Umbilical Cord Blood

as Alternative for

Infant Blood in Neonatal Sepsis Evaluation

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Author Note

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Abstract

Early onset sepsis, primarily with group-B streptococci (GBS), remains a leading cause of neonatal morbidity and mortality in the United States. Long-term sequelae of GBS sepsis include neurologic, growth, sensory, developmental and physical delays or abnormalities. Before antibiotics, neonatal sepsis was almost always fatal (95-100% mortality rate). One of the recommendations published by the Centers for Disease Control and Prevention (CDC) that has caused a striking decline in GBS infection is to obtain a complete blood count and blood culture from infants at risk for sepsis. Currently, these blood tests are taken from the infant. Studies suggest that using umbilical cord blood may be an alternative for sepsis evaluation. A retrospective review of previously collected data from 165 charts, comparing infant blood and cord blood results was performed to examine the validity of using cord blood to avoid a painful procedure for baby and improve time and resource utilization. A statistically significant moderate correlation exists between umbilical and infant I:T ratio. For both volume and culture time, there were significant statistical differences ($p<0.001$) with umbilical cord blood achieving higher volume with less time from birth to laboratory analysis. The study was unable to determine if there was a statistical correlation between the blood cultures because there were no positive blood cultures in either sample.

Keywords: umbilical cord blood, cord blood, group B streptococci, neonatal sepsis evaluation, neonatal pain, pain prevention.

Umbilical Cord Blood as Alternative for Infant Blood in Neonatal Sepsis Evaluation

In spite of improved antimicrobial agents, infection remains a significant cause of neonatal morbidity and mortality. Neonatal sepsis is classified into two distinct illnesses based on an infant's age at onset. Early onset sepsis typically occurs in the first 7 days of life and manifests as a fulminant, multisystem illness usually acquired by vertical transmission from the mother. Early onset sepsis has a higher fatality rate than late-onset sepsis (Edwards, 2006). Late-onset sepsis may occur as early as postnatal day 3, but is more common after the first week of life and is usually a progressive illness characterized by focal infection, often meningitis (Mohan, Merenstein, Adams, & Weisman, 2006).

Common organisms found in early onset infection include Group B streptococcus (GBS), *Escherichia coli* (E coli), *Haemophilus influenza* (type B and nontypable), and coagulase-negative Staphylococcus (Mohan et al., 2006). In the pre-antibiotic era, neonatal sepsis was almost always fatal (95-100% documented mortality rates). Since 1990, the fatality rate has declined, with recent fatality estimates at 5% for late-onset sepsis and ranging from 5% to 20% for early-onset sepsis (Edwards, 2006).

Approximately 25-35% of neonates with a bacteremia develop adverse sequelae. In other infants, bacteria are successfully eliminated by the body's defenses before adverse effects occur (Mohan et al., 2006). Signs and symptoms of early-onset neonatal sepsis are nonspecific and nonlocalizing. Awaiting clinical emergence of sepsis diminishes the opportunity for a successful outcome. Rapid and accurate detection of newborn infants with sepsis, and the early initiation of antibiotic therapy are essential to decreasing illness and death (Polin et al., 1981). Infections must be identified and treated as soon as suspected to prevent serious complications such as

septic shock, necrotizing enterocolitis, renal tubular necrosis, persistent pulmonary hypertension, meningitis, disseminated intravascular coagulation and death (Mohan et al., 2006). Neonates who survive sepsis may have long-term sequelae, which may include neurologic, growth, sensory, developmental, and physical delays or abnormalities (Mohan et al., 2006).

Group B Strep (GBS) remains the leading cause of early-onset neonatal sepsis, mortality and morbidity in the United States. In 1996, the Centers for Disease Control and Prevention (CDC), in collaboration with relevant professional societies, published guidelines for the prevention of perinatal GBS disease. These guidelines were updated in 2002. The implementation of these guidelines resulted in a dramatic decrease in the incidence of GBS, GBS infection rates decreased 80%, from 1.7 cases per 1,000 births to 0.34-0.37 cases per 1,000 births in recent years. Guideline recommendations included universal screening of pregnant women for GBS colonization at 35-37 weeks gestation, with subsequent administration of intrapartum antibiotic prophylaxis to carriers (CDC, 2005). In 2009, clinical and health representatives assembled to reevaluate prevention strategies on the basis of the data collection following the 2002 guidelines. The continued burden of GBS disease and newly available data using an evidence-based approach prompted further revisions of CDC recommendations for early-onset sepsis prevention in 2010. The implementation of the new 2010 guidelines is expected to prevent even more cases of early-onset GBS disease (CDC, 2010). The CDC also recommended continued surveillance to monitor the impact of revised recommendations and guide direction of future interventions (CDC, 2007).

Early clinical signs and symptoms of neonatal GBS infection are nonspecific, and the risk factors for disease are common occurrences. The evaluation of newborns for potential early sepsis, therefore, is difficult for neonatal clinicians. A complete blood count (CBC) is

commonly ordered to help determine the likelihood of sepsis and the need for antibiotics in infants who are symptomatic or who have a history of risk factors. Although the CBC test is an insensitive GBS screening tool, which should not be used exclusively to predict infection, the CBC is helpful diagnostic modality in the presence of clinical signs of infection (Newman, Puopolo, Wi, Draper, & Escobar, 2010). The CDC guidelines for the prevention of GBS recommend both a CBC and blood culture for term infants born to mothers who were GBS positive but not adequately treated with antibiotics and for preterm infants with positive or unknown GBS status (CDC, 2010). Based on CDC guidelines, between 324,000 and 608,000 newborns require a sepsis evaluation annually (Hansen, Forbes, & Buck, 2005). Currently, both the CBC and blood culture used to evaluate GBS sepsis status are drawn from a peripheral site of at-risk newborns (CDC, 2007).

Complete blood counts (CBCs) are typically obtained as a component of a partial sepsis evaluation. Immature to total ratio granulocyte count (I:T ratio) is calculated to assist with diagnosis of acute sepsis. In response to GBS infection, newborns often exhibit an increase in percentages of immature cells released from bone marrow that is above the upper limits of normal, which would increase the I:T ratio (Edwards, 2006).

Blood cultures, the second component of a sepsis evaluation, are important determinants of the identification of pathogens causing infections, and this identification determines the direction of appropriate antibiotic treatment. Although many factors influence the yield of blood cultures, blood volume is the single most important factor. According to several studies, the rate of isolation of pathogens from blood cultures is increased with the quantity of blood inoculated into the culture bottle (Gonsalves, Cornish, Moore, Chen, &Varman, 2009). It is possible for a blood culture to be falsely negative with inadequate blood volume. Inadequate amount of blood

inoculated in the blood culture bottle may also result in delay in interpretation of bacterial growth (Polin et al., 1981). There is also an inverse correlation between contamination rate of blood culture and blood volume (Connell, Rele, Cowley, Buttery, & Curtis, 2007). Blood culture contamination impairs decision making in patient care (Gonsalves et al, 2009).

It is difficult to obtain an adequate volume of blood from newborns who often have small, delicate veins. One to two milliliters of blood should increase microorganism recovery in sepsis in those instances of low-colony count of pathogens (Schelonka, Yoder, Brockett, & Ascher, 1996). Blood sampling from the neonate may require multiple venous or arterial sticks. These punctures are exquisitely painful, and the break in the skin exposes the neonate to potential infection (Costakos, Walden, Rinzel, & Dalen, 2009). Umbilical cord blood is a readily available source of blood that is produced by the infant in utero. The quantity of umbilical blood available within the umbilical cord is more than adequate for blood cultures.

