This chapter will focus on techniques that have been developed to measure transcutaneous bilirubin (TcB). The first electronic TcB device proved to be useful when used as a screening method for identifying newborns who needed a serum bilirubin determination. Newer TcB devices can be used not only as screening tools but also as reliable substitutes for serum bilirubin measurements. The Chromatics Colormate III is still based on the colour of the skin, estimating serum bilirubin from skin-reflectance (skin colour) whereas the bilirubin by utilizing the BiliCheck measures transcutaneous entire spectrum of visible light (380 to 760 nm) reflected by the skin.

Key words: jaundice, newborn, bilirubin, kernicterus, transcutaneous bilirubin determination, bilirubin measurement, laboratory

Jaundice is seen in 30-60% of full-term newborns [11] and in nearly all premature infants but the incidence varies substantially in different populations depending on racial composition, feeding regimens etc. In our nurseries only about 5% of full-term neonates develop total serum bilirubin (TSB) concentrations of more than 12.9mg/dl (220gmol/1) [2,3] and heel punctures to measure the TSB levels are performed on many newborns. This procedure is painful, time consuming, and occasionally dangerous [4].

Estimation of the bilirubin level by visual inspection of the skin is not reliable. To address this problem, Rowntree and Brown, in 1925 proposed a 'linctometer' for the evaluation of skin colour [5], and subsequently, Gosset described the use of the Ingram Icterometer [6]. The first sophisticated device for non-invasive bilirubin measurement was the Minolta/Air Shields Jaundice Meter, which operates by evaluating the light reflected from the skin (after emission from a photo tube). The meter measures the optical densities of blue and green light, thus providing a measure of intensity of the yellow colour. In homogeneous populations of term infants [7-10] the correlation between the TSB and TcB index was excellent but was poor when the population included preterm infants and infants of different skin pigmentation [11]. This instrument proved to be a useful screening device but could not replace the measurement of serum bilirubin. In addition, the Jaundice Meter provided only a 'transcutaneous index' that had to be converted to a TSB level. The TSB level depended, in turn, upon the individual hospital laboratory.

New transcutaneous bilirubin devices

The original devices used to measure TcB measured the yellowness of the skin as a reflection of the TSB level. One of the newer devices also uses skin colour (Chromatics Colormate 111, Chromatics Color Sciences International Inc., New York, NY) but employs a sophisticated computer algorithm for assessing the underlying skin colour [12]. The algorithm allows for the determination of yellow colour regardless of the underlying skin pigmentation, provided that an early determination of skin colour measurement is completed within the first 30 h of life. When an initial baseline skin colour measurement was performed in neonates, the correlation coefficient with TSB measured in the clinical laboratory was >0.95 [12]. One criticism of this study is that the TSB determination was measured by a number of different techniques (in different clinical
laboratories) and not by the technique of high performance liquid chromatography (HPLC, considered to be the gold standard for bilirubin determination [13]. On the other hand, physicians have always relied on the clinical laboratory for measuring TSB and all of the data correlating outcome with TSB levels are based on clinical laboratory measurements. A major drawback of the Colormate III, however, is that every infant, regardless of its risk for developing hyperbilirubinaemia, requires a baseline measurement.

The latest commercially available TcB device is the BiliChecV9 (SpectRx, Inc., Norcross, GA, USA) which measures transcutaneous bilirubin by utilizing the entire spectrum of visible light (380 to 760 nm) reflected by the skin [14]. While light is transmitted into the skin of the newborn and the reflected light is collected for analysis (Fig. 1). By mathematically isolating the light absorption of certain interfering factors (haemoglobin, melanin, and dermal thickness), the absorption of light due to the presence of bilirubin in the capillary beds and subcutaneous tissue can be isolated by spectr subtraction. In theory, this allows for an unblase measurement that is independent of the race, age and weight of the newborn. In a multicentre study performed with this device, the close correlation between BiliChecO and HPLC was shown to be equivalent to that of HPLC and laboratory tests [14]. In addition, as expected a close correlation was also found between BiliChecV~ and various methods of determining serum bilirubin concentration [14]. Analysis of covariance demonstrated that TcB accuracy was independent of race, birth weight, and post-natal age.

The accuracy of the TcB determinations when performed on the forehead and sternum were comparable [14] but TcB measurements on the sternum were on average 0.8 to 0.9 mg/dl (13.7-15.4 umol/l) higher than on the forehead. This is possibly due to the effect of natural phototherapy on the exposed forehead [14]. Nevertheless, the ease of measurement on the forehead has advantages. These results and those of Bhutani et al. [15] suggest that BiliChecV~ TcB measurements can be substituted for TSB measurements in most circumstances.

