Original Article

Accuracy of transcutaneous bilirubin level measured by a JM-105 bilirubinometer

Akira Ohishi a,*, Miyuki Kondo a, Tomoka Fujita a, Toru Baba b, Shigeo Iijima b

a Maternal-Fetal and Neonatal Care Center, Hamamatsu University School of Medicine, Hamamatsu, Japan
b Department of Regional Neonatal and Perinatal Medicine, Hamamatsu University School of Medicine, Hamamatsu, Japan

Received Oct 20, 2021; received in revised form Mar 17, 2022; accepted May 10, 2022
Available online

Key Words
hyperbilirubinemia; neonate; screening; transcutaneous bilirubin

Background: Transcutaneous bilirubin (TcB) measurement is useful, but dissociation with total serum bilirubin (TSB) is a clinical problem in measurement. We verified the accuracy of the latest version of the JM-105 jaundice meter.

Methods: The TcB, TSB, and hematocrit (Hct) measurements obtained in the first 4 days of life in 2788 term neonates were analyzed.

Results: When divided into 2-mg/dL classes, the difference between the TcB and TSB measurements did not change as TcB increased, but both overestimation and underestimation of TcB increased as TcB increased. At TcB greater than 11 mg/dL, inaccurate measurements with dissociation greater than 2 mg/dL exceeded 10% of the TcB measurements. The Hct value was associated with overestimation and underestimation.

Conclusion: To evaluate neonatal jaundice accurately, it is desirable to measure TSB by blood sampling before discharge from obstetrics or in the case of worsening jaundice on day 4 or 5 of life.

Copyright © 2022, Taiwan Pediatric Association. Published by Elsevier Taiwan LLC. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

* Corresponding author. Maternal-Fetal and Neonatal Care Center, Hamamatsu University School of Medicine, 1-20-1 Handayama, Higashi-ku, Hamamatsu city, Shizuoka, 431-3192, Japan.
E-mail address: a-ohishi@hama-med.ac.jp (A. Ohishi).

https://doi.org/10.1016/j.pedneo.2022.05.012
1875-9572/© 2022, Taiwan Pediatric Association. Published by Elsevier Taiwan LLC. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Please cite this article as: A. Ohishi, M. Kondo, T. Fujita et al., Accuracy of transcutaneous bilirubin level measured by a JM-105 bilirubinometer, Pediatrics and Neonatology, https://doi.org/10.1016/j.pedneo.2022.05.012
Key note

Transcutaneous bilirubin measurement is useful, but dissociation with total serum bilirubin is a clinical problem in measurement. At transcutaneous bilirubin greater than 11 mg/dL, inaccurate measurements with dissociation greater than 2 mg/dL exceeded 10% of the TcB measurements. It is desirable to measure total serum bilirubin by blood sampling before discharge from obstetrics.

1. Introduction

Neonatal jaundice is a common condition in primary care that can result in adverse neurological outcomes if left untreated. Although some treatment initiation criteria have been established,1 there is no consensus regarding an authorized policy for screening of primary jaundice or timing of blood sampling. A simple, noninvasive transcutaneous bilirubin measurement is widely used in the screening for neonatal jaundice, and the American Academy of Pediatrics (AAP) guidelines recommend routine jaundice monitoring in all infants every 8 or 12 h.1 However, transcutaneous bilirubin (TcB) and total serum bilirubin (TSB) values obtained by blood sampling may occasionally show deviations. A previous study described a monogram of TcB for jaundice screening that requires TSB measurement by blood sampling for TcB values ≥15 mg/dL.2

The manufacturers of the latest version of a TcB measurement device (JM-105; Konica Minolta, Tokyo, Japan) state that the stabilization of light emission has enabled measurement variations (repetition error) in a single measurement to be reduced to approximately half in the new version compared with older versions.3 Thus, this study aimed to verify the accuracy of TcB measured with the latest version of JM-105 and to explore caveats to keep in mind when interpreting TcB measurements.

2. Methods

This retrospective study was conducted in Hamamatsu University Hospital, Japan, that has 700–800 deliveries per year. Healthy newborns usually stay for approximately 4 days with their mother in a newborn room that has windows facing south. Midwives measure TcB values by JM-105 at the forehead and sternum every morning and record the median value of three measurements. Pediatricians measure TSB on day 4 of life by the absorbance measurement method, with Bilimeter F (Mochida Siemens Medical Systems Co., Ltd., Tokyo, Japan) using capillary blood obtained by heel puncture. The hematocrit (Hct) value is calculated by placing whole blood in a glass tube and centrifuging; thereafter, the ratio of the blood cell length/whole blood length is measured.

We conducted a retrospective review of the medical records of healthy babies born between July 2013 and June 2018. Almost all newborns were Japanese. The TcB values on days 3 and 4, TSB and Hct values on day 4, body weight on day 4, and breast-/bottle-fed data were recorded. The body weights were measured at birth and daily until babies were discharged from the hospital using an electric resistance-type infant scale NS-608N (Atom Medical Corp. Japan) that was maintained and calibrated regularly. Weight gain on day 4 was calculated by the following equation (body weight on day 4 − birth weight)/birth weight.

