

PHILIPS

Mother &
Child Care

Jaundice management

Transcutaneous bilirubin measurements in the assessment and management of neonatal jaundice

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In 2004, the American Academy of Pediatrics (AAP) published guidelines for assessing newborns at risk for jaundice.¹ The purpose of the guidelines was to promote an evidence-based approach to reduce the frequency of severe neonatal hyperbilirubinemia and associated neurological sequelae as well as to minimize the risk of unintended harm such as increased parental anxiety, decreased breastfeeding, or unnecessary treatment. Coupled with these goals was the desire to provide optimal care to infants and families in a cost-effective manner. The purpose of this white paper is to review the importance of early jaundice detection and critically examine the variability in current practice in order to promote the most safe, efficacious, and cost-effective approach to care.

Pathophysiology of jaundice

Jaundice is defined as the yellowish discoloration of the skin, mucous membranes and conjunctival membranes caused by hyperbilirubinemia, which is an excess of bilirubin in the blood. Discoloration is most noticeable in the face and descends cephalocaudally; with clearance of the yellowish hue occurring in the opposite direction. Most adults are visibly jaundiced when serum bilirubin exceeds 2.0mg/dL, four times the usual value of 0.5mg/dL. Infants are visibly jaundiced when serum bilirubin levels exceed 7.0mg/dL.

Adverse outcomes

Neonatal hyperbilirubinemia is usually a benign condition that peaks between the second and fourth day of life.² However, when a pathological process interferes with the

normal functioning of the metabolism and excretion of bilirubin, severe hyperbilirubinemia occurs and immediate treatment with phototherapy and/or exchange blood transfusions is required.^{3,4} Kernicterus is defined as increased levels of unconjugated bilirubin that deposits in the brainstem nuclei and cerebellum. Although preventable, kernicterus is associated with significant neonatal morbidity such as cognitive impairment, cerebral palsy and neurosensory hearing loss. In response to the increasing numbers of infants affected by kernicterus, the Provisional Committee for Quality Improvement and Subcommittee on Hyperbilirubinemia of the AAP produced guidelines for the early detection and management of hyperbilirubinemia in the healthy term newborn. Based on best evidence, the following guidelines are recommended.¹

1. Promote and support successful breastfeeding.
2. Establish nursery protocols for the identification and evaluation of hyperbilirubinemia.
3. Measure the total serum bilirubin (T_sB) or transcutaneous bilirubin (T_cB) level on infants jaundiced in the first 24 hours.
4. Recognize that visual estimation of the degree of jaundice can lead to errors, particularly in darkly pigmented infants.
5. Interpret all bilirubin levels according to the infant's age in hours.
6. Recognize that infants at less than 38 weeks' gestation, particularly those who are breastfed, are at higher risk of developing hyperbilirubinemia and require closer surveillance and monitoring.
7. Perform a systematic assessment for the risk of severe hyperbilirubinemia on all infants before discharge.
8. Provide parents with written and verbal information about newborn jaundice.
9. Provide appropriate follow-up based on the time of discharge and the risk assessment.
10. Treat newborns, when indicated, with phototherapy or exchange transfusion.

Applying the guidelines to clinical practice

The AAP guidelines enable practitioners to systematically identify which infants are at risk for serious hyperbilirubinemia and which ones require immediate treatment. While serum bilirubin levels are the standard of care by which one defines hyperbilirubinemia, not all infants require such intensive monitoring. Therefore, utilizing noninvasive monitoring offers a less painful and safer alternative for select infants. Historically, visual inspection was used to diagnose hyperbilirubinemia. In fact, despite studies suggesting that visual inspection is prone to error in 60% of cases, it continues to be used as the initial assessment of jaundice. In the 1940s, Davidson and colleagues⁵ noted wide variability between visible jaundice and serum bilirubin levels. Later, studies by Kramer and colleagues in the 1960s⁶ reported that a single observer noting the presence or absence of jaundice in five dermal zones (progressing cephalocaudally) had poor correlation with serum bilirubin levels in each of the dermal zones. Ebbesen in the 1970s⁷ examined the correlation between serum bilirubin levels and degree of "yellowness" in healthy term infants in daylight rather than fluorescent light. Wide ranges of bilirubin values were reported in each of the dermal zones. Results of these studies indicate that visual cues alone are not sufficient in detecting jaundice and should not be used as a screening mechanism for further assessment. A more systematic approach to detection of jaundice is, therefore, required.

