Skin Bilirubin Measurement during Phototherapy in Preterm Jaundice Infants

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Abstract

Objective: To evaluate the correlation between skin bilirubin (transcutaneous bilirubin: TcB) and total serum bilirubin (TSB) levels in preterm jaundice infants during phototherapy.

Methods: Levels of TcB and TSB during phototherapy were measured in preterm jaundice neonates who required phototherapy during September 2011, 1st to July 2012, 31st in Charoenkrung Pracharak Hospital. The TcB was measured over the unexposed (TcBUE) skin underneath the eye pad (glabella region) and exposed skin (TcBE) of the forehead. Pearson's correlation coefficients were determined. Factors possibly influencing TSB, including TcBUE and TcBE, were analysed with a stepwise multiple linear regression analysis. Factors with significant correlation with TSB were entered into the equation to obtain the predicted TSBs. The predicted TSBs derived from TcBUE and from TcBE were then compared with the actual TSB.

Results: Sixty preterm infants were involved in this study. We found strong correlation between TcBUE - TSB ($r=0.73$; p-value < 0.001) and TcBE - TSB ($r=0.71$; p-value < 0.001). Factors which impacted the predicted TSB from TcB during phototherapy were birth weight. The predicted TSB from multiple regression analysis using TcBUE = 0.363 + (0.002 birth weight) + (0.501 TcBUE). While the predicted TSB using TcBE = - 4.230 + (0.005 birth weight) + (1.176 TcBE) - 0.367 (birth weight $\times$ TcBE). Defining a difference of $\pm$ 1.5 mg/dl as similar, we found that the predicted TSB from TcBUE was similar to the actual TSB in 53.3% and underestimated in 41.7%. The corresponding comparison of the predicted TSB from TcBE to TSB demonstrated 66.7% were similar and 25.0% were underestimated.

Conclusion: Skin bilirubin (TcB) in preterm jaundice infants showed strong correlation with TSB. However, the TcB cannot predict TSB during phototherapy well. Underestimation rate of the predicted TSB during phototherapy was found in high percentage. It is not safe to replace TSB with the TcB, both in exposed and unexposed areas, for a clinical care of preterm infants because it may lead to earlier termination of phototherapy.

Keywords: hyperbilirubinemia, skin bilirubin, transcutaneous bilirubin, preterm infants, phototherapy

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บทคัดย่อ

การวัดค่าบิลิรูบินทางผิวหนังในทารกเกิดก่อนกำหนดตัวเหลืองระหว่างได้รับการรักษาโดยวิธีส่องไฟ

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วัตถุประสงค์: เพื่อศึกษาความสัมพันธ์ระหว่างค่าบิลิรูบินที่วัดทางผิวหนังกับค่าบิลิรูบินในเลือด ในทารกเกิดก่อนกำหนดระหว่างส่องไฟรักษาภาวะตัวเหลือง

วิธีดำเนินการวิจัย: การศึกษานี้ศึกษาในทารกเกิดก่อนกำหนดตัวเหลืองที่ได้รับการรักษาด้วยวิธีส่องไฟที่โรงพยาบาลเจริญกรุงประชารักษ์ ตั้งแต่เดือนกันยายน พ.ศ. 2554 ถึง เดือนกรกฎาคม พ.ศ. 2555 โดยมีการวัดค่าบิลิรูบินทางผิวหนังบริเวณที่ไม่ถูกแสงที่อยู่ใต้ต่อผ้าปิดตา และบริเวณที่ถูกแสงที่หน้าผากของทารกระหว่างส่องไฟเทียบกับค่าบิลิรูบินในเลือด วิเคราะห์สถิติเพียร์สันเพื่อหาสัมประสิทธิ์สหสัมพันธ์ และวิเคราะห์ปัจจัยที่มีผลต่อความสัมพันธ์ระหว่างค่าบิลิรูบินทางผิวหนังกับค่าบิลิรูบินในเลือดโดยใช้การวิเคราะห์ถดถอยและสหสัมพันธ์เชิงซ้อน และสร้างสมการเพื่อทำนายค่าบิลิรูบินในเลือด และทำการเปรียบเทียบแบบคู่ระหว่างค่าบิลิรูบินที่คำนวณจากสมการกับค่าบิลิรูบินในเลือดจากห้องปฏิบัติการ

