

Term Neonatal Jaundice Screening by Transmission Transcutaneous Bilirubinometer

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บทคัดย่อ: การคัดกรองภาวะตัวเหลืองในทารกแรกเกิดด้วยการตรวจวัดบิลิรูบินทางผิวหนังแบบส่องผ่าน

วิวัฒน์ เจริญศิริวัฒน์ พ.บ.

กลุ่มงานกุมารเวชศาสตร์ โรงพยาบาลเลิดสิน, สถาบันร่วมผลิตแพทย์ กรมการแพทย์, มหาวิทยาลัยรังสิต

ภูมิหลัง: ศึกษาความน่าเชื่อถือในการคัดกรองด้วยเครื่องวัดบิลิรูบินทางผิวหนังแบบส่องผ่าน **วิธีการ:** เป็นการศึกษาไปข้างหน้าในทารกแรกเกิดที่มีภาวะตัวเหลือง เปรียบเทียบการวัดค่าบิลิรูบินในทารกแรกคลอดด้วยการวัดทางผิวหนังแบบส่องผ่านกับการเจาะเลือดตามเกณฑ์มาตรฐาน เพื่อเป็นข้อมูลพื้นฐานในการตัดสินใจเลือกใช้เครื่องวัดบิลิรูบินในทารกแรกคลอดเป็นอุปกรณ์ในการคัดกรองขั้นต้นต่อไป **ผล:** พบว่า จากจำนวนทารกที่มีปัญหาสงสัยว่า ตัวเหลือง จำนวน 100 ราย อายุครรภ์ 39.15 ± 1.29 สัปดาห์ น้ำหนักแรกเกิด $3,066.70 \pm 382.62$ กรัม การคัดกรองด้วยเครื่องวัดบิลิรูบินทางผิวหนังแบบส่องผ่าน มีความไวระหว่างร้อยละ 91.67-100 ความจำเพาะระหว่างร้อยละ 44.00 - 78.02 บิลิรูบินที่วัดได้สามารถนำไปสร้างสมการความสัมพันธ์เชิงเส้นตรงระหว่างระดับบิลิรูบินที่ผิวหนังแบบส่องผ่าน และที่วัดจากเลือด ซึ่งมีค่าสัมประสิทธิ์แสดงการตัดสินใจ เท่ากับ 0.636 **สรุป:** ความสามารถของการวัดระดับบิลิรูบินทางผิวหนังแบบส่องผ่านในการทำนายระดับบิลิรูบินในเลือดอยู่ในระดับปานกลาง สามารถใช้เป็นการคัดกรองเบื้องต้นได้

คำสำคัญ: ภาวะตัวเหลืองในทารกแรกเกิด ค่าบิลิรูบินทางผิวหนังแบบส่องผ่าน ค่าบิลิรูบินในเลือด

Abstract

Background: To find reliability of bilirubin measurement in term neonates using transcutaneous bilirubinometer. **Methods:** This was a cross-sectional descriptive study. Term neonates who had jaundice were collected blood for serum bilirubin and transcutaneous bilirubin also collected in the same time. Correlation between transcutaneous bilirubin and serum bilirubin level was calculated. **Result:** 100 term neonates born at gestational age of 39.15 ± 1.29 weeks and birth weight of $3,066.70 \pm 382.62$ grams were measured for bilirubin level. The result of the screening test using bilirubinometer has sensitivity 91.67-100%, specificity 44.00 - 78.02 % with correlation between transcutaneous bilirubin and serum bilirubin level could be created as a linear equation with coefficient of determination (r^2) was equal to 0.636. **Conclusions:** Transmission transcutaneous bilirubin measurement had moderate level of accuracy in measuring serum bilirubin level and could be used as a screening method.

Keywords: Neonatal non-hemolytic jaundice, Phototherapy with T8 (18 watt) fluorescent tubes mounted on light reflecting lamp holder

Introduction

Neonatal jaundice is a common problem which might lead to kernicterus¹. Early diagnosis and treatment can reduce severe brain damage². Nowadays, heel-stick technique is the standard method to collect neonatal blood for bilirubin measurement. The collected blood in hematocrit tubes were then measured for bilirubin by spectrophotometry. Only neonates suspected of jaundice by physicians or attending nurses would be measured for bilirubin level which required high experiences health care professionals.

Today, efficacy of transcutaneous bilirubinometer for screening of neonatal jaundice have been reported³⁻⁶. Principle of this method depends on reflection of light from the equipment placed at forehead or sternum⁷⁻¹². This requires experiences from examiner and is easy to have errors in interpretation¹³⁻¹⁶. Therefore, pitfalls in measuring techniques had been corrected

by placing the equipment at the back of ear pinna instead of forehead or sternum. One study in 60 term neonates¹⁷ found that transmission transcutaneous bilirubinometer had high predictive value for serum bilirubin level and can be used as a screening method.

In this study, the investigator wants to study the possibility of using transmission transcutaneous bilirubinometer as screening test for term neonatal jaundice. If the results are accurate in assessing term neonatal jaundice, it will be used as policy data for using the equipment as screening test instead of eyesight.

