Diagnostic accuracy of transcutaneous bilirubinometer devices compared with the total serum bilirubin measurement in preterm (≤35 weeks) very low birth weight neonates during the neonatal period up to 7 days of life

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Abstract

**Introduction:** Hyperbilirubinaemia is the commonest morbidity in preterm neonates, most of whom are of very low birthweight (VLBW ≤1500g) babies. Repeated blood sampling in preterm VLBW neonates not only causes pain but may lead to sepsis and anaemia. Transcutaneous measurement of bilirubin by a device called transcutaneous bilirubinometer (TcB) is an effective alternative tool to predict neonatal hyperbilirubinaemia in late preterm and term neonates, most of whom have birthweights >2000g.

**Objectives:** To evaluate diagnostic accuracy of TcB devices in comparison to total serum bilirubin (TSB) measurements in VLBW neonates.

**Method:** We evaluated 128 preterm neonates with gestational ages ranging from 28 to 35 weeks and birthweights ≤1500g till 7 days of post-natal age. A total of 1003 TcB readings were taken, along with concurrent heel prick capillary samples, for laboratory measurement of TSB. For TcB, Drager JM-103 transcutaneous bilirubinometer was used and for TSB, Microlab’s Easybil instrument was used. Coefficient of correlation (r) and Bland-Altman plot were calculated to check correlation between TSB and TcB.

**Results:** Total number of neonates was divided into 2 groups: i) ≤1000g and ii) 1001-1500g. Paired readings of TSB and TcB were taken before and after starting phototherapy. All the paired readings were analysed for correlation between TcB and TSB. Correlation co-efficient (r) value for group i) was 0.87 and for group ii) was 0.89 (p<0.0001). Before and after starting phototherapy, readings were analysed separately to see the effect of phototherapy on correlation between TcB and TSB. Correlation co-efficient (r) values for paired readings before starting phototherapy were 0.97 & 0.90 respectively for both groups and for paired readings after starting phototherapy were 0.81 & 0.83 respectively for both groups.

**Conclusions:** TcB measurements correlate significantly with TSB levels in early preterm neonates with VLBW. Phototherapy does not affect the correlation significantly.

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(Key words: Hyperbilirubinaemia, preterm neonate, transcutaneous bilirubin, VLBW)

**Introduction**

Preterm neonates are more at risk for hyperbilirubinaemia due to immature hepatic function, polycythaemia, delay in starting feeds, sepsis, etc. Hyperbilirubinaemia is potentially more dangerous in premature VLBW (birthweight ≤1500g) neonates due to the immature blood brain barrier which can lead to bilirubin induced neuronal damage. Rough bilirubin estimation can be made visually as neonatal hyperbilirubinaemia progresses cephalocaudally. However, recent studies showed that visual assessment correlates poorly with SB. Blood sampling to estimate SB is the commonest investigation done in the neonatal intensive care unit (NICU). This is frequently performed by heel prick, a painful procedure with long-term sequelae. Therefore, an accurate non-invasive method of SB estimation is required. Transcutaneous estimation of bilirubin by a handheld device called transcutaneous bilirubinometer (TcB) uses the principle of reflectance photometry and colorimetry. TcB devices estimate SB by directing light into the neonatal skin and measuring the intensity of specific wavelengths. There are several devices for transcutaneous estimation of bilirubin like “Bili Med”, “Drager JM-102”, “Drager JM-103”, “Drager JM-105”. We used “Drager JM-103” for current study. These devices correlated well with SB in term and near-term neonates in various studies. Most neonates in these groups were of birthweight >2000g. American Academy of Pediatrics recommends utilisation of TcB devices for evaluating jaundice in infants >35 weeks’ gestation. However, the
accuracy of TcB devices for estimating SB in preterm (≤35 weeks) VLBW neonates remains unclear\textsuperscript{12-15}.

**Objectives**

To evaluate diagnostic accuracy of TcB devices in comparison to total serum bilirubin (TSB) measurements in VLBW neonates.

**Method**

This was a time bound prospective cohort study done at the Department of Paediatrics at SSG Hospital and Medical College, Baroda from January to October 2017 after obtaining approval from the Institutional Ethical Committee on Human Research. We included VLBW neonates till 7 days of postnatal age with jaundice. All the VLBW neonates in our study were preterm babies of ≤35 weeks gestational age. Written pre-informed consent was taken from the parents. However, neonates with multiple anomalies incompatible with life, neonates who died within 7 days of birth and those where parental consent to participate was not given, were excluded.

Gestational age was decided by LMP-EDD, and if this was not reliable, then early trimester USG was considered. If no antenatal care was taken or no documents were available, then gestational age was estimated by the “new Ballard score”\textsuperscript{16}. If any VLBW neonate who was part of the study showed signs of jaundice, a serum sample was obtained by heel prick and at the same time (+/-30 minutes) TcB value was obtained by using Drager JM-103 transcutaneous bilirubinometer. Serum sample was processed in microlab’s easybili-p instrument which measured serum bilirubin (TSB) by the spectrometric method using 450 nm and 570 nm wavelength light. As all the neonates were preterm babies of ≤ 35 weeks, intervention was decided by the gestational age specific National Institute for Health and Care Excellence (NICE) guideline charts. Thereafter, serial monitoring of bilirubin was done by paired readings of TcB and TSB till 7 days of postnatal age. Maximum efforts were done to obtain TSB and TcB readings at the 24\textsuperscript{th} hour of life (HOL), 48\textsuperscript{th} HOL, 72\textsuperscript{nd} HOL, 96\textsuperscript{th} HOL, 120\textsuperscript{th} HOL, 144\textsuperscript{th} HOL and 168\textsuperscript{th} HOL. A maximum of 30 minutes was tolerated between TSB and TcB. During phototherapy, an area over the sternum approximately double the size of JM-103 tip was covered with well thickened cotton swabs to keep the area unaffected by phototherapy. A total of 168 neonates were enrolled; however, 128 neonates were considered for statistical analysis as the rest did not have enough readings (<2) for analysis and in some neonates time lag between TcB and TSB was more than 30 minutes. Data analysis was carried out using MedCalc v-17.9.7. Correlation coefficient (r) and Bland Altman plot were done to check diagnostic accuracy of TcB value to TSB.

