INTRODUCTION

Newborn bilirubin levels are monitored to help prevent bilirubin encephalopathy (kernicterus), irreversible brain damage caused by an elevation of indirect bilirubin.1,2 Kernicterus is currently rare in the United States, with <100 cases per year,3 but as many as 60% of newborns have elevated bilirubin levels in the first few days of life.4,5 Most cases of hyperbilirubinemia resolve,4 with 20% requiring medical intervention.4 Infants at risk for persistent hyperbilirubinemia can be difficult to detect in the hospital, because normal bilirubin levels vary over time and may not peak until the fifth day of life or later, requiring a follow-up after discharge from the hospital.6 In 1999, Bhutani et al7 created a nomogram based on total serum bilirubin (TSB) measurements of 13000 healthy term and near-term newborns until 120 hours of age. This nomogram became the basis for the BiliTool.org Web site available to all practitioners. Neonates considered at high risk (HR) for dangerous hyperbilirubinemia have levels above the 95th percentile on the nomogram, and
those between the 75th and 95th percentile are at high-intermediate risk.

When transcutaneous bilirubin (TcB), a noninvasive measurement of bilirubin, emerged, efforts were made to maximize its use in practice. TcB meters produce light at several wavelengths and then measure its reflection after interacting with the bilirubin in the subcutaneous microcirculation. TcB results have repeatedly been found to correlate to TSB measurements, despite changes in infant weight and severity of disease, and are reliable across different ethnicities, gestational ages, and postnatal ages. In previous studies, screening with TcB has decreased blood draws by 60% to 80%, with each measurement saving 5 minutes and at least $2.9 TcB-specific nomograms have been developed to stratify the risk of adverse outcomes by age and TcB percentile, encouraging the use of TcB as a screening method. However, these nomograms miss some neonates classified as HR on the Bhutani nomogram. They may be difficult to standardize and tend to underestimate serum bilirubin at higher values, when close correlation is most important.

Given the specifics of our clinical environment, we felt that the simplest and safest way to screen neonates would be to use a single TcB cutoff to trigger a TSB in follow-up. We sought to identify the single TcB value that would balance the competing demands of judicious use of resources with a desire to protect all infants from the potential for kernicterus. Our specific aim was to analyze all existing TcB results from our healthy newborn nursery cohort to evaluate how well a cutaneous screening cutoff would exclude newborns with TSB in the HR or high-intermediate risk categories by using the Bhutani nomogram.

METHODS

All available TcB and TSB measurements from a convenience cohort of newborns ≥37 weeks’ gestation born between July 13, 2009 and July 12, 2010, were analyzed in a retrospective chart review of an urban university hospital well-infant nursery’s electronic medical records. The study was an unfunded, exempt analysis approved by the Thomas Jefferson University Institutional Review Board and followed the quality improvement ethical guidelines.

This hospital’s well-infant nursery policy is to order a TSB if the routine screening TcB value is ≥6 mg/dL or if there is any clinical suspicion of hyperbilirubinemia. Only the first recorded TcB and TSB values were used for this study, because these values determine further testing and treatment. Preterm infants, who are automatically considered high-intermediate or HR, were screened directly with a TSB and were not included in the study. However, term infants at increased risk, due to ethnicity, birth trauma, or other causes, who underwent both a TcB and TSB were included in these analyses.

By hospital protocol, TcB measurements are collected with the Minolta JM-103 (Draeger Medical Systems, Inc, Telford, PA) by the nurses in the well-infant nursery, who average the measurements from 5 areas on a infant’s forehead or chest to display a single TcB value (personal communication with the unit director Gary Emmett, MD, Department of Pediatrics, Thomas Jefferson University). The Minolta JM-103 measures bilirubin levels between 0 and 25 mg/dL with accuracy within 2 SDs of ±1.5 mg/dL, according to company research. TSB samples are sent to the inpatient laboratory and analyzed by the Synchron Beckman Coulter LX-20 (Beckman Coulter, Inc, Brea, CA).

By this hospital’s protocol, TcB measurements are acquired in most cases between 2:00 and 4:00 AM on the second day of life, whereas the majority of blood draws for TSB measurements were collected by phlebotomists between 6:00 and 8:00 AM on that same day. The corresponding age of the newborns should range from 27 to 51 hours of age for TcB measurements and from 31 to 56 hours of age for TSB measurements. All charts with both a TcB ≥6.0 mg/dL and a TSB drawn within 6 hours of the TcB were selected and then stratified into groups based on TcB level. These groups were analyzed for their negative predictive values (NPVs) for HR or high-intermediate/HR by using the TSB-based BiliTool.org Web site.

