University of Groningen

Transcutaneous bilirubin measurements

Dani, Carlo; Hulzebos, Christian V.; Tiribelli, Claudio

Published in:
Pediatric Research

DOI:
[10.1038/s41390-020-01242-3](https://doi.org/10.1038/s41390-020-01242-3)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2021

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Dani, C., Hulzebos, C. V., & Tiribelli, C. (2021). Transcutaneous bilirubin measurements: useful, but also reproducible? *Pediatric Research*, 89(4), 725-726. <https://doi.org/10.1038/s41390-020-01242-3>

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

COMMENT

Transcutaneous bilirubin measurements: useful, but also reproducible?

Carlo Dani^{1,2}, Christian V. Hulzebos³ and Claudio Tiribelli⁴

Pediatric Research (2021) 89:725–726; <https://doi.org/10.1038/s41390-020-01242-3>

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 worldwide³ 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 $\mu\text{mol/L}$, 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 ($0.5\text{--}181.3\text{ }\mu\text{mol/L} = 0.03\text{--}10.52\text{ mg/dL}$) of bilirubin concentrations. They found that the intra-device difference was very low ($11.0\text{ }\mu\text{mol/L} = 0.64\text{ mg/dL}$), while the inter-device difference increased with increasing TcB and was as high as $65.0\text{ }\mu\text{mol/L}$ (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 $50\text{ }\mu\text{mol/L}$ (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 minimized. 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.

¹Division of Neonatology, Careggi University Hospital of Firenze, Firenze, Italy; ²Department of Neurosciences, Psychology, Drug Research and Child Health, Careggi University Hospital of Florence, Florence, Italy; ³Beatrix Children's Hospital, Division of Neonatology, University Medical Center Groningen, Groningen, The Netherlands and ⁴Fondazione Italiana Fegato, Trieste, Italy

Correspondence: Carlo Dani (cdani@unifi.it)

Received: 12 October 2020 Accepted: 13 October 2020

Published online: 10 November 2020

ADDITIONAL INFORMATION

Competing interests: The authors declare no competing interests.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

REFERENCES

- Bhutani, V. K. et al. PredischARGE screening for severe neonatal hyperbilirubinemia identifies infants who need phototherapy. *J. Pediatr.* **162**, 477–82.e1 (2013).
- Le Pichon, J. B., Riordan, S. M., Watchko, J. & Shapiro, S. M. The neurological sequelae of neonatal hyperbilirubinemia: definitions, diagnosis and treatment of the kernicterus spectrum disorders (KSDs). *Curr. Pediatr. Rev.* **13**, 199–209 (2017).
- Bhutani, V. K. et al. Neonatal hyperbilirubinemia and Rhesus disease of the newborn: incidence and impairment estimates for 2010 at regional and global levels. *Pediatr. Res.* **74**, 86–100 (2013).
- Bang, A. T., Bang, R. A., Baitule, S., Deshmukh, M. & Reddy, M. H. Burden of morbidities and the unmet need for health care in rural neonates—a prospective observational study in Gadchiroli, India. *Indian Pediatr.* **38**, 952–965 (2001).
- Maisels, M. J. et al. Hyperbilirubinemia in the newborn infant > or =35 weeks' gestation: an update with clarifications. *Pediatrics* **124**, 1193–1198 (2009).
- Maisels, M. J. et al. Evaluation of a new transcutaneous bilirubinometer. *Pediatrics* **113**, 1628–1635 (2004).
- Ebbesen, F., Vandborg, P. K. & Trydal, T. Comparison of the transcutaneous bilirubinometers BiliCheck and Minolta JM-103 in preterm neonates. *Acta Paediatr.* **101**, 1128–1133 (2012).
- Olusanya, B. O., Mabogunje, C. A., Imosemi, D. O. & Emokpae, A. A. Transcutaneous bilirubin nomograms in African neonates. *PLoS ONE* **12**, e0172058 (2017).
- Rubio, A. et al. Diagnosis accuracy of transcutaneous bilirubinometry in 310 very preterm newborns. *Neonatology* **111**, 1–7 (2017).
- Sanpavat, S. & Nuchprayoon, I. Comparison of two transcutaneous bilirubinometers—Minolta AirShields Jaundice Meter JM103 and Spectrx Bilicheck—in Thai neonates. *Southeast Asian J. Trop. Med. Public Health* **36**, 1533–1537 (2005).
- Grohmann, K. et al. Bilirubin measurement for neonates: comparison of 9 frequently used methods. *Pediatrics* **117**, 1174–1183 (2006).
- Qualter, Y. M., Allen, N. M., Corcoran, J. D. & O'Donovan, D. J. Transcutaneous bilirubin—comparing the accuracy of BiliChekW and JM 103W in a regional postnatal unit. *J. Matern. Fetal Neonatal Med.* **24**, 267–270 (2011).
- Raimondi, F. et al. Measuring transcutaneous bilirubin: a comparative analysis of three devices on a multiracial population. *BMC Pediatr.* **12**, 70 (2012).
- Jones, D. F. et al. A prospective comparison of transcutaneous and serum bilirubin within brief time intervals. *Clin. Pediatr.* **56**, 1013–1017 (2017).
- Dam-Vervloet, A. J. et al. Inter-device reproducibility of transcutaneous bilirubin meters. *Pediatr. Res.* <https://doi.org/10.1038/s41390-020-01118-6>. Online ahead of print (2020).
- Maisels, M. J., Coffey, M. P. & Kring, E. Transcutaneous bilirubin levels in newborns <35 weeks' gestation. *J. Perinatol.* **35**, 739–744 (2015).
- Wainer, S., Parmar, S. M., Allegro, D., Rabi, Y. & Lyon, M. E. Impact of a transcutaneous bilirubinometry program on resource utilization and severe hyperbilirubinemia. *Pediatrics* **129**, 77–86 (2012).
- Maisels, M. J. et al. Transcutaneous bilirubin levels in an outpatient and office population. *J. Perinatol.* **31**, 621–624 (2011).
- Wickremasinghe, A. C., Karon, B. S. & Cook, W. J. Accuracy of neonatal transcutaneous bilirubin measurement in the outpatient setting. *Clin. Pediatr.* **50**, 1144–1149 (2011).
- American Academy of Pediatrics Subcommittee on Hyperbilirubinemia. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. *Pediatrics* **114**, 297–316 (2004).
- Romagnoli, C. et al. Italian guidelines for management and treatment of hyperbilirubinaemia of newborn infants ≥35 weeks' gestational age. *Ital. J. Pediatr.* **40**, 11 (2014).