A more recent study in the 1990s⁸ evaluated the accuracy and agreement of physicians, nurses, and parents in detecting jaundice in newborns. Participants were asked to judge whether the infant was jaundiced or not. Correlation between participants,

irrespective of their relationship to the infant, and serum bilirubin levels was poor. Moyer⁹ sought to determine whether pediatric experience affected accuracy of clinical judgement of infant jaundice. At the time of bilirubin determination, two trained individuals independently recorded their assessments of jaundice as absent, slight or obvious. Each observer also classified the infant's skin tone as light or dark. One hundred twenty-two healthy infants were examined, with a mean age of two days. All infants were more mature than 36 weeks gestation. Although the agreement between observers was good for whether or not the infant was light or dark skin toned, agreement for jaundice ranged from 16–23%, which is poor. Riskin¹⁰ examined the correlation between visual assessment of jaundice and serum bilirubin levels in term and late preterm infants before discharge home. Five neonatologists and 17 nurses were asked to rank infants as low or high risk for jaundice. Although correlation was good for infants in the low risk group (Pearson's $r = 0.752$, $p < .001$), 62% of infants in the high risk group were misclassified and, therefore, at risk for significant neurological sequelae. These data over the past 60 years suggest that agreement between experienced examiners regarding the extent of jaundice in otherwise healthy newborns is poor and that alternative methods of noninvasive monitoring should be sought.

Reliability and validity of the BiliChek

The BiliChek noninvasive hyperbilirubin assessment tool works by directing white light into the skin of a newborn and measuring the intensity of the specific wavelengths that are reflected. By knowing the spectral properties of the components of the skin (hemoglobin, melanin, collagen and bilirubin), one can determine the concentration of bilirubin.

In a racially diverse population of 490 term and late preterm infants (59.1% white, 29.5% black, 3.46% Hispanic, 4.48% Asian, and 3.46% other), ranging from 12 to 98 hours of life, Bhutani¹¹ compared T_cB levels using the BiliChek to T_sB levels. In 23 of 419 of the study population infants, the pre-discharge T_sB levels designated them to be at high risk for subsequent excessive hyperbilirubinemia. For these infants, the negative predictive value of the BiliChek was 100% and the positive predictive value was 86%; sensitivity 100% and specificity 88.1%. These data were in good agreement with the T_sB measurements and therefore demonstrate the accuracy and reproducibility of the pre-discharge BiliChek measurements in term and near-term newborn infants of diverse races and ethnicities. The authors concluded that infants with pre-discharge BiliChek values above the 75th percentile of hour-specific T_sB values on the bilirubin nomogram may be considered to be at high risk for subsequent excessive hyperbilirubinemia.

Slusher¹² compared BiliChek measurements with TsB in 127 infants with dark pigmented skin. Infants from two hospitals were included in the analysis. Measurements were made on the forehead of each infant, while blood samples were taken simultaneously. The BiliChek was chosen specifically because of its ability to correct for different degrees of skin pigmentation as well as correcting for other interfering factors such as collagen and hemoglobin. Irrespective of degree of skin pigmentation, the BiliChek and TsB measurements were highly correlated (r values of 0.90 and 0.88) for the respective hospitals.

Bental¹³ obtained TsB levels on 1,069 term and near-term infants and compared them to TcB in order to develop nomograms for the prediction of significant hyperbilirubinemia. Measurements were performed on the infants' foreheads and mid-sternum, and the mean of both measurements was calculated. Linear regression showed a significant relation between TsB and TcB (R² of 0.846). Gestational age, birthweight, age at sampling, and ethnicity had a negligible influence on the relationship. The authors concluded that a nomogram based on TcB could be used to assess the risk of jaundice during hospital stay and pre-discharge.