ผลการวิจัย: จากการศึกษาทารกเกิดก่อนกำหนดตัวเหลืองระหว่างการรักษาด้วยการส่องไฟจำนวน 60 ราย พบค่าสัมประสิทธิ์สหสัมพันธ์ระหว่างค่าบิลิรูบินทางผิวหนังบริเวณไม่ถูกแสงกับค่าบิลิรูบินในเลือด และระหว่างค่าบิลิรูบินทางผิวหนังบริเวณที่ถูกแสงกับค่าบิลิรูบินในเลือดอยู่ระดับสูง ($r=0.73$; p–value <0.001 และ $r=0.71$; p–value <0.001 ตามลำดับ) เมื่อวิเคราะห์ความถดถอยและสหสัมพันธ์ เชิงซ้อน พบน้ำหนักแรกเกิดเป็นปัจจัยซึ่งมีผลต่อการทำนายค่าบิลิรูบินในเลือดจากค่าบิลิรูบินทางผิวหนังในช่วงที่ส่องไฟ โดยมีสมการสหสัมพันธ์เชิงซ้อน ทำนายค่าบิลิรูบินในเลือดจากค่าบิลิรูบินทางผิวหนังบริเวณที่ไม่ถูกแสงคือ 0.363 + (0.002 × น้ำหนักแรกเกิด) + (0.501 × ค่าบิลิรูบินทางผิวหนังบริเวณที่ไม่ถูกแสง) และสมการสำหรับทำนายค่าบิลิรูบินในเลือดจากค่าบิลิรูบินทางผิวหนังบริเวณที่ถูกแสงคือ −4.230 + (0.005 × น้ำหนักแรกเกิด) + (1.176 × ค่าบิลิรูบินทางผิวหนังบริเวณถูกแสง) − 0.367 (น้ำหนักแรกเกิด × ค่าบิลิรูบินทางผิวหนังบริเวณถูกแสง) จากการทดสอบเปรียบเทียบแบบคู่ระหว่างค่าทำนายบิลิรูบินในเลือดจากสมการถดถอยกับค่าบิลิรูบินในเลือดที่ได้จากห้องปฏิบัติการ กำหนดให้ค่าเทียบเท่าเมื่อค่าทั้งสองต่างกันไม่เกิน 1.5 มก./ดล. พบค่าเทียบเท่าบริเวณไม่ถูกแสงร้อยละ 53.3 และในบริเวณที่ถูกแสง ร้อยละ 66.7 และพบค่าทำนายบิลิรูบินในเลือดจากสมการถดถอยมีค่าต่ำกว่าค่าบิลิรูบินในเลือดจากห้องปฏิบัติการบริเวณไม่ถูกแสงร้อยละ 41.7 และบริเวณที่ถูกแสง ร้อยละ 25.0

สรุป: ค่าบิลิรูบินทางผิวหนังในทารกเกิดก่อนกำหนดตัวเหลืองมีความสัมพันธ์กับค่าบิลิรูบินในเลือดในระดับสูง อย่างไรก็ตามค่าบิลิรูบินทางผิวหนังไม่สามารถทำนายค่าบิลิรูบินในเลือดระหว่างการรักษาโดยวิธีส่องไฟเนื่องจากค่าบิลิรูบินในเลือดที่ทำนายจากการสมการมีค่าต่ำกว่าค่าบิลิรูบินในเลือดจากห้องปฏิบัติการในอัตราที่สูง จึงไม่ปลอดภัยที่จะนำมาใช้แทนกันทางคลินิกเนื่องจากทารกอาจเกิดอันตรายจากภาวะตัวเหลืองได้หากมีการหยุดส่องไฟเร็วกว่าเกณฑ์

