Assessment of a transcutaneous bilirubinometer in the evaluation of neonatal Hyperbilirubinemia in hospitalized neonates

Abstract

Transcutaneous bilirubinometer is useful in screening and monitoring neonatal hyperbilirubinemia. The aim of this study was assessment of a Transcutaneous bilirubinometer in the prediction of neonatal hyperbilirubinemia in hospitalized neonates. Descriptive observational prospective study methods was used in the present study. Estimation of transcutaneous serum bilirubin (TCB) was measured using the device and was compared with serum bilirubin concentration in neonates at MGIMS Hospital. Transcutaneous bilirubin (TCB) readings were taken on the forehead. 99 neonates were enrolled for the present study, mean and standard deviations of serum bilirubin concentration and TCB were 12.03±5.69 and 9.63±4.69 mg/dl, respectively. Results from the present study indicate that TCB measurement is a useful in screening the high risk neonate to determine significant hyperbilirubinemia. Although TCB tend to underestimate serum bilirubin, it is a useful technique as a screening tool in the evaluation of hyperbilirubinemia.

Key Word: Transcutaneous bilirubinometer, neonate, hyperbilirubinemia, diagnostic accuracy
1.0 Introduction
Neonatal jaundice or hyperbilirubinemia occurs commonly in newborns affecting nearly 60% of term and 80% of preterm neonates during first week of life. It is one of the most frequently encountered diagnostic and therapeutic problem in the newborn. The standard method of serum bilirubin estimation requires blood specimen taken by heel prick or venepuncture which is both painful and expensive. In 1980, Yamanouchi introduced Transcutaneousbilirubinometry as a non invasive screening tool in the management of neonatal jaundice [1-3]. It measures the intensity of yellow color of the skin and subcutaneous tissue and correlates with the serum bilirubin concentration in newborns. It is safe, simple, reproducible, cost effective method of monitoring of neonatal jaundice and immediacy of the test result availability. Previously, authors have reported the significant correlation between serum bilirubin and transcutaneous bilirubin(TCB). But the correlation is affected by gestational age, use of phototherapy, birth weight, color of skin, degree of jaundice and race. If a newborn is at higher risk for clinically significant hyperbilirubinemia, TSB should be measured [4,5]. The objectives of the study was to evaluate the accuracy of Transcutaneousbilirubinometer (TCB) measurements for assessing hyperbilirubinemia in the term neonates, by using Total Serum Bilirubin (TSB) as the reference standard.

2.0 Material and methods
This study was performed in the Neonatology unit at Mahatama Gandhi Institute of Medical Sciences, Sevagram, from May 2009 and July 2009. A diagnostic study of the index test (TCB) as compared to a reference standard (laboratory confirmed hyperbilirubinemia) in an independent manner was employed as study design. All the healthy full-term newborns who are admitted in postnatal ward were selected for the present study. A written informed consent was sought from one of the parents (preferably the mother) of the neonates for inclusion in the study. Neonates who would have received exchange transfusion or phototherapy prior to inclusion (day 3) were excluded. In addition, eligible neonates, whose parent(s) do-not agree for inclusion in the study were also excluded.

TCB determination was made in accordance with the manufacturer’s recommendations, and the device was calibrated before each measurement. All determinations were obtained from the infant’s forehead, and readings were taken by one investigator only while the infant was in a quiet state. For each infant, readings was obtained with TCB devices used in the study for data analysis. TCB determinations performed 5 minutes before blood sampling for total serum bilirubin (TSB). No study patients were receiving phototherapy when the transcutaneous values or blood samples were obtained. A serum bilirubin test was performed immediately within 10 minute. The TSB estimation will be done by calorimetrically using green filter with 540nm wavelength (KLETTE) method.

