Pre-Discharge Screening Trans-Cutaneous Bilirubinometry in Healthy Newborns in Mahdieh Hospital, Tehran

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1. Background

Jaundice is one of the most common diseases in neonatal period. More than 60% of newborns develop clinical jaundice in the first week of life (1, 2). Pathologic levels of bilirubin may lead to irreversible complications such as bilirubin encephalopathy called kernicterus associated with cerebral palsy, deafness, dental dysplasia, ophthalmomalia with upward gaze, and personality disorders (3, 4). Early discharge of neonates from nursery aggravates its danger (5). Awareness of risk factors causing severe jaundice, and early diagnostic and treatment interventions may prevent this severe irreversible complication. Estimation of the severity of jaundice and anticipation of its progression solely based on clinical observations is often not accurate enough and could lead to missed diagnosis. Transcutaneous bilirubin (TcB) measurement may be an effective method for prompt diagnosis of jaundice and prevention of its rapid progression (3). Some studies have recommended predischarge bilirubin screening for early detection of neonates at risk, so that treatment could be started as soon as possible, although evidences showing better outcome for these neonates is inadequate (6).

According to the American academy of pediatrics guidelines, all neonates should be evaluated for hyperbilirubinemia before discharge from hospital and serum bilirubin should be checked in neonates at risk (7). Moreover, the Canadian Academy of Pediatrics recommends serum bilirubin levels measurement by TcB (transcutaneous bilirubin) and TsB (total serum bilirubin) 24 to 72 hours after birth (prior to hospital discharge) for all neonates (8). TcB may be used as an estimate of the bilirubin level, since in various studies linear relationship between TcB and TsB has been specified (r = 0.87 to 0.96).

Although hyperbilirubinemia is highly prevalent in Iran and neonates are usually discharged before 24 hours of delivery, no strict evaluation for hyperbilirubinemia currently must be done.

2. Objectives

The goal of our study was comparison of transcutane-
ous and serum bilirubin levels in order to determine the sensitivity (positive predictive value) of this non-invasive method in term and late preterm infants.

3. Patients and Methods

This cross-sectional prospective study was conducted between 22 December 2010 and 20 March 2011 in Mahdieh hospital, a maternity university hospital in Tehran, Iran covered by Shahid Beheshti university and has 4,000 - 5,000 annually delivery. The study had received the approval of ethics committee of Shahid Beheshti university. Inclusion criterion was all healthy term and some late preterm neonates (those with gestational age more than 35 weeks) with birth weight over 1,800 g that were born in this period of time. In addition to physical examination for visible jaundice, the neonates were tested by forehead bilirubin 8,000 KJ Kejian, transcutaneous bilirubinometry just before discharge from hospital. In neonates with TcB levels of bilirubin ≥ 5 mg/dL in 24 hours after birth and ≥ 8 mg/dL in age of 48 hours, serum bilirubin level was checked by drawing capillary blood from foot heel to compare the results with TcB.

Selection of the above mentioned cut off levels was based on minimal pathologic level of serum bilirubin according to age specific Bhutani curve in American academy of pediatrics (AAP) guideline in neonatal hyperbilirubinemia (7). In cases with high serum bilirubin levels, neonates were admitted to neonatal wards for phototherapy, but in cases with lower bilirubin levels neonates were discharged from hospital advising parents to come back at a specific time interval for rechecking bilirubin to excise risk factors.

Our exclusion criteria were neonates with birth weight lower than 1,800 g and gestational age less than 35 weeks, as well as sick babies who needed admission for other causes in special care units.

All demographic data including mother’s and infant’s blood group, neonate’s gestational age, sex, and birth weight, mode of delivery, and bilirubin levels obtained by both TcB and TsB methods were registered in designed check lists. Data were analyzed by SPSS software.

4. Results

During the study period, 800 newborns were delivered in Mahdieh hospital and 613 neonates were enrolled in study. Of these 51% were boys, 57.5% were delivered by cesarean section. Mean birth weight was 3130 gram and mean gestational age 38.2 weeks.

