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A Comparison between Transcutaneous Bilirubin (TcB) and Total Serum Bilirubin (TSB) Measurements in Term Neonates

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Abstract

Introduction

Transcutaneous Bilirubinometry (TcB) is a simple method for estimating bilirubin levels in neonates. This method is noninvasive, quick, and painless. We aimed to compare serum and cutaneous bilirubin measurements in term neonates.

Materials and Methods

In this descriptive cross-sectional study, 200 neonates with icter and birth weights of at least 2,500 grams were studied. TcB was measured using a bilirubinometer three times on the forehead and mean levels were calculated. Then, during the subsequent 30 minutes blood samples were obtained and sent to the laboratory for determining the Total Serum Bilirubin (TSB) levels.

Results

Of the 200 neonates, 124 (62%) were boys and 76 (38%) were girls, with an age range of 1-22 days. The mean±SD serum and cutaneous bilirubin levels were 18.75±5.38 and 17.85±4.46 mg/dl, respectively. A high correlation (r=0.89) was observed between TSB and TcB. The sensitivity and specificsity of cutaneous bilirubin measurement were 95.1% and 68%, respectively.

Conclusion

Because of its high sensitivity, TcB can be a suitable tool for predicting neonatal icter. However, it is not a suitable substitute for TSB measurement in neonates at a high risk of jaundice.

Key Words: Neonatal icter, Serum bilirubin, Transcutaneous bilirubin.

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Introduction

Hyperbilirubinemia is a common finding in neonates. 60% of term neonates and 80% of preterm neonates suffer from jaundice during the first week of life (1). Transient encephalopathy and kernicterus are among the complications induced by hyperbilirubinemia (2, 3).

For the better treatment of neonatal jaundice, measuring bilirubin levels is vital; which is usually done by visual, cutaneous, and serum evaluations (4). Although visual assessment is simple, it has two major shortcomings; it is dependent on the physicians experience with no accurate and reliable criteria, and possible estimations in this method are based on the cephalocaudal trend of jaundice. Moreover, the color of skin and clothes as well as the lighting affect visual estimation (4-6).

Total serum bilirubin (TSB) measurement is also not an ideal method of measurement because it could have complications such as infection, anemia, pain, and stress because of frequent blood sampling. Moreover, this method is stressful, time consuming and expensive (1). In cases at a high risk of kernicterus such as day-one icter, hepatosplenomegaly, etc, TSB measurement, follow-up and hospitalization are necessary (7, 8).

In recent decades, noninvasive bilirubin measurements have been presented for reducing patients' stress, laboratory expenses, and the need for blood sampling. One of these noninvasive methods is transcutaneous bilirubinometry (TcB) (9). In TcB, the bilirubinometer is pressed against the skin causing pallor, and bilirubin levels are measured in different ways using light waves (10, 11) (Figures.2, 3).

Fig.2, 3: Measurement of bilirubin level in Neonates by bilirubinometer

Studies comparing the correlation between TSB and TcB have yielded different results. Briscoe and colleagues found a relatively high correlation between TSB and TcB (12); while Janjindamai and colleagues did not find a clear relationship between the results of the two measurements (13). In the later study, the researchers have mentioned that TcB is as accurate as TSB and can replace it (13). Karon et al. showed that TcB is a sensitive but nonspecific method for predicting the risk of neonatal icter (14).

Schwartz et al. in 2011 presents a comprehensive study on the different methods for the diagnosis and management of hyperbilirubinemia (15). In 2012, different researchers like Mantagou et al. (16), Wainer et al. (17), Bosschaart et al. (18) and Sajjadian et al. in Iran (19) addressed the bilirubin measurements especially in neonates.

Due to importance of bilirubin measurement, there are several studies recently published about this topic (20-24).

Considering the importance of this issue and the inconsistencies between previous studies regarding the accuracy of TcB, we aimed to compare the relationship between TcB and TSB measurements in term neonates. Moreover, we also studied the sensitivity and specificity of TcB based on the age of the neonates and bilirubin levels.

Materials and Methods

In this descriptive cross-sectional study, 200 full term (37 gestational weeks) neonates weighing ≥ 2500g referred to Besat Hospital, Sanandaj_ Northwestern Iran, were studied. This study was conducted from October 2009 to January 2010. The documented research project code is 88/47. The study was approved by the Ethics Committee of Kurdistan University of Medical Sciences (No.82199). Moreover, the aim of the study was described for the parents and then, written informed consent was obtained from the parents before enrollment.

Fig.1: Location of Kurdistan province, Northwest of Iran

The neonates had not previously undergone phototherapy or blood transfusion. Premature neonates, those less than 2,500 g, or neonates suspected of septicemia, meningitis, and cholestasis were also excluded from the study. Neonates who seem icteric visually at the clinic were examined by a pediatric resident and if they had the inclusion criteria for the study, their bilirubin levels were measured three times on the forehead for avoiding any bias induced by the bilirubinometer (JH20-1, Japan). Cutaneous bilirubin was measured by a pediatric resident. The skin was blanched due to the pressure when the apparatus is put on the skin and then the bilirubin was measured by using light waves in different ways. The radiated light goes to sub-cutaneous layer through the skin and reflected. Based on the reflected wave specifications, the cutaneous bilirubin is calculated.

