CEP Clin Exp Pediatr Vol. 68, No. 7, 539–545, 2025
https://doi.org/10.3345/cep.2024.01249

Original article

Evaluation of total serum bilirubin thresholds for discontinuing phototherapy in jaundiced neonates: a randomized study

Ajay Kumar, MD, Nidhi Jain, DM

Department of Neonatology, Maulana Azad Medical College, New Delhi, India

Background: To evaluate the outcomes of jaundiced neonates using 2 different total serum bilirubin (TSB) thresholds for discontinuing phototherapy.

Purpose: The study aims to evaluate the outcomes of jaundiced neonates by comparing 2 different TSB thresholds for discontinuing phototherapy.

Methods: All consecutive jaundiced neonates in a tertiary care hospital with a gestational age of ≥35 weeks and ≥3 days postnatal age were randomly assigned to 2 groups.

Results: Eighty neonates were included. The mean±standard deviation TSB at the time of phototherapy discontinuation was 13.1±2.2 mg/dL in the recommended threshold group and 10.5±2.5 mg/dL in the low threshold group. After discontinuing phototherapy, 17 infants in the recommended threshold group and 21 in the low threshold group experienced an increased TSB, with 3 and 9 crossing the treatment threshold, respectively. Following the National Institute for Health and Clinical Excellence (NICE) guidelines, there was a 14.3% increase in the reinstitution of treatment, averaging 28.11 hours with no reported adverse outcomes.

Conclusion: Discontinuation of phototherapy in neonates led to increased TSB levels, with a reinstitution rate of 14.3%. While adherence to the NICE guidelines is important, careful posttreatment monitoring is essential. Incorporating the 2022 American Academy of Pediatrics guidelines into future research could provide a more comprehensive understanding of safe practices in this area.

Key words: Neonate, Hyperbilirubinemia, Phototherapy discontinuation

Key message

Question: What are the outcomes of jaundiced neonates when phototherapy is discontinued at 2 different total serum bilirubin (TSB) thresholds?

Findings: The study involved 80 neonates, comparing a recommended TSB threshold and a lower threshold for phototherapy discontinuation. Results showed a 14.3% reinstitution rate of treatment, with no adverse outcomes.

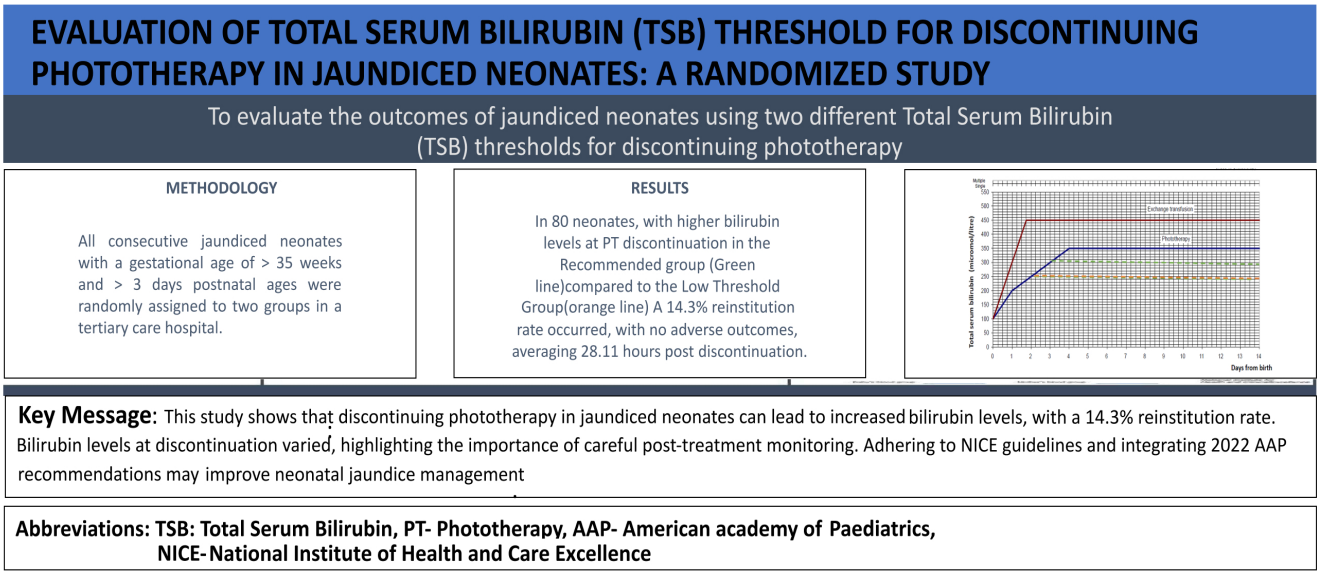
Meaning: Careful posttreatment monitoring is essential when discontinuing phototherapy, and future research should consider updated guidelines like those from the American Academy of Pediatrics.

Introduction

Jaundice is a prevalent neonatal condition that often necessitates hospital admission. It affects approximately 60% of term newborns and 80% of preterm newborns within the first week of life.[1] Phototherapy remains the principal treatment for managing elevated bilirubin levels. The guidelines for discontinuing phototherapy, particularly concerning the total serum bilirubin (TSB) level, have evolved over time. In 1994, the American Academy of Pediatrics (AAP) recommended discontinuing phototherapy at a TSB level of 14–15 mg/dL for term infants.[1] This threshold was not reaffirmed in the 2004 AAP guidelines, which instead proposed a discontinuation threshold of 13–14 mg/dL for readmitted infants with a gestational age of 35 weeks or more.[2] This single "cutoff" recommendation does not account for variations in postnatal age, particularly for younger infants where phototherapy might be initiated at lower TSB levels.

In contrast, the 2010 guidelines from the National Institute for Health and Clinical Excellence (NICE) suggest that phototherapy may be discontinued when the serum bilirubin level is 3 mg/dL (50 μmol/L) below the treatment

Corresponding author: Nidhi Jain, MD. Department of Neonatology