Introduction

Hyperbilirubinemia is a common complication of neonates. The incidence varies from approximately 80% in preterm to 50% in term neonates.[1] Neonatal hyperbilirubinemia or jaundice is mostly physiologic which requires no therapeutic intervention. In other situations when hyperbilirubinemia is pathologic, phototherapy is indicated. Treatment which aims to reduce neonatal indirect bilirubin is especially important in preterm infants because their immature blood-brain barrier allows better bilirubin diffusion to the brain,[2,3] with higher risk of consequent bilirubin encephalopathy and long term neurologic sequelae.[4] Determination of total serum bilirubin (TSB) is an important means to assess bilirubin level for a recognition of neonates at risk for bilirubin encephalopathy. However, skin puncture for blood sample collection is invasive and painful. It may also lead to significant blood loss particularly in affected neonates requiring phototherapy who require serial serum bilirubin measurements of a daily basis or more frequently as clinically indicated. A non-invasive method to measure skin bilirubin (transcutaneous bilirubin: TcB) has been proposed as an alternative approach. Transcutaneous bilirubinometer works by directing light to the skin of the neonate then an intensity of specific wavelength returned is measured. The procedure is safe, easy and convenient to evaluate the severity of jaundice. Most studies in healthy term and near-term neonates found high accuracy of TcB.[5-9] However, controversial data in preterm jaundice neonates exist regarding the reliability of TcB as a screening method[10-14] and as a monitor tool during treatment with phototherapy.[15-18] This study aimed to evaluate the correlation of TcB and TSB measurement in preterm jaundice neonates during phototherapy. Predicted values of TSB from the TcB by statistical means were also obtained to assess whether they can replace the actual TSB in clinical practice.

Methods

The descriptive prospective study was approved by the Bangkok Metropolitan Administration Committee for Research in Human Subjects. The study was performed in preterm jaundice infants born with gestational age less than 37 weeks who were admitted in Nursery Intensive Care Unit and sick newborn ward of Charoenkrung Pracharak Hospital during September 2011 and July 2012. Other inclusion criteria were infants whose postnatal age was less than 7 days, had birth weight over 1,000 grams, and had high TSB value requiring phototherapy. Exclusion criteria were: preterm jaundice infants who had unstable hemodynamic status, had prophylactic phototherapy, or had any of the followings: history of exchange transfusion, congenital anomalies or chromosomal abnormalities. Neonates whose parents declined to participate in the study were also excluded. Parental written informed consent of each participant was obtained upon agreement to enter into the study.

The use of phototherapy was determined by the panel of attending pediatricians who usually follow the Clinical Practice Guideline of Department of Pediatrics, Faculty of Medicine Siriraj Hospital for preterm jaundice neonates.[19] Phototherapy was administered with blue light with a high intensity of 400 to 500 wavelengths which yield the highest efficacy for isomerization of unconjugated bilirubin in the skin. The eye pads made of gauzes inserted with old x-ray film covering from just above the glabella to lower parts of orbits were placed to protect the eyes of the infants.

The TcB in this study was measured with a transcutaneous bilirubinometer (Minolta Airshields Jaundice Meter JM-103 ; Osaka, Japan). After the phototherapy light was turned off, the optic head of the meter is gently pressed on the skin of neonates on the glabella area underneath the eye pads for TcB in the unexposed area (TcBUE) and skin on the forehead above the eye pads for TcB in exposed area (TcBE). Two readings were taken on each site and the mean value

was obtained as the final values. All TcB measurements were done by well-trained nurses specialized in intensive care of preterm infants. Total serum bilirubin was measured in our hospital's laboratory using a spectrophotometric method by Bilirubinometer Model BR 400 which measured dual wavelength (455 nm, 575 nm) to minimize the interference of hemolysis and turbidity as frequently seen in the serum of jaundice neonates. The machine was calibrated daily as a quality control. Blood sampling was collected within half an hour after TcB measurement. The values of TcB and TSB in this study were taken from the value or specimen taken in the following morning after phototherapy initiation.

Aside from the levels of TSB and TcB during phototherapy, other data collected were: gender, ethnicity, birth weight, gestational age at birth, postnatal age, and other co-morbidities. Gestational age was obtained from the maternal last menstrual period and by the modified Ballard Score assessment. If the difference between two methods was less than 2 weeks, gestational age from the last menstrual period was used. Preterm LGA (large for gestational age) was defined as preterm infants with birth weight greater than 90th percentile for specific age. Preterm infant with birth weight below the 10th percentile was classified as preterm SGA (small for gestational age).