<table>
<thead>
<tr>
<th>Particulars</th>
<th>TCB cut off</th>
<th>Correctly Correlation</th>
<th>Sn</th>
<th>Sp</th>
<th>LR+</th>
<th>LR-</th>
</tr>
</thead>
<tbody>
<tr>
<td>S.Bil 15mg/dl</td>
<td>12</td>
<td>88.89</td>
<td>72.4</td>
<td>95.7</td>
<td>16.8</td>
<td>0.28</td>
</tr>
<tr>
<td>S.Bil 12mg/dl</td>
<td>9</td>
<td>87.8</td>
<td>83.6</td>
<td>92</td>
<td>10.4</td>
<td>0.17</td>
</tr>
<tr>
<td>S.Bil 10mg/dl</td>
<td>7</td>
<td>95.6</td>
<td>98.4</td>
<td>91.6</td>
<td>11.8</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Sn= Sensitivity, Sp= Specificity, LR+= Positive Likelihood ratio, LR- = Negative Likelihood ratio
Statistical analysis
The diagnostic accuracy of TCB was measured by computation of sensitivity, specificity, positive likelihood ratios (LR+), negative likelihood ratios (LR–), and positive and negative predictive values. The precision of these estimates was evaluated by using 95% confidence intervals (95% CI). The receiver operating characteristics (ROC) curve was employed for predicting sensitivity and specificity of different cutoff TCB values to estimate whether the TSB was >10mg/dl, or >12mg/dl or >15mg/dl subsequently.

3.0 Results and discussion
Of 99 eligible neonates, 54 were male and 45 were female. The mean gestational age was 39 weeks; mean birth weight was 2.6±0.7; and the mean age at the time of data collection was 3.2±0.4. The TSB levels ranged from 1.8 to 27.3 mg/dL with mean of 12.03±5.69. The TCB levels ranged from 1.1 to 18.3 mg/dL with mean of 9.63±4.69. The Area under curve by ROC was 0.93 (CI: 0.88-0.98) for TSB was >15mg/dl by TCB, similarly for the for s.bilirubin >12mg/dl & for s.bilirubin >10mg/dl was 0.95(CI:0.91-0.98) and 0.97(CI:0.94-1.00) subsequently. A cut-off TCB level 12 mg/dl had high specificity of 95.7 and satisfactory sensitivity of 72.4 with correctly correlation (88.89) for identifying babies with s.bilirubin 15mg/dl.

A cut-off TCB level of 9 mg/dl had high specificity of 92 and satisfactory sensitivity 83 with correctly correlation (83.6) for identifying babies with s.bilirubin 12mg/dl. A cut-off TCBS level 7 mg/dl had high specificity 91.6 and high sensitivity 98.4 with correctly correlation.
(95.6) for identifying babies with s.bilirubin 10mg/dl (Table-1). The area under the ROC curve was 0.93 as shown in figure-1. Thus the TCBS would be considered to be "good" at separating that predicted serum bilirubin > 15mg from serum bilirubin <15mg. Analysis of the ROC curve showed that the TCBS value that predicted serum bilirubin > 15mg/dl with a TCBS cut off value of 12 having sensitivity 72.4%, specificity 95.5 with 95% CI of 0.88 - 0.98.

The area under the ROC curve was 0.96 as shown in figure-2. Thus the TCBS would be considered to be "good" at separating that predicted serum bilirubin > 12mg from serum bilirubin <12mg. Analysis of the ROC curve showed that the TCBS value that predicted serum bilirubin > 12mg/dl with a TCBS cut off value of 9 having sensitivity 83.6%, specificity 92 with 95% CI of 0.91 - 0.98.

**Figure-3: Prediction of serum bilirubin level of > 10 mg/dL**

The area under the ROC (receiver operator characteristic) curve was 0.97 as shown in figure-3. Thus the TCBS would be considered to be "good" at separating that predicted serum bilirubin > 10mg from serum bilirubin <10mg. Analysis of the ROC curve showed that the TCBS value that predicted serum bilirubin > 10mg/dl with a TCBS cut off value of 7 having sensitivity 98.4%, specificity 91.6 with 95% CI of 0.94-1.00

