Delayed cord clamping with and without cord stripping: a prospective randomized trial of preterm neonates

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OBJECTIVE: Autologous blood transfusion from the placenta to the neonate at birth has been proven beneficial. Transfusion can be accomplished by either delayed cord clamping or cord stripping. Both are equally effective in previous randomized trials. We hypothesized that combining these 2 techniques would further improve outcomes in preterm neonates.

STUDY DESIGN: This was a prospective randomized trial for singleton deliveries with estimated gestational ages between 22 and 31 6/7 weeks. The control protocol required a 30-second delayed cord clamping, whereas the test protocol instructed a concurrent cord stripping during the delay. The primary outcome was initial fetal hematocrit. We also examined secondary outcomes of neonatal mortality, length of time on the ventilator, days to discharge, peak bilirubin, number of phototherapy days, and neonatal complication rates.

RESULTS: Of the 67 patients analyzed, 32 were randomized to the control arm and 35 were randomized to the test arm. The gestational ages and fetal weights were similar between the arms. Mean hematocrit of the control arm was 47.75%, and the mean hematocrit for the test arm was 47.71% ($P = .98$). These results were stratified by gestational age, revealing the infants less than 28 weeks had an average hematocrit of 41.2% in the control arm and 44.7% in the test arm ($P = .12$). In the infants with gestational ages of 28 weeks or longer, the control arm had an average hematocrit of 52.9%, which was higher than the test arm, which averaged 49.5% ($P = .04$). The control arm received an average of 1.53 blood transfusions, whereas the test arm received 0.97 ($P = .33$). The control arm had 3 neonatal deaths, and the test arm had none ($P = .10$). The average number of days until discharge was 71.2 for the control arm and 67.8 for the test arm ($P = .66$). The average number of days on the ventilator was 4.86 for the control arm and 3.06 for the test arm ($P = .34$).

CONCLUSION: Adding cord stripping to the delayed cord clamp does not result in an increased hematocrit. Data suggest trends in lower mortality and higher hematocrit in neonates born less than 28 weeks, but these were not statistically significant.

Key words: delayed cord clamping, umbilical cord stripping

Cite this article as: Krueger MS, Eyal FG, Peevy KJ, et al. Delayed cord clamping with and without cord stripping: a prospective randomized trial of preterm neonates. Am J Obstet Gynecol 2015;212:394.e1-5.

Preterm neonates are vulnerable to many complications associated with their prematurity. There are extensive data supporting the routine use of delayed cord clamping in preterm deliveries to allow autologous placental transfusion. This practice has been studied extensively and is well known to improve neonatal outcomes.[1-8] Saigal et al[1] published early research on this topic in 1972, which concluded that delayed cord clamping increased red cell volume and hematocrit by 50% in preterm infants. Since that study, several more studies have reaffirmed higher hematocrits with delayed cord clamping.[2-8]

In addition to increasing hematocrit, studies have found that delayed cord clamping improves secondary outcomes including overall morbidity, mortality, a need for transfusions, a need for respiratory support, incidence of intraventricular hemorrhage, incidence of late-onset sepsis, and days to discharge.[5,7,8]

In addition to performing delayed cord clamping, many obstetricians and pediatricians also advocate for stripping or milking of the umbilical cord. This practice has also been studied and found to be independently beneficial.[9] Recent studies have demonstrated an improvement in neonatal outcomes, including a decreased need for blood transfusions, a decreased need for respiratory support, the stabilization of blood pressure, and an improvement in urine output in those neonates who received cord stripping.[9,10] In a 2011 study, Rabe et al[11] concluded that umbilical cord stripping alone was equal in benefit to delayed cord clamping alone.

Because both delayed cord clamping and cord stripping have been previously analyzed independently and have been shown to be beneficial, we sought to examine outcomes when the 2 practices were combined. The purpose of this study was to compare delayed cord clamping alone with delayed cord clamping plus cord stripping in preterm

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Received Aug. 15, 2014; revised Nov. 13, 2014; accepted Dec. 15, 2014.

The authors report no conflict of interest.

Presented in oral format at the 81st annual meeting of the Central Association of Obstetricians and Gynecologists, Albuquerque, NM, Oct. 8-11, 2014.

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0002-9378/$36.00 • http://dx.doi.org/10.1016/j.ajog.2014.12.017

neonates. The primary outcome was initial neonatal hematocrit. Our hypothesis was that delayed cord clamping plus cord stripping would yield at least a 5% higher neonatal hematocrit and improve neonatal outcomes beyond delayed cord clamping alone.

