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Original Article

Transcutaneous bilirubinometry to estimate total serum bilirubin in neonatal jaundice

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Abstract

Background The gold standard for diagnosis of neonatal jaundice is total serum bilirubin (TSB) measurement. This method, however, is invasive, painful, and costly in terms of workload, time, and money. Moreover, repeated blood sampling may lead to significant blood loss, which is of particular concern in preterm infants. To overcome these drawbacks, non-invasive methods of bilirubin measurement have been proposed. Transcutaneous bilirubinometry (TcB) determines the yellowness of the subcutaneous tissue of a newborn infant by measuring the difference between optical densities for light in the blue and green wavelength regions.

Objective To evaluate the accuracy of transcutaneous bilirubinometry for estimating TSB levels in neonatal jaundice.

Methods Subjects were infants aged < 28 days with jaundice who had never been treated with phototherapy or exchange transfusion. The study was done from February to July 2016 in Mohammad Hoesin Hospital. Subjects underwent transcutaneous bilirubin (TcB) and TSB assays, with a maximum interval of 15 minutes between tests.

Results One hundred fifty patients were included in this study. The TcB values > 5 mg/dL were correlated to TSB > 5 mg/dL, with 100% sensitivity and 83.3% specificity. This cut-off point was obtained from a receiver-operator characteristic (ROC) curve with AUC 99.3% (95%CI 97.9 to 100%; P< 0.001).The correlation coefficients (r) for TSB and TcB measurements on the forehead were 0.897 (P<0.001).

Conclusion Transcutaneous bilirubinometry can be used to accurately estimate TSB levels in neonatal jaundice, and may be useful in clinical practice as a non-invasive method to reduce blood sampling. **[Paediatr Indones. 2017:57:8-11. doi: 10.14238/pi57.1.2017.8-11]**.

Keywords: *JM-105; transcutaneous bilirubin; total serum bilirubin*

Neonatal jaundice is often found in term and preterm infants. Most cases donot require treatment, but because of the potential toxicity of bilirubin, all newborns should be monitored.[1-4] In areas with limited health facilities, serum bilirubin concentration may be assessed using Kramer's scale, but the gold standard remains to be TSB measurement. This method, however, is invasive, painful, and costly, in terms of workload, time, and money. Moreover, repeated blood sampling may lead to significant blood loss, which is of particular concern in preterm infants. To overcome these drawbacks, non-invasive methods of bilirubin measurements have been proposed. Transcutaneous bilirubinometry has been shown to be correlated to serum bilirubin concentration in infants.[5-9]

The new Drager Jaundice Meter JM-105 uses 2 wavelengths and a dual optical path system. The operational principles have been described in detail by Yasuda *et al.* who used the JM-103 model, the predecessor to the JM-105.10 The jaundice meter has two optical beams, one of which reaches only

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the shallow areas of subcutaneous tissue, while the other penetrates the deeper layers. The differences between the optical densities are detected by blue and green photocells. Bilirubin accumulated primarily in the deeper subcutaneous tissue should decrease the influence of other pigments in the skin, such as melanin and hemoglobin. In a study of 77 Japanese infants, TcB levels with the JM-103 had a strong correlation well toTSB levels and performed better than the JM-102 model.[10]

There are significant variations among the different instruments for TcB measurement. When TcB is used as a clinical substitute for TSB, the new instruments should always be compared to TSB performed by the laboratory, in order to ensure good correlation.11 We aimed to evaluate the accuracy of transcutaneous bilirubinometry at Mohammad Hoesin Hospital, Palembang for the following reasons; (1) for early estimation of TSB so that invasive blood sampling procedures can be reduced; and (2) because to date, such a study has not been done in Mohammad Hoesin Hospital, Palembang, South Sumatera.

Methods

This study was conducted in the maternity ward, intermediate care, and the neonatal intensive care unit (NICU) at Mohammad Hoesin Hospital, Palembang, from February to July 2016. Subjects were infants aged < 28 days with jaundice which was measured by Kramer's scale. We excluded patients who had been treated with phototherapy or exchange transfusion, or whose parents did not consent to participation. The study was approved by the Medical Ethics Committee of Mohammad Hoesin Hospital. Subjects' parents provided informed consent.

The TcB and TSB assays were performed for all patients, with a maximum interval of 15 minutes between tests. All TcB measurements were performed by one investigator, using transcutaneous bilirubinometry (Drager Jaundice Meter, Minolta JM-105). The measurements were obtained from the forehead of the infants, while they were lying in a supine position. The fiber optic probe was placed against the forehead and gentle pressure was applied to exert even contact between the probe and the skin. The TSB assay was performed using a diazo-based method12 in the clinical chemistry laboratory of Mohammad Hoesin Hospital, Palembang, which was calibrated daily before use, in accordance with the manufacturer's instructions. Demographic data, TcB, and TSB values were analyzed using SPSS version 17.0. Pearson's linear regression analysis was used to find a correlation coefficient between TcB and TSB. We assessed cut-off point, sensitivity, and specificity using ROC curve analysis.

Results

One hundred and fifty neonatres were included in this study. The male to female ratio was 1: 1.2. **Table 1** shows the general characteristics of subjects. The majority of subjects were in < 7 day-old age group (139 neonates, 92.7%). The majority of subjects had fullterm gestational age (105 neonates, 70%) and normal birth weight of 2,500-4,000 grams (94 neonates, 62.7%). Most subjects had TSB > 5 mg/dL (144 neonates, 96%) and TcB > 5 mg/dL (145 neonates, 96.7%).

