EFFECTS OF AN INCREMENTAL HEALTH SYSTEMS APPROACH TO THE
MANAGEMENT OF NEONATAL HYPERBILIRUBMINEMIA.

A RESEARCH PAPER
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ABSTRACT


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Neonatal hyperbilirubinemia is a common occurrence yet it is often dismissed due to failure of clinicians to recognize the significance of jaundice. To better guide outpatient diagnosis and treatment of neonatal hyperbilirubinemia, healthcare providers should consider a systems approach to provide standardized, guidelines in initiating identification, treatment and follow-up for newborns. The purpose of this study is to evaluate the effect of pre-discharge and guided follow-up transcutaneous bilirubin measurement in the neonate to determine the effects on management of neonatal hyperbilirubinemia and prevention of kernicterus. This is a replication of the first part of the 2006 study by Bhutani, Johnson, Schwoebel, and Gennaro. The sample will include 1,800 infants for pre-implementation data who have been discharged from the “well-baby” nursery at a northeast Indiana hospital. The test group will include infants born in a two year period after implementation. The intervention will be routine transcutaneous bilirubin measurement to diagnose clinical jaundice, along with routine serum bilirubin testing pre-discharge, and use hour specific, percentile based bilirubin nomogram. Findings will provide information for clinicians in the application of evidence based practices that incorporate a systems approach to prevent complications of neonatal hyperbilirubinemia.
Chapter I

Introduction

Most people in the United States are at least minimally aware of newborn jaundice and may have known someone, or had a child of their own that had a slight case of jaundice shortly after birth. However, far less common is the devastating consequence of severe neonatal hyperbilirubinemia called kernicterus, or acute bilirubin encephalopathy (ABE). Kernicterus is a form neuropathology caused by the neurotoxic effects of bilirubin upon the brain. Kernicterus is characteristically identified by icteric staining within the basal ganglia of the brain, discovered through autopsy or an MRI. Kernicterus can have a myriad of effects from death secondary to respiratory failure, seizures, hearing loss, hypertonia of the muscles, behavioral problems, and staining of the primary teeth (Bhutani, Vilmis, & Hamerman-Johnson, 2010).

The actual incidence of kernicterus in the United States is not known, and at the time of this publication, there is no national reporting registry. Even the U.S. Preventive Services Task Force is unable to provide accurate data on its incidence describing, “kernicterus, a rare condition traditionally diagnosed at autopsy” (US Preventive Services Task Force, 2009). However, nearly 80% of neonates experience hyperbilirubinemia according to Bhutani, et al. (2010). Bhutani et al. (2010) further broke down the incidence and severity into percentiles based on total serum bilirubin levels:
### Table

<table>
<thead>
<tr>
<th>Adjective</th>
<th>TSB level</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Significant</td>
<td>&gt;17mg/100mL</td>
<td>8.1-10%</td>
</tr>
<tr>
<td>Severe</td>
<td>&gt;20mg/100mL</td>
<td>1-2%</td>
</tr>
<tr>
<td>Extreme</td>
<td>&gt;25mg/100mL</td>
<td>0.16%</td>
</tr>
<tr>
<td>Hazardous</td>
<td>&gt;30mg/100mL</td>
<td>0-0.032%</td>
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(Bhutani, et al., 2010).

Another important factor in the incidence of newborn jaundice and kernicterus is that bilirubin levels peak between three to four days after birth. This is a time when many infants have already been released from the hospital. The average hospital stay after an uncomplicated vaginal birth in the United States is 2 days or 48 hours after delivery (De Luca, Carnielli, & Paolillo, 2009). This does not allow for elevated levels of bilirubin to be manifested in the neonate prior to discharge. Instead, the burden falls upon the practitioners in the outpatient setting to observe and monitor for this potential pathology. The outpatient practitioner may not have access to transcutaneous bilirubin measurements and is less likely to order serum bilirubin lab assessment than in the inpatient setting (Petrova, Mehta, Birchwood, Ostfeld, & Hegyi, 2006). This puts the infant at increased risk of severe hyperbilirubinemia due to delay of treatment and thereby increased risk of complication such as kernicterus.

**Background and Significance**

Historically, the United States has not closely monitored the incidence of acute bilirubin encephalopathy, or kernicterus. However, enough infants have experienced this potentially preventable form of neurological encephalopathy that their families have come forward and created an online support group, prompting the researchers Bhutani, Johnson, Schwoebel, and Gennaro (2006) to formulate a plan to help reduce the incidence of kernicterus. The research of Bhutani, et al. (2006) was supported by the American Academy of Pediatrics (AAP).
recommendations regarding measurement of bilirubin pre-discharge, or assessment for risk factors, or a combination of the two in order to identify infants at higher risk of development of severe hyperbilirubinemia. The researchers felt that by using the AAP recommendations as a guideline, they could further expand upon the recommendations by incorporating a systems based approach. This included allowing the nurses to obtain serum or transcutaneous bilirubin measurements, routine bilirubin measurement, and follow-up appropriate for risk group. The researchers also utilized an hour specific nomogram in order to evaluate the neonates’ bilirubin level to determine specific risk (Bhutani, et al., 2006).

Bhutani et al. (2006) found that by implementing their systems based approach, they reduced the number of infants whose bilirubin levels rose to dangerous levels of >25mg/dl. By identifying and treating infants at risk sooner, the researchers proved that their system helps to keep infants safe and prevent adverse effects from hyperbilirubinemia.

Problem Statement

Neonatal hyperbilirubinemia is a common occurrence yet it is often dismissed due to failure of clinicians to recognize the significance of jaundice. If left untreated, hyperbilirubinemia can lead to the more significant problem of kernicterus which can cause an increase in mortality as well as long term implications to the neonate’s health. To better guide outpatient diagnosis and treatment of neonatal hyperbilirubinemia, healthcare providers should consider a ‘systems’ approach to provide standardization of guidelines in initiating identification, treatment and follow-up for newborns.
**Purpose of the Study**

The purpose of this study is to evaluate the effect of pre-discharge and guided follow-up transcutaneous bilirubin measurement in the neonate to determine the effects on management of neonatal hyperbilirubinemia and prevention of kernicterus.