Statistic analysis was performed by SPSS for Windows Releases 11.5. Demographic data were reported as number with percentage or mean with standard deviation. Pearson linear regression analysis was used to determine the correlation coefficients between TSB and TcB as well as other variables (birth weight, gestational age, and postnatal age). The relationship was perfect positive linear relationship if r values were between 0.91 and 1.00, strong positive with 0.71 and 0.90, moderate positive with 0.51 and 0.70, weak with 0.31-0.50, and very weak with 0.00 and 0.30.[20] The corresponding negative r values indicated inverse relationship. Factors that were significantly correlated with TSB along with their interaction terms were entered into a linear regression model. The beta coefficients from the model were used to generate an equation to predict the level of TSB. Pair comparisons of predicted TSB (derived from an equation) with actual TSB (derived from our laboratory-BR 400) were then performed. The two values of actual and predicted TSB levels were determined as similar if the difference was ± 1.5 mg/dl (based on the Minolta manufacturer's reference), overestimation if predicted TSB was higher than actual TSB > 1.5 mg/dl), and underestimation if predicted TSB was lower than actual TSB > 1.5 mg/dl. A p-value < 0.05 was considered statistically significant.

Results

From approximately 4,800 deliveries and 350 preterm infants per year in our hospital, 60 preterm neonates during the study period met inclusion criteria and were involved in this study. Majority of the participants (96.7%) were Thai and slightly more than half were male (51.7%). The gestational age ranged from 28 to 36 weeks (mean 33.6 ± 2.1 weeks) with their birth weights between 1,050 to 3,680 grams (mean 2,043.1 ± 536.0 grams). One preterm baby born of diabetic mother with birth weight of 3,680 grams was defined as preterm LGA by a Ballard Score assessment. Aside from jaundice, up to half of the neonates had one or more co-morbidities. The three most common were: respiratory distress syndrome (29 neonates or 48.3%), bacterial sepsis (16 or 26.7%), and hypoglycemia (15 or 25.0%).

Mean postnatal age of the preterm babies at the beginning of phototherapy was 71.2 ± 27.7 hours (range, 12-126 hours). Twenty nine (48.3%) had phototherapy when their postnatal ages were less than 72 hours and 31 (51.7%) when they aged between 72 to 126 hours. All demographic data and baseline clinical characteristics of preterm babies are shown in Table 1.

Mean TcBUE and mean TcBE values obtained during phototherapy were significantly lower than TSB

Table 1 Demographic data and baseline characteristics (n=60)

	Number	Percent (%)	mean ± SD
Sex			
Male	31	51.7	
Female	29	48.3	
Race			
Thai	58	96.7	
Others	2	3.3	
Birth weight (g)			2,043.1 ± 536.0
1,000-1,500	9	15.0	
1,501-2,000	23	38.4	
2,001-2,500	17	28.3	
≥ 2,500	11	18.3	
Gestational age (weeks)			33.6 ± 2.1
28-33	23	38.3	
34-36	37	61.7	
Method of GA assessment			
By score	50	83.3	
By date	10	16.7	
Postnatal age at the time of beginning phototherapy			71.2 ± 27.7
0-71 hours	29	48.3	
72-126 hours	31	51.7	
Associated diseases			
Respiratiory distress syndrome (RDS)	29	48.3	
Bacterial sepsis	16	26.7	
Hypoglycemia	15	25.0	
Hypothermia	9	15.0	
Birth asphyxia	3	5.0	
Large for gestational age (LGA)	3	5.0	
Small for gestational age (SGA)	3	5.0	
Others*	10	16.7	

* Others: enterocolitis, apnea, potassium imbalance, sodium imbalance, transient tachypnea, feeding problem, G-6-P-D deficiency, renal cyst, hypocalcemia, pneumonia

Table 2 Comparison of transcutaneous bilirubin in both unexposed (TcBUE) and exposed (TcBE) areas to total serum bilirubin (TSB)

	Transcutaneous bilirubin (mg/dl) ± SD	Total serum bilirubin (mg/dl) $\overline{X}$ ± SD	Mean difference (mg/dl) $\overline{X}$ ± SD	95% CI of mean difference
Unexposed area during phototherapy	8.49 ± 2.81	9.22 ± 2.76	0.72 ± 2.04	0.26-1.25
Exposed area during phototherapy	7.41 ± 2.98	9.22 ± 2.76	1. 80 ± 2.20	1.24-2.37