Neonatal research has shown that newborns experience pain (Kanwaljeet, Anand, Aranda, Berde, et al., 2006). An expectation of care providers is to prevent infants from experiencing pain, if possible (Franck, Allen, Cox, & Winter, 2006). In 2006, the American Academy of Pediatrics published guidelines recommending that health care facilities that treat neonates should establish a neonatal pain control program. One of these recommendations was to reduce the number of painful procedures (Batton, Barrington, &Wallman, 2006).

Often, health care providers with increased skills are needed to perform venipuncture from a neonate. This means that highly skilled neonatal clinicians must leave other higher acuity tasks in order to obtain a newborn blood sample (Costakos et al., 2009).

Well infants at risk for GBS sepsis are removed from their families, disrupting the bonding process and causing distress to the family (Costakos et al., 2009). In a study conducted

by Franck et al. (2006), parents indicated that they believed that medical procedures were the major source of pain for their newborn. Parents also articulated that their newborn's pain caused personal emotional distress.

Purpose

The purpose of this project was to perform a retrospective review of previously collected research data to compare the complete blood count immature to total (I:T) granulocyte ratio and blood culture results between paired samples of umbilical cord blood and infant blood. This analysis provided evidence needed to determine that umbilical cord blood could be a valid alternative for infant blood for evaluation of group B streptococcus sepsis in newborns. Significant correlations were demonstrated between umbilical cord blood and infant blood for the I:T ratio and pathogen cultured, showing painless blood testing to screen for GBS in neonates is possible. This method of blood sampling would spare trauma to the infant, distress to the family, and provide improved utilization of time and resources.

The site of this study was a large acute care hospital in Bell County, Texas. The mission of this hospital is to provide personalized, comprehensive, and quality health care, enhanced by medical education and research. The purpose of this study supports this mission. Providing services to meet the special needs of children has been an important part of the hospital's mission.

Problem Statement

Despite prevention strategies and improved antibiotics, early onset bacterial sepsis, primarily with group B streptococci (GBS), remains a significant cause of neonatal morbidity and mortality (Edwards, 2006; Hansen et al., 2005; Nandyal, 2008). About one in 2000 newborn babies acquire group B streptococcus bacterial infections, which are typically manifested as a

fulminant, multisystem illness characterized by respiratory disease, general sepsis or meningitis, within the first week of life (Edwards, 2006; Ohlsson & Shah, 2009). Signs and symptoms of early onset neonatal sepsis are nonspecific and nonlocalizing. If clinicians wait for the emergence of signs of sepsis in the newborn, the opportunity for early initiation of treatment needed to decrease morbid sequelae of GBS infection dwindles. Rapid and accurate detection of newborn infants with sepsis and the early initiation of antibiotic therapy are essential to decreasing illness and death (Polin et al., 1981).

The recommendation by the 2002 CDC guidelines for asymptomatic infants who are at risk for GBS sepsis is to obtain a CBC with differential and blood culture (CDC, 2010). Sepsis evaluation has become the most common cause for triage admission to the nursery. Between 324,000 and 608,000 newborns require a sepsis evaluation in the United States annually (Hansen et al., 2005).

To understand the impact of using cord blood as an alternative to using infant blood, one must understand the disadvantages of current practice. Shortly after delivery, well infants at risk for GBS sepsis are removed from their families and transported to the nursery for venipuncture procedures, thus disrupting the bonding process. This is distressing to the family, knowing that their newborn infant will experience a painful procedure alone without benefit of parental comfort measures (Franck et al., 2006). If the venipuncture is unsuccessful, the needle stick may need to be repeated multiple times producing pain to the neonate and increasing an infant's risk for subsequent infection (Costakos et al., 2009; Franck et al., 2006). Venipuncture in newborns often requires neonatal clinicians with an increased skill level, which removes these highly-trained providers from higher acuity tasks (Hansen et al., 2005). Often it is difficult to obtain an

adequate volume of blood from a newborn, which may cause a falsely negative culture result or a delay in the interpretation of bacterial growth (Gonsalves et al., 2009; Schelonka et al., 1996).

Results from the study provided support for the validity of the use of umbilical cord blood as an alternative to infant blood, which would allow the entire sepsis evaluation to be performed in the delivery room with the mother. The specimen would be obtained at the earliest possible time, which would facilitate rapid initiation of antibiotic therapy. This method is noninvasive and nontraumatic and may be performed by a less skilled member of the health care team (Polin et al., 1981). An adequate volume of blood could be easily obtained from the umbilical cord. Substitution of umbilical cord blood for infant blood to detect bacteremia would spare trauma to the infant, decrease distress within the family, facilitate earliest possible sepsis detection, and provide improved utilization of time and resources (Beeram, 2000; Hansen et al., 2005).

Research Questions

This research project will address the following research questions:

1. In newborns, is the use of umbilical cord blood a valid alternative to infant blood, in the evaluation of group B streptococcus sepsis through I:T ratio?
2. In newborns, is the use of umbilical cord blood a valid alternative to infant blood, in the evaluation of group B streptococcus sepsis through blood culture?
3. Is there a significant difference in length of time from delivery to obtaining the umbilical cord blood sample compared to the infant blood sample, as measured by length of time from birth to sample collection?
4. Is there a significant difference in the volume of blood taken from the umbilical cord for blood culture compared to the volume obtained from the infant?

Research Hypotheses

1. Results obtained from the complete blood count immature to total granulocyte ratio between blood drawn from the umbilical cord and blood taken from the infant are equivalent.
2. Blood culture results from blood drawn from the umbilical cord and blood taken from the infant are equivalent regarding whether positive or negative.
3. Significantly less time is required to obtain the umbilical cord blood sample compared to the time needed to obtain a sample from a peripheral site, as measured from birth to sample collection.
4. Umbilical cord blood samples are more likely to produce greater than 1.0 ml of blood compared to samples obtained from a peripheral venous site in the newborn.

PICO Question

In newborn infants at risk for group B streptococcus sepsis, is blood drawn from the umbilical cord as effective for identifying Group B streptococcus through use of the complete blood count immature to total granulocyte ratio and blood culture compared to results of the currently acceptable practice of obtaining blood from the infant?

Conceptual Framework

Synactive Theory of Infant Development

The synactive theory of infant development, conceptualized by Als (1982), provides a theoretical model to understand the individual infant and neonatal development. This model focuses on how the individual infant handles the experiences of the surrounding world. The infant's functioning is seen as continuous interactions within the infant in turn with continuous interactions with the environment.

The synactive theory of infant development provides the viewpoint that the inherently stressful environment of the neonatal intensive care unit, caused by light, sound, activity and care giving techniques, is constantly impinging on the neurobehavioral infant development. The infant is continuously striving toward balance within this hostile environment. Each infant is not only the recipient of care but is an active participant in caregiving. Essential to the appreciation of the infant's reactions in the midst of procedures is the ability to recognize pain and discomfort. The caregiver who acknowledges pain will modify the procedure in order to limit or prevent the infant's pain. The professional caregiver understands the goals of the infant and modifies their approach to care giving interventions (Franck & Lawhon, 1998).

A newborn is suddenly delivered from a warm, safe environment to an environment full of noxious stimuli, including sequelae resulting from the stress of delivery, bright lighting, colder temperatures, eye treatments, and injections. In addition to this, caregivers may be required to perform painful or uncomfortable procedures, which are needed to ensure the infant's long-term well-being. Neonates who require procedures in an intensive care setting must be cared for within this challenging environment in a manner that is respectful and mindful of each child's individual development. Although a painful procedure may be necessary for the infant's health or survival, there are significant methods to decrease the potential negative effects of the tests or interventions. The care approach should be individualized and developmentally supportive, incorporating respect for infant development within the context of the family and providing necessary care in an attempt to optimize neurobehavioral development (Franck & Lawhon, 1998). The implementation of environmental strategies can provide a preventative approach for minimizing an infant's pain and stress, while maximizing the infant's ability to regulate and cope with the stressors. Recognition of the impact of the environment on the infant's developing brain

will lead to the prevention or lessening of pain, which would promote neurobehavioral development (Franck & Lawhon, 1998). The complex behavioral response to pain in the neonate has long-term as well as short-term implications.