**Research Question**

What is the effect of incorporating transcutaneous bilirubin measurement prior to discharge and at four to five days of age for term infants on identification and management of neonatal hyperbilirubinemia?

**Conceptual Theoretical Framework**

A ‘systems’ approach for the treatment of neonatal hyperbilirubinemia is based on the work of Betty Newman and her Systems Model (Reed, 1993). Newman’s theory describes individuals as being in a state of flux within their environment from the constant interactions with other individuals, stressors within the environment, and numerous variables interacting with the individual. An individual experiences illness when these forces cause the individual to fall out of a balanced state within their environment, this is due to the lack of the individual to be able to compensate for the shift within their environment (Tomey & Alligood, 2006). This theoretical approach demonstrated the needs of the researchers, Bhutani, et al. (2006) in finding a methodology to reduce the incidences of severe effects of neonatal hyperbilirubinemia by utilizing all available resources and changing the normal approach to care of the infant. This is important as hospitalizations are becoming shorter and the time spent with the newborn infant in hospital is shifting toward more out-patient based. In the outpatient setting it becomes more critical to quickly recognize symptoms and identify and treat neonatal hyperbilirubinemia.
Limitations

The limitation of this study will be its small sample size and short duration in comparison to the original study, and confinement to one geographical location. This will make the results of the study difficult to generalize to the entire United States population. Participants of the study will include all infants that meet the criteria of the study at the selected location. This does offer some randomization in that it is unknown what the number, and the diversity of the infants yet to be born at the location will be.

Assumptions

The consequences of increased bilirubin within the body are highly individualized and no two individuals will react in the same manor to similar levels of bilirubin within the blood. This is due to such factors as binding capacity of albumin, and numerous other internal and external variables. According to Bhutani, et al. (2006) there is no specific safe and definitively danger zones in which to classify infants. Furthermore a serum or transcutaneous bilirubin level alone without consideration of other risk factors cannot accurately predict the incidence of kernicterus. Therefore the study will always place the safety of the neonate as top priority. If a neonate is displaying signs of kernicterus or has a level of bilirubin above the recommendation by the AAP in concurrence with one or more risk factors, the physician will be notified immediately and emergent care sought as necessary per the judgment of the nurse assessing the neonate.

Summary

Prevention of the incidence of kernicterus is important in the undertaking of this replication research study. Researchers Bhutani, et al. (2006), found the transcutaneous measurement of bilirubin in the neonate incorporated with a ‘systems’ based approach helped to improve patient safety and prevent hyperbilirubinemia complications. It is important that this
research be replicated in order increase generalizability of the findings to the United States population as a whole, and further validates their findings.
Chapter II
Literature Review

Introduction

Neonatal hyperbilirubinemia continues to exist within the community. According to the Centers for Disease Control (2013), approximately 60% of infants exhibit some form of hyperbilirubinemia or jaundice. If severe hyperbilirubinemia is left untreated in the infant, it can lead to death or brain damage called Kernicterus. Kernicterus is a highly preventable outcome. It has been noted in nearly all cases of kernicterus that there was a demonstrated need for early recognition and management of hyperbilirubinemia in the neonate (Bhutani, et al., 2006). The purpose of this study is to evaluate the effect of pre-discharge and guided follow-up transcutaneous bilirubin measurement in the neonate to determine the effects on management of neonatal hyperbilirubinemia and prevention of kernicterus. This study is a replication of the first part of a ten year study completed by Bhutani, et al. (2006).

The following literature review focuses on the theoretical concepts behind the original research by Bhutani, et al. (2006), as well as examines complementary and supportive research studies in a brief review. The literature review is organized into four areas recognition and risk assessment in the neonate, measurement of bilirubin levels, lactation support, and postdischarge follow up. The final study reviewed is a discussion of the original research by Bhutani et al. (2006) from which this replication study is based.

Theoretical Framework

In considering a theoretical framework for this study, it was noted that Bhutani et al. (2005) did not specifically identify a theoretical framework for their study. However, a ‘system approach’ for the treatment of neonatal hyperbilirubinemia could build upon the work of Betty
Newman and her Systems Model (Reed, 1993). Newman describes individuals as being in a state of flux within their environment from the constant interactions with other individuals, stressors within the environment, and numerous variables interacting with the individual. An individual experiences illness when these forces cause the individual to fall out of a balanced state within their environment, this is may be due to lack of the individual being able to compensate for a shift within their environment (Tomey & Alligood, 2006). This is important as hospitalizations are becoming shorter and the time spent with the newborn infant in hospital is shifting towards more outpatient based. In the outpatient setting it becomes more critical to quickly recognize symptoms and identify and treat neonatal hyperbilirubinemia.

Newman’s systems theory demonstrates how stressors experienced by the individual interact with their normal lines of defense. The degree to which these stressors affect the basic structure of the individual within their environment includes internal, external and created environments (Tomey & Alligood, 2006). Neuman describes the individual or family as a set of circles surrounding the core structure. Each line surrounding the core represents a level of defense to protect the client and maintain homeostasis (Reed, 1993). They include factors such as genetics, strenghts and weaknesses. An additional outer ring called the flexible line of defense is the first line of defense against stressors as well as improving the optimal state of wellness such as supplementation of the neonates diet of breastmilk with formula to promote weight gain, hydration and elimination of excess bilirubin from the system. The further the stressor penetrates the lines of defense the more effect they have on the wellbeing of the individual.

Neuman’s theoretical concept provides basis for a theoretical framework when planning the basis for systems based approach for neonatal hyperbilirubinemia, all components for neonatal care included in the plan by viewing the neonate as a whole when considering cause and
effects of hyperbilirubinemia. For example, the stressors as identified by Neuman may be
defined as: the internal buildup of bilirubin, potential ABO blood incompatability, method of
delivery, and/or method of nutrition and hydration. These stressors, when acting upon the infant
simultaneously, allow for further penetration of the neonate’s lines of defense and thereby cause
more damage to the core of the neonate. This ‘systems approach’ can utilize various components
within the neonate’s environment in the treatment of hyperbilirubinemia prior to needing
hospitalization. For example, the breastfed infant can be supplemented with formula, education
can be given to the parents on signs and symptoms to watch for, and the neonate at risk for
hyperbilirubinemia followed more closely by the practitioner.