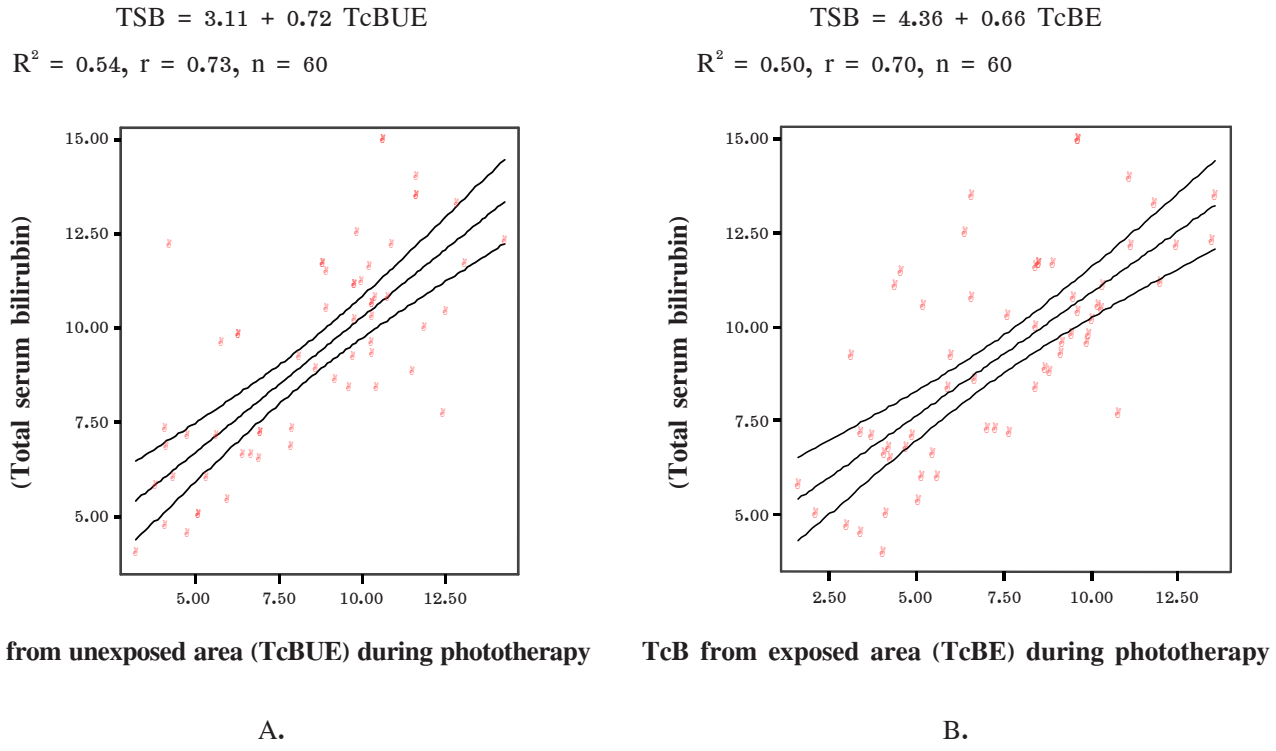

Figure 1 A. Correlation between TcBUE (transcutaneous bilirubin from unexposed area) and TSB (total serum bilirubin) B. Correlation between TcBE (transcutaneous bilirubin in exposed area) and TSB

(p-value < 0.001). Levels of TcB in both exposed and un-exposed areas during phototherapy and TSB are shown in Table 2. Figure 1 presents the correlation between TcBUE and TcBE with TSB. We found a strong positive correlation between both TcBUE vs TSB and TcBE vs TSB during phototherapy (r=0.73; R^2=0.54, p-value < 0.001; and r=0.71; R^2=0.50, p-value < 0.001 respectively).

Since the R^2 between TcBUE or TcBE and TSB were only 0.54 or 0.50, we searched for other variables that might also have correlation with TSB. We found various degrees of correlation between TSB and these factors: very weak correlation with postnatal age, weak correlation with gestational age, and moderate correlation with birth weight. Details of their correlations are presented in Table 3.

We entered TcB, birth weight and gestational age

Table 3 Correlation of gestational age, birth weight, postnatal age, and transcutaneous bilirubin in unexposed (TcBUE) and exposed area (TcBE) during phototherapy with total serum bilirubin (n=60)

Factors	correlation (r)	p-value	level of correlation
Gestational age (week)	0.417	0.001	weak
Birth weight (g)	0.697	< 0.001	moderate
Postnatal age (hour)	0.130	0.321	very weak
TcBUE (mg/dl)	0.732	< 0.001	strong
TcBE (mg/dl)	0.708	< 0.001	strong