**Results**

A total of 128 neonates with gestational ages of ≤35 weeks and birthweights ≤1500g were included in the present study. These 128 neonates were subdivided into two groups i) ≤1000g (18 neonates) and ii) 1001-1500g (110 neonates). Gender and gestational age distribution are shown in Tables 1 and 2.

| Table 1: Gender distribution of neonates (n=128) |
|-----------------|-----------------|-----------------|
| Birth weight (g) | Gender          | Number of neonates |
| ≤1000           | Male            | 06              |
|                 | Female          | 12              |
| 1001-1500       | Male            | 53              |
|                 | Female          | 57              |

| Table 2: Gestational age distribution of neonates (n=128) |
|-----------------|-----------------|-----------------|
| Birth weight (g) | Gestational age (weeks) | Number of neonates |
| ≤1000           | 28-30           | 11              |
|                 | 31              | 01              |
|                 | 32              | 02              |
|                 | 33              | 01              |
|                 | 34              | 03              |
|                 | 35              | 00              |
| 1001-1500       | 28-30           | 17              |
|                 | 31              | 15              |
|                 | 32              | 21              |
|                 | 33              | 27              |
|                 | 34              | 18              |
|                 | 35              | 12              |
Correlation co-efficient (r) value for subgroup i) total 146 and subgroup ii) total 857 paired data of TcB and TSB were collected and analysed and the r value was 0.87 and 0.89 respectively with the p value being <0.0001 suggesting statistically significant strong correlation (Table 3, Figure 1).

### Table 3: Correlation coefficients (r) of subgroups

| Group                | Observations            | Number of paired data | ‘r’ Value | p value  |
|----------------------|-------------------------|-----------------------|-----------|----------|
| Subgroup i)          | All the observations    | 146                   | 0.87      | <0.0001  |
| Birthweight <1000g   | Before phototherapy     | 13                    | 0.97      | 0.97     |
| n=18                 | After phototherapy      | 82                    | 0.81      | <0.0001  |
| Subgroup ii)         | All the observations    | 857                   | 0.89      | <0.0001  |
| Birthweight 1001-1500g | Before phototherapy    | 168                   | 0.90      | <0.0001  |
| n=110                | After phototherapy      | 529                   | 0.83      | <0.0001  |

Data collected before starting phototherapy and after phototherapy were analysed separately for 13 neonates among subgroup i) and 101 neonates among subgroup ii). Correlation co-efficient r values for before phototherapy was 0.97 and 0.90 respectively for subgroup i) & ii) (Table 3, Figure 2).

However, for subgroup i) only 13 readings were available and hence more data are required to comment on statistical significance. Correlation co-efficient r values for after phototherapy were 0.81and 0.83, p value being <0.0001, for respectively for subgroup i) & ii) (Table 3, Figure 3). Hence TcB and TSB shows strong correlation in VLBW even after phototherapy.
As Pearson’s correlation co-efficient is a poor indicator for agreement between two different methods of bilirubin estimation (i.e. TSB and TcB), we used Bland Altman Plot analysis. Figures 4 and 5 are the Bland-Altman plot analysis for subgroup-i) & subgroup-ii) respectively. These plots are suggestive of a statistically significant (p<0.0001) agreement between TcB and TSB in VLBW preterm neonates, and phototherapy does not affect the agreement.
Discussion

The Drager Jaundice Meter-103 assesses yellowness of neonatal subcutaneous tissue by measurement of the difference between optical densities for light in the blue and green wavelength areas. As this optical density difference demonstrates a linear correlation with the SB concentration, it is converted into TSB and indicated digitally. Advantages of this non-invasive technique are real-time results, cost-efficacy and avoidance of pain and local infection. Drager JM-103 TcB assessment can be used to identify the need for blood sampling for TSB levels in term and near-term neonate. For the preterm infant current evidence is controversial. Several previous studies were done with various results and correlation coefficients ranged from 0.68 to 0.96.

In a study by Bhutani et al there was a strong correlation between TcB and TSB in >2500g neonates. Negar et al estimated the r value which was 0.83 in >2500g neonates. However, r values estimated in VLBW neonates in 2009 by Karolayi et al, Sui ly et al, Stillova et al suggest that there is strong correlation among VLBW neonates also. In our study we found that there is a strong correlation between TcB and TSB in VLBW neonates and this correlation is not affected even after phototherapy. In our study, we found that there is a statistically significant agreement between TcB and TSB in VLBW neonates as well and that phototherapy did not affect this agreement.

Conclusions

TcB measurements correlate significantly with TSB levels in early preterm neonates with VLBW. Phototherapy does not affect the correlation significantly.

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