**Literature Review**

**Recognition and risk assessment**

Bilirubin in the healthy newborn typically peaks between 72 and 96 hours after birth. However the hospital stay for a healthy newborn continues to decrease, resulting in a large
number of infants being discharged from the hospital and subsequently being readmitted for
hyperbilirubinemia when blood levels peak (De Luca, Carnielli & Paolillo., 2009). De Luca and
colleagues (2009) completed a meta-analysis of research literature on topics related to
hyperbilirubinemia. This review was used to compile an evidence based practice model for
jaundice management. De Luca et al. (2009) employed an evidence-based research methodology
in order to collect and review data simultaneously based on prior research and proven methods,
as well as to compile a ‘best practice’ model for practitioners.

The researchers extracted data from PubMed on studies completed between 1999 and
2008 using the search terms of “hyperbilirubinemia,” “bilirubin,” “jaundice,” and “early
discharge,” as the primary qualifiers and further refined their search to include only those studies
that contained data on neonatal readmission. The percentages of readmission ranged from nine to 74% with a total of six infants who were readmitted requiring exchange transfusion. Of those readmitted due to jaundice, the percentage of those discharged before 48 hours of age ranged from 0.01% to 7.8%. The researchers included data from multiple countries including the United States, United Kingdom, India, Canada, Israel, Spain, and France (De Luca, et al., 2009).

De Luca, et al. (2009) then appraised the most recent evidence-based practices including hour-specific nomogram to evaluate neonatal bilirubin levels with specification further into pre-term and full-term infants. They also examined research utilizing multiple hour-specific readings which further identified infants at risk for development of hyperbilirubinemia and also required treatment prior to discharge. This method allows practitioners opportunity to evaluate the actual level of bilirubin and also increase in bilirubin level between readings. This provided an opportunity to determine trends and identify those at higher risk within the population.

Upon examination of the available data De Luca et al. (2009) created an algorithm for a “jaundice prediction protocol.” The algorithm included identification of a nomogram for the population served, validation of the nomogram, measurement of transcutaneous or serum bilirubin at two different times, and calculation of the rise of bilirubin level with division into low risk or increased risk. Infants at increased risk could then be identified and should have a follow-up visit scheduled prior to discharge. Additionally, evaluation of bilirubin levels and parental education related to recognition of jaundice and complications of hyperbilirubinemia should be reinforced (De Luca, et al., 2009).

De Luca et al. (2009) also created a list of ‘practical advice’ for practitioners that included an effective list of “do not’s” such as: visual only evaluation, evaluation in days versus hours, utilization of the wrong curve for the wrong data, and forgetting ethnic and genetic
factors. An important aspect brought forth by the authors emphasized that complications from hyperbilirubinemia are rare, but they can have devastating, life-long consequences.

The researchers concluded that it is important to periodically review jaundice management protocols that help practitioners with recognition and treatment of hyperbilirubinemia. This is especially important as hospital stays are becoming shorter. Careful monitoring in-hospital as well as post discharge is necessary to prevent the severe complication of kernicterus (De Luca, et al., 2009).

Risk assessment was a key focus in the study completed by Chawla, Jain, Dhir, and Rani (2011). The objective of Chawla, et al.’s (2011) retrospective study was to evaluate effectiveness of identified clinical risk factors with transcutaneous bilirubin measurement, in order to predict the need for treatment of hyperbilirubinemia in healthy term and late preterm infants. Chawla et al.’s study population consisted of infants born at a teaching hospital in India between August and October 2009. In order to be included in the study, infants needed to be greater than 35 weeks gestation and have a birth weight of over 2000g. Exclusion from the study included: any major congenital defect, admission to the NICU, positive direct Coomb’s test, or phototherapy prior to first bilirubin measurement. Another significant exclusion fact included infants who were unable to complete a follow-up appointment after discharge. The researchers enrolled 462 infants in the study, however only 392 were able to complete the final follow-up assessment. The median gestational age of the infants who participated was 38 weeks, with 52% being male and 48% female. Ethnicity was not specifically discussed in the study findings, however it is implied that the neonates were of “East Indian” origin.

In order to maintain accuracy and eliminate variables within the study, the researchers assigned a risk score, measured serum bilirubin using an automated analyzer, as well as
measuring transcutaneous bilirubin levels using a Bilichek device. Transcutaneous measurement of bilirubin levels was the measurement of choice. This measurement was performed on all infants enrolled in the study between 18 to 42 hours of age. It was noted in the study, that if transcutaneous readings were unable to be performed due to staining with ichor, or results of the transcutaneous readings were within 2mg/dL of the phototherapy therapeutic range, the serum measurements were performed. In this region of India, Chawla et al. (2012) also noted that the incidence of glucose-6-phosphate dehydrogenase deficiency is present in all newborns unless proven otherwise by genetic screening.

The findings revealed that of the 392 neonates who completed the study, 65 developed pathological hyperbilirubinemia which required treatment. Using the assigned risk factors and transcutaneous or serum bilirubin measurements, Chawla et al. (2012) were able to correctly classify 84.9% of the subjects considered to be high risk. However, the researchers stated that non-optimal breastfeeding post discharge may have increased the neonates’ risk for hyperbilirubinemia and this risk factor was less predictable and required close follow up in the outpatient setting.

Chawla, et al. (2012) concluded that utilization of risk scoring tools greatly helps in the identification of infants at risk for developing hyperbilirubinemia requiring treatment. There was a recognized weakness noted in their study in relation to a relatively small sample of infants with a 15% loss to follow-up, which the authors acknowledge as a key factor in recognition and treatment of neonatal hyperbilirubinemia.

Gamalelaidin, et al. (2011) examined the relationship between total serum bilirubin levels in neonates and the risk factors in predicting kernicterus. The purpose was to determine the risk
of development of bilirubin encephalopathy in neonates and identify biological factors relevant to the neonates’ tolerance of hyperbilirubinemia.