Hyperbilirubinemia is one the most frequently observed condition and common reason for readmission after early hospital discharge. In neonatal jaundice, the binding capacity of plasma albumin is exceeded, which allows free bilirubin to diffuse and accumulate within extravascular tissues, such as the central nervous system and may develop kernicterus. Earlier discharge from the hospital, may lead to inadequate monitoring of jaundice may sometimes leads to kernicterus. Previous studies were unable to demonstrate the clinical application and reliability of the visual assessment of jaundice to predict subsequent hyperbilirubinemia, especially in darker skinned babies [6]. Blood is required for serum bilirubin measurement which is taken by heel prick or venepuncture may causes the neonatal pain and time consuming procedure. Unnecessary skin puncture would be performed if every visibly jaundiced neonate had serum bilirubin estimation done. And these unnecessary puncture can be decreased if only jaundiced neonates at risk for bilirubin encephalopathy were sampled. The use of TCB reading as a screening device for neonatal hyperbilirubinemia is based on the assumption that serum and tissue bilirubin are in constant equilibrium. A non invasive, transcutaneous measurement of bilirubin concentration is developed to be an alternative method as a reliable for the screening method to detect hyperbilirubinemia. It may be a useful screening device to decrease the risks and discomfort associated with blood sampling
in neonates. TCB sampling is easy to perform and pain-free for the infant, and the test gives immediate results. Knudsen [7] concluded that use of the TCB reduced (50%) the need for invasive serum bilirubin testing. It measures the transcutaneous serum bilirubin by determining the intensity of specific wavelength bands that are reflected from the skin, independent of the age of the neonate. Previous studies have reported that TCB is not affected by haemoglobin level, gestational age, or ethnicity [8,9]. The bilirubin measurement by TCB is also supposedly unaffected by melanin component of the skin and therefore suitable for use on any skin colour [10,11].

Samanta S et al [12] found that TCB identified significant jaundice (serum bilirubin above 250 micromol/l) with a sensitivity (95% confidence interval) of 91% (88% to 94%) and specificity of 66% (60% to 71%). The area under the receiver operator characteristic curve was 0.85. Whereas it found that a cut-off TCBS level 12 mg/dl had high specificity 95.7 and satisfactory sensitivity 72.4 with correctly correlation (88.89) for identifying babies with s.bilirubin 15mg/dl and the Area under curve by ROC was 0.93. Similarly, a cut-off TCBS level 7 mg/dl had high specificity 91.6 and high sensitivity 98.4 with correctly correlation (95.6) for identifying babies with s.bilirubin 10mg/dl and the Area under curve by ROC was 0.97. Dai et al reported that [14] although TcB measurements correlate well with SB levels, they cannot accurately predict SB. Yap SH et al(8) also reported that TCB and TSB were significantly correlated (r=0.890). Similarly, Carceller AM(14) found that the correlation between TCB and serum bilirubin was adequate (r= 0.7768). Nanjundaswamy S et al [15] observed that the significant (r = 0.78) correlation between bilirubin levels obtained transcutaneously and those measured in the infant’s blood. As well as TcB measurements can accurately predict TSB values lower than 11 mg/dl in a multiracial preterm and term neonatal population. In another view, Marco Lozano N et al [16] concluded that the bilirubinometer measurements tend to underestimate serum bilirubin, especially in patients with high levels, although it is a useful technique as a screening tool in the evaluation of hyperbilirubinaemia. Ochoa Sangrador C et al [17] reported that the error intervals in which predictions of serum bilirubin were found were #+ 2 mg/dl for low values and #+ 4 mg/dl for high values (#> 15mg/dl). Whereas we found that for the prediction of bilirubin >10mg/dl; >12mg/dl or >15mg/dl, the TCBS measurement can accurately predict TSB value which is lower than 2mg/dl. In conclusion, TCB measurement it may be stated that it is a useful screening for high risk neonate to determine significant hyperbilirubinemia. Although TCB tend to underestimate serum bilirubin, is a useful technique as a screening tool in the evaluation of hyperbilirubinemia.

4.0 Conclusion

Estimation of bilirubin is one of the important step in identification of Neonatal jaundice. Eventhough the present methods where blood is withdrawn and analyzed is highly useful, there is a need for usage of non-invasive method. Results from the present study indicate that TCB measurements using Transcutaneousbilirubinometer may used as non-invasive method for detection of neonatal jaundice. However further studies involving large sample may substantiate the usefulness of the method.

References