



NONINVASIVE AND MINIMAL INVASIVE DEVICES TO IDENTIFY NEONATAL HYPERBILIRUBINEMIA: ARE THEY RELIABLE?

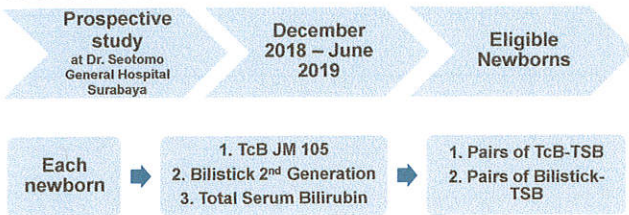
Siti Annisa Dewi Rani¹, Mahendra Tri Arif Sampurna², Zahra Safithry Irawan¹, Risa Etika²
¹Faculty of Medicine Universitas Airlangga Surabaya Indonesia
²Department of Pediatrics Faculty of Medicine Universitas Airlangga Surabaya Indonesia

BACKGROUND

Jaundice is a common condition in neonatal period, but it may become severe and potentially harmful. Early detection along with proper treatment are necessary^{1,2}. Kramer score is often inaccurate and not reliable³. Total Serum Bilirubin is gold standard for detecting and diagnosing hyperbilirubinemia⁴. But not all health facilities have reliable laboratory access⁵. However, blood sampling for total serum bilirubin measurement itself is invasive procedure, painful, stressful and has greater risk of infection⁴. Transcutaneous bilirubinometer (TcB), noninvasive device and Bilistick®, minimal invasive device have been developed. This study aims to evaluate reliability of TcB JM 105 and 2nd generation of Bilistick® compared with TSB and determine the agreement.

METHODS

STUDY DESIGN



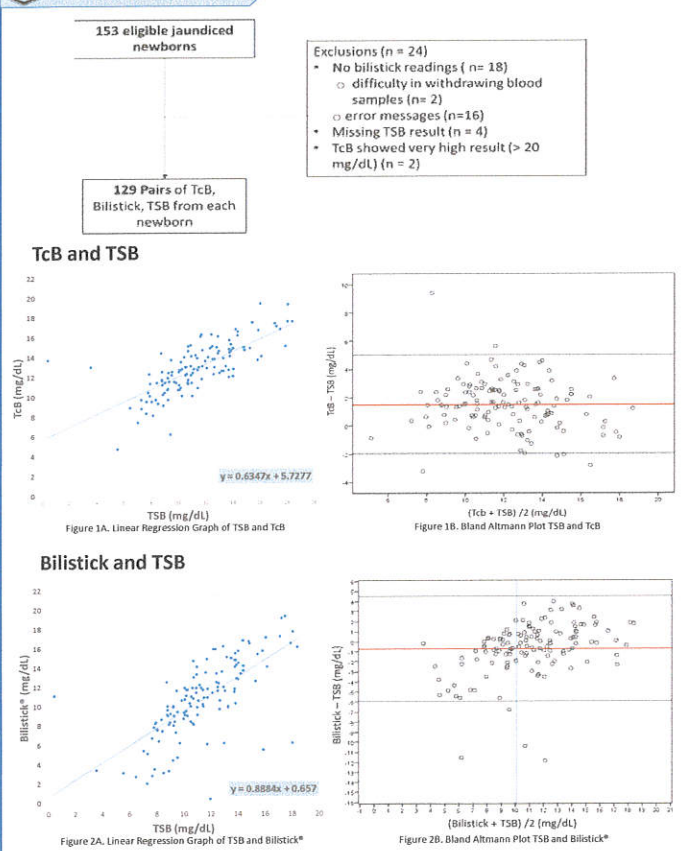
SAMPLE RECRUITMENT

Inclusion Criteria	Exclusion Criteria
1. Clinically jaundiced	1. Has massive congenital diseases
2. Birth weight is \geq 1500 gram	2. Use invasive respiratory support
3. Gestational age is $>$ 31 weeks + 6 days	3. Has condition affecting skin circulation, such as sepsis and/or heart failure
4. 0-14 days old.	4. Receive phototherapy within 24 hours prior to examination