This prospective cohort study was carried out in Cairo Egypt. In 2008, infants who admitted to the neonatal intensive unit at Cairo University Children’s Hospital were enrolled in the study. Exclusion criteria included: estimated gestational age of less than 34 weeks or admission weight less than 2000g, postnatal age of 14 days or younger, and total serum bilirubin (TSB) level of over 25mg/dL (Gamaleldin, et al., 2011). All infants were born at out-lying birthing facilities. This feature created a challenge and made birth history, documentation of birth weight, and gestational age difficult to obtain. There were 135 were male and 114 female infants included in the sample.

The infants had a neurological examination using a bilirubin-induced neurologic dysfunction protocol, or BIND, performed within 12 hours of their admission to Cairo University Children’s Hospital (Gamaleldin, et al., 2011). Other variables measured included admission weight, Rh incompatibility, ABO incompatibility, and sepsis through positive blood culture, elevated C-reactive protein levels, or elevated leukocyte counts (Gamaleldin, et al., 2011).

Data was analyzed using multiple logistic regression to examine the relationship between the variables and the total serum bilirubin levels upon the neurological assessment of the neonate. A limitation of this study was the lack of birth history information, unreliable direct antiglobulin testing, and a lack of long term follow-up for subtle effects of bilirubin encephalopathy such as auditory system dysfunction.

A large number of infants in this study (207) received exchange transfusion. Additionally all infants in the study were treated with phototherapy. In Gamaleldin’s et al. (2011) findings, 44 infants has moderate to severe acute bilirubin encephalopathy (ABE), 55 had subtle signs of
neurotoxicity, and 150 had no signs of ABE. At the time of discharge only nine infants had signs of continued bilirubin encephalopathy, while 26 infants had post mortem evidence of bilirubin encephalopathy. There was a positive predictive outcome in infants who had BIND scores of >6 at admission assessment and 22 out of 25 infants experienced an anticipated adverse outcome. Only three out of the 35 infants with a presenting BIND score of 3 deteriorated and experienced bilirubin encephalopathy. One infant had a rapid decline after admission with a total serum bilirubin level of 55.5mg/dL, and another infant became septic. Finally, one infant was noted to have Rh hemolytic disease and progressed to bilirubin encephalopathy post-discharge.

Gamaleldin, et al. (2011), concluded that in the absence of other neurotoxicity risk factors, neonates are able to tolerate higher bilirubin levels with a low risk of development of kernicterus. This demonstrated that the risk of ABE was greatly dependent on the etiology of the neonates’ hyperbilirubinemia. This led to the conclusion by Gamaleldin, et al. (2011) that the effects of plasma or other defense variables within the neonate in relation to development of bilirubin encephalopathy require further examination.

**Measurements of bilirubin levels**

It has been noted transcutaneous measurement of bilirubin in the outpatient setting can help practitioners more accurately assess the level of bilirubin in the neonate versus visual inspection alone (Wainer, Parmar, Allegro, Rabi, & Lyon, 2012). The purpose of a study by Wainer, et al. (2012) was to assess the impact of instruction of practitioners on the accurate use of transcutaneous bilirubin measurement for newborns, to assess if there was a decrease in the diagnosis of severe hyperbilirubinemia in this population, as well as to measure the accuracy of the transcutaneous bilirubin measurement (Wainer, et al., 2012). The researchers used a
prospective cohort study with an historical control group” to compare the use of the new tool to historical data within the parameters of their research study.

The target population for this study was all healthy newborns born between June 1, 2006 to May 31, 2008 in Calgary, Canada that were greater than or equal to 35 weeks gestation. Infants delivered at home, discharged after 10 days of age or less than 35 weeks gestation were excluded from the study. This inclusion and exclusion criteria lead to a sample size of 14,796 infants in the experimental group and a database of 14,112 infants in the historical data group (Wainer, et al., 2012). During the time of the study, a transcutaneous bilirubin screening program for well-infant nurseries was implemented in Calgary. This program also included post discharge follow-up utilizing the public health nurse system already in place in the community. During the ‘study period,’ infants in Calgary were seen by a public health nurse within 2 days of discharge for weight check, lactation support, and to provide increased support for infants identified as high risk. These follow-up activities were in addition to routine follow-up by the physician or midwife (Wainer, et al., 2012).

The instruments used in the study by Wainer, Parmar, Allegro, Rabi, and Lyon (2012), was the Dräger Jaundice Meter JM-103. The researchers took a mean of three measurements on the infants’ foreheads. The researchers validated the equipment by wavelength verification at time of purchase as well as periodic measurements according to the manufacturer’s recommendations. Measurement of serum bilirubin was done by the Roche Modular Hitachi 912 and 917 machines; there was no description of the method to validate the accuracy of the equipment. The researchers used a Strata 9.0, OpenEip, and Microsoft Excel 2010 to analyze the data (Wainer, et al., 2012).
Study findings demonstrated a significant decrease in the incidence of severe hyperbilirubinemia and enhanced early identification of neonatal hyperbilirubinemia. This finding allowed for prompt treatment of neonatal hyperbilirubinemia and a decrease in risk for complications. Wainer, et al. (2012), also found that there was a decrease in number of serum bilirubin measurements obtained by 22.9%, as well as a reduction in the pre-discharge use of phototherapy. It was also noted that infants were admitted sooner post discharge for phototherapy with the use of transcutaneous bilirubin measurement and their length of stay was reduced slightly (Wainer, et al., 2012).

The researchers concluded transcutaneous measurement in the presence of an organized implementation system improved patient safety as well as reduced utilization of hospital resources. However, it may increase the use of community health agencies (Wainer, et al., 2012).

