

PRO: CELL SALVAGE SHOULD BE USED IN OBSTETRICS

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One of the leading causes of death during childbirth is hemorrhage.^{1,2} When hemorrhage occurs it can be massive. The use of cell salvage would naturally be attractive in this setting. Use of cell salvage in obstetrics is classically contraindicated; however, little data are available to substantiate this contraindication. In fact, significant data exists which supports the use of cell salvage in obstetrics. This contraindication arises from a fear that shed blood can be contaminated with amniotic fluid, and readministration may lead to an iatrogenic amniotic fluid embolism. Fortunately, or unfortunately, the incidence of amniotic fluid embolism is so rare a study to demonstrate safety of cell salvage use would require a study incorporating 1.7 million patients. Since this sample size is unrealistic, an evaluation of what we do know about cell salvage use along with an evaluation of the alternative therapy, allogeneic transfusion, is warranted.

Support for the use of cell salvage in obstetric hemorrhage now encompasses 390 reported cases where blood contaminated with amniotic fluid has been washed and readministered without filtration.^{3,4,5} None of these cases were complicated by amniotic fluid embolism. Only one adverse report has been made. In this letter to the editor, a 22 y.o. Jehovah's Witness patient at 30 weeks gestation with preeclampsia and HELLP syndrome is described.⁶ Her presenting laboratory values were a Hgb of 7.1 g/dl; platelet count of 48,000; AST of 194 u/L; and an ALT of 330 u/L. A Continuous Auto Transfusion System (CATS, Fresenius) was utilized to scavenge 600 mL of blood/amniotic fluid which was subsequently processed to 200 mL. It is important to note that no leukocyte depletion filter was used. Ten minutes after starting the reinfusion, the patient became dyspnoeic, hypoxic (O2 Sat = 85%) then arrested. A clinical

diagnosis of amniotic fluid embolism was followed by a pathologic diagnosis which “Did not reveal any other cause...”

This report is highly suspect as to whether cell salvage was responsible for the death of the patient. First, the patient was severely ill when presenting to the labor suite and may have succumbed from a number of different mechanisms. Secondly, little description is made of how the blood was processed other than that a CATS machine was used. This is important because cell salvage can be associated with the “cell salvage syndrome” which is a coagulopathy due to the readministration of a partially washed product and is typically due to a lack of knowledge of the parameters necessary for a quality wash. Lastly, the volume of reinfused blood can be questioned as being adequate to cause an amniotic fluid embolism. Tio⁷ demonstrated a therapeutic effect of amniotic fluid when he infused amniotic fluid into 27 peripartum women with prolonged coagulation times. Volumes ranged from 5-500 mL and resulted in resolution of the clotting abnormalities. He then proceeded to administer amniotic fluid to 73 patients of all ages without effect.⁸ Thus, it seems unlikely that any remnant amniotic fluid in the 200 mL of cell salvaged blood could be responsible for the demise of the aforementioned patient.

Because of the rarity of amniotic fluid embolus, evaluation of surrogate markers of amniotic fluid have been made. Unfortunately, since the mechanism for amniotic fluid embolism is not clear, any studies demonstrating that salvaged blood is clean for one parameter may not extrapolate to the unknown mechanism of amniotic fluid embolism. Tissue factor is thought to be involved in the disseminated intravascular coagulopathy that typically follows the acute embolic event.⁹ Bernstein and colleagues¹⁰ evaluated

the washout of tissue factor and found that routine washing eliminated all tissue factor activity. Since tissue factor may be only one of many components that lead to the syndrome of amniotic fluid embolism, washing of this tissue factor would not guarantee that amniotic fluid embolism would not occur.^{11,12} This being said, several studies evaluating efficacy of cell salvage washout including studies on the removal of free hemoglobin, bromocresol green dye, and heparin, have suggested that if one factor is effectively removed than the other factors are equally removed.^{13,14} Therefore, if tissue factor is effectively removed from blood contaminated with amniotic fluid, these previous studies would suggest that the other biochemical components of amniotic fluid would also be similarly removed or reduced significantly in concentration.

In a pig model, clear amniotic fluid (meconium free) injected into the pig in quantities up to 10 ml/kg caused only minor effects.¹⁵ However, when meconium stained amniotic fluid was infused at volumes of 3 ml/kg, a severe coagulopathy and cardiorespiratory abnormalities ensued. This would suggest that the particulate matter of amniotic fluid is important to remove. Durand and colleagues¹⁶ showed cell washing alone did not remove fetal squamous cells. Waters et al. demonstrated that leukocyte depletion filters along with cell washing will remove fetal squamous cells to an extent comparable to the concentration of these cells in a maternal blood sample following placental separation.¹⁷ From this study it was concluded that the combination of cell salvage washing and filtration produces a blood product comparable to circulating maternal blood with the exception of the fetal hemoglobin contamination. The filters work through the use of a small-pore microfiber web and a negative surface charge.¹⁸

All of this discussion may be irrelevant because recent articles^{19, 20,21} have

suggested that amniotic fluid embolus is, in fact, not an embolic disease but rather an anaphylactic reaction. This would imply that it would occur with or without cell salvage since amniotic fluid is routinely entrained during delivery. Thus, any debate regarding remnant amniotic fluid in cell salvage blood may be irrelevant.