Table 2 shows the subjects' TSB and TcB concentrations. The TSB levels ranged from 4.15 to 21.66 mg/dL [mean 12.32 (SD3.4) mg/dL] and TcB levels ranged from 4.03 to 19.50 mg/dL [mean 13.05 (SD 3.5) mg/dL].

The ROC curve had an area under the curve (AUC) of 99.3% (95%CI 97.9 to 100%; P<0.001). A TcB cut-off point of > 5 mg/dL had 100% sensitivity, 83.3% specificity, 99.3% positive predictive value, and 100% negative predictive value.

Figure 1 shows the relationship between TSB and TcB, as represented by the linear equation y=0.9+0.87*x. This equation was able to correctly predict TSB with an accuracy of 80% (r2=0.805). The correlations between TSB and TcB were found to be significant and close to Pearson's correlation coefficient (r) for TSB and TcB measurements (r=0.897; P<0.001).

Discussion

A number of studies have demonstrated the possibility of predicting serum bilirubin concentration in neonates by the spectral reflectance from the

Table 1. Subjects' characteristics

Characteristics	N=150
Gender, n(%)	
Male	68 (45.3)
Female	82 (54.7)
Age, n(%)	
< 7 days	139 (92.7)
7-14 days	6 (4)
15-28 days	5 (3.3)
Gestational age, n(%)	
< 38 weeks	41 (27.3)
38-42 weeks	105 (70)
> 42 weeks	4 (2.7)
Birth weight, n(%)	
1,000- < 1,500 g	5 (3.3)
1,500 - < 2,500 g	50 (33.3)
2,500 - 4,000 g	94 (62.7)
> 4,000 g	1 (0.7)
Kramer's scale, n(%)	
I	16 (10.7)
II	24 (16)
III	75 (50)
IV	31 (20.7)
V	4 (2.6)
TSB, n(%)	
> 5 mg/dL	144 (96)
≤ 5 mg/dL	6 (4)
TcB, n(%)	
> 5 mg/dL	145 (96.7)
≤ 5 mg/dL	5 (3.3)

Table 2. Subjects' TSB and TcB concentrations (N=150)

Characteristics	Minimum	Maximum	Mean (SD)
TSB, mg/dL	4.15	21.66	12.32 (3.4)
TcB, mg/dL	4.03	19.50	13.05 (3.5)

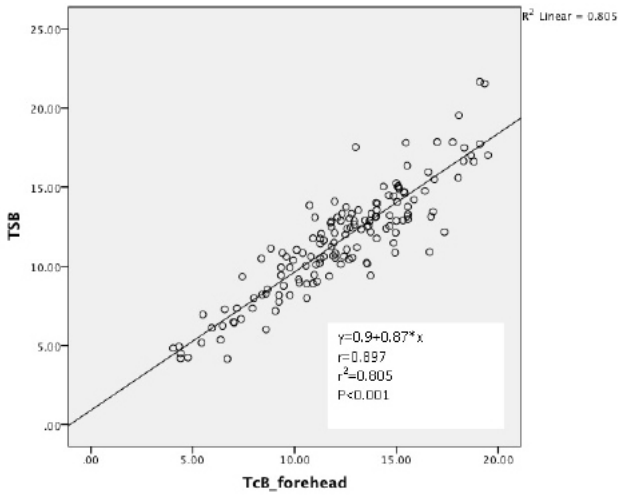

Figure 1. Scatter plot correlation between TSB and TcB measurements

skin. However, the accuracy of these techniques is complicated by variations in skin pigmentation and dermal maturity. Hence, the results of studies in Caucasion infants may not be applicable to the racially heterogeneous Indonesian population.[13,14] The overall correlation between JM-103 measurements and total serum bilirubin estimation was reported to be linear (r = 0.89). The measurements were independent of gestation, race, and ethnicity.[15]

In our study, the correlation coefficient between TSB and TcB (JM-105, at the forehead site) concentrations was high and significant (r = 0.897; P< 0.01), in agreement with studies by Maisels *et al.* in China (r=0.83) and Lamet al.(r=0.83).[16,17] The correlation coefficient does not provide information about clinical significance of the diagnostic test. But we found that as TSB level increased, the difference between values of TcB and TSB increased as well. In addition, the lower the TSB level at which treatment began can lead to frequent blood sampling, a painful procedure with possible complications. The TcB can be used as a screening test to determine the need for TSB measurement.[18]

When comparing TcB and TSB measurements, it is important to remember that the two methods of measurement may be evaluating different physiologic entities. Rubaltelli *et al.* suggested that TcB methods measure the amount of bilirubin that has moved from the serum into the tissue, possibly mimicking the movement of bilirubin across the blood–brain barrier and into brain issue, whereas laboratory-based methods measure only bilirubin that is circulating in the blood. Thus, TcB may actually offer additional information not provided by TSB measurements, although this hypothesis remains to be proven.[19]

The TcB cut-off point obtained from the subjects was > 5 mg/dL, with an AUC of 99.3% (95%CI 97.9 to 100%; P <0.001), sensitivity of 100%, specificity of 83.3%, positive predictive value of 99.3%, and negative predictive value of 100%. A number of studies found different cut-off points. Panburana et al. reported that TcB levels of >12 mg/dL had the

best sensitivity (87.5%) and specificity (96.9%) for predicting TSB.[20]

In conclusion, transcutaneous bilirubin, as assessed by JM-105 has a strongly significant correlation to total serum bilirubin, as measured by chemical laboratory method. The non-invasive TcB measurement (JM-105) is useful as a screening tool to identify those who need serum bilirubin measurements, and can be used in clinical practice to reduce blood sampling. But TcB cannot substitute for total serum bilirubin estimation.

Conflict of interest

None declared.

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