In 2004 the American Academy of Pediatrics instituted guidelines regarding treatment of neonatal hyperbilirubinemia. However, there were concerns in the medical community regarding a possible resurgence of kernicterus (Slaughter, Anniblae, & Suresh, 2009). When there are “normal” bilirubin levels noted in the neonate noted prior to hospital discharge, there may be a false sense of security, which may lead to delayed follow up, and treatment. This could ultimately lead a greater incidence of severe neonatal hyperbilirubinemia. The purpose of Slaughter et al.’s (2009) study was to examine the incidence of readmission of newborns for neonatal hyperbilirubinemia when the neonates where they were discharged with normal bilirubin levels (i.e. false negative results). The framework for this study was retrospective chart review. The researchers reviewed neonatal total bilirubin levels and also neonatal readmission for treatment of serum bilirubin levels >17 mg/dl.
In their study, Slaughter et al. (2009) reviewed charts from a population of infants from the Children’s Hospital of the Medical University of South Carolina. These infants were born between July 1, 2002 and September 30, 2006 and were at least 35 weeks gestation. Only neonates who were admitted to the normal newborn nursery were enrolled in the study. Other exclusion criteria included: illness, gestation less than 34 weeks, jaundice beginning within first 24 hours, or findings indicative of the presence of hemolysis. Infant readmission was further clarified to include having TSB level of 17mg/dl or more and occurring within the first 28 days after birth. If multiple bilirubin assessments were made, the final pre-discharge assessment was used for data collection. The hospital uses a BiliChek® Noninvasive Bilirubin Analyzer at 24hrs age on all infants in the newborn nursery. This tool was evaluated briefly by the researchers and determined that the transcutaneous measurement was comparable to total serum bilirubin (TSB) levels.

Slaughter et al. (2009) accessed several sources for information from the target hospital’s records-database. They accessed data including diagnostic codes for neonatal jaundice, hemolytic disease due to isoimmunization, and perinatal jaundice. In addition, infants who were readmitted were identified and their individual hospital records were reviewed including their pre-discharge TSB level. It was noted that of the 6220 infant charts that were reviewed, 28 were readmitted with a bilirubin reading of at least 17mg/dl. All infants were successfully treated with phototherapy. Additionally, none of the infants in the study had any signs or symptoms of kernicterus.

One of the major flaws of this study was the number of infants that were lost to follow-up and the inconsistency in practitioners checking bilirubin levels vs. visual only examination. Of
the infants readmitted for elevated bilirubin levels, 46% were in the low to intermediate risk zone utilizing the AAP-recommended nomogram (Slaughter, et al., 2009).

The researchers concluded that infants with a low risk nomogram may develop significant hyperbilirubinemia that may require treatment. This finding demonstrated the significance of providing a universal follow-up for all newborns discharged from the hospital, as well as reevaluation of risk assessment tools in the prediction of newborns that may develop hyperbilirubinemia (Slaughter, et al., 2009).

**Lactation support**

Breast milk jaundice is a factor that is considered to be significant in infants with hyperbilirubinemia. Breast-fed newborns have variable amounts of fluid and nutrients which may impact excretion of bilirubin through urine and feces. If breastfeeding is too brief or infrequent in the exclusively breastfeeding infant, hyperbilirubinemia may result due to dehydration, weight loss and decreased excretion of bilirubin. The purpose of the study by Chen, Chen, and Chen (2011), was to identify the risk factors for breastfed infants in development of severe hyperbilirubinemia and help to pinpoint the specific factors that lead to breast milk jaundice.

Chen et al. (2011) used a retrospective study to examine the data of neonates born at Taipei Medical University Hospital from August 2009 to July 2010. Infants transferred to the neonatal intensive care unit were excluded from the database. Careful attention to body weight changes was documented for each newborn in the study noting differences between birth and discharge weight, as well as discharge weight and follow up discharge weight. There were a total of 323 infants included in the study.
Researchers used transcutaneous bilirubin measurement (BiliCheck) device on the infants’ forehead, to measure bilirubin levels (Chen, et al., 2011). The researchers did not discuss the calibration of scales used to weigh the infants. The data was analyzed using t test, Pearson’s correlations and Fisher’s exact test.

The study findings demonstrated that of the 323 infants included in the study, the incidence of hyperbilirubinemia was 35.3% with 81.4% of infants being exclusively breastfed (Chen, et al., 2011). The infants with hyperbilirubinemia had a larger mean body weight decrease from birth to discharge than those without hyperbilirubinemia, (8.1% vs. 6.3%). The rate for hyperbilirubinemia in the exclusively breastfed group was 35.3%. It was observed these infants had a smaller amount of weight gain from discharge to follow-up. The researchers also noted a relationship between the length of the hospital stay and the risk of developing hyperbilirubinemia, as well as method of birth (Chen, et al., 2011).

Chen, et al. (2011) concluded that neonatal jaundice is not directly connected to breastfeeding but may be related to a decrease in consumption of calories and fluids. Thus, when breastfeeding is not optimal, parents should be educated to increase frequency and duration of breastfeeding and possibly supplement with formula if milk supply is suboptimal within the first few days of life.

**Post-discharge follow up**

Management and education regarding neonatal hyperbilirubinemia is the focus of a study by Petrova, Mehta, Birchwood, Ostfeld and Hegyi (2006). Petrova et al.’s (2006) study focused on the management of neonatal hyperbilirubinemia by individual practitioners in the outpatient setting. A questionnaire survey used by the researchers focused on practitioners’ beliefs and knowledge related to compliance with recommendations by American Academy of Pediatrics.
Petrova et al. (2006) mailed surveys to a random sample of 800 pediatricians in New Jersey chosen from a listing of the New Jersey Fellows of the American Academy of Pediatrics. The survey was mailed two times in order to capture responses from those who did not respond to the first survey. Physicians were excluded from the survey if they were in their residency, retired, did not provide newborn services, or completed less than half of the survey.

The tool for this study was a 25 question survey on the management of neonatal hyperbilirubinemia. Questions were multiple choice, yes/no, or scale format. Question content was evaluated by seven pediatricians in order ensure that questions were clear and not repetitive (Petrova, et al., 2006). After final review, the researchers had 356 surveys that met their criteria for the study. Data was analyzed using STATISTICA 6.0 software with an accepted P value of <0.05.

