Transcutaneous bilirubin measurements

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COMMENT

Transcutaneous bilirubin measurements: useful, but also reproducible?

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Jaundice is the most frequent clinical problem in both preterm and term infants, and it has been reported that ~80% develop unconjugated hyperbilirubinemia.[1] Fortunately, only a small but non-negligible proportion of these infants progresses to a severe neonatal hyperbilirubinemia (SNH). Newborn infants with SNH are at risk of acute bilirubin encephalopathy (ABE) and of its neurological sequelae, namely kernicterus spectrum disorders (KSDs).[2] Approximately one million newborns suffer from SNH worldwide[3] and the prevalence rate of KSDs is very high in low- and middle-income countries, that is, as high as 73 per 100,000 live births in Eastern Europe, Latin America, sub-Saharan Africa, and Asia,[3] with an associated mortality rate of 119 per 100,000 live births, which rises to 730 per 100,000 live births in India.[4] As such, bilirubin screening programs are crucial to timely discover infants with SNH, to treat them promptly, and thus prevent ABE, KSDs, and mortality in a population that, let us remember, would otherwise remain healthy. Nowadays, transcutaneous bilirubin (TcB) measurement has become widely used in high-income countries as a screening tool for SNH, because this method is inexpensive, painless, and easy to use. TcB screening reduces the need for heel pokes and, consequently, also reduces the risk of anemia resulting from repetitive blood sampling. Yet, specific decision rules that indicate when to obtain a TSB are imperative to correct for the reported underestimation of TSB, especially at higher TSB concentrations, and not to miss an infant with SNH and imminent bilirubin neurotoxicity.[5] Moreover, TcB devices have a limited measuring scale, that is, up to 340 µmol/L, and TcB readings may vary depending on infants' skin pigmentation, and may be also on postnatal age.[6–9]

Different TcB devices with unique specifications and principles of measurement may coexist in the same unit or may be used alternately posing the question if their readings are interchangeable. To that end, several authors have analyzed and compared the diagnostic accuracy of frequently used TcB devices in preterm and term neonates.[7,10–13] Almost all tested TcB devices proved to be reliable screening devices. To account for the intra-device variability, three or more repetitive measurements are recommended.

Although numerous studies report on inter-device differences in vivo, relating this difference to the technical differences of the devices is difficult as the test conditions may vary.[14] The paper by Dam-Vervloet et al.[15] in this issue of *Pediatric Research* addresses for the first time the specific issue of inter-device reproducibility of TcB devices by using an aqueous phantom that optically mimics neonatal skin. Thirteen devices of one brand were studied in vitro for evaluating and comparing their measurement capabilities over an acceptable range (0.5–181.3 µmol/L = 0.03–10.52 mg/dL) of bilirubin concentrations. They found that the intra-device difference was very low (11.0 µmol/L = 0.64 mg/dL), while the inter-device difference increased with increasing TcB and was as high as 65.0 µmol/L (3.77 mg/dL) between two similar TcB devices. The latter value is higher than that reported by the manufacturers (https://www.draeger.com/en_seeur/Products/Jaundice-Meter-JM-105), and above all, exceeds the commonly used safety limit of 50 µmol/L (2.9 mg/dL), which is added to the measured TcB value to correct for the underestimation of TcB before the decision to carry out a heel poke to measure TSB.[16]

This study also underlines the need for frequent device validation and quality assurance in clinical practice, apart from the daily calibration of the device.[17] Although this study does not address the divergent results of TcB measurement as a screening tool for SNH in outpatient settings,[18,19] it is tempting to speculate that the use of different TcB devices may, at least in part, have contributed to this discrepancy. The in vitro setting of this study leaves open relevant points such as the effect of skin color and ethnicity on TcB readings, as well as the accuracy of TcB measurements during phototherapy.

The paper by Dam-Vervloet and colleagues raises awareness of the device-depending variability of TcB measurements. When we measure TcB for the screening of SNH, it is utmost importance not only to know the technical specifications of the measurement principle of the TcB device but first of all the accuracy and the limitations of the device we are using. We concur with Dam-Vervloet's recommendation to use whenever possible the same TcB device in a single infant. In this way, device-specific effects will be minimalized. The data of this study claim for caution in the use of different TcB devices in a single infant given the higher inter-device variability at higher TSB concentrations, when the need for phototherapy may become more likely. Keeping this in mind, TcB measurements are useful and can be safely applied to identify newborn infants at risk for SHN or having SNH in agreement with current guidelines of different (inter)national pediatric and neonatal societies.[20,21]

AUTHOR CONTRIBUTIONS

C.D., C.V.H., and C.T. equally contributed to the conception, writing, and revision of this article. All authors approved the text of the manuscript.

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ADDITIONAL INFORMATION

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