Table 1 reports the sensitivity and specificity of TcB in relationship to the HPLC measurement of serum bilirubin at various clinically relevant cutoff points. As previously noted, the accuracy and precision of the TcB measurement with BiliChecV~ in the multicentre study was comparable to standard laboratory tests [14]. Nevertheless, in order to evaluate the performance of a new device it is necessary to focus primarily on the aspects of precision, accuracy and technique dependence. We therefore tested the BiliChecV~ device for technique dependence and calculated the inter-device and inter-operator coefficient of variation in 30 infants over a range of bilirubin levels. The TSB levels in each group of infants were < 8 mg/dl (137 -tmol/l), 8.1-12.9 mg/dl (139-221 pmol/l) and > 12.9 mg/dl (221 jamol/l). There were 10 infants in each group and TcB measurements were performed by a neonatologist and two resident physicians on the forehead of each infant. As shown in Table 2, the calculated coefficient of variation (CV) was 6% and ranged from a low of 4% for TSB levels > 12.9 mg/dl (221 gmol/l) to 11% for TSB levels: < 8 mg/dl (13.7 gmol/l). To test inter-device variation, 15 newborns in three groups of five were studied. Each group had the same range of TSB levels listed above (Table 3). The same operator used three different BiliCheck devices, sequentially. As shown in Table 3, the CV was 9.3% and ranged from a low of 7.2% for TSB levels > 12.9 mg/dl (221 [tmol/l) to a high of 17.6% for TSB levels < 8 mg/dl (13.7 gmol/l). The fact that the CV decreases as the TSB increases is positive as it is most important that this type of instrument is able to accurately screen higher levels of bilirubin that are potentially toxic.

Knudsen and Brodersen have indicated that the mechanism by which bilirubin is deposited in the skin is similar to the mechanism by which it traverses the blood brain barrier [16]. If so, they suggest that the TcB could be a better predictor of potential cerebral damage than the serum bilirubin concentration [16] and this hypothesis needs to be tested. Using the Air Shields 101 Jaundice Meter in premature infants, Knudsen and Ebbesen found that for a given increase in bilirubin concentration, the expected increase in TcB is greater in infants with a gestational age below 34 weeks than for infants with a gestational age of 34 weeks or more [17]. Knapfer et al. found that the correlation coefficient between TcB (BiliCheck) and TSB (Roche Diagnostics, Mannheim, FRG) increases with gestational age from 0.42 for very low birth weight infants (23-28 wk) to 0.72 for the 35-36 wk neonates [18] indicating that this instrument currently should not be used in infants whose gestational age is <35 weeks.
Recent reports of cases of kernicterus have rekindled the debate about the guidelines for the management of neonatal hyperbilirubinaemia [19-23]. Early discharge requires a different approach to follow-up and management and severe hyperbilirubinaemia is the leading cause for re-hospitalization of neonates in the first 2 weeks of life [24].

The TS13 concentration usually peaks on the fourth to fifth day of life, yet newborns are now commonly discharged by age at 48 h and must therefore be followed carefully to identify the few that develop severe hyperbilirubinaemia. TcB measurement is ideal for outpatient use and should provide very helpful in ensuring appropriate surveillance of infants after they are discharged from the hospital.

To establish normative data for TcB levels in our population, we performed BiliChecK measurements on 175 infants in our nursery. All were delivered via the vaginal route and were healthy term neonates who displayed no risk factors for the onset of significant hyperbilirubinaemia. We excluded those with ABO incompatibility (blood typing was performed on all mothers and infants) a positive Coomb's test or bruising. The neonates were divided into three gestational age groups: 37-0/7-38-6/7 wk (n = 30), 39-0/7-40-6/7 wk (n = 109) and >o= 41 weeks of gestation (n = 36). TcB measurements were taken 24 h after birth and then every 24 h until day 5. Infants discharged before day 5 returned to our clinic each day at the scheduled time for a follow-up TcB measurement. Neonates requiring phototherapy were excluded from the study. Figure 2 shows the 5th, 50th and 95th percentiles for TcB levels in the three populations studied. These data provide normal values for our population of healthy, vaginally delivered infants >o= 37 weeks of gestation and allow us to identify infants at risk for the subsequent development of severe hyperbilirubinaemia.

There are no appropriate studies comparing the cost of Bilicheck TcB measurements with the cost of laboratory measurement of TSB. Such studies are urgently needed. Another problem to be considered when using the BiliCheck is the fact that the results are not documented by a laboratory technician either by hand or in a computer. This places additional responsibilities on nursing staff to ensure appropriate documentation.

References


