SCVMC Hyperbilirubinemia QI Project Summary

Author:

Christopher Cahill, MD
Pediatric Hospitalist,
Department of Pediatrics
Santa Clara Valley Medical Center
May 2023

Background:

The newest 2022 American Academy of Pediatrics guidelines for treating hyperbilirubinemia described why higher phototherapy and exchange transfusion thresholds are appropriate and provided a means to help clinicians use higher thresholds.[1] Nevertheless, providers that are accustomed to the 2004 guidelines may have their doubts regarding these higher thresholds. Are these new thresholds safe? Do changing these thresholds make a significant clinical difference? The new AAP guidelines are so recent there is limited clinical experience to answer these doubts, but a similar, higher phototherapy guideline published by the Northern California Neonatal Consortium (NCNC) in 2016 could offer a preview[2].

Significant evidence for the safety of higher phototherapy thresholds than the 2004 AAP guidelines already exists from multiple population-based studies. These studies show kernicterus only in bilirubin levels >30[3–8], normal developmental outcomes at bilirubin levels >25 but <30[9] and analyses that suggest the number needed to treat to prevent exchange transfusion to be overly high for many groups.[10] Furthermore, other studies suggest phototherapy may have unintended consequences with associations with epilepsy[11,12], cancer[13,14], and reduced rates of breastfeeding in certain populations[15].

Method:

We recently conducted a QI study when our large well baby nursery and 10 outpatient clinics transitioned from the 2004 AAP hyperbilirubinemia guidelines[16] to the 2016 NCNC guidelines. From July 2018 to December 2020, we assessed all 6,173 infants admitted to the well baby nursery and tracked serum bilirubin levels, phototherapy, IVIG, and exchange transfusion. For the first 6 months of data collection, we used the 2004 AAP hyperbilirubinemia guidelines for phototherapy thresholds. We drew serum bilirubin levels when transcutaneous bilirubin levels were in the “high” or “high-intermediate” risk zone. After a 3 month introductory period where we disseminated the NCNC guidelines via grand rounds, email, and paper guidance to providers, as well new protocols and order sets for nursing staff, we analyzed data for 9 more months. Under NCNC guidelines, the serum bilirubin levels were obtained when transcutaneous bilirubin was within 3 points of the phototherapy threshold.

Result:

Our study found changing from the 2004 AAP to the 2016 hyperbilirubinemia guidelines resulted in a significant shift in the proportion of infants receiving phototherapy from a baseline

of 6.4% to 4%. We also observed a significant shift in the proportion of infants requiring TSB, from a baseline of 70% in the pre-group to 26% in the post-group.

For balancing measures, there was a similar rate of readmission for phototherapy and infants with bilirubin within 2 mg/dL of the exchange transfusion thresholds, or those who received exchange transfusion, between the pre- and post-groups. For bilirubin > 25 mg/dL, there were 0 such babies in our pre group, and 7 babies in our post group; this difference was not statistically significant. One baby in the pre-group was readmitted with a bilirubin level just above the 2004 AAP exchange transfusion threshold. This baby was later diagnosed with auditory neuropathy spectrum disorder which was improved by age two. One baby in the post-group discharged at 48hr of life did not return to care until day of life 9 and developed kernicterus with a peak bilirubin of 39.9 mg/dL. Ten of the remaining 11 children with bilirubin >25 or within 2 points of exchange transfusion had follow-up within our system and did not have any neurodevelopmental concerns identified at routine checkups by pediatricians or by parents using the Ages and Stages Questionnaire.

Discussion:

While there were more infants with bilirubin >25 under 2016 NCNC guidelines, evidence from multiple studies has suggested that bilirubin values between 25 and 30 mg/dL do not result in adverse neurologic outcomes. [3–9,17] Most detailed was the study by Newman et al[9] where infants with bilirubin in the range of 25 mg/dL to 29.9 mg/dL (who received treatment) had neurologic outcomes on formal developmental assessments that were equivalent to control infants. However, timely identification and aggressive treatment of bilirubin between 25 and 30 is critical since kernicterus can occur at high bilirubin levels.

Conclusion:

Our experience changing from the 2004 AAP to the 2016 NCNC guidelines offers insight to providers considering adopting higher phototherapy thresholds such as the very similar 2022 AAP guidelines. Adopting these new guidelines is feasible, reduces phototherapy exposure, and bilirubin laboratory draws significantly while maintaining similar amounts of clinical complications from hyperbilirubinemia. Timely identification and aggressive treatment of bilirubin between 25 and 30 is critical to prevent kernicteus.