Materials and Methods

This was a cross-sectional descriptive study in term neonates born at Lerdsin Hospital between April 2015 and June 2015 that attending health care personnel suspected of jaundice. All neonates were collected blood for serum bilirubin

measurement and collected transcutaneous by equipment placed at the back of ear pinna as described above. Detailed information of neonates including maternal pregnancy history, maternal gestational age, sex, birth weight and time of blood collection were recorded. The consent from all participants were done by their parents and the study was approved by ethics committee of Lerdsin Hospital.

Equipments

1. A transmission transcutaneous bilirubinometer (Natus®), model BiliCare, serial number S/N 141270 (figure 1).
2. A serum bilirubin measurement equipment (Optima Inc, Japan), model BR 400, which was calibrated regularly as scheduled (last calibration was December 3rd, 2014).

Samples

Term neonates who were born at Lerdsin hospital between April 2015 to June 2015

Inclusion criteria:

Term neonates who were born at Lerdsin Hospital and were suspected to have jaundice by attending physicians.

Exclusion criteria:

1. Neonates who were in critical condition.
2. Neonates with ear pinna abnormality.
3. Request for withdrawal from custodians
4. Previous treatment for neonatal jaundice

Sample size was calculated according to preliminary study in 60 neonates (17) as follows,

$$n = \frac{Z_{\alpha/2}^2 \text{Spec}(1-\text{Spec})}{d^2(1-\text{Prev})}$$

$$Z_{\alpha/2} = 1.96$$

$$\text{Spec} = 61.54\% = 0.6154$$

$$1 - \text{Spec} = 0.3846$$

$$d = 0.15$$

$$= 95 \text{ cases}$$

Sample size was round to 95 cases and added up to 100 cases.

Research methodology

According to standard Lerdsin Hospital Protocol, term neonates who were born at the hospital will be assessed for jaundice by attending physicians' eyes. If they were suspected of jaundice, they would be checked blood for serum bilirubin level using our standard equipment. Signed informed consent form from custodians would be needed before blood collection. If the bilirubin levels are above the standard value for neonatal age, they would be treated according to the standard treatment protocol.

All participants needed to have consent from their custodians. The investigator and team will measure transcutaneous bilirubin level at ear pinna (figure 2) with Natus® transmission transcutaneous bilirubinometer, model BiliCare for 5 seconds. Results will be recorded in case report forms (CRFs) in mg/dL.

Blood will be collected from participants' heel no less than 30 minutes later and measured for bilirubin level and recorded in the CRFs.



Figure 1 Transmission transcutaneous Bilirubinometer



Fig 2 Transcutaneous bilirubin measurement at ear pinna

Definition of variables

Jaundice means yellowish discoloration seen at neonates face, body and trunks by attending physicians.

Transmission transcutaneous bilirubin (tTcB) index is bilirubin level measured from transmission transcutaneous bilirubinometer which is a new equipment to assess jaundice transcutaneous at ear pinna and unit measurement of mg/dL.

Serum bilirubin level (TSB) is bilirubin level measured heel stuck blood with serum bilirubin equipment (Optima Inc, Japan), model BR400 which was calibrated regularly as scheduled.

Data analysis

Results from the study were analyzed to find the sensitivity and specificity of the equipment used for screening test in neonatal jaundice. In addition, we also calculate the association between tTcB index and TSB in a form of simple linear regression equation. The derived coefficient of determination (r^2) was used to assess how good the linear regression equation can predict TSB from tTcB index.

Results

One hundred neonates who participated in the study had average gestational age of 39.15 ± 1.29 weeks and birth weight of $3,066 \pm 382.62$ grams. They were 44 cases of male (44 percent) and 56 cases of female (56 percent). The average age of the neonates at the time of bilirubin measurement was 50.36 ± 2.82 hours as shown in table 1.

Table 1 Samples characteristics

| Number (cases) | 100 |
|--|-------------------|
| Male (percent) | 44 (44.0) |
| Female (percent) | 56 (56.0) |
| Average gestational age (weeks) | 39.1 ± 1.29 |
| Average birth weight (grams) | 3,066.70 ± 382.62 |
| Average age at time of bilirubin measurement (hours) | 50.36 ± 2.82 |
| Routes of delivery | |
| Normal delivery (percent) | 68 (68.0) |
| C/S (percent) | 27 (27.0) |
| Forceps (percent) | 3 (3.0) |
| V/E (percent) | 2 (2.0) |
| Skin color | |
| White/yellow (percent) | 100 (100.0) |
| Black (percent) | 0 (0.0) |

When transcutaneous bilirubinometer was used to screen neonates who had bilirubin level ≥ 11 mg/dl, we found that 33 cases had serum bilirubin level higher than 11 mg/dl. We found the sensitivity and specificity to be 91.67 percent and 59.38 percent respectively (table 2).