Table 4 Multiple linear regression models to predict total serum bilirubin (TSB) from transcutaneous bilirubin (in unexposed (TcBUE) and exposed area (TcBE)) during phototherapy and other factors

Variables	First model		Second model		Final model	
	coefficient	p-value	coefficient	p-value	coefficient	p-value
During phototherapy in unexposed area						
TcBUE	0.505	< 0.001	1.007	0.003	0.501	< 0.001
Gestational age	-0.030	0.799	-	-	-	-
Birth weight	0.002	0.001	0.004	0.003	0.002	0.001
Birth weight × TcBUE	-	-	-0.252	0.109		
Constant value	1.244		-3.882		0.363	
r	0.824		0.832		0.824	
R^2	0.679		0.693		0.678	
During phototherapy in exposed area						
TcBE	0.424	< 0.001	1.176	< 0.001	1.176	< 0.001
Gestational age	0.066	0.604	-	-	-	-
Birth weight	0.002	0.001	0.005	0.001	0.005	0.001
Birth weight × TcBE	-	-	-0.367	0.009	0.367	0.009
Constant value	-0.394		-4.230		-4.230	
r	0.792		0.818		0.818	
R^2	0.627		0.669		0.669	

(which had significant correlations with TSB) into a first linear regression model. Factors that had statistical significant in the first model (birth weight and TcBUE or TcBE) including their interaction terms were then tested in the second model. The results are shown in Table 4. We found no interaction between birth weight and TcB in unexposed area while there was an interaction between both variables in exposed area. Hence, from

Table 5 Paired comparison between predicted total serum bilirubin (TSB) level calculated from transcutaneous bilirubin (TcB) in unexposed and exposed area and actual TSB (n=60)

Comparison between predicted TSB and Actual TSB	Underestimate		Similar		Overestimate	
	Number	%	Number	%	Number	%
Unexposed area	25	41.7	32	53.3	3	5.0
Exposed area	15	25.0	40	66.7	5	8.3

TcBUE a final model to predict the level of TSB was derived from coefficient values of birth weight and TcBUE while from TcBE was derived from coefficient values of birth weight, TcBE, and birth weight × TcBE.

The equations used to calculate the predicted TSB from TcB in unexposed and exposed area were:

Predicted TSB = 0.363 + (0.002 birth weight) + (0.501 TcBUE)

Predicted TSB = −4.230 + (0.005 birth weight) + (1.176 TcBE) − 0.367 (birth weight × TcBE)

A pair comparison between actual TSB and predicted TSB from the regression equations above were performed (Table 5). Between predicted TSB from TcB in unexposed area and actual TSB; similar results were found in 53.3%, underestimation in 41.7%, and overestimation in 5.0%. For predicted TSB from TcB in exposed area and actual TSB; 66.7% were similar, 25.0% were underestimation, and 8.3% were overestimation.

Discussion

Previous studies suggested that TcB could be used for screening neonatal hyperbilirubinemia in healthy term and near-term infants.[5-9] However, function of TcB in preterm neonates are still a controversial issue. Some studies showed that TcB of preterm jaundice infants with phototherapy particularly in the unexposed area, could predict TSB value.[15-18] Others demonstrated that TcB had good reliability in preterm infants; however, its performance was not as good as in healthy term infants.[12-14] Few studies found limiting factors for the TcB function. One study by Knüpfer et al[12] found TcB was reliable only in preterm infants who had gestational age more than 30 weeks. Another study by Karolyi et al[13] also reported that TcB could not precisely predict TSB in very low birth weight ≤ 1,500 g neonates. We did not find these factors contributing to the limited function of TcB. Most of our preterm infants were older than 30 weeks gestation, with only 7 neonates born prior to 30 weeks of gestation. Furthermore, only 9 cases had birth weight ≤ 1,500 g. Despite these favorable clinical features in our participants, we found TcB could not satisfactorily predict TSB.

Our study found both TcBUE and TcBE were strongly correlated with TSB (r=0.73 and 0.71 respectively). These degrees of correlation in our study were relatively low compared to 0.7-0.8 found in other studies involving preterm neonates who did not have phototherapy.[12,14,16,18] Nevertheless, a better TcBUE-TSB than TcBE-TSB correlation in our study was accordant to other studies.[15,17] Nanjundaswamy et al[17] also found higher correlation of TcBUE-TSB (r=0.77) than TcBE-TSB (r=0.70) in preterm infants receiving phototherapy.

