National Academy of Clinical Biochemistry (NACB

Laboratory Medicine Practice Guidelines (LMPG):

Evidence-Based Practice for Point of Care Testing

Transcutaneous Bilirubin

Steven Kazmierczak
Professor of Pathology
Oregon Health & Science University
Portland, Oregon

Members of Bilirubin Study Group

- Steven Kazmierczak, Ph.D. - Chair
- Vinod Bhutani, M.D.
- Glenn Gourley, M.D.
- Scott Kerr
- Sal Sena, Ph.D.
- Karen Shattuck, M.D.
- Patrick St. Louis, Ph.D.

Neonatal Hyperbilirubinemia

- Aggressively treated up to 1970s due to high incidence of Rh hemolytic disease
- Studies performed in 1980s suggested that kernicterus was rare and infants treated unnecessarily.
- 1990s: increase in early hospital discharge and rise in breastfeeding rates has led to increase in cases of reportable kernicterus.
- These factors have led to development of techniques to detect hyperbilirubinemia.

Neonatal Hyperbilirubinemia: Scope of the Problem

- Difficult to assess:

  Neither hyperbilirubinemia nor kernicterus are reportable diseases.

Extrapolation of population studies to US

- **4 million births per year**
  - **80,000 with TSB > 20 mg/dL (2.0%)**
  - **6,000 with TSB > 25 mg/dL (0.15%)**
  - **400 with TSB > 30 mg/dL (0.01%)**

Clinical Practice Guidelines: AAP*

- Establish protocols for evaluation of hyperbilirubinemia.
- Measure TSB or TcB in first 24 hours and within 24 h of discharge
- Recognize limitations of visual assessment of hyperbilirubinemia
- Perform systematic bilirubin assessment of infants prior to discharge

*Management of Hyperbilirubinemia in the Newborn Infant 35 or More Weeks of Gestation. *Pediatrics* 2004;114:297-316

Clinical Questions: TcB Screening

- 1. Effect of TcB on clinical outcome, LOS, and readmission rates.
- 2. Optimum timing, frequency and site of analysis
- 3. Contraindications for use of TcB
  - Breastfeeding
  - Phototherapy
  - Ethnic origin
  - Transfused newborns
  - Postpartum age

Clinical Questions: Bilirubin Screening

- 4. Evidence of decreased morbidity (infection, blood loss/usage) with TcB use.
- 5. How does TcB compare with TSB with respect to accuracy and precision when using HPLC serum bilirubin analysis as reference.
- 6. Are TcB measurements more cost effective compared with laboratory-based serum measurements

Literature Review

- 1966 – January 2004
- Medical Subject Headings:
  - Hyperbilirubinemia, Noninvasive, Transcutaneous
- Abstracts
  - Human, English language
    - 99 Articles for Full Text Review
    - 57 for Systematic Review
      - 54 appropriate for data abstraction
      - 3 articles did not address any of clinical questions being considered

Methods to assess TcB

- Perspex Icterometer: semiquantitative
- Chromatics Colormate III
- Minolta Jaundice meter (1980)
- BiliCheck (Respironics/SpectRx)

Evaluation of TcB Methods

- Minolta AirShields and Chromatics Colormate
  - Dual wavelength instruments (460 & 550 nm)
  - Baseline reading recommended to correct for skin color
- Respironics BiliCheck
  - Multiple wavelengths (137; 380 – 700 nm)
  - Corrects for skin pigmentation
  - No baseline reading required

Clinical Question 1

- 1. What is the effect of TcB on clinical outcome, LOS, and readmission rates for hyperbilirubinemia as compared to newborns assessed with TSB.
- 0 of 54 studies addressed this issue.
- Recommendation: Evidence is insufficient to address whether TcB has a positive impact on clinical outcome, LOS, or readmission rates. Well designed prospective studies needed.

Clinical Question 2

- What are the optimum timing, frequency, and site of TcB measurements that result in best agreement with TSB measurements?