Table 2 Accuracy, sensitivity and specificity of the equipment (comparing tTcB with TSB)

| TSB | tTcB | prevalence | Sensitivity | Specificity | PPV | NPV | Accuracy |
|-----|-------|------------|-------------|-------------|-------|--------|----------|
| 10 | 12.00 | 50.00 | 94.00 | 44.00 | 62.67 | 88.00 | 69.00 |
| 11 | 12.84 | 36.00 | 91.67 | 59.38 | 55.93 | 92.68 | 71.00 |
| 12 | 13.67 | 26.00 | 92.31 | 62.16 | 46.15 | 95.83 | 70.00 |
| 13 | 14.51 | 15.00 | 93.33 | 72.94 | 37.84 | 98.41 | 76.00 |
| 14 | 15.35 | 9.00 | 100.00 | 78.02 | 31.03 | 100.00 | 80.00 |

When the transcutaneous bilirubinometer was used to screen neonate whose serum bilirubin level ≥ 12 mg/dl, we found that 24 neonates had serum bilirubin level higher than 12 mg/dl and sensitivity and specificity from using the simple linear regression equation were 92.31 and 62.16 respectively (table 2).

When the derived simple regression equation was used to calculate serum bilirubin level from tTcB index, resulted in the following equation, $tTcB = 3.623 + 0.837$ TSB

The coefficient of correlation (r) was equal to 0.849 and coefficient of determination (r^2) was equal to 0.636 as shown in diagram 1.

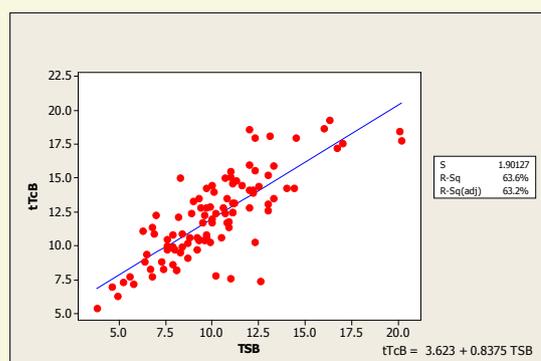


Diagram 1 Linear correlation between tTcB index and TSB

Discussion

Neonatal jaundice is a common pediatrics problem that can be diagnosed from measurement of serum bilirubin level. Today, decision to withdraw blood measurement depends on physicians' judgment from the appearance of skin color of the neonates. The judgment of each physician can be different so the transcutaneous bilirubinometer had been developed to screen for neonatal jaundice. The objectives were to reduce blood withdrawal, expense and reduce complications from drawing blood. Our study found that tTcB index is highly associated with serum bilirubin level and the derived simple regression equation could predict TSB with coefficient of determination (r^2) of 0.636. This means that the accuracy in predicting serum bilirubin level from tTcB index is 63.6 percent.

Care for neonatal jaundice and decision to treat it depend on neonatal age and serum bilirubin level including other risk factors leading to harmful effect from severe jaundice. Selecting too low level of serum bilirubin for treatment leads to over admission of neonates while selecting too high level leads to neonatal risks from severe jaundice. Term neonates born at Lerdsin Hospital are discharged at 48 - 72 hours after birth where their serum bilirubin level should not exceed 11-12 mg/dl (75th percentile of bilirubin level) (10, 11). When

we used tTcB index to screen for term neonatal jaundice, we found that this method had sensitivity in predicting serum bilirubin level of ≥ 12 mg/dl more than serum bilirubin level ≥ 11 mg/dl. So the criteria to treat neonatal jaundice at serum bilirubin level of 12 mg/dl seem to be appropriate and safe for the neonates.

When we compared these results with our previous study that used the traditional transcutaneous bilirubin measurement method, we found that the value of coefficient of determination (r^2) differed in the range of 0.57 - 0.95 (12-16). The equipment had sensitivity and specificity of diagnosing neonatal jaundice around 80 - 100 percent and 45-95 percent respectively (12, 13). The traditional transcutaneous bilirubin measurement needed experienced users as measurement from the same site three times in three minutes yield different results of 1-2 mg/dl so that we have to use the average of the three measurements (17). Our findings from measuring the same site for three times in three minutes with transmission transcutaneous bilirubinometer yielded the different results of 0.1-0.2 mg/dl (the first ten cases of measurement). When we compared results from each ear pinna, we also found the different of 0.1 - 0.2 mg/dl. Our study performed tests in 100 term neonates and showed that it is convenient to use and had moderate efficacy. We did not have black-skin color neonates in our study and would extend our study in pre-term neonates in the future.

Conclusions

Our study of 100 neonates found that tTcB index and the derived regression equation could predict serum bilirubin level with moderate efficacy. In using transmission transcutaneous bilirubinometer for screening term neonatal jaundice, we should know the efficacy of the equipment to predict serum bilirubin level and aware of the errors that could happen. It should be used to screen only neonates who fit to the inclusion criteria as described above and suspected of jaundice as there is still no supported evidence so far for the use in other types of neonates such as pre-terms or sick neonates. The decision to treat should be based on serum bilirubin level only. Users should also operate the equipment with correct technique to prevent errors from the measurements and interpretation of the results.

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