damage that occurs during the process of scavenging. In orthopedic procedures, a considerable proportion of red cells may be damaged during the collection and washing of the red cells.

In summary, acute normovolemic hemodilution allows patients to tolerate moderate degrees of blood loss without the requirement for allogeneic blood. The technique is an effective method to store autologous red cells prior to the operation and return the blood at a time when surgical blood loss has abated. The main advantage of ANH is that the technique can be used intraoperatively, without the need for long-term blood storage and testing. In order for hemodilution to reduce red cell losses, normovolemia must be maintained throughout the intraoperative period.

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