The mean levels were recorded and blood samples were obtained within 30 minutes and sent to the laboratory for determining TSB. Sampling was performed from brachial vein of neonates by the nurse of neonatal ward of Besat Hospital. TSB was measured using a bilirubinometer (Model BR-5000N, Japan). The two measurements obtained from the two methods were then compared.

Neonatal data were also collected including: age, sex, birth weight, current weight, height, onset of jaundice, birth order in the family, history of jaundice in the family, type of delivery, type of feeding, history of hospitalization, neonatal and maternal blood group, history of phototherapy, priority and distance of measurements in serum and skin bilirubin, history of blood transfusion in newborn, and maternal prenatal care.

Data were analyzed using SPSS software, version 16. Independent t-test (to compare the quantitative variable in the two studied groups) and Pearson's correlation coefficient (to evaluate effective parameter on dependent variable) were used accordingly.

Results

Of the 200 neonates, 124 (62%) were boys and 76 (38%) were girls, with a Mean ± SD (Standard Deviation) age of 5.3±4.5 days (range: 1-22 days). 99% of the neonates were breastfed and 39 (19.5%) neonates had a history of icter. The mean ± SD weight of the neonates were 3002±379 grams. Most of the neonates were the first child (55%). Moreover, 32% were the second child, and 12.4% were the third child and the next. 12%, 27.5%, and 60.5% of the neonates became icteric on days 1, 2-3, and 4 or more of birth respectively (Table.1).

Table 1: Frequency distribution of different study variables

Variables		N (%)
Gender	Boy	124 (62)
	Girl	76 (38)
Weight	2500-3000	119 (59.5)
	3001-3500	62 (31)
	≥3500	19 (9.5)
History of icter	Yes	39 (19.5)
	No	161 (80.5)
Rating birth	First	110 (55)
	Second	65 (32.5)
	Third or more	25 (12.5)

No significant relationship was observed between serum and cutaneous bilirubin and history of jaundice in the family. Moreover, no significant relationship was found between type of delivery and hyperbilirubinemia. In this study, no significant relationship was observed between history of hospitalization and serum and cutaneous bilirubin. Moreover, no significant relationship was found between nutrition and serum and cutaneous bilirubin.

Most neonates with hyperbilirubinemia have B+ blood group and then A+ blood group have the highest frequency in the study. O + blood group in mothers of newborns with jaundice was the most common (49 %), and then A+ blood group have the highest frequency in the mothers (37 %).

The mean ± SD serum and cutaneous bilirubin levels were 18.75±5.38 and 17.85±4.46 mg/dl, respectively. A high correlation (0.89) was observed between TSB and TcB.

We also assessed the sensitivity and specificity of different TcB measurements. Table.2 shows the sensitivity and specificity of this method for different bilirubin levels. As shown, the highest specificity and sensitivity was related to bilirubin levels between 12-15 mg/dl.

Table.3 shows the frequency and percentage of serum bilirubin as compared with cutaneous bilirubin in normal and abnormal states for calculating positive and negative predictive values of cutaneous bilirubin based on serum bilirubin. In this table bilirubin levels below 12 are considered normal. In this study the positive and negative predictive values of TcB were 93.9 and 69.2.

We also calculated the sensitivity and specificity of TcB measurements with respect to age. The highest sensitivity and specificity was seen on day three after birth (Table.3). In general, the sensitivity and specificity of TcB compared with TSB was 95.1% and 67.7%, respectively.

Table 2: Specificity and sensitivity of cutaneous bilirubin measurement based on bilirubin levels

Bilirubin Levels (mg/dl)	Specificity (%)	Sensitivity (%)
8<	25	100
8-12	25	95
12-15	100	96.1
15≥	80	96

Table 3: Frequency and percentage of Serum bilirubin versus cutaneous bilirubin

Variables		Serum bilirubin		Total
		Abnormal	Normal	
Cutaneous bilirubin	Abnormal*	155 (93.9%)	10 (6.1%)	165 (100.0%)
	Normal	8 (30.8%)	18 (69.2%)	26 (100.0%)
Total		163 (85.3%)	28 (14.7%)	191 (100.0%)

* Bilirubin levels above 12 (mg/dl) are considered abnormal.