ANALYSIS



RESULTS



DISCUSSION

This study found strong correlation for TcB and Bilistick® compared with TSB. We found that TcB tend to overestimate TSB. Meanwhile, the Bilistick® tend to underestimate TSB. The previous studies comparing TcB with TSB used the previous version of TcB reported strong correlation ranging $r=0.83-0.889$. But, during phototherapy it will be only moderate correlation⁶⁻⁸. TcB tends to overestimate TSB by 1.5 mg/dL with LoA -2.0 to 5.0 mg/dL. Other study also found similar results TcB overestimates TSB by 0.41 – 0.81 mg/dL (LoA -2.69 to 3.77 mg/dL)⁹ and 0.3 mg/dL (-5.4 to 6.0 mg/dL)⁹. Due to its overestimation, the high bilirubin level that need treatment will not be missed even though the TcB device we used cannot show exact result if the bilirubin level reach $>$ 20 mg/dL. In healthy term neonates whose TcB level is close to treatment threshold, it will lead to overtreatment if it is not confirmed with TSB level. This study found that 2nd generation of Bilistick® has 12.4% of failures. It is an improvement compared with the previous study that reported almost 50% errors¹⁰. But unpredictable false low levels are still present. Most of errors were due to high hematocrit level. Our study found strong correlation between Bilistick® and TSB. Other studies also reported strong correlation ($r=0.78 - 0.94$ ($p < 0.001$))^{8,10,11}. We found that Bilistick® underestimates TSB by -0.7 mg/dL with LoA -5.9 to 4.6 mg/dL. The wide range LoA clinically is unacceptable. Especially in the levels were falsely lower than treatment threshold. This will be too dangerous for preterm baby. It will lead to undertreatment and risk of bilirubin encephalopathy. Other studies reported the same problem^{8,10,11}. We found that the Bilistick® gave false low readings in cases. According to the manual, it might be caused by not enough blood volume is used. The need of trained people to withdraw the blood from the heel in order to avoid low blood volume is mandatory. In lower bilirubin level ($<$ 10 mg/dL) Bilistick® underestimated TSB and it is not clinically important. Because the level below 10 mg/dL does not need treatment. However unpredictable false low level in bilirubin above 10 mg/dL will put the baby in danger.

CONCLUSION

TcB and Bilistick® may help to identify hyperbilirubinemia but both devices are supposed to be used with considerations and TSB confirmation is still needed before deciding the treatment. In addition, TcB will be less reliable during phototherapy, meanwhile Bilistick® still can be used during phototherapy.

REFERENCES

- Olusanya B, Ogunlesi T, Slusher T. Why is kernicterus still a major cause of death and disability in low-income and middle-income countries?. Archives of Disease in Childhood. 2014;99(12):1117-1121.
- Burke B, Robbins J, Bird T, Hobbs C, Nesmith C, Tilford J. Trends in Hospitalizations for Neonatal Jaundice and Kernicterus in the United States, 1988-2005. PEDIATRICS. 2009;123(2):524-532
- Keren R, Tremont K, Luan X, Nnaan A. Visual assessment of jaundice in term and late preterm infants. Archives of Disease in Childhood - Fetal and Neonatal Edition. 2009;94(5):F317-F322.
- Grabenhenrich J, Grabenhenrich L, Buhner C, Berns M. Transcutaneous Bilirubin After Phototherapy in Term and Preterm Infants. PEDIATRICS. 2014;134(5):e1324-e1329.
- Coda Zabetta C, Iskander I, Greco C, Bellarosa C, Demarini S, Tiribelli C et al. Bilistick: A Low-Cost Point-of-Care System to Measure Total Plasma Bilirubin. Neonatology. 2013;103(3):177-181.
- Nagar G, Vandermeer B, Campbell S, Kumar M. Reliability of Transcutaneous Bilirubin Devices in Preterm Infants: A Systematic Review. PEDIATRICS. 2013;132(5):871-881.
- Nagar G, Vandermeer B, Campbell S, Kumar M. Effect of Phototherapy on the Reliability of Transcutaneous Bilirubin Devices in Term and Near-Term Infants: A Systematic Review and Meta-Analysis. Neonatology. 2016;109(3):203-212.
- Rohsiswatno R, Oswari H, Amandito R, Sjakti H, Windiastuti E, Roeslani R et al. Agreement test of transcutaneous bilirubin and bilistick with serum bilirubin in preterm infants receiving phototherapy. BMC Pediatrics. 2018;18(1).
- Greco C, Iskander I, Akmal D, El Houchi S, Khaliry D, Bedogni G et al. Comparison between Bilistick System and transcutaneous bilirubin in assessing total bilirubin serum concentration in jaundiced newborns. Journal of Perinatology. 2017;37(9):1028-1031.
- Thielemans L, Hashmi A, Priscilla D, Kho Paw M, Pimolsontong T, Ngerseng T et al. Laboratory validation and field utility assessment of a point-of-care test for serum bilirubin levels in neonates in a tropical setting. Wellcome Open Research. 2018;3:110.
- Greco C, Iskander I, El Houchi S, Rohsiswatno R, Rundjan L, Ogala W et al. Diagnostic Performance Analysis of the Point-of-Care Bilistick System in Identifying Severe Neonatal Hyperbilirubinemia by a Multi-Country Approach. Eclinicalmedicine. 2018;1:14-20.

Analysis

	Correlation Coefficient	p	Mean Difference (SD) mg/dL	Limits of Agreement (LoA) mg/dL
TcB and TSB	0.784	$<$ 0.001	1.5 (1.8)	-2.0 to 5.0
Bilistick® and TSB	0.723	$<$ 0.001	-0.7 (2.7)	-5.9 to 4.6

	Mean Difference (SD) mg/dL	Limits of Agreement (LoA) mg/dL
Bilistick® and TSB		
$<$ 10 mg/dL	-1,2 (2.3)	-5.7 to 3.3
\geq 10 mg/dL	-0.5 (2.8)	-6 to 5