According to Gardner, Hagedorn, and Dickey (2006), an alteration in brain development and mal-development of sensory systems can occur when distorted or inappropriate sensory input occurs during a critical period in development. Because of a neonate's memory, painful experiences increase his or her sensitivity to subsequent medical encounters. These initial experiences may affect future attitudes, fears, anxiety, conflicts, wishes, expectations, and patterns of interactions with others. The evidence shows that pain that is experienced in early life may lead to an exaggerated response to painful events in the future. This phenomenon may be a consequence of painful stimuli during a critical period of brain development that might produce changes in the nervous system (Stork, 2006).

The American Academy of Pediatrics (AAP), the Canadian Pediatric Society (CPS), and other professional groups have issued policies, positions, and consensus statements. Their position is that pain and stress are problems in the neonate, and their recommendations are designed to reduce exposure to pain (Stork, 2006). According to the AAP policy statement, the prevention of pain should be the goal of neonatal caregivers and is an expectation of parents (AAP, 2006).

According to Kanwaljeet et al. (2006), one of the discussions from the Neonatal Pain-Control Group was to decrease procedural pain by avoiding or eliminating laboratory tests or other interventions that are not necessary. It is important to use behavioral/environmental approaches to infant care. Clinicians should create strategies to reduce the number of painful procedures, the most obvious and effective of which is to rigorously limit invasive testing such

as heel sticks and venipunctures. Recognition of neonatal pain and appreciation for the strong influence that environment has on infant neurodevelopment will lead caregivers to lessen or prevent pain and optimize neurobehavioral development (Franck & Lawhon, 1998).

Definitions of Terms

For the purpose of this clinical inquiry project, the following terms were defined for clarity:

Umbilical Cord Blood

Umbilical cord blood is blood that is drawn either from a vein or an artery of a segment of umbilical cord that has been clamped on both ends, separated from the placenta and the infant (Beeram et al., 2000).

Infant Blood

Infant blood is a specimen of blood that has been obtained peripherally, arterially or centrally from an infant (Gonsalves et al., 2009).

Sepsis

"Sepsis is a toxic condition due to spread of bacteria or their products in the body" (Merriam-Webster, 1994, p. 662).

Group B Streptococci

Group B streptococci (GBS) is an organism that may colonize a woman's vagina. During pregnancy, women can contract infections caused by GBS. Infants can become infected with GBS during passage through the birth canal. GBS causes severe invasive disease in young infants, which is characterized by sepsis, pneumonia, meningitis, osteomyelitis, or septic arthritis (CDC, 2002).

Risk Factors for Perinatal GBS Disease

In addition to GBS colonization, other factors increase the risk for early-onset sepsis. The CDC guidelines for risk factors are:

- Maternal fever $\geq 100.4^{o}$F.
- Prolonged (>18 hours) rupture of membranes at < 37 weeks gestation
- History of an infant with GBS sepsis from a previous pregnancy
- Presence of positive urine or genital cultures for GBS during the present pregnancy
- Infants born at < 35 weeks gestation or ≥ 35 weeks gestation to at risk mothers who received < 2 doses of penicillin or 1 dose of a cephalosporin at least 4 hours prior to delivery, which is considered adequate prophylaxis (CDC, 2010).

Immature to Total Ratio (I:T Ratio)

The I:T ratio is calculated on the complete blood count (CBC) differential white blood cell count. It is a ratio of the immature (I) to total (T) granulocytes. The immature count is defined as the absolute number of all neutrophils excluding the mature or segmented neutrophils. The I:T ratio is sensitive to infection in neonates. If the I:T ratio is ≥ 0.2, it is significant for possible infection. The current standard of care is to base the decision to initiate antibiotics on whether the I:T ratio is normal or elevated (Hansen et al., 2005).

Blood Culture

A blood culture is performed when a person is at risk for a blood infection. Blood is drawn from the person and tested in a laboratory to identify any microorganism present and growing within the blood. Blood cultures are vital for identifying pathogens causing infections and remain the standard method for detecting bacteremia in ill patients (Gonsalves et al., 2009).

For the purpose of this study, the final blood culture result is determined at 72 hours after inoculation.

Review of Literature

Databases of scientific publications were accessed using a meta-database via Texas Woman's University Library and Richard D. Haines Medical Library. The databases evaluated included Cochrane Library (OVID), MeSH, PubMed, and Centers for Disease Prevention and Control (CDC). Search terms included (a) umbilical cord blood, (b) cord blood, (c) group B streptococci, (d) neonatal sepsis evaluation,(e) neonatal pain, and (f) pain prevention. The articles reviewed were limited to publications in English and those pertaining to newborn infants. Only those articles concerning use of umbilical cord blood for neonatal sepsis evaluation, treatment, and management of group B streptococci sepsis and variables related to pain management were evaluated. In order to expand the scope of the reviewed literature, articles dating back to 1981 were included. Using these search terms, only three articles were found that directly addressed the use of cord blood obtained from a section of the umbilical cord for detection of neonatal group B streptococcal bacteremia. Articles not included in the review of literature were those that focused on the use of umbilical cord blood for unrelated laboratory tests. Articles regarding (a) guidelines for prevention and treatment of GBS sepsis, (b) potential use of umbilical cord blood, (c) blood culture and complete blood count, and (d) prevention and management of neonatal pain were reviewed.

Guidelines for Prevention and Treatment of Group B Streptococcus Sepsis

Despite improved antibiotics, Group B Streptococcus (GBS), remains a leading cause of neonatal sepsis, mortality, and morbidity in the United States (Edwards, 2006; Nandyal, 2008).

Approximately 25-35% of neonates with a bacteremia develop serious adverse sequelae (Mohan, Merenstein, Adams, & Weisman, 2006).

In 1996, the Centers for Disease Control and Prevention (CDC) first issued guidelines for the prevention of GBS sepsis. These guidelines were revised in 2002, when recommendations and reports that were prepared by the National Center for Infectious Diseases were published in the *Morbidity Mortality Weekly Report* (CDC, 2002). Revised guidelines for the prevention of perinatal GBS disease were presented with key changes, differences, and similarities, as compared to the 1996 guidelines, highlighted. This article also reported the impact of implementation of the 1996 guidelines and the evidence supporting changes in practice. Future prevention technology was addressed, and updated recommendations were made based on critical appraisal of multistate population-based observational data.

Several studies had been completed since the previous 1996 CDC recommendations. These guidelines were rated for strength and quality (CDC, 2002). Institutional adherence to implementation of the 2002 guidelines was good and resulted in a significant decrease in GBS disease. An article published in 2007 described the results of an analysis performed by the CDC utilizing data from the Active Bacterial Core surveillance (ABCs) during the period of 2003 to 2005, comparing these findings with data from 2000 to 2001 (the period prior to the universal screening recommendations). The results of this analysis indicated the incidence of early onset GBS disease in infants 0 to 6 days of age was 33% lower during the period of 2003 to 2005 as compared to the period of 2000 to 2001. The authors emphasized the importance of continued surveillance to monitor the impact of CDC guidelines on perinatal GBS disease trends and to guide further interventions. Continued surveillance was also aimed at detection of specific

antibiotic-resistant organisms that might develop following CDC guideline initiation (CDC, 2007).