References:

1. Kemper AR, Newman TB, Slaughter JL, et al. Clinical Practice Guideline Revision: Management of Hyperbilirubinemia in the Newborn Infant 35 or More Weeks of Gestation. *Pediatrics*. 2022;150(3):e2022058859. doi:10.1542/peds.2022-058859

2. Landman G, Hoffman K, Sun Y, et al. *Northern California Neonatal Consortium: Hyperbilirubinemia in Neonates >35 Weeks Gestational Age*.; 2017. https://www.ucsfbenioffchildrens.org/-/media/project/ucsf/ucsf-bch/pdf/hyperbilirubinemia_consensus_guideline.pdf

3. Ebbesen F, Bjerre JV, Vandborg PK. Relation between serum bilirubin levels ≥450 μmol/L and bilirubin encephalopathy; a Danish population-based study. *Acta Paediatr Oslo Nor 1992*. 2012;101(4):384-389. doi:10.1111/j.1651-2227.2011.02565.x

4. Le Pichon JB, Riordan SM, Watchko J, Shapiro SM. The Neurological Sequelae of Neonatal Hyperbilirubinemia: Definitions, Diagnosis and Treatment of the Kernicterus Spectrum Disorders (KSDs). *Curr Pediatr Rev*. 2017;13(3):199-209. doi:10.2174/1573396313666170815100214

5. Kuzniewicz MW, Wickremasinghe AC, Wu YW, et al. Incidence, etiology, and outcomes of hazardous hyperbilirubinemia in newborns. *Pediatrics*. 2014;134(3):504-509. doi:10.1542/peds.2014-0987

6. Johnson L, Bhutani VK, Karp K, Sivieri EM, Shapiro SM. Clinical report from the pilot USA Kernicterus Registry (1992 to 2004). *J Perinatol Off J Calif Perinat Assoc*. 2009;29 Suppl 1:S25-45. doi:10.1038/jp.2008.211

7. Wu YW, Kuzniewicz MW, Wickremasinghe AC, et al. Risk for cerebral palsy in infants with total serum bilirubin levels at or above the exchange transfusion threshold: a population-based study. *JAMA Pediatr*. 2015;169(3):239-246. doi:10.1001/jamapediatrics.2014.3036

8. Vandborg PK, Hansen BM, Greisen G, Mathiasen R, Kasper F, Ebbesen F. Follow-up of extreme neonatal hyperbilirubinaemia in 5- to 10-year-old children: a Danish population-based study. *Dev Med Child Neurol*. 2015;57(4):378-384. doi:10.1111/dmcn.12603

9. Newman TB, Liljestrand P, Jeremy RJ, et al. Outcomes among newborns with total serum bilirubin levels of 25 mg per deciliter or more. *N Engl J Med*. 2006;354(18):1889-1900. doi:10.1056/NEJMoa054244

10. Newman TB, Kuzniewicz MW, Liljestrand P, Wi S, McCulloch C, Escobar GJ. Numbers needed to treat with phototherapy according to American Academy of Pediatrics guidelines. *Pediatrics*. 2009;123(5):1352-1359. doi:10.1542/peds.2008-1635

11. Maimburg RD, Olsen J, Sun Y. Neonatal hyperbilirubinemia and the risk of febrile seizures and childhood epilepsy. *Epilepsy Res*. 2016;124:67-72. doi:10.1016/j.eplepsyres.2016.05.004

12. Newman TB, Wu YW, Kuzniewicz MW, Grimes BA, McCulloch CE. Childhood Seizures After Phototherapy. *Pediatrics*. 2018;142(4):e20180648. doi:10.1542/peds.2018-0648

13. Cnattingius S, Zack M, Ekbom A, Gunnarskog J, Linet M, Adami HO. Prenatal and neonatal risk factors for childhood myeloid leukemia. *Cancer Epidemiol Biomark Prev Publ Am Assoc Cancer Res Cosponsored Am Soc Prev Oncol*. 1995;4(5):441-445.

14. Newman TB, Wickremasinghe AC, Walsh EM, Grimes BA, McCulloch CE, Kuzniewicz MW. Retrospective Cohort Study of Phototherapy and Childhood Cancer in Northern California. *Pediatrics*. 2016;137(6):e20151354. doi:10.1542/peds.2015-1354

15. Kemper K, Forsyth B, McCarthy P. Jaundice, terminating breast-feeding, and the vulnerable child. *Pediatrics*. 1989;84(5):773-778.

16. American Academy of Pediatrics Subcommittee on Hyperbilirubinemia. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. *Pediatrics*. 2004;114(1):297-316. doi:10.1542/peds.114.1.297

17. Kuzniewicz MW, Escobar GJ, Wi S, Liljestrand P, McCulloch C, Newman TB. Risk factors for severe hyperbilirubinemia among infants with borderline bilirubin levels: a nested case-control study. *J Pediatr*. 2008;153(2):234-240. doi:10.1016/j.jpeds.2008.01.028