Statistical analysis was performed with IBM SPSS Statistics for Windows, version 25 (IBM Corp., Armonk, NY, USA). The Kruskal–Wallis test was used to examine the difference in the median of each class divided into 2 mg/dL according to TcB or TSB. Further statistical analysis was made to determine which factors lead to increased inaccurate measurements. The Mann–Whitney test was used to analyze the birth weight, gestational age, maternal age, Apgar score (1 min/5 min), postnatal age at the time of examination, weight gain on day 4, and Hct value on day 4. Pearson’s chi-square test was used to analyze the nutrition method (breastfeeding, mixed feeding, or formula only), delivery method (normal vaginal delivery, vacuum vaginal delivery, scheduled cesarean section, or emergency cesarean section), and sex.

The study was approved by the institutional review board of Hamamatsu University School of Medicine (No. 18–120). Individual consent was waived because it was a retrospective, non-interventional study.

3. Results

A flow chart of the subject selection process is shown in Fig. 1. Of the 3979 live births in the maternity ward of Hamamatsu University Hospital during the research period, 3117 healthy babies stayed in a newborn room. Premature infants; those with respiratory distress who were admitted to the neonatal intensive care unit (NICU); newborns who started phototherapy treatment for jaundice in the NICU by day 3; those with birth weight <2500 g or ≥4000 g, gestational age <37 weeks or ≥42 weeks; or those who had incomplete data were excluded. A final total of 2788 neonates (including two neonates with hyperbilirubinemia admitted to the NICU on day 4 or later) were enrolled in the study, and their data were analyzed. Table 1 lists the characteristics of the subjects. There were 1390 boys (49.9%), the mean gestational age was 39.4 weeks, the mean birth weight was 3028 g, and 72.3% were born by normal vaginal delivery. At day 4, 89.4% of the infants were fed with both breast milk and formula.

The TSB value ranged from 1.6 to 24.3 mg/dL and was >15 mg/dL in 317 (9.5%) measurements. Overall, the difference between the TcB and TSB values on day 4 in 2788 complete data was −0.82 ± 1.45 mg/dL (mean ± SD), which ranged from −7.9 to 2.5 mg/dL. The correlation rate between the pairs of TcB and TSB measurements on day 4 was 0.858. The regression line of TcB and TSB was defined as 0.911 × TcB + 1.771. TSB that was obtained by substituting TcB for this regression line was termed estimated TSB (EstTSB).

To examine the accuracy of TcB, we divided the difference between TcB and TSB into 2-mg/dL classes according to the TSB value. In the 49 pairs of TcB and TSB measurements in which the TSB value was <5 mg/dL, the difference...
between TcB and TSB measurements was $-0.39 \pm 0.29$ mg/dL. The difference between TcB and TSB measurements widened progressively, as the TSB level increased, and was $-2.05 \pm 0.10$ mg/dL in the 300 pairs of TcB and TSB measurements in which the TSB level was $>15$ mg/dL. This finding indicates that the dissociation between TcB and TSB increased as the TSB value increased and that the TcB value tended to be lower than that of TSB. This tendency was similar to that reported in a previous study that used an earlier JM-103 model and recommended that TSB should be measured by blood sampling in the case of TcB $>15$ mg/dL.

To match the situation from the clinical viewpoint, we then divided the difference between TcB and TSB measurements into 2-mg/dL classes according to TcB (Fig. 2a). Despite variations in the TcB value, the mean difference between TcB and TSB measurements was almost the same:
Figure 2 Box plots of difference between TcB and TSB divided into 2-mg/dL classes according to TcB. (a) Box plots of TcB (day 4) – TSB (day 4). The mean value of the difference between TcB and TSB was similar among the classes. As TcB increased, the difference between TcB and TSB increased, and they dispersed both positively and negatively. A significant difference was observed between the classes according to TcB (Kruskal–Wallis test, p < 0.001). (b) Graph and table of the rate of dissociation in samples with >2 mg/dL. The gray cells indicate a rate of proper estimation of <90%, which indicates the low accuracy of the TcB measurement. The number of TcB measurements with low accuracy increased to a clinically relevant level when the TcB was ≥11 mg/dL. NICU, neonatal intensive care unit; TSB, total serum bilirubin; TcB, transcutaneous bilirubin.
the difference between TcB and TSB measurements when TcB < 5 mg/dL was −0.66 ± 0.07 (n = 63), and when the TcB level was 15 mg/dL, the difference was −0.26 ± 0.07 (n = 134). However, as the TcB value increased, more variations occurred, and the difference between TcB and TSB measurements dispersed both positively and negatively. The Kruskal–Wallis test revealed significance in the difference between TcB and TSB measurements among classes according to the TcB value (p < 0.001).