Materials and Methods

This was an institutional review board–approved, prospective, randomized trial performed at the University of South Alabama Children's and Women's Hospital between the dates of August 2012 and November 2013.

When endeavoring a study of neonatal outcomes, it would be ideal to use long-term outcomes of morbidity and mortality as primary variables; however, the sample size required to power these analyses is a difficult task in a prospective randomized control trial; therefore, previous studies have set a precedent to use hematocrit as a surrogate marker of therapy success.[1,2,5,6] In addition, previous studies have set a precedent of hypothesizing at least a 10% increase in hematocrit when either delayed cord clamping or cord stripping was performed over an immediate cord clamping.[2,11]

In designing our study, we were attempting to speculate an additive increase in hematocrit when cord stripping was done in conjunction with delayed cord clamping. In an attempt to choose an increase in hematocrit that would be clinically significant but still reasonably attainable, we deduced that a 5% relative difference between our control and test arms would be considered a valuable increase. Therefore, a power analysis with the G*power application was performed for a goal of obtaining a 5% relative increase in hematocrit. In this calculation, we used a predicted average hematocrit of 50%, which was simply chosen by examining the typical hematocrits of neonates admitted to the neonatal intensive care unit (NICU). With an alpha of 0.05, a power of 80%, and a predicted SD of 3.5%, it was determined that a minimum of 32 patients were to be recruited in each arm.

Informed consent was obtained from obstetric patients at risk for preterm delivery, with randomization occurring just prior to delivery. Randomization was performed with opaque envelopes contained on the labor and delivery unit containing cards with instruction on either delayed cord clamping alone or delayed cord clamping plus cord stripping. An equal number of envelopes were created for each arm and were scrambled by a third-party registered nurse.

Using a protocol designed by Mercer et al,[7] delayed cord clamping instructed holding the neonate below the level of the placenta, which was done below the perineum in a vaginal delivery or to the maternal side in a cesarean delivery. The 30-second delay was verbally stated in 5 second increments by the neonatal nurse practitioner present at the delivery. After the cord clamp, the neonate was immediately transferred to the warmer and care was assumed by the awaiting pediatric team.

The cord stripping protocol was designed to mimic a previous protocol by Rabe et al[11] in which, in addition to the above 30 second delay, the full length of the visible cord, which is estimated to be one third to two thirds of the full cord length, is manually stripped between 2 fingers by the surgeon or assistant toward the neonate. This stripping was done 4 times during the above-described delay with instructions to allow 4-5 seconds between strippings to allow the cord to refill completely.[11]

Protocol also dictated that uterotonic agents were not to be used until after cord clamping, except in cases in which pitocin was already being administered to achieve vaginal delivery. In those patients pitocin administration was allowed to continue at the existing rate.

Singleton deliveries from both cesarean deliveries and vaginal deliveries with estimated gestational ages between 22 0/7 weeks and 31 6/7 weeks were included. Patients at periviable gestational ages received counseling and were included only if they desired full interventions on behalf of the fetus both prior to and after delivery. Patients were excluded if the fetus had known anomalies or there was a suspected placental abruption. The primary outcome was initial hematocrit, which was obtained as soon as reasonably possible within the first 30 minutes of life from either venous or arterial blood draws.

The protocol allowed arterial blood draws if an arterial line was available because this was deemed to be in the best interest of the neonate. Venous draws were initiated if an arterial line was not yet established. Capillary hematocrits were not obtained because these can differ from venous and arterial hematocrit too widely. The secondary outcome variables were the length of time on the ventilator, days to discharge, neonatal mortality, peak bilirubin, number of phototherapy days, and neonatal complication rates.

The ideal randomized control trial has double blinding. We obviously could not blind the surgeon to the therapy; however, because randomization occurred just prior to delivery, all care leading up to delivery, including the decision to deliver and delivery timing, was done prior to the providers being aware of randomization.

NICU protocol requires a team of neonatal providers to be present at delivery when possible. This team includes either a neonatologist or a neonatal nurse practitioner. The neonatal team was not told which patients were participating in the study, and the randomization arm was not documented on the infants' charts. This was done in an effort to avoid alteration in subsequent management and achieve blinding of the care team.

The care provided to the neonate after delivery was at the discretion of the attending neonatologist. A study by Hosono et al[9] created a protocol for postnatal management, which required serial blood counts with specific guidelines for transfusions. In contrast, Mercer et al[7] allowed the clinical management of the infant to be at the discretion of the neonatologist in their study.

Our protocol reflected the latter, rationalized by the fact that strict transfusion parameters might not be appropriate, given differences in estimated gestational ages, age of life, and complications encountered. In addition, not all