TcB was performed in all cases just before discharge from hospital. Demographic characteristics of patients are shown in Table 1.

| Characteristics          | TcB+, % | Total Numbers | P Value | TsB+, % | TsB+, (%) | P Value |
|--------------------------|--------|---------------|---------|---------|-----------|---------|
| Sex                      |        |               |         |         |           |         |
| Male                     | 250 (50.9) | 306 (49.9) | 0.22  | 201 (50.5) | 49 (32.6) | 0.2     |
| Female                   | 241 (49.1) | 307 (50.1) |        | 197 (49.5) | 44 (47.3) |         |
| Weight, g                |        |               | 0.034  |         |           | 0.09    |
| < 2500                   | 27 (14.1) | 59 (9.6)     | 0.22  | 18 (15) | 9 (25.7)  | 0.2     |
| ≥ 2500 - 4000            | 157 (82.2) | 534 (87.1) |        | 131 (83.9) | 26 (74.2) |         |
| ≥ 4000                   | 7 (3.7) | 20 (3.2)     |        | 7 (4.4) | 0         |         |
| Mode of delivery         |        |               | 0.001  |         |           | 0.0001  |
| Vaginal                  | 196 (39.9) | 260 (42.4) |        | 135 (33.9) | 61 (65.6) |         |
| Cesarean                 | 295 (60.1) | 353 (57.6) |        | 263 (66.1) | 32 (34.4) |         |
| Rank of children         |        |               | 0.3    |         |           | 0.8     |
| First child              | 208 (42.4) | 254 (41.5) |        | 170 (42.7) | 38 (41.3) |         |
| Second child and over    | 282 (57.6) | 358 (58.5) |        | 228 (57.3) | 54 (58.7) |         |
| Gestational age, wk      |        |               |        |         |           |         |
| 35 - 37                  | 132 (26.8) | 132 (26.8) |        | 120 (30.2) |          |         |
| 37 - 40                  | 347 (70.9) | 347 (70.9) |        | 253 (63.8) |          |         |
| > 40                     | 11 (2.3) | 11 (2)        |        | 25 (6.2) |           |         |

a Data are presented as No. (%).
b N = 491.
c N = 398.
According to the study protocol, 491 (80%) neonates revealed high TcB levels. This consisted of 240 (49%) infants with bilirubin levels of ≥ 5 mg/dL during the first 24 hours and 251 (51%) cases with bilirubin level > 8 mg/dL within 48 hours. TcB ranged 3.3 - 17.1 mg/dL, average TcB level was 7.1 ± 9.6 mg/dL (mean 6 mg/dL) in first 24 hours and 2.1 ± 9.1 (mean 10 mg/dL) in second 24 hours.

In this study we assessed the correlation between TcB and TsB measurements and comparing, a precise reference of a local TcB nomogram, and selection of appropriate TcB cut-off level was not available. In this regard more expanded studies with higher cut off levels need to be conducted. Recently in a publishment by institute of health economics about transcutaneous bilirubinometry for the screening of jaundice, it is more suitable than TsB (11). In our study visual screening was not done.

5. Discussion

This study showed that TcB screening of hyperbilirubinemia in healthy term or late preterm neonates has high predictive value and can be recommended for early detection of jaundice in nurseries. American academy of pediatrics (AAP) has also recommended this technique as a suitable and noninvasive method in assessment of hyperbilirubinemia progression (7). In this study we assessed the correlation between TcB and TsB (as the gold standard test for bilirubin) in the diagnosis of jaundice with a PPV of 81%. Several studies on the role of TcB as an inexpensive, suitable, and noninvasive tool for pre-discharge screening of jaundice in all neonates have been performed in different countries. In a study conducted in China on 113 neonates, TcB showed a good correlation with TsB (correlation coefficient: 0.83 and P value < 0.001). According to this study Bili check type 103 JM estimates bilirubin higher than serum levels (9), whereas in another study performed in Thailand with the same type of Bili check, correlation between TcB and TsB was reported as significant (correlation coefficient 0.8 and P-value < 0.001) and according to this study, this type of TcB reveals bilirubin levels about 0.7 mg/dL lower than serum levels (10). Also in our study, TcB and TsB were consistent (correlation coefficient 0.72 and P value < 0.001) confirming the results of two previous studies. It seems that Bili check type 8,000 KJ with a PPV of 81% in the diagnosis of hyperbilirubinemia is a suitable tool for screening of neonatal jaundice.