RISKS OF ALLOGENEIC BLOOD TRANSFUSION

Since most medical therapies encompass some degree of risk, an analysis of the risks associated with the alternative to cell salvage use is necessary. The primary alternative would be the use of allogeneic blood. There are many risks associated with allogeneic transfusion. This author believes that these risks outweigh any theoretical risk of cell salvage.

The risk of infectious complications is foremost on most people's minds when they think about allogeneic transfusion. Modern blood banking and screening have markedly reduced the risk of disease transmission; however this risk is raised considerably when multiple units are transfused. For instance, the risk of having an infectious complication of any type (HIV, Hepatitis C, HTLV, etc.) is approximately 1:30,000 following exposure to a single unit of blood.²² With ten units, the probability of exposure increases so that the patient receiving 10 units now has an exposure risk close to 1:3000. When obstetrical patients need transfusion, it is frequently in large amounts making this an important risk.

The leading cause of death following allogeneic transfusion involves clerical error and hemolytic transfusion reaction. Hemolytic transfusion reaction occurs at rates ranging from 1:12,000 to 1:21,000 units transfused and has a mortality of 20-40%. More recently, Transfusion Related Acute Lung Injury (TRALI) has been recognized to be a

significant cause of morbidity. TRALI occurs within 1-2 hours following transfusion and results in severe hypoxemia, bilateral pulmonary edema, hypotension and fever and is indistinguishable from ARDS. The incidence remains unknown but has been estimated to occur somewhere between 1:300-5000 transfusions.

The risk of immunosuppression following allogeneic blood transfusion is less often mentioned but is of greater importance to short and long-term patient outcome than are the risks of viral transmission.²³ An increased incidence of postoperative infection and cancer recurrence is thought to occur from immunosuppression following allogeneic blood. The immunosuppression following transfusion was first observed in renal transplant patients who had higher graft survival rates when they received allogeneic transfusion.²⁴ Thus, this practice became the standard of care for a period of time. This standard changed when potent immunosuppressive drugs were developed. Thus, this immunosuppressive effect has been manipulated to some patient's benefit. Conversely, this immunosuppression can be detrimental for most surgical patients. Studies evaluating postoperative infection rate following allogeneic transfusions have demonstrated as much as a 10-fold greater rate of infection in patients receiving allogeneic blood.^{25,26,27} In obstetrics, post-cesarean infection rates range from 5-25%.^{28,29} Thus, increases in infection rate due to immunosuppression offers a profound effect on patient outcome.

In addition to being associated with the risks of immunomodulation and viral exposure, blood is altered by storage. The most significant of these storage injuries being decreased levels of 2,3-diphosphoglycerate (2,3 DPG) in red blood cells. Decreased levels of 2,3 DPG shift the oxyhemoglobin dissociation curve to the left, making it more difficult for oxygen to bind with hemoglobin as its carrier. Restoration of normal levels

of 2,3-DPG can take up to a day to occur following reinfusion of stored blood which means that the oxygen delivery of transfused blood is not initially comparable to *in vivo* blood. This storage defect applies to both allogeneic and stored autologous blood but does not apply to cell salvaged blood. In recent studies, there has been a suggestion that the reduction in 2,3-DPG along with an associated red cell shape change may lead to a worsening of tissue oxygen levels despite an increase in blood oxygen content.³⁰

Storage of blood can also lead to electrolyte abnormalities. Increases in patient potassium concentrations can occur from lysis of red cells as they age during storage. This lysis can lead to life threatening hyperkalemia. This occurs under circumstances of massive transfusion where the kidney's ability to remove the potassium is overwhelmed. Another electrolyte abnormality occurring from transfusion is hypocalcemia which can occur from calcium binding by the citrate anticoagulant in the transfused unit. Normally, citrate is rapidly metabolized in the liver and its presence is clinically insignificant; however, at rapid transfusion rates or in patients who metabolize citrate slowly (small children, hypothermic or hypotensive patients, or patients with liver dysfunction), hypocalcemia will occur. This hypocalcemia can lead to myocardial dysfunction and clotting dysfunction.

Lastly, an interest has arisen over the possibility of transmission of disease-producing genes via blood transfusion.³¹ Studies concerning the risk of this transmission in humans are limited to an increased risk of non-Hodgkins lymphoma in patients who have received a blood transfusion.³² Nevertheless, it is interesting to speculate on the ramifications of such a finding and it is another good reason to avoid allogeneic blood.

CONCLUSION

The practice of medicine frequently requires evaluation of risks when applying different treatment strategies. In this debate, we have the purely theoretical risk of cell salvage use in obstetrics being compared to allogeneic blood which has multiple, known adverse consequences. Until proven otherwise, the use of cell salvaged blood would appear to offer the safer treatment modality for the hemorrhaging obstetric patient.

Despite what appears to be substantial reassuring data, several precautions should be taken when salvaging blood in obstetrics. First, minimizing the aspiration of amniotic fluid through a double suction setup is advisable. One suction should be connected to the cell salvage reservoir and used for suctioning of blood. The other should be connected to the regular wall suction and used only for aspiration of amniotic fluid. In this way, the volume of amniotic fluid contamination is minimized. Secondly, the utilization of leukocyte reduction filters at the completion of processing can reduce the fetal squamous cell contamination to a level comparable to maternal blood contamination. These filters should be used by the anesthesiologist with pressure of < 300 mm HG being placed on the reinfusion bag. Lastly, fetal red cell contamination is present. An Rh incompatibility between mother and infant may suggest that the Rhogam dose following delivery may need to be modified.

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