Petrova, et al. (2006) found that few pediatricians tested transcutaneous or serum bilirubin with the presentation of jaundice in the outpatient setting, and relied primarily on cephalocaudal progression of jaundice and visual inspection. However, in terms of initiation of treatment, physicians were more likely to start phototherapy and even exchange transfusion at lower levels than the accepted American Academy of Pediatrics practice recommendation. It was noted that pediatricians did not take into account all risk factors for severe hyperbilirubinemia and kernicterus. These risk factors included early gestational age, breastfeeding, bruising, and prior siblings with jaundice (Petrova, et al., 2006).

In conclusion, Petrova et al. (2006) found that physicians surveyed in this research were concerned enough about the severe effects of kernicterus resulting from neonatal hyperbilirubinemia to initiate treatments sooner. However, a distinct knowledge gap related to monitoring bilirubin levels and assessment of individual risk factors for severe
hyperbilirubinemia was noted in the study findings. The authors found that this was an opportunity to encourage practitioners to review best practice guidelines and incorporate them into use.

**Systems approach to neonatal hyperbilirubinemia**

Acute bilirubin encephalopathy (ABE) resulting from neonatal hyperbilirubinemia is a preventable outcome. The purpose of the research by Bhutani, Johnson, Schwoebel, and Gennaro, (2006) was to propose and implement a systems approach to manage newborn jaundice to prevent complications such as ABE. The researchers used an observational framework, in which they observed established data including use of intensive phototherapy and exchange transfusion. They then implemented changes slowly over time including staff education on visual assessment of jaundice, authorizing nurses to collect transcutaneous or serum bilirubin levels at their discretion without a physician order, lactation support, parent education, and scheduled post-discharge follow-up. This was done in order to monitor for adverse outcomes to determine if their approach produced a measurable decrease in the incidence of four main measureable outcomes. The four main measureable outcomes were a “never event” where neonates had a total serum bilirubin (TSB) level >30 mg/dl, extreme hyperbilirubinemia with a TSB level >25 mg/dl, use of exchange transfusion, or readmission of newborns for intensive phototherapy.

This is a unique study which looked at the evolution and sequential changes in a facility regarding management of newborns related to bilirubin screening. There were several activities implemented over time in this facility: these were development of an hour-specific bilirubin nomogram, in-services for faculty, a revision of lactation support programs, parent education, and post discharge screening for follow up planning.
Bhutani, et al. (2006), conducted their study in a semiprivate urban birthing hospital from 1990 to 2000. A population of 31,059 well babies discharged as healthy were recruited for their study. The researchers defined term infants as at least 38 weeks gestation or infants with a birth weight of 2500g for 35 weeks gestation, or 2000g for 36 weeks gestation or more. Study exclusion criteria included: low birth weight infants, or infants admitted to and treated in the neonatal intensive care unit.

The researchers assessed for four known adverse outcomes for early and late onset severe hyperbilirubinemia before, during, and after implementation of their systems approach. The four outcomes were a “never event” where neonates had a total serum bilirubin (TSB) level >30 mg/dl, extreme hyperbilirubinemia with a TSB level >25 mg/dl, use of exchange transfusion, or readmission of newborns for intensive phototherapy (Bhutani, et al., 2006). One drawback of this study was that the use of home phototherapy could not be confirmed for infants who were enrolled in the study. Total serum bilirubin levels were completed with the 2,5-dichlorophenyldiazonium tetrafluoroborate, diazo method. Standard National Institute for Standardized Testing guideline levels was used for accuracy and variance values were assessed every three months and ranged from 2-3% (Bhutani et al., 2006).

Bhutani et al. (2006) also examined the use of intensive phototherapy and exchange transfusion over a seven year period. The use of phototherapy decreased from 4.49-5.44% in 1993-1998 to 2.49% in 1999 and 2000. The incidence of readmission for phototherapy also decreased from 14 to 5.5 per 1000 discharged infants. The researchers also noticed a decrease in the incidence of exchange transfusions; from 1990 through 2000. During this period there were a total of 17 infants who required exchange transfusion (1 in 1,822). After the implementation of
the systems based approach from 1999-2003, it was noted that there were three infants who required exchange transfusions, this reduced the statistics to one in 6,130 (Bhutani et al., 2006).

The researchers found that this slow, steady introduction and implementation of the systems based approach demonstrated a concurrent decrease in the incidence of newborn jaundice adverse events. It was noted that the incidence of readmission for phototherapy decreased from 14 to 5.5 infants per 1000. In this group infants were primarily identified by early onset jaundice. The authors summarized that monitoring for jaundice and testing bilirubin appears to be superior to blood typing and Coombs testing (Bhutani et al., 2006).

Bhutani et al. (2006) concluded that sequential implementation of the systems-based approach had a direct effect on decreasing adverse events related to neonatal jaundice and hyperbilirubinemia. It was noted that researches avoided statistical comparison of adverse events that had low incidence and relied entirely on observational data in certain areas. This could be perceived as a potential weakness of this study. Another aspect the researchers failed to measure was the use of home phototherapy. The authors did note that usage and prescriptions for phototherapy by home nursing agencies did not increase between 1995 and 2000. The researchers also noted that the development of physician practices in the outpatient setting during this time may have positively affected outcomes. They related that communication between healthcare providers was promoted. Additionally, a standard for follow-up timelines was initiated for infants with “at-risk” levels of serum bilirubin in order to provide ongoing evaluation and treatment as needed (Bhutani et al., 2006). This study report synthesized the findings over ten years and discussed these findings. Ultimately the researchers found that even with this large number of infants (31,059), over time it was shown that there were steady,
continuous decrease in adverse events in newborns related to newborn jaundice and hyperbilirubinemia.

**Summary of findings**

De Luca et al. (2009) performed a review of the research literature regarding neonatal hyperbilirubinemia and early discharge in order to aid in the development of an evidence-based practice model for jaundice management. Upon examination of the available research, De Luca et al. (2009) created an algorithm for a, “jaundice prediction protocol.” They concluded that it is important to periodically review jaundice management protocols, especially as hospitalizations are becoming shorter, and that all parents should continue to be educated about the signs and symptoms of jaundice prior to discharge.