The NPVs for HR and high-intermediate/HR of integer cutoff values between 6 and 12 mg/dL were calculated. The number of neonates with a TcB level below each potential cutoff value, who were not HR (according to their age and TcB level on the Bhutani nomogram), was divided by the total number of infants with TcB below that potential cutoff to determine each NPV for HR. NPVs for high-intermediate/HR were calculated by dividing the number of neonates with TcB levels below the tested cutoff who were low/low-intermediate risk by the total number of infants with TcB below the potential cutoff. Neonates in the high-intermediate category are considered healthy but were included because
they might require closer follow-up by their physician. Data regarding gestational age, weight, gender, phototherapy during initial hospitalization, and Coombs test results were also collected. The readmission rates for infants requiring phototherapy could not be collected, because discharge summaries were the primary source of our data. In addition, patients delivered in our nursery may be readmitted to another hospital, where the information would be inaccessible.

RESULTS

Risk Analysis

As displayed in Fig 1, of the 1288 infants discharged from the well-infant nursery during our study, 1071 (83.2%) had a recorded TcB level. TcB levels ranged from 0 to 15.6 (mean = 6.6 mg/dL, median = 6.6 mg/dL). Five hundred thirty-eight infants were male (50.2%). The mean age at TcB measurement was 36 hours, with a range from 26.4 to 67 hours of age (96% were within the nursery protocol’s 27–51 hours of age). Data regarding gender, Coombs test results, mean birth weight, and gestational age of our cohort by TcB level and risk category can be found in Table 1.

Six hundred forty-seven neonates had TcB levels ≥6 mg/dL and TSB measurements recorded; of these, 76 were high-intermediate risk by TSB level on the Bhutani nomogram and 14 were HR. Table 2 shows the NPV of using TcB screening levels of 6 to 13 mg/dL; the NPV decreases as the TcB cutoff is increased, with no high-risk infants missed at TcB <7 mg/dL. Infants with TcB ≥8 mg/dL had an odds ratio >3 of being HR in comparison with those with a TcB <8 mg/dL.

Figure 2 shows the correlation between TSB and TcB levels and the distribution of low/low-intermediate risk, high-intermediate risk, and high-risk neonates. There is a degree of scatter between TcB and TSB values in our institution, with correlation coefficient ($R^2$) equal to 0.3574.

The NPV for HR and high-intermediate/HR showed no statistically significant difference when separated by gestational age, which ranged from 37 to 41 weeks (data not shown).

Eleven term infants in the well-infant nursery received phototherapy on initial hospitalization. Of these 11, only 3 had a TcB measurement recorded, with values of 7.4, 7.6, and 9.8 mg/dL. Only the latter was high-intermediate risk by TSB.

Cost Analysis

On average, a Minolta JM-103 TcB meter costs a hospital $7000 and, in our institution, it has an average lifetime of 7 years; as advertised, it could last up to 150,000 measurements. It has no disposable parts but does require some maintenance. The cost per use comes to −$1.*

Although the hospital charge for a TSB exceeds $50, the actual cost, including personnel, machine, and material costs, is probably closer to $12.† In our institution, every TSB that we do not draw could save $11, a few minutes of pain, and a few milliliters of blood loss. If 300 blood draws are avoided each year, this hospital can save $3300 per year in the well-infant nursery. A hospital with a higher volume of newborns each year would use their TcB meter more efficiently and therefore save even more money per child. Hospitals have varied labor costs, which could also change the cost per infant to some degree. In the United States, ~4 million infants are born every year. Assuming a similar proportion of savings of $3300 for the 2000 infants born yearly at our institution, the savings in the United States would be $6.6 million each year.

DISCUSSION

Nursery protocols for bilirubin screening differ widely across the country. Our well-infant nursery, balancing suboptimal follow-up rates and staff availability, is particularly conservative. This chart review suggests that, by using 8 mg/dL instead of 6 mg/dL, the

*In our hospital, the cost of the machine is $7000, maintenance and repair are $300 per year, average lifespan is 7 years, and it is used for 1200 infants per year. This creates a cost of $9100 per 7 years, and over this time it is used for 8400 infants, coming to $1.08 per use.