Overestimation occurred when EsTSB obtained by substituting TcB for the regression line (0.911 × TcB + 1.771) was greater than the TSB value by 2 mg/dL, and underestimation was defined as EsTSB less than the TSB value by 2 mg/dL. Proper estimation indicated that the difference between EsTSB and TSB measurements was ≤ 2 mg/dL or less. We used 2 mg/dL as the cutoff value because it has been used in previous studies and because, in clinical terms, dissociation of <2 mg/dL is regarded as being in the range of measurement error and does not have a significant effect on treatment policy. Fig. 2b shows the rates of dissociation >2 mg/dL according to overestimation and underestimation and divided into 2-mg/dL classes according to TcB for a clinical perspective. The accuracy of the TcB value was judged to be low when proper estimation was <90%. The accuracy decreased for TcB ≥ 11 mg/dL and when both overestimation and underestimation had increased. For the class of TcB 13 < 15, 10.3% were overestimated, 11.1% were underestimated, and only 78.6% of TcB measurements were properly estimated. We analyzed how the overestimation/underestimation groups differed from the proper estimation group in samples with TcB ≥11 mg/dL. When the TcB value was >11 mg/dL, 17.1% of the samples had inaccurate measurement. The Hct value on day 4 was lower in the overestimation group, 53 [49, 57] (median [25th percentile, 75th percentile]) and higher in the underestimation group, 56 [53, 60], than in the proper estimation group, 51 [47, 55].

4. Discussion

In their guidelines regarding the need for and methods of screening for neonatal jaundice, the AAP states that clinicians should ensure that all infants are routinely monitored no less than every 8–12 h for the development of jaundice. They recommend measuring TcB along with TSB for the assessment of jaundice in the first 24 h and if jaundice appears excessive for the infant’s age in those aged ≥35 gestation weeks. All newborns should be screened for neonatal jaundice. However, the methods should include noninvasive testing because frequent blood sampling can be painful and invasive for infants.

The TcB and TSB measurements may differ given their different measurement principles. TcB is lower than TSB when not in equilibrium (TSB rises sharply and TcB drops after phototherapy), when there is abundant subcutaneous melanin pigment, and when TSB is very high. TcB is higher than TSB after exchange transfusion and if there is copious unbound bilirubin. When performing and interpreting TcB measurements, it is important to recognize that TcB is not a substitute for TSB. Thus, the AAP guidelines recommend noninvasive TcB measurement devices only for infants with TSB levels <15 mg/dL,¹ and some authors have suggested including TSB measurement with blood sampling in the routine screening of all newborns.⁴–¹⁰

JM-105 is the latest model of a noninvasive instrument for measuring TcB by optical density difference measurement that employs two wavelengths of light and has been in clinical use for a long time. The fluctuations in measured values are reduced by half compared with that with the previous model, which was achieved by stabilizing the light emission.³ Studies using the same model of the device also showed that TSB ≥15 had a large dissociation between TcB and TSB, which is easy to underestimate, as reported previously.⁴–¹⁰ In the present study, it is clinically problematic that TSB was underestimated by ≥2 mg/dL in approximately half of the cases with TSB ≥15.

We divided the difference between TcB and TSB values into 2-mg/dL classes according to TcB for a clinical perspective. Although the mean difference between TcB and TSB values did not change as the TcB value increased, clinically important dissociation of >2 mg/dL increased when the TcB level was >11 mg/dL. Moreover, the difference between TcB and TSB values increased both positively and negatively, i.e., as a result of increasing overestimation and underestimation, the accuracy of the TcB measurement was inferior when the TcB level was >11 mg/dL. Because 46.7% of the term neonates have TcB level >11 mg/dL at day 4, the finding that TcB measurements are inaccurate in almost half of the newborns in the newborn room is clinically important. For smaller values, dividing the classes according to TcB resulted in less accurate TcB measurements than when dividing by TSB. This may be due to differences in the distribution of TcB and TSB. The TSB level was 11.4 mg/dL (interquartile range, 9.8–13.3), whereas the TcB level was distributed at 10.8 mg/dL (interquartile range, 9.1–12.4), reflecting the underestimation. If this is indeed the case, then more measurements may have been categorized as lower TcB class.

The Hct value differed between the proper estimation group and the overestimation/underestimation groups. To our knowledge, no study has reported the effect of Hct value on TcB measurement. Because the absorption spectra of bilirubin and Hb overlap, Hb may affect TcB, as TcB measurement decreased with increased Hb concentration.⁴¹¹ As Hct and Hb have a positive correlation, Hct may be similarly associated with TcB measurements.

In this study, we changed our perspective from mean and variance and focused on the proportion of measurement points that showed clinically significant dissociation >2 mg/dL. Because the study is conducted in a single facility, there is no need to consider differences in the types of equipment used for control, measurement skills, and clinical routines. However, it cannot be denied that there may be a bias due to the light environment around the neonates and how to handle the measuring instrument.

5. Conclusions

Dissociation from TSB increased when TcB values were high. In addition, the accuracy of TcB measurement decreased when the TcB level rise to 11 mg/dL or higher, which is
lower than the previously reported TSB value of 15 mg/dL, and accurate measurements were in less than 90% of the samples.

TcB is useful as a noninvasive jaundice screening test but is not a substitute for TSB. To evaluate neonatal jaundice accurately, measuring TSB by blood sampling before discharge from obstetrics is desirable.

Declaration of competing interest

None declared.

References