In June 2009, a group of clinical and public health representatives met to reevaluate prevention strategies on the basis of data collected after the issuance of the 2002 guidelines. Universal screening for maternal GBS colonization and use of intrapartum antibiotics has resulted in a substantial (80%) decrease in the burden of early-onset GBS disease (CDC, 2010). Continued efforts are needed to improve on the progress previously attained in the prevention of GBS disease. There is also a need to monitor for adverse events related to intrapartum antibiotic prophylaxis. Treating a mother with intrapartum antibiotic prophylaxis (IAP) during labor is associated with a decrease in early onset GBS. Some providers proposed that treating all women who are colonized with GBS exposes a large number of women and infants to adverse effects of possibly unnecessary antibiotic administration (Ohlsson & Shah, 2009).

Potential Use of Umbilical Cord Blood

There is little recent literature published on the subject of using umbilical cord blood as an alternative for infant blood for neonatal sepsis evaluation. Two original studies examined the use of umbilical cord blood as a substitute for infant blood for the detection of neonatal bacteremia.

Polin et al. (1981) conducted a study comparing the incidence of positive umbilical cord blood cultures (UCBCs) to the incidence of positive peripheral venous cultures and determined whether a meticulous UCBC technique prevented contamination of culture specimens.

There were 200 umbilical cultures obtained, but only 29 neonatal peripheral cultures were drawn. The incidence of clinically significant false-positive UCBCs was 0.5%. In addition, the single case of true bacteremia was detected in both the UCBC and peripheral

venous blood culture. This study demonstrates that contamination of UCBC can be avoided by meticulous attention to sterile technique. The authors concluded from this study that umbilical cord blood may prove to be a satisfactory alternative to infant blood culture for the evaluation of neonatal bacteremia. Due to the small number of neonatal cultures that were available for comparison to umbilical cultures, the researchers determined that it would be statistically difficult to conclude that umbilical cord blood cultures were a valid alternative. A larger prospective study to document the sensitivity and specificity would be required to determine suitability of this method.

An original paper published by Hansen et al. (2005) addressed the potential substitution of cord blood for infant blood in the neonatal sepsis evaluation. Paired samples of umbilical cord blood and infant peripheral venous blood from 113 infants were compared, assessing the correlation of CBC differential white blood cell counts and blood culture results. The population of this study included only term infants. All 113 cord and infant blood culture results were negative. Therefore, the false-positive blood culture rate was zero. The false-negative blood culture rate is not measurable as there were no positive cultures. Spearman's correlation of the I:T ratio between cord and infant blood was 0.32 ($p=0.0001$). The 0% false-positive blood culture result is consistent with the only other two published studies on the subject (Costakos et al., 2009; Polin et al., 1981) and strongly contradicts the impression that UCBCs have an unacceptably high false-positive rate. The limitations of this study are that there were no positive cultures to assess the cord blood for false-negative results. Nevertheless, this was not the goal of the study because it was not the concern raised by clinicians who were skeptical of cord blood testing. The study was also limited to term infants. These researchers concluded that cord blood could be safely substituted for infant blood in sepsis evaluations of asymptomatic

term infants based on both the low false positive cord blood culture rate and the significant association between I:T ratios in cord and infant blood.

An unpublished study conducted by Beeram et al. (2000) evaluated the validity of umbilical cord blood sampling for CBC and blood cultures as compared to infant's blood that was obtained from a peripheral site for the purpose of GBS sepsis screening in both term and preterm newborns. The conclusions of this study were that the CBC results, which are required for GBS screening, were similar from cord blood and infant blood samples. Only three infants had positive cultures (one cord blood sample and two infant blood samples). There were no cases where both cord and infant blood cultures were positive. None of the samples grew GBS. In one infant, the cord blood sample grew microaerophilic streptococci. In the other infant, the peripheral sample grew coagulase negative staphylococci. Both were considered contaminants. In a third case, the neonatal culture grew *Escherichia coli*. This study provided support for the proposition that contamination of carefully prepared cord blood samples for culture is uncommon (0.6%). The authors concluded that cord blood could be used for GBS sepsis screening, which would avoid inflicting pain and trauma to neonates and save significant professional time. In order to recommend a change in the blood sampling source (umbilical blood versus infant peripheral site) for evaluation of sepsis, a large, paired sample population of term and preterm infants would be required to ensure that both sample sources yield similar results.

In a published paper, Costakos et al. (2009) proposed the process of testing for GBS using umbilical cord blood. In their first 130 umbilical blood cultures and in their subsequent surveillance strategies, the false-positive rate was 3.8%, which they report as being similar to the

other two published studies. Additionally, there were no false-negative cord blood cultures reported.

Blood Culture and Complete Blood Count

The blood culture is the gold standard for detection of bacteremia (Gonsalves et al., 2009). Over the past 20 years culture media and automation of instruments have been refined in an attempt to shorten the time to detection of infection, as well as increase the yield from a sample. One of the advances in technology has been continuously monitored automated blood culture systems that are in widespread clinical use. In adults, the most important factor influencing yield is the volume of blood for culture. Nevertheless, extrapolating adult literature data to children is problematic. Withdrawing large amounts of blood from a neonate can be challenging and may also lead to a necessary blood transfusion. The most widely accepted recommendation for sample size for culture from small children is 0.5-1.0 ml of blood. (Schelonka et al., 1996).

Schelonka et al. (1996) conducted a study to determine the minimum volume of blood and the absolute number of organisms required for detecting bacteria using the BacT/Alert, Organon Teknika system. According to this study, if a 0.5 ml sample of blood is inoculated into the culture bottle, the prediction is an 81% ability to detect bacterial growth. The authors of this study concluded that blood culture yield would be improved in neonates by obtaining 1 to 2 ml of blood for culture.

Clinical decision-making and patient care is greatly affected by blood culture contamination. The presence of microbial contaminants results in longer hospital stays, unnecessary antibiotic therapies, and additional blood testing. Extra cost is incurred by the

hospital and the lab. According to Gonsalves, although many factors can influence blood culture yield, blood volume is the single most important factor (Gonsalves et al., 2009).

The optimal volume of blood to be drawn from infants and children has not been absolutely determined, but retrospective data indicates the presence of a direct relationship between the volume of blood cultured and bacteremia detection. Gonsalves et al. (2009) conducted a study that determined that the blood culture contamination rate was inversely correlated with the blood volume of the culture. Limitations to this study included study design, as this was a retrospective study. Only a portion of the total blood cultures drawn during the time period were analyzed, which could contribute to bias in interpretation of these results.

For infants and children, blood sampling by venipuncture can be difficult. Smaller-volume blood samples can be submitted from children. This is offset to some extent because the level of bacteremia is usually higher in infants and children. Inappropriately large (> 5 ml) or small (< 0.5 ml) amounts of blood inoculated into blood culture bottles can affect isolation rates because of altered blood/broth ratios. Connell et al. (2007) conducted a study to determine the volume of blood submitted for culture in routine clinical practice. Results from Cornell's research supported the proposition that in routine clinical practice a large proportion of negative blood cultures were almost inevitable because of the submission of an inadequate volume of blood. Of 1358 blood cultures, 169 contained less than 0.5 ml of blood. Of 859 blood cultures submitted in a pediatric culture bottle, 77 were inadequate (8.9%) because they were submitted with a volume greater than 5 ml. According to this study, blood cultures that were submitted with appropriate volume were more likely to yield a positive culture than those with inadequate volume.