Chawla, et al.’s (2011) objective was to evaluate the effectiveness of clinical risk factors with transcutaneous bilirubin measurement in order to predict the need for treatment of hyperbilirubinemia in healthy term and late preterm infants. In the process of their study, the researchers were able to correctly classify 84.9% of the subjects at high risk. The researchers conclude that utilization of risk scoring tools greatly helps in the identification of infants at risk for developing hyperbilirubinemia requiring treatment.

Gamaleldin, et al., (2011) concluded from their research, that neonates are able to tolerate higher bilirubin levels with a lower risk for development of kernicterus when other neurotoxicity risk factors are absent. The risk of ABE was greatly dependent on the etiology of the neonates’ hyperbilirubinemia. This led to the conclusion by Gamaleldin, et al. (2011), that the effects of plasma or other defense variables within the neonate in relation to development of bilirubin encephalopathy need further examination.
Wainer, et al. (2012) sought to assess the impact of instruction and use of transcutaneous bilirubin measurement upon the incidence of severe hyperbilirubinemia. The researchers found that infants who were screened using transcutaneous bilirubin measurement were admitted sooner post discharge for phototherapy, and phototherapy was of shorter duration than those who were not screened post discharge. Wainer et al. concluded transcutaneous measurement in the presence of an organized implementation system improved patient safety.

Slaughter, et al. (2009) examined the incidence of false-negative results, that infants with a low risk nomogram may develop significant hyperbilirubinemia that may require treatment within their patient population. Within their study Slaughter et al. (2009), had 28 readmissions with a bilirubin reading of at least 17mg/dl out of the 6,220 infants included in the study. The researchers concluded that infants even at low risk for hyperbilirubinemia may well develop significant hyperbilirubinemia that requires treatment.

The purpose of the study by Chen, et al. (2011), was to identify the risk factors for breastfed infants associated with the development of severe hyperbilirubinemia. The infants with hyperbilirubinemia had a larger mean body weight decrease from birth to discharge, than those without hyperbilirubinemia. Chen et al. (2011) concluded that neonatal jaundice is not directly connected to breastfeeding but in fact may be related to a decrease in consumption of calories and fluids.

Petrova, et al. (2006) focused their study on the management of neonatal hyperbilirubinemia in individual pediatric practices in outpatient settings. They found that few pediatricians tested transcutaneous or serum bilirubin with the presentation of jaundice in the outpatient setting. The researchers concluded there is a distinct knowledge gap associated with
monitoring bilirubin levels and assessment of individual risk factors for severe hyperbilirubinemia.

The purpose of Bhutani, et al.’s (2006) study was to propose and implement a systems approach to manage newborn jaundice to prevent complications such as kernicterus. Bhutani, et al. (2006) completed a decade long study in order to implement nurse initiated bilirubin testing, routine bilirubin screening on all infants, and targeted follow-up based on risk for severe hyperbilirubinemia. The researchers found that a slow steady introduction and implementation of a systems-based approach was associated with a concurrent decrease in the incidence of newborn jaundice adverse events.
Chapter III

Methodology and Procedures

Introduction

Kernicterus or acute bilirubin encephalopathy (ABE) is a neuropathology that is caused by neurotoxic effects of elevated levels of bilirubin upon the brain. Newborns’ immature central nervous systems are highly susceptible to the toxic effects of elevated levels of bilirubin. Management of hyperbilirubinemia requires the joint efforts of nursing, in-hospital practitioners, as well as practitioners in the outpatient setting due to decreased length of stay after birth and the timeframe for peak bilirubin levels. The purpose of this study is to evaluate the effect of pre-discharge and guided follow-up transcutaneous bilirubin measurement in the neonate to determine the effects on management of neonatal hyperbilirubinemia and prevention of kernicterus. This is a replication of the first part of a ten-year study completed by Bhutani, et al. (2006), the use of transcutaneous measurement of bilirubin on all healthy newborns prior to discharge. The focus of this chapter is a description of the methods, procedures, and data analysis to be used in the completion of this study.

Research Question

What is the effect that an initial intervention of transcutaneous measurement of bilirubin levels will have on the management of neonatal hyperbilirubinemia as a part of an incremental health systems approach on identification and management of neonatal hyperbilirubinemia?

Population and Sample Setting

This study will take place in an urban hospital in Fort Wayne, Indiana that has approximately 1000 deliveries a year (Indiana Business Research Center, 2013). The sample will
include two parts. A retrospective sample chart review from the prior two years, including approximately 1,800 infants who have been discharged from the “well-baby” nursery. This collection of data will serve as pre-implementation data for comparison. Additional enrollment will include 1800 infants admitted to the “well-baby” nursery during the 24 months study period. Enrollment criteria for inclusion in the study will include: (a) full term infants born at 37 weeks gestation or more, (b) birth weight of 6lbs or more, (c) infants discharged from the well-baby nursery, (d) infants without any known health concerns or conditions, and (e) no chromosomal abnormalities.

**Protection of Human Subjects**

This study involves infants as a vulnerable population. Approval from the Office of Research Integrity will be obtained through an institutional review procedure process before any collection of data begins. The study proposal will be submitted to Ball State University’s Institutional Review Board (IRB) and to the Fort Wayne Hospital’s research committee board. After approval from the IRB and the hospital’s research committee, the nurse manager for the labor and delivery unit as well as the well-baby nursery will be consulted prior to initiation of the study in their department. The study poses a low risk of harm and an opportunity-for benefit as the subjects will receive closer supervision than the current standard of care.

Parents of potential infant participants for the on-going enrollment will be informed verbally and in writing about the study. If parents agree to allow their infants to participate, written informed consent will be obtained. The information given to parents will include the study details including: purpose, what data will be collected, how the personal data will be protected, and the risk and the potential benefit of study participation. It is important that parents
fully understand what the research entails in order to make an informed choice regarding participation in the study.

Subjects in the study will be protected by HIPPA privacy rule, as no identifying information will be used in the analysis of data, or the release of results. Data to be collected will include: nationality, birth weight, gestational age, hour-specific bilirubin measurements, method of nutrition (exclusive breastfeeding, exclusive formula feeding, or a combination of the two), method of delivery, and blood type incompatibility information, and readmission or outpatient treatment data. All research personnel collecting information will have training on Federal Research Ethics guidelines and HIPPA privacy laws. This training will be documented accordingly and reported to IRB.

Procedures

Research staff will educate staff members regarding use and documentation of results of the transcutaneous measurement of bilirubin. Workshops and lunch in-services will be provided for staff, allowing several opportunities to learn per shift. This will be scheduled with the nursing education department and nurse manager. The research staff will also educate hospital staff on the inclusion guidelines that will be utilized for enrollment regarding potential infants who may be included in the study. The researchers will also train the nursing education department to be super users through more in-depth training that will offer free CEUs for staff as well as a gift certificate for the super users. The rationale for training these super users is that they will be an onsite resource to staff and be able to train new nurses to the unit.

Parents of infants who participate will receive an incentive of a $30 gift certificate to Babies-R-Us. This incentive is not considered to be coercive due to the small amount of the incentive and that it will go toward infant care items. Nursing staff members who participate will
receive an incentive of a $10 gift certificate to a local restaurant every four months (one up to six certificates) during the 24 month enrolment period ($60 total). Again this is not considered to be coercive due to the small amount of the incentive.

Methods of Measurement

Retrospective data from the past two years for 1800 infants discharged from the “well baby” nursery will be obtained. Data will be collected using the hospital’s medical records department. Information from practitioners within the hospital network will also be available as this hospital has EPIC electronic records that are shared with all network physicians to maintain one complete medical record for patients served by hospital physicians.

Research staff will contact new parents within 24 hours after delivery to obtain consent from parent to enroll “well” infants in the study. Again, parents of potential infant participants for the on-going enrollment will be informed verbally and in writing about the study. If parents agree to participate, written informed consent will be obtained.

Serum bilirubin levels will be obtained by trained nursing staff using the hospital’s current laboratory tools and collection methods. Transcutaneous bilirubin levels will be obtained by nursing staff also to allow for direct comparison of the two measurements. The lab will follow standard practice for calibration and maintenance of equipment per hospital protocols. The validity and reliability of serum bilirubin measurements is already established and will be maintained using current practices. Testing of the validity and reliability of transcutaneous measurement will be explored as part of this study.

Care of the infant will be determined by examining for risk factors by questionnaire to be completed by the nurse assessing the infant, as well as by using the hour specific nomogram as established by Bhutani et al. (2006). The questionnaire will include the following questions:
• Do they have sibling with history of newborn jaundice?
• Is there a blood type incompatibility between mother and infant?
• Is the mother exclusively breastfeeding?
• Has the infant lost >8% of body weight since birth?
• Does the hour specific bilirubin level chart indicate a need for early follow-up?

An answer of yes to one or more of these questions may indicate that the infant is at increased risk to develop significant jaundice which may require treatment and more frequent follow-up after discharge. These questions correlate to an increased risk of development of hyperbilirubinemia and allow the nurse to evaluate additional factors that may affect the neonate’s resistance to higher bilirubin levels (Gamaleldin, et al., 2011).

Research Design

The design for this study will be that of a retrospective/prospective cohort study. In this type of study we examine a group at risk, the neonate, for development of an event, severe hyperbilirubinemia (Burns & Grove, 2005). The group is examined with the variable in place to determine if there is a pattern to those who develop severe hyperbilirubinemia and to recognize these neonates sooner to provide treatment to prevent the extreme adverse event of kernicterus. The study will also measure the reliability of the transcutaneous measurement of bilirubin in the neonate.

The research will enroll 1800 babies from the “well baby” nursery over a 24 month period. Additionally a chart review of 1800 infants discharged from the “well baby” nursery will be included from the prior 24 months. Infants enrolled in the study will have transcutaneous measurement performed at this time. Infants will be brought back to the hospital at four to five days of age when bilirubin levels typically peak and have repeat serum bilirubin level testing
through heel stick, as well as repeat transcutaneous measurement. This post-discharge assessment will be conducted in the outpatient weigh-in room that is free for parents to come and have their newborn’s weight assessed post discharge as well as consulting with a lactation consultant in house if the neonate is being breastfed. This is a free service to the community already in place.

All bilirubin measurement results will be reported to the primary care physician of the newborn. Utilizing the guidelines of the American Academy of Pediatrics, (2004) newborns at high risk (two or more answers of ‘YES’ to screening questions) with transcutaneous bilirubin measurement of \( \geq 14.5 \text{mg/dL} \), infants at medium risk (one answer of ‘YES’ to screening questions) with a bilirubin level of \( \geq 17 \text{mg/dL} \), and healthy infants with no other risk factors with a bilirubin level of \( > 20 \text{mg/dL} \) should be considered for phototherapy, and on-call physician will be notified immediately of results by nurse without waiting for confirmation by serum bilirubin levels. Any infant exhibiting signs of kernicterus will be immediately sent to the ER for evaluation by a physician.

**Statistical Data Analysis**

Chart audits will be completed by the researchers utilizing the EPIC records system at the Fort Wayne Indiana hospital. Researchers will collect demographic data as well as available bilirubin measurements at discharge and at follow-up, if obtained. Data will be collected on pre-discharge bilirubin measurement on infants readmitted for treatment of hyperbilirubinemia or outpatient treatment of hyperbilirubinemia using a bili-blanket. Data will be averaged based on nationality, gestational age, birth weight, and breastfeeding in order to further determine the cause and effect ratios of these variables within the sampled population. Data will be analyzed
using descriptive statistics including bivariate analysis to graph the serum bilirubin measurement and compare with the transcutaneous measurement.

Summary

This proposed study offers an opportunity to increase screening for risk of the serious complication from kernicterus. A systems based approach utilized by Bhutani et al. (2006), has been shown to be beneficial in the monitoring of neonates and prevention of the detrimental effects of severe hyperbilirubinemia. This research implementing phase one of Bhutani et al.’s (2006) systems based approach will further support the use of transcutaneous bilirubin measurement and universal screening of bilirubin in all neonates.