†Materials cost ~$7, phlebotomists’ time comes to ~$3 including benefits (assuming an average hourly wage of $12.50 + benefits), and equipment costs another $2, with the hospital receiving an average reimbursement of $12.
current cutoff used in our well-infant nursery, could have prevented >300 blood draws over a year-long period and would have only missed 1 high-risk infant of 1000. Physicians less averse to risk could safely use a cutoff of 12 mg/dL, missing up to 7 high-risk infants who would be identified with universal follow-up.

Some nurseries use visual inspection to determine the need to check a serum bilirubin level. However, studies have shown that visual inspection is unreliable, especially in a diverse population. Although we were unable to collect demographic information for our study, we know that our hospital’s Labor and Delivery patient population is composed of ~65% African American, 20% white, and 7% each Asian- and Latino-surnamed infants. However, ethnicity-based protocols are unreliable because the ethnicity of the infant’s father and the complete background of the mother are often unknown. The American Academy of Pediatrics guidelines, although supportive of the use of visual inspection, remark that TcB or TSB are the most reliable methods for determining a neonate’s risk, especially in darkly pigmented infants.

Other nurseries use hour-of-life–specific TcB or TSB nomograms to determine neonatal risk. Because our institution’s well-infant nursery is covered by many different nurses, the use of a single cutoff TcB value for screening was thought to engender fewer possible mistakes than use of a nomogram. Previous studies using TcB cutoff levels found that levels of 13 mg/dL were 100% sensitive for HR in an analysis of 121 Hispanic newborns, as were those of 9 mg/dL in a study of 54 infants in Turkey. These studies, however, are limited by sample size and an ethnically uniform group of neonates, making these values difficult to generalize, especially in a risk-averse environment.

The 95th percentile (HR) value in the Bhutani TSB nomogram ranges from 9 mg/dL at 27 hours to 14.5 mg/dL at 56 hours, the age window within which our newborns are screened according to protocol. Studies comparing TcB and TSB have found them to correlate...
most closely at lower levels. With this close correlation, a cutoff of 8 mg/dL would catch even the youngest well-infant nursery neonate with an dangerous bilirubin level without requiring a nurse to look up the time of birth and reference a nomogram.

Although we evaluated risk based on bilirubin values, we did not attempt to correlate risk to need for phototherapy. A 2009 study found that 20% of infants with a diagnosis code for jaundice in the first 30 days of life required phototherapy. In our cohort, only 11 term infants (0.85%) had documented phototherapy, and only 3 had been screened by TcB; however, because we were unable to collect jaundice diagnosis codes and readmission rates, these include only phototherapy rates during initial hospitalization.

Another study estimates that 2.3% of total newborns require phototherapy (0.9%–3.2%, depending on hospital policy), and our rate may simply be on the lower end of this spectrum, possibly because of the ethnic make-up of our patient population and the exclusion of infants discharged from the NICU. In addition, 8 of our 11 newborns requiring phototherapy did not have a TcB measurement, likely because of clinically increased risk requiring an immediate TSB without a screen.

Unfortunately, as a quality-control initiative, we could not change nursery protocols and the patient population studied was limited to the 1000 newborns in our well-infant nursery in the year-long period. This limits the generalizability of our results outside of the environment we evaluated. We wanted to find a cutoff level that could be generalized to our diverse population without requiring ethnicity-specific nomograms, but our sample size cannot be generalized to all hospital populations. Multicenter cohort studies would help further evaluate methods of cutaneous bilirubin screening on a nationwide scale. To best study and compare TcB and TSB, these should be measured simultaneously; in our nursery, there may be as much as a 6-hour difference between the measurements, and normal bilirubin levels can vary significantly within that time. In addition, as demonstrated in Fig 2, there was a high degree of scatter between TcB and TSB results. Although the goal of this initiative was not to compare modes of bilirubin measurement, the relationship between TSB and TcB is certainly an important factor that requires further investigation. In addition, more data such as infant feeding method, because breastfeeding is associated with higher neonatal bilirubin levels, needs to be taken into account in future studies. Further research would provide more reliable information.

Our goal was to have an NPV of 100%, and it is true that 1 high-risk neonate would have been missed with a TcB screening level of 8 mg/dL. However, the neonate’s TcB screen was performed at 26.5 hours of life. The protocol in the well-infant nursery usually does not screen infants <27 hours of age, and it is possible that a later measurement would have been >8 mg/dL. A second TcB may be considered for infants who are screened earlier in life than their peers.

**REFERENCES**


Neonatal Bilirubin Triage With Transcutaneous Meters: When is a Blood Draw Necessary?
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