Jangaard¹⁴ compared TcB with TsB in well full-term infants not requiring phototherapy, as well as in ill term and preterm infants. TcB measurements obtained with the BiliChek instrument were accurate for measuring bilirubin levels in term jaundiced infants not receiving phototherapy and in those receiving phototherapy if an area of skin was patched. TcB was not as sensitive in the small sample of preterm infants. The authors suggest that a larger study is required before recommending the use of this instrument in that population.

Cost effectiveness and clinical utility of the BiliChek

Petersen¹⁵ retrospectively compared the newborn readmission rates for hyperbilirubinemia, length of stay and the number of bilirubin measurements before and after initiation of transcutaneous (BiliChek) bilirubin testing. Between August 2002 and December 2003, 8,974 infants were admitted to one newborn nursery. Infants who did not fit the diagnosis-related group of "normal" were excluded, leaving 6,933 infants who were analyzed. Approximately 7% of these infants required phototherapy before discharge home. In the eight months before and after initiation of the transcutaneous monitoring, the number of bilirubin measurements did not change, nor did the length of stay or duration of time requiring phototherapy. However, the number of readmissions for significant hyperbilirubinemia decreased significantly ($p=0.044$) after BiliChek monitoring was instituted. The sensitivity of the BiliChek to predict infants at risk for jaundice and subsequent readmission further support its use in routine clinical practice.

Recent information suggests that hospitals may be reluctant to purchase the BiliChek device due to the "high" cost of the replacement tips in relation to serum bilirubin tests. A cost comparison study of heel stick procedures and transcutaneous bilirubin measurements was published by Jim McKenzie, et al.¹⁸ using the BiliChek jaundice assessment device. Specific manufacturer and part number information was gathered and prices were provided from a national distribution company. Clinical experts completed a survey and an observation of current practice was conducted. Each well baby nursery had a protocol for jaundice assessment, but variation in the timing of assessment existed. Two units based the assessment on visual inspection of jaundice. If the infant was determined to be jaundiced, a BiliChek assessment was performed. Depending on BiliChek results, serum bilirubin would be obtained. The third well baby nursery used the BiliChek as a standard screening tool at the time of home discharge. Time to obtain serum bilirubin results ranged from 60-120 minutes, compared to one to two minutes using the BiliChek.

This pilot study showed increased cost to the hospital for a heel stick test compared with a BiliChek. The list price for the BiliCal tip is \$6.80. Given the two minutes of testing time required, the cost of labor at \$25-\$35/hour rate for nursing time would be \$0.83-\$1.16. Heel sticks have a cost of parts in the range of \$4.17 to \$9.07 depending on the specific parts used for testing. The labor costs for the hospital included 10-15 minutes of nursing time at \$25-\$35/hour and 10 minutes of lab technician time at \$18-\$23/hour for a total labor rate of \$9.25-\$12.58 for a heel stick test. Given this information, the cost of a noninvasive test could total \$7.63-\$7.96 compared to the total cost of a heel stick, which ranges from \$13.42-\$21.65.

The number of people involved in obtaining serum bilirubin levels compared to BiliChek values (nurse, phlebotomist, lab technician, parent) were three and one, respectively. The likelihood of having to repeat the testing was similar in both groups, but the time, cost and pain implications for the infant were significantly higher when performing the serum bilirubin. Participants indicated several advantages to using the BiliChek, including the ability to perform the test with parents present, less disturbance of the infant, less likelihood of pain/stress, less equipment required, and less likelihood of losing the specimen. Areas for concern included uncertainty about how to use the BiliChek device, where to store the product, and how to assure infection control practices are followed.

Summary

Neonatal jaundice is a common physical finding that most often is benign in nature.¹⁷ Preterm infants are at higher risk for adverse outcomes associated with jaundice and therefore rely on astute practitioners to identify the phenomena and treat accordingly.¹ AAP has clearly articulated best practice guidelines and practitioners, researchers and industry leaders need to follow the evidence-based guidelines while continuing to identify alternative approaches to quality care.

- Jaundice is physiologically normal¹
- Preterm infants are at higher risk for jaundice¹
- Visual assessment of jaundice leads to error
- Serum bilirubin is the “gold standard” but
 - Blood tests are painful
 - Noninvasive monitoring may provide an alternative to blood tests in specific cases
- BiliChek has established preliminary reliability and validity and is easy to use

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