Table 4: Mean±SD cutaneous bilirubin levels based on age, sensitivity, and specificity

Age	Bilirubin	Number	Mean±SD (mg/dl)	Specificity (%)	Sensitivity (%)
One day	Cutaneous	24	10.6±2.44	25	100
	Serum		10.6±2.90		
Two days	Cutaneous	28	15.64±3.33	25	95.6
	Serum		15.37±3.53		
Three days	Cutaneous	27	17.47±2.86	100	91.6
	Serum		18.93±4.08		
Four or More days	Cutaneous	121	19.8±3.53	80	96
	Serum		18.93±4.38		

Discussion

We found a high correlation between TcB and TSB measurements in neonates (r=0.89). Consistently, in another study on 490 neonates over 2.5 kg a high correlation (r=0.91) was observed between TcB and TSB (8). Several studies have been done in this regard (25-28). One study on 388 healthy term neonates showed a correlation coefficient of 0.8; which is very similar to our study (28). In another study on 490 neonates with a gestational age of more than 35 weeks, a correlation coefficient of 0.91 was observed (8).

Briscoe and colleagues also found a correlation coefficient of 0.76 by studying 285 neonates (12). Minor differences between the mentioned studies could be attributed to differences in the type of bilirubinometers, skin color, ethnicity, laboratory methods and kits, etc.

We found that TcB had a high specificity for bilirubin levels over 12 mg/dl, especially for levels between 12-17 mg/dl. For levels lower than 12 mg/dl, its specificity decreased while its sensitivity increased; therefore, increasing the number of false positives. Also, for levels higher than 17 mg/dl, false negative cases would increase. In a study on 200 Brazilian neonates, higher correlations between TSB and TcB measurements were observed for bilirubin levels lower than 14 mg/dl. The researchers concluded that for levels over 14 mg/dl, serum measurements should be done (29). Few studies have been done on specificity and sensitivity based on birth age, and most studies have calculated the sensitivity and specificity of TcB based on gestational age, sex, ethnicity, and weight. However, we also evaluated the former variable in our study.

Day one and day two TcB yielded low specificity and high sensitivity. Therefore, during these days false positive cases would increase and the accuracy of TCB would decrease. From day three onward false positive cases would decrease considering its higher specificity and accuracy would rise. Therefore, TcB measurements are closer to TSB measurements on days three and four.

Our results are relatively comparable with another recent study in Italy that showed a significant increase in the specificity of bilicheck 61-96 hours after birth compared with 0-60 hours (P=0.074). However, the mentioned study did not assess the sensitivity of bilicheck as well as its specificity after 96 hours from birth (30). In a study on 560 neonates, a good correlation was found between TcB and TSB after 24 hours from birth. However, the mentioned study did not evaluate the association between TcB and TSB on the first day of birth. The specificity and sensitivity of bilicheck was also not assessed (31).

The practical application of these findings is that considering the high sensitivity of TcB, we can predict neonatal icter using a noninvasive method without spending much time and money. The highest levels of bilirubin are seen on the fifth and sixth days of birth. This is while most neonates are discharged 48 hours after birth. Therefore, they should be followed accurately with respect to icter after discharge. TcB is an ideal method for outpatient followup and aid the quick diagnosis of icter in order to prevent its consequent side effects.

However, because of its relatively low specificity, in this study we emphasize that in neonates with progressive jaundice, those with risk factors such as hemolysis or infection, or those with higher than normal bilirubin levels detected by TcB, serum bilirubin levels must be checked. Briscoe and colleagues also emphasized that TcB does not have the accuracy of TSB and the need for checking TSB in neonates with icter could be determined by TcB measurements (12). On the other hand, Janjindamai et al. found that TcB is as accurate as TSB and can replace it (13). Some researchers do not recommend the bilirubinometer as a suitable screening tool (12, 32). This could be attributed to the method of patient selection and higher bilirubin levels in patients.

With respect to the effect of gestational age on the correlation between TcB and TSB, De Luca and colleagues reported a correlation coefficient of 0.79 and confirmed a lower correlation coefficient in term neonates as compared with premature ones (33). On the other hand, other researchers found that the correlation coefficient between TcB and TSB increase as the gestational age increases (from 0.43 for 23-28 weeks to o.72 for 35036 weeks) (34). Douville et al., also found an excellent correlation between TcB and TSB in term neonates as compared with premature ones (35). Further research is needed in this regard. In our study, we did not consider gestational age since all neonates were term.

We did not evaluate the effect of phototherapy on the association between TcB and TSB. Tan and Dong found a lower correlation coefficient in regions exposed to phototherapy compared with the control group in their assessment of 310 neonates (36).

Our study was done in Kordestan province and 98.5% of the neonates were of Kord ethnicity and only 1.5% were of Fars ethnicity. Therefore, we could not assess the effect of ethnicity of the correlation between TcB and TSB. In a study evaluating the effect of ethnicity on the association between TcB and TSB, the researchers found a correlation coefficient of 0.89, which did not yield statistically significant results (37).

Since TcB is a quick, inexpensive, and noninvasive method, it seems that parental follow-up would be facilitated using this method. This issue could be studied in the future.

Conclusion

We found a high correlation between TcB and TSB measurements in term neonates. Due to its simplicity and painlessness, serial cutaneous bilirubin measurements would be helpful in following neonatal icter. Although TcB has a high sensitivity in detecting icter, it should not replace TSB due to its relatively low specificity. Therefore, in high risk neonates, measuring TSB alongside TcB is necessary.

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Conflict of interest: None.

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