A complete blood count (CBC) with differential is the most commonly ordered test to evaluate newborns at risk for sepsis. The American Academy of Pediatrics endorses the CDC guidelines for early-onset GBS prevention (Newman et al., 2010). These recommendations included collection of blood for a CBC for high risk infants. A retrospective cross-sectional study conducted by Newman et al. (2010) indicated that among newborns with infection, mean white blood counts (WBCs) were 29% lower, mean absolute neutrophil counts (ANCs) were 39% lower, and I:T ratios were 133% higher than in those newborns who were not septic. Both WBC and ANC counts were associated with increased risk of sepsis only when they were low. Very high values for both WBC and ANC counts, although not worrisome, are not reassuring.

Prevention and Management of Neonatal Pain

Clinical work with infants is enhanced when strategies are congruent with an established theory which enhances understanding of infant development. Sensory, cognitive, and social capacities of infants have been the center of much work over the last ten years. The focus of the synactive theory of development is on the continuous interaction of the various subsystems within the infant and interaction with the environment.

The synactive theory of infant development provides the viewpoint that the stressful environment of the neonatal intensive care unit (NICU), caused by light, sound, activity, and care giving techniques, is constantly impinging on the neurobehavioral infant development. The infant is continuously striving towards internal balance within this hostile environment. Each infant is not only the recipient of care, but is an active participant in caregiving. The caregiver who acknowledges pain should modify interventions in order to limit or prevent the infant's pain (Als, 1982). The professional caregiver understands the goals of the infant and modifies

approaches to care giving to achieve internal, pain-free neonatal equilibrium (Franck & Lawhon, 1998).

Caregivers may be required to perform painful or uncomfortable procedures in order to ensure the infant's well-being. Although a painful procedure may be necessary for the infant's health or survival, there are significant interventions which can decrease the potential negative effects of the tests or procedures. The care approach should be individualized and developmentally supportive, incorporating respect for infant development within the context of facilitation of family bonding, with necessary care provided within a context that optimizes neurobehavioral development (Franck & Lawhon, 1998). The implementation of environmental strategies can provide a preventative approach for minimizing an infant's pain and stress, while maximizing the infant's ability to regulate and cope with the stressors. Recognition of the impact of the environment on the infant's developing brain will relate to the prevention or lessening of pain, which subsequently promotes neurobehavioral development (Franck & Lawhon, 1998).

According to Gardner, Hagedorn, and Dickey (2006), an alteration in brain development and maldevelopment of sensory systems can occur when distorted or inappropriate sensory input occurs during a critical period in development. Because of a neonate's memory, painful experiences increase sensitivity to subsequent medical encounters. These initial experiences may affect the development of attitudes, fears, anxiety, conflicts, wishes, expectations, and patterns of interactions with others.

Stork (2006) discussed evidence that supports the proposition that pain experienced in early life may lead to an exaggerated response to painful events in the future. This phenomenon

may be a consequence of the infliction of painful stimuli during a critical period of brain development, which subsequently produces changes in the nervous system.

The American Academy of Pediatrics (AAP), the Canadian Pediatric Society (CPS), and other professional groups have issued policy, position, and consensus statements. Their position is that pain and stress are problems in the neonate. These pediatric professional societies agree that clinicians should reduce exposure to pain (Stork, 2006). The AAP policy guideline states:

> The prevention of pain in neonates should be the goal of all caregivers, because repeated painful exposures have the potential for deleterious consequences. Every health care facility caring for neonates should implement an effective pain-prevention program, which includes strategies for routinely assessing pain, minimizing the number of painful procedures performed.

Pain prevention is not only an ethical expectation, but repeated exposures to pain can have deleterious consequences. These consequences include emotional and behavioral problems, as well as learning disabilities.

Franck et al. (2006) stated that pain prevention in infants is expected by the child's parents. The purpose of a study conducted by Franck et al. (2006) was to describe parents' perceptions and feelings about their infant's pain experience and pain care in the NICU. A questionnaire was completed by 257 parents from 9 NICUs in the United Kingdom and 2 NICUs in the United States. According to their comments, parents perceived medical procedures as the major source of pain for their baby. Parents also indicated that their infant's pain affected them personally and emotionally. The findings of this study expanded knowledge about how parents perceive painful procedures and provided direction for clinical practice interventions.

Pain assessment is a necessary part of managing neonatal pain. Because of the inability to communicate, detecting and measuring a neonate's pain can be difficult. According to Batton et al. (2006) it is an expectation that care providers prevent any baby from experiencing pain if at all possible. Clearly, the simplest way to reduce pain is to reduce the number of painful procedures and minimize the number of repeat procedures after failed attempts.

Recent advances in neurobiology have established that infants experience pain. The neonatal pain-control group, as part of the Newborn Drug Development Initiative (NDDI) Workshop addressed concerns regarding pain management. In the summary of the proceedings from the Neonatal Pain-Control Group, Kanwaljeet et al. (2006) stated that caregivers must consider strategies for reducing procedural pain by avoiding or eliminating unnecessary laboratory tests. The authors also pointed out gaps in knowledge regarding pain perception, pain assessment, and consequences of pain. Clinical trials are needed to evaluate the long-term outcome measures of pain management in neonates.

Instrumentation

A data collection tool, the Umbilical Cord Blood Study Form, (Appendix A) developed by the researcher was utilized to collect data. The Umbilical Cord Blood Study Form was completely de-identified and compared the complete blood count I:T ratio and blood culture results from the umbilical cord blood and the infant blood for similarity. If there had been a positive blood culture, the organism would have been recorded. The length of time from delivery to obtaining the blood for testing was recorded for both umbilical blood and infant blood. The volume of blood obtained from each culture was recorded.

Population and Sample

A convenience sample of charts of term and preterm infants born at a large, acute-care facility in central Texas were accessed for this study. These charts were from infants who were considered at risk for infection because of maternal factors and qualified for intrapartum prophylaxis with antibiotics per CDC guidelines and were included in previously collected research data. This population was comprised of multiple ethnicities, including Caucasian, Hispanic, Asian, and African American infants.

To qualify for *inclusion* in the previously performed chart review, infants/mothers met the following criteria:

- Estimated gestational age was ≥ 36 weeks gestation and the mother had received less than 2 doses of intrapartum antibiotics for GBS prophylaxis
- Preterm infants whose estimated gestational age was ≤ 35 weeks gestation regardless of the number of doses of intrapartum antibiotics received by the mother
- Infants whose mother had presumed or documented chorioamnionitis
- Infants with a CBC and blood culture obtained from the neonate (standard practice)
- Infants with an additional CBC and blood culture obtained from the umbilical cord

Neonates were *excluded* from the previous study for the following reasons:

- Difficulty in obtaining cord blood for any reason
- Inability to obtain sufficient amount of blood from the neonate

This study used a sample size of 165 participants. The effect size was 0.23. Significance (alpha) was set at 0.05. The power estimated was .832.

Implementation

Project Objectives

Three objectives were constructed in order to provide the essential information needed to answer the research questions. These objectives were the guide for the investigator throughout the implementation of the project.

1. Determine the validity of using umbilical cord blood as an alternative to infant blood for the evaluation of neonatal group B streptococcus sepsis in newborn infants.
2. Compare the difference in length of time from delivery to obtaining an umbilical cord blood culture and the length of time from delivery to obtaining an infant blood culture.
3. Assess the volume of blood obtained for blood culture from the umbilical cord and compare this to the volume of blood obtained from the infant.