In the study of Kaplan and colleagues, visual screening with TcB in identifying neonates with jaundice was made. They concluded that since blood sampling is not required in TcB, it is more suitable than TsB (11). In our study visual screening was not done.

Some studies revealed that routine pre-discharge TcB screening program is associated with significant reduction in the overall incidence of admission in neonates with higher bilirubin levels and phototherapy rate and reduced age at readmission for phototherapy and more frequent contacts with public health nurses after introduction of the TcB program (12). In our study 6.5% of patients had readmission for treatment.

High prevalence of hyperbilirubinemia with TcB and TsB measurements (about 80%) in our study, was because of our low cut off levels obtained from Bhutani curve based solely on serum bilirubin levels. Normally the lowest pathologic level for TsB is 5 mg/dL in first 24 hours and 8 mg/dL in second 48 hours, whereas pathologic levels of bilirubin vary with some other factors such as gestational age, weight, and hours passed birth. As our study was the first expanded study of the kind performed in Iran on the prevalence of hyperbilirubinemia by means of TcB and TsB measurements and comparing, a precise cut off level was not available. In this regard more expanded studies with higher cut off levels need to be conducted. Recently in a publishment by institute of health economics about transcutaneous bilirubinometry for the screening of jaundice, it is reported that pre-discharge TcB cut-off of ≥ 75th percentile at 48 to 72 hours is a good predictor of TsB of ≥ 95th percentile. If the cut-offs are set toward high sensitivity; a large number of false positives are acceptable and result in additional unnecessary TsB testing, but this is without serious clinical consequences. They emphasize that in TcB screening program, development of a local TcB nomogram, and selection of appropriate TcB cutoff is needed (13). Some researchers concluded that if TcB values were plotted on the TsB nomogram resulted in a trend towards a higher false negative rate but plotting TcB on transcutaneous nomogram resulted in better predictive value, with the best sensitivity (90.0%) and specificity (87.79%) (14), but we compared TcB and TsB measures simultaneously in the same nomogram.
According to the present study, the prevalence of hyperbilirubinemia is higher in cesarean deliveries (C/S) and in ABO and Rh incompatibility, which are similar to the results of other studies conducted in Thailand (9), China (8) and on Hispanic infants (15), although neonates delivered with C/S stayed longer in nursery and detection of jaundice in these infants was more probable.

Estimation of bilirubin by TcB may be inaccurate in some situations, especially in severe cases of hyperbilirubinemia, in preterm infants and during phototherapy. We excluded preterm newborns from our study and used TcB just as a screening test. None of our cases received phototherapy, and because our study was done in a nursery where a high percentage of cases were discharged early from hospital, only a few of our patients had high bilirubin levels. We matched the results of TcB with our finding in physical examination at pre-discharge visits, it is logical that in icteric cases with underestimation of TcB test, we checked TsB to confirm the diagnosis of hyperbilirubinemia.

A limitation of our study was exclusion of the premature and low birth weight infants because precise diagnosis of hyperbilirubinemia in preterm infants is questionable and TcB measurements in this group of neonates should be further evaluated.

A point of strength in our study was more documented diagnosis of icterus with TcB in comparison with visual diagnosis in pre-discharge visits and more infants came back to recheck the bilirubin in follow up clinics, of which 6.5% were hospitalized to receive treatment. This was mainly (95%) with phototherapy, and only in one case blood exchange was utilized. This highlights the importance of screening tests and parental notification towards the follow up of jaundice, especially in late preterms and low birth weight neonates.

TcB is an inexpensive, noninvasive and precise method for screening of hyperbilirubinemia with a high (81%) PPV. According to high prevalence of neonatal jaundice, pre-discharge TcB measurement is recommended as the first line in screening of jaundice in all neonates.

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