- 18 studies addressed issue.
  - 16 Minolta AirShields (Baseline measurement)
  - 2 BiliCheck

Supporting Literature

- Minolta AirShields
  - Baseline reading needed 4h, 6h following birth
    - no baseline: $r \cong 0.60$ baseline: $r \cong 0.90$
  - Sternum readings show similar or better correlation with TSB compared with forehead.
    - Infants exposed to natural light
    - No baseline measurement taken
    - 0-3 d: forehead >4 d: sternum

Supporting Literature

- BiliCheck
  - Randomized controlled trial
    - Forehead correlated with TSB better than Sternum
  - Mixed race population
    - None on phototherapy/direct exposure to natural light
  - TSB by HPLC and various lab methods
    - TcB = 1.07 HPLC + 0.17 (r = 0.93)

Recommendations

- Insufficient data is available to recommend the preferred site of TcB measurements for MAS.
  - Baseline measurements for the MAS are needed (also manufacturer's recommendation).
  - Exposure to natural light may degrade TcB/TSB correlation.
- MAS: Grade: II-2 observational and retrospective cohort studies
- For BC, forehead is optimum site. Grade: I

Clinical Question 3

- Is the use of TcB measurement contraindicated in certain patient populations?
  - Preterm infants
  - Breastfed newborns
  - Newborns undergoing phototherapy
  - Newborns of particular ethnic origin
  - Newborns above a certain age (days)

Supporting Literature

- Preterm: 3 studies found use in babies $\leq$ 32 weeks to be contraindicated (BC & MAS).
- Phototherapy: PT degrades TcB/TSB
  - Most noticeable in first 6 hours
    - TcB 50% of TSB
  - TcB/TSB correlation returns 24 h post PT
- Newborns of particular ethnic origin
  - MAS: TcB underestimates TSB in darker skinned individuals
    - Baseline measurement (MAS)
  - BC: 2 studies (1 RCT) showed no effect of race

Recommendations

- Preterm: Both MAS and BC contraindicated for use in infants ≤32 weeks. Grade: I
- PT: Significantly degrades TcB/TSB correlation (MAS). Grade II-2
- Ethnicity: Incorrect TcB readings may occur in darker skinned individuals (MAS). Grade II-2

  BC: No effect due to ethnicity. Grade I

Clinical Question 4

- Is there evidence of decreased morbidity (infection, osteomyelitis, blood loss) with use of TcB when compared with blood sampling associated with TSB measurements.

Supporting Literature

- 6 studies (4 MAS: 2 MAS/BC)
- Based on NPV and PPV: 20% - 34% decrease in samples for TSB.
- 1 study found a 12% decrease in TSB orders following implementation of TcB. Another found no net decrease in neonatal TSB requests.
  - TSB ordered with other labs.
- Comparison of MAS & BC
  - Due to higher NPV of BC, use of MAS would result in 124 more TSB for every 1000 babies screened with TcB.

Recommendations

- Utility of TcB in decreasing infant morbidity is largely unstudied.
- Current studies suggest that TcB may decrease need for blood collection associated with TSB. Grade II-2

Clinical Question 5

- How do analytical aspects of TcB (precision, accuracy) compare with TSB and bilirubin measured by HPLC.
- Does use of TcB eliminate interference effects with neonatal specimens in the laboratory (hemolysis, lipemia).

Supporting Literature

- Many studies report that TcB (BC and MAS) tend to underestimate TSB.
- BC found to correlate better with HPLC compared with lab TSB
  - Do lab methods overestimate TSB
- Precision: Using HPLC as reference, SD of MAS 3.0 to 4.0 mg/dL; SD of BC was 1.2 to 2.0 mg/dL at TSB of 12 mg/dL.
- Setting NPV to 100% yields PPV 8% - 33% (MAS and BC)

Recommendations

- Although TcB methods appear to correlate reasonably well with TSB, relatively large imprecision (MAS) may limit utility. Better designed studies with rigorously controlled laboratory methods for TSB determinations are needed. Grade II-2

Clinical Question 6

- Are TcB measurements more cost effective when compared to laboratory based bilirubin measurements.

Supporting Literature

- Effect of TAT: Use of TcB decreased total TAT by average of 2 h 22 min.
  - 12% decrease in TSB requests
- Implementation of TcB resulted in no net decrease in neonatal TSB requests.

Recommendations

- Insufficient data is currently available to evaluate potential cost savings associated with TcB measurements.

  Grade: III limited clinical experience and opinion

Clinical Practice Guidelines: AAP Future Research

- "Additional studies are needed to validate noninvasive (transcutaneous) measurements of serum bilirubin and to understand the factors that affect these measurements. These studies should also assess the cost-effectiveness and reproducibility of TcB measurements in clinical practice"

Pediatrics 2004;114:297-316

kazmierc@ohsu.edu