However, in Nanjundaswarmy's study bilirubinometer (BiliCheck™) was used and they measured the intensity of the phototherapy light under the eye pads to assure that there was no measureable transmission of light through the pads in unexposed area. Tan & Dong[15] also found high degree of TcBUE-TSB correlation (r=0.74) in term infants during phototherapy but only weaker TcBE-TSB correlation (r=0.60).

Findings R^2 of 0.54 and 0.50 in unexposed and exposed area implied that 54% of or 50% of TSB level during phototherapy were dependent on TcBUE or TcBE while the remaining 46% or 50% were due to other factors. In an effort to identify other factors, multiple stepwise regression analysis was performed. The results showed birth weight and TcB had impacted the predicted TSBs level. Other reports also suggested that TcB measurements itself can be affected by various factors, including gestational age, postnatal age, and phototherapy.[12,14,16,21] These studies found that as the gestational age decreased or postnatal age advanced, TcB-TSB correlation decreased.[12,14,16] One study also found that the TcB measurement was not reliable when phototherapy was being administered to the infants.[21]

We attempted to explore further role of TcB. With the two structured equations derived from multiple regression analysis data, we calculated the predicted TSB from TcBUE and TcBE, respectively. Pair comparison between actual TSB (derived from our laboratory) and predicted TSB (derived from regression equation) did not show better function of TcB in the unexposed area. Nevertheless, only 53.3% of predicted TSB from TcBUE and 66.7% of TSB from TcBE were similar with actual TsB. Approximately one fourth to nearly one half of predicted TsBs would underestimate the actual TsB.

The suboptimal function of TcB measurement to predict TSB was also found in other studies.[17,22,23] Sanpavat & Nuchprayoon[22] demonstrated that TcB measurement (which had positive correlation with TSB) had a tendency to underestimate TSB levels. The mean difference between TSB and TcB measured by Minolta JM 103 was 0.7 mg/dl (SD = 1.6 mg/dl, and 95% confidence interval (CI) of the mean of 0.4 and 1.0). This was, however, in contrast to the other two studies by Panburana et al[23] and Nanjundaswamy et al[17] who found that TcB value tended to overestimate TSB value. In Panburana's study, TcB levels tended to be higher than TSB with mean difference of 0.44 mg/dl (95% CI: 0.13-0.74 mg/dl) and SD: 1.6 while in Nanjundaswamy's study,[17] paired comparisons between TcB and TSB were done with overestimatation of TSB by 64% before phototherapy, by 42% and 27% during phototherapy in unexposed and exposed area. Nevertheless, these other studies directly compared the measured TcB and actual TSB while our study used the multiple stepwise regression analysis. Hence, our result of TcB having a tendency to underestimate the TSB should be more convincing.

We were aware of few limitations in our study. First we did not measure the intensity of light under the eye pads to confirm that the unexposed skin was completely protected from the phototherapy exposure. With the smaller preterm babies, the smaller the eye pads are generally used. This might allow the scattered light along the edge of eye pads. Furthermore, there was only small area under the small eye pads for the probe to measure TcBUE. These reasons might cause the lower percentage of similarity in the unexposed area. Second, factor of other co-morbidities could not be taken into the analyses because each preterm neonate frequently had complex problems with more than one illness. These limitations should be concerned in future researches.

Although our study found strong correlation of TcB and TSB, we could not recommend the replacement of TSB with TcB particularly during phototherapy. Predicted TSB during phototherapy had only suboptimal clinical function, with approximately 53% or 67% having similar values to TSB. The underestimation was as high as 42% in unexposed or 25% in exposed areas. These rates of underestimation are clinically unacceptable because these preterm jaundice babies may have risk of bilirubin encephalopathy with an early termination of phototherapy.

In conclusion skin bilirubin measurement in preterm jaundice neonates had strong correlation with TSB. However, skin bilirubin cannot predict total serum bilirubin well. Only half or two thirds of predicted TSB obtained from calculation had similar values with actual TSB while approximately one fourth to nearly half had underestimation.

Acknowledgement

The authors thank the Director of Charoenkrung Pracharak Hospital, Dr.Somchai Jungmeechoke, for his support to this research work and the manuscript preparation as well as Prof. Manit Sripramote for his advice on research methodology and Miss Sumalee Thanindratarn for statistic analysis.

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