Methodology

Study design. This project used a retrospective review of previously collected data to compare umbilical cord blood to infant blood for the purpose of sepsis evaluation. Paired samples of the I:T ratio, blood culture results, volume of blood collected, and time from delivery to sample collection were assessed. Approval for the project was obtained from the hospital Institutional Review Board (Appendix B) and Texas Woman's University Institutional Review Board (Appendix C).

Data collection. Data for this study was extracted and de-identified onto a paper data collection tool (Appendix A) from a paper data collection tool that was used to previously retrieve data from the charts of term and preterm infants who were born at this large acute care facility in central Texas. Feasibility was not required, as this study only involved a retrospective review of previously collected research data. Data was then entered into the Software Package

for Social Sciences (SPSS), version 17, program on the researcher's laptop computer. To ensure correct data entry, every tenth chart underwent a second review by a data collection assistant.

Statistical analysis. The agreement between the umbilical cord blood sample and infant sample with respect to the I:T ratio was measured using Spearman rho correlation of coefficients. The length of time from birth to sample collection and volume of blood obtained were assessed by comparing medians using the Wilcoxon Signed Ranks test. McNemar χ^2 was the statistical test that was planned to be used to compare blood culture results. Because there were no positive blood culture results in either sample, this test could not be used to evaluate positive and negative blood culture results. An overview of the statistical analysis is presented in Appendix D.

Project Timeline

The timeline for this project was from October 2010 to May 2011 and is summarized in Appendix E. Data collection began in March 2011, once approval was granted by the hospital Institutional Review Board (IRB), TWU Institutional Review Board (IRB) and by the university DNP faculty. Statistical analyses were initiated once data was collected and compiled in March 2011. Final results of the project were presented to the DNP faculty and students in May 2011. A poster and podium presentation of the results was presented at the DNP Scholarly Projects and Poster Presentation on April 29, 2011.

Project Requirements and Resources

The large acute-care facility in central Texas that was the site of the study provided support of the study through the Institutional Review Board (IRB) approval of the study (Appendix B). Texas Woman's University provided support of the study through the Institutional Review Board (IRB) approval of the study (Appendix C). Appropriate steps were

taken to protect the rights and welfare of the participants and to preserve anonymity through de-identification of all records accessed for this study. Following the IRB approvals, the primary investigator implemented the following protocol.

1. Eligible participants were identified and assigned a unique identifier by the data collection assistant from previously collected research data collection paper tools.
2. The de-identified data extracted from the previously collected research data were entered on the data collection tool for this study (Appendix A).
3. All completed data collection tools were placed in a 10" x 13" manila envelope. Identifying information was removed from the previously collected research data to protect the anonymity of the participants. The data was stored in a locked drawer in a locked office. The key to this drawer storage was secured by the investigator.

The study site was a large acute care hospital in Bell County, Texas. Hospital support consisted of approval of the project and consent to allow use of previously collected research data. The personnel and support for the project consisted of the data collection assistant and the nurse practitioner. The support needed from the hospital site was the cooperation of the primary investigator of the previously collected research data to allow use of the data and approval of the facility that is the site of the study.

In addition to IRB approval, Texas Woman's University provided support of this project through the student's Capstone committee review with approval. Throughout the course of the study, a statistician was consulted.

Evaluation and Recommendations

This project investigated four research questions. The first research question addressed the comparison of umbilical cord blood and infant blood (independent variables) for I:T ratio (dependent variable) for the purpose of sepsis evaluation. The results of this project indicated that there is a statistically significant moderate correlation between umbilical cord blood and infant blood I:T ratio (*Spearman Rho* = .536, p = .001, N= 165).

The second research question addressed the comparison of umbilical cord blood and infant blood (independent variables) for blood culture (dependent variable) for the purpose of sepsis evaluation. All cultures were negative and there were no positive cultures in either sample. Therefore, with this sample, the McNemar chi square test could not be used and was unable to determine if there was statistical significance. Umbilical cord blood and infant blood were equivalent in being negative predictors. There were no false positive results in this study.

The third research question addressed the comparison of umbilical cord blood and infant blood (independent variables) on length of time from birth to sample collection (dependent variable). As illustrated in Table 1, the results of this project indicated that there is a statistically significant difference (p<0.001) with umbilical cord blood requiring less time from birth to laboratory analysis than infant blood.

Table 1

Comparison of volume and time of umbilical cord blood versus infant blood

Measure	Umbilical Cord Blood		Infant Blood		Statistics		
	M	*SD*	*M*	*SD*	*Wilcoxon z*	*p*	*Effect size*
Culture volume	1.84	0.68	1.05	0.23	-5.822	<0.001	.45 (medium)
Time from delivery	36.92	31.07	56.05	36.29	-9.526	<0.001	.74 (large)

Note: N=165

The fourth question addressed the comparison of umbilical cord blood and infant blood (independent variables) on volume of blood obtained (dependent variable). As illustrated in Table 1, the results of this project indicated that there is a statistically significant difference ($p<0.001$) with umbilical cord blood achieving higher volume than infant blood.

Study Population

The study site was chosen for the convenience of the sample of previously collected data. The number of charts reviewed was 165. Effect size was .23. Power was .832. Alpha was 0.05. Since there were no positive cultures, a sample from a site with potential positive cultures is recommended. The population of this study was paired samples with umbilical cord blood and infant blood from the same infant for comparison. The sample consisted of multiple ethnicities.

End Products

A study of the use of umbilical cord blood as an alternative to infant blood for the evaluation of neonatal sepsis was completed to assess the validity of substituting umbilical cord blood for infant blood in diagnosing infection. There were no positive blood cultures so with this population there was an inability to determine if there was statistical significance. Nevertheless, there were no false positive results, and none of the infants with negative cultures became ill. Because a moderate statistical correlation exists between the complete blood count I:T ratio and because umbilical cord blood can be obtained in sufficient volume within a shorter time period, umbilical cord blood could become an accurate and preferred site for blood sampling in the evaluation of neonatal GBS infection. Utilizing umbilical cord blood would spare the infant a painful procedure, spare the family distress, provide improved utilization of time for healthcare providers, and allow earlier initiation of necessary treatment.

The sponsoring university and the hospital located in Bell County will receive copies of the completed study and results comparing umbilical cord blood to infant blood for the purpose of neonatal sepsis evaluation. Based on the study findings, the hospital will be able to change the standard of practice for method of obtaining blood for sepsis evaluation.

Conclusion

The results of this project revealed no significant difference between I:T ratio of blood taken from the umbilical cord and blood taken from the infant. Therefore, the I:T ratio of blood drawn from the umbilical cord is an effective diagnostic option to that of infant blood. All blood culture results were negative. Therefore, the researcher was unable to determine statistical significance in the comparison of positive cultures from umbilical cord blood and infant blood. There were no false positives, which is similar to results reported in other published studies. A repeat study is recommended in a population where there would be positive blood cultures to determine if both types of samples yield the same blood culture results.

Umbilical cord blood, instead of infant blood, should be the option when tests are sensitive to volume of the blood sample. Umbilical cord blood, instead of infant blood should be the option when decreased time for sample collection is required. This project also adds to the literature regarding use of umbilical cord blood as an alternative to infant blood for the purpose of group B streptococcus sepsis evaluation.

References

Als. H. (1982). Toward a synactive theory of development: A promise for the assessment and support of infant individuality. *Infant Mental Health Journal, 3,* 229-243.

American Academy of Pediatrics. (2006). Prevention and management of pain in the neonate: An update. *Pediatrics, 118*(5), 2231-2241.

Batton, D.G., Barrington, K. J., &Wallman, C. (2006). Prevention and management of pain in the neonate: An update. *Pediatrics, 118,* 2231.

Beeram, M. R. (2000). *Utilization of umbilical cord blood for complete blood count (CBC) and blood cultures in group B streptococcal (GBS) sepsis screening.* Abstract presented at the Pediatric Academy Societies & American Academy of Pediatrics Joint Meeting, Boston, MA.

Beeram, M. R., Loughran, C. L., Krauss, D. R., & Riggs, M. (2000). *Umbilical cord blood for the evaluation of infection.* Unpublished manuscript. Pediatrics, Scott & White Clinic/ Texas A&M Health Sciences Center, Temple, TX.

Centers for Disease Control and Prevention: Early-Onset and Late-Onset Neonatal Group B Streptococcal Disease-United States, 1996-2004. *MMWR Morbidity and Mortality Weekly Report 2005*, *54*(47), 1205-1208.

Centers for Disease Control and Prevention: Prevention of perinatal group B streptococcal disease: Revised guidelines from CDC. *MMWR Morbidity Mortality Weekly Report 2007*, *56*(28), 1-22.

Centers for Disease Control and Prevention: Prevention of perinatal group B streptococcal disease: Revised guidelines from CDC. *MMWR Morbidity Mortality Weekly Report 2010*, *59*(RR10), 1-32.

Connell, T. G., Rele, M., Cowley, D., Buttery, J. P., & Curtis, N. (2007). How reliable is a negative blood culture result? Volume of blood submitted for culture in routine practice in a children's hospital. *Pediatrics, 119,* 891–896. doi:10.1542/peds.2006-0440

Costakos, D., Walden, J., Rinzel, M., & Dahlen, L. (2009). Painless blood testing to prevent neonatal sepsis. *Wisconsin Medical Journal, 108*(6), 321-322.

Edwards, M. S. (2006). Postnatal bacterial infections. In R. J. Martin, A. A. Fanaroff, & M. C. Walsh, (Eds). *Fanaroff and Martin's neonatal-perinatal medicine: Diseases of the fetus and infant: Vol. 2.* (8th ed., pp.791-804). Philadelphia, PA: Mosby Elsevier.

Franck L. S., Allen, A., Cox, S., & Winter, I. (2006). Parents' views about infant pain in neonatal intensive care. *Clinical Journal of Pain, 21,* 133.

Franck, L. S., & Lawhon, G. (1998). Environmental and behavioral strategies to prevent and manage neonatal pain. *Seminars in Perinatology, 99*(5), 434-443.

Gardner, S. L., Hagedorn, M. I. E., & Dickey, L. A. (2006). Pain and pain relief. In Merenstein, G.B., & Gardner, S. L. (Eds). *Handbook of neonatal intensive care.* (6th ed., pp. 223-272). St. Louis, MA: Mosby Elsevier.

Gonsalves, W. I., Cornish, N., Moore, M., Chen, A., & Varman, M. (2009). Effects of volume and site of blood draw on blood culture results. *Journal of Clinical Microbiology, 47*(11), 3482-3485. doi:10.1128/JCM.02107-08

Hansen, A., Forbes, P., & Buck, R. (2005). Potential substitution of cord blood for infant blood in the neonatal sepsis evaluation. *Biology of the Neonate, 88,* 12-18. doi:10.1159/000083946

Kanwaljeet, J. S., Anand, D., Aranda, J. V., Berde, C. B., Buckman, S., Capparelli, E. V…&Walco, G. A. (2006). Summary proceedings from the neonatal pain-control group. *Pediatrics, 117*(3), S9-S22.

Merriam-Webster (1994). Springfield, MA: Merriam-Webster.

Mohan, V., Merenstein, G. B., Adams, K. M., &Weisman, L. E. (2006). Infection in the neonate. In G. B. Merenstein, & S. L. Gardner (Eds). *Handbook of neonatal intensive care* (6th ed., pp. 582-585). St. Louis, MO: Mosby Elsevier

Nandyal, R. R. (2008). Update on group B streptococcal infections: Perinatal and neonatal periods. *Journal of Perinatal and Neonatal Nursing, 22*(3), 230-237.

Newman, T. B., Puopolo, K. M., Wi, S., Draper, D., & Escobar, G. J. (2010). Interpreting complete blood counts soon after birth in newborns at risk for sepsis. *Pediatrics, 126*(5), 903-909. doi:10.1542/peds.2010-0935

Ohlsson, A. & Shah, V. (2009). Intrapartum antibiotics for known maternal group B streptococcal colonization. Retrieved from *Cochrane Database of Systematic Reviews* 2009, Issue 3. Art. No.: CD007467.doi: 10.1002/14651858.CD007467.pub2

Polin, J., Knox, I., Baumgart, S., Campman, E., Mennuti, M., & Polin, R. (1981). Use of umbilical cord blood culture for detection of neonatal bacteremia. *Obstetrics and Gynecology, 57*(2), 233-237.

Schelonka, R. L., Chai, M. K., Yoder, B. A., Hensley, D., Brockett, R. M., & Ascher, D. P. (1996). Volume of blood required to detect common neonatal pathogens. *Journal of Pediatrics, 8*(129), 275-278.

Stork, J. E. (2006). Anesthesia in the neonate. In R. J. Martin, A. A. Fanaroff, & M. C. Walsh, (Eds). *Fanaroff and Martin's Neonatal-perinatal medicine: Diseases of the fetus and infant: Vol. 1*. (8th ed., pp.630-631). Philadelphia, PA: Mosby Elsevier.

Appendix A

UMBILICAL CORD BLOOD STUDY FORM

Case Number: _____Gestational Age:_____weeks

Umbilical Cord Blood Sample:

CBC:
I:T Ratio:_____

Blood Culture: □Negative □Positive
Organism: □ Group B Streptococcus
□ E Coli
□ Haemophilus Influenza
□ Other_____
□ None

Volume of Blood Obtained:_____ml
Time of Culture from Delivery:_____min

Neonatal Blood Culture:

CBC:
I:T Ratio:_____

Number of Neonatal Blood Cultures:_____

Blood Culture #1: □Negative □Positive
Organism: □ Group B Streptococcus
□ E Coli
□ Haemophilus Influenza
□ Other_____
□ None

Volume of Blood Obtained:_____ml
Time of Culture from Delivery:_____min

Blood Culture #2: □Negative □Positive
Organism: □ Group B Streptococcus
□ E Coli
□ Haemophilus Influenza
□ Other_____
□ None

Volume of Blood Obtained:_____ml
Time of Culture from Delivery:_____min

Appendix B

Scott & White Institutional Review Board
Federalwide Assurance #FWA00003358
IRB Registration #IRB00000706

Notification of IRB Action

To: Teresa Baker, MS/sDNP cc: Madhava Beeram
OSRA

Project ID: 110020

Title: Umbilical Cord Blood as Alternative for Infant Blood In Neonatal Sepsis Evaluation

Level of Review: Expedited
Expedited Review Category: 45 CFR 46.110(b)(1)(5)

Type of Action: Approval

Date of Action: 2/1/2011

Pediatric Category: 45 CFR 46.404 *(Research not involving greater than minimal risk)*

Approval period: 2/1/2011 to 1/31/2012

Continuing review deadline: 12/30/2011*

***You are responsible for ensuring IRB approval is obtained for the continuation of your project by submitting the required progress report and supporting documentation by the continuing review deadline.**

Items reviewed: Submission reference #: 026577
1. Initial Review Submission Form Version 1.0
2. Application Version 1.0
3. Research plan Version 1.0

*****Please ensure the IRB approval letter from TWU is submitted via a study update in iRIS once it is received.***

Waiver of consent/authorization: The IRB has waived the requirement for informed consent based on 45 CFR 46.116 (d). The IRB has 1) waived the requirement for authorization based on 45 CFR 164.512 (2) (ii) and 2) determined the use of existing protected health information is necessary to do the research.

Please be advised that in addition to obtaining IRB approval, you must ensure all contractual and budgetary issues are resolved prior to initiating your research.

2401 S. 31st St., Temple, Texas 76508 Phone: 254-215-9030/9031 Fax: 254-215-9061

Appendix C

TWU
TEXAS WOMAN'S UNIVERSITY
DENTON DALLAS HOUSTON

Institutional Review Board
Office of Research and Sponsored Programs
P.O. Box 425619, Denton, TX 76204-5619
940-898-3378 FAX 940-898-4416
e-mail: IRB@twu.edu

March 8, 2011

Ms. Teresa Z. Baker
3525 Centennial Drive
Belton, TX 76513

Dear Ms. Baker:

Re: Umbilical Cord Blood as Alternative for Infant Blood in Neonatal Sepsis Evaluation (Protocol #: 16577)

The above referenced study has been reviewed by the TWU Institutional Review Board (IRB) and was determined to meet requirements in regard to protection of individuals' rights and is exempt from further review.

Any modifications to this study must be submitted for review to the IRB using the Modification Request Form. Additionally, the IRB must be notified immediately of any unanticipated incidents. If you have any questions, please contact the TWU IRB. The Institutional review board is pleased to acknowledge your sense of responsibility for ethical research.

Sincerely,

Suh-Jen Lin

Dr. Suh-Jen Lin, Chair
Institutional Review Board - Dallas

cc. Dr. Stephanie Woods, College of Nursing - Dallas
Dr. Peggy Mancuso, College of Nursing - Dallas
Graduate School

Appendix D

Statistical Analysis

Questions	Independent Variable	Dependent Variable	Operational Definition	Statistical Test	Power Analysis	Results
1. In newborns, is the use of umbilical cord blood a valid alternative to infant blood, in the evaluation of group B streptococcus sepsis through I:T ratio?	IV#1:Umbili-cal Cord Blood IV #2: Infant Blood	DV: I:T Ratio	IV#1: Umbilical Cord Blood →Blood drawn either from a vein or an artery of a segment of umbilical cord that has been clamped on both ends, separated from the placenta and the infant. IV#2: →A specimen of blood that has been obtained systemically from an infant. DV: I:T Ratio →The ratio of the immature to total granulocytes as defined by I ÷T to obtain a decimal value	Spearman Rho correlation of coefficients	Sample size, N=165 Effect size = .23 Alpha = 0.05 Power = .832	Assumption of normality not met. *Spearman Rho* = .536, *p* = .001, *N*= 165

Questions	Independent Variable	Dependent Variable	Operational Definition	Statistical Test	Power Analysis	Results
2. In newborns, is the use of umbilical cord blood a valid alternative to infant blood, in the evaluation of group B streptococcus sepsis through blood culture?	IV#1:Umbili-cal Cord Blood IV #2: Infant Blood	DV: Blood culture results (+versus-)	IV#1: Umbilical Cord Blood →Blood drawn either from a vein or an artery of a segment of umbilical cord that has been clamped on both ends, separated from the placenta and the infant. IV#2: →A specimen of blood that has been obtained systemically from an infant. DV: Blood culture results → Results of positive or negative for microorganisms growing in the sample of blood taken for culture sample, as reported by the laboratory.	McNemar Chi Square	Sample size, N=165 Effect size = .23 Alpha = 0.05 Power = .832	Assumption of normality not met. Unable to determine due to no positive blood cultures in either sample.

Questions	Independent Variable	Dependent Variable	Operational Definition	Statistical Test	Power Analysis	Results
3. Is there a significant difference in length of time from delivery to obtaining umbilical cord blood sample as compared to the length of time from birth to sample collection?	IV#1:Umbili-cal Cord Blood IV #2: Infant Blood	DV: Time measured in minutes from birth to sample collection	IV#1: Umbilical Cord Blood →Blood drawn either from a vein or an artery of a segment of umbilical cord that has been clamped on both ends, separated from the placenta and the infant. IV#2: →A specimen of blood that has been obtained systemically from an infant. DV: Time measured in minutes from birth to sample collection → length of time from birth to time of sample collection.	Wilcoxon Signed Ranks Test	Sample size, N=165 Effect size = .23 Alpha = 0.05 Power = .832	Assumption of normality not met. Wilcoxon z score=-5.822 *N*=165, <.001 (mean = 36.9 SD =31.07), (mean 56.05 SD = 36.29)

Questions	Independent Variable	Dependent Variable	Operational Definition	Statistical Test	Power Analysis	Results
4. Is there a significant difference in the volume of blood taken from the umbilical cord for blood culture compared to the volume obtained from the infant?	IV#1:Umbili-cal Cord Blood IV #2: Infant Blood	DV: Volume of blood measured in ccs taken for blood culture	IV#1: Umbilical Cord Blood →Blood drawn either from a vein or an artery of a segment of umbilical cord that has been clamped on both ends, separated from the placenta and the infant. IV#2: →A specimen of blood that has been obtained systemically from an infant. DV: Volume of blood measured in ccs taken for blood culture → the volume of blood obtained for the purpose of blood culture.	Wilcoxon Signed Ranks Test	Sample size, N=165 Effect size = .23 Alpha = 0.05 Power = .832	Assumption of normality not met. Wilcoxon z score=-9.526 *N*=165, <.001 (mean = 1.84, SD =0.68), (mean = 1.05, SD = 0.23)

	Umbilical cord		Infant		
	Mean	Std. Deviation	Mean	Std. Deviation	*p*-value
blood culture volume	1.84	0.68	1.05	0.23	<0.001
blood culture time from delivery	36.92	31.07	56.05	36.29	<0.001

Wilcoxon Signed Ranks Test

Ranks

		N	Mean Rank	Sum of Ranks
Umbilical cord I:T ratio - Infant I:T ratio	Negative Ranks	59[a]	60.22	3553.00
	Positive Ranks	52[b]	51.21	2663.00
	Ties	54[c]		
	Total	165		

a. Umbilical cord I:T ratio < Infant I:T ratio

b. Umbilical cord I:T ratio > Infant I:T ratio

c. Umbilical cord I:T ratio = Infant I:T ratio

Test Statistics[b]

	Umbilical cord I:T ratio - Infant I:T ratio
Z	-1.311[a]
Asymp. Sig. (2-tailed)	.190

a. Based on positive ranks.

b. Wilcoxon Signed Ranks Test

Correlations

			Infant I:T ratio	Umbilical cord I:T ratio
Spearman's rho	Infant I:T ratio	Correlation Coefficient	1.000	.536**
		Sig. (2-tailed)	.	.000
		N	165	165
	Umbilical cord I:T ratio	Correlation Coefficient	.536**	1.000
		Sig. (2-tailed)	.000	.
		N	165	165

**. Correlation is significant at the 0.01 level (2-tailed).

Appendix E

Time Line

1. Created the Umbilical Cord Blood Study Form data collection tool in December 2010.
2. Submitted the research plan to Scott & White Hospital (S&W) Institutional Review Board (IRB) for exempt status approval in January 2011.
3. Wrote the capstone proposal and obtained approval from my Capstone committee members in March, 2011.
4. Submitted the project concept proposal to Texas Woman's University (TWU) IRB for exempt status approval in March 2011.
5. Extracted data from previously collected research data utilizing the Umbilical Cord Blood Study Form data collection tool in March 2011.
6. Submitted data collected for analysis in March 2011.
7. Submitted completed capstone paper to the Texas Woman's University committee in May 2011.
8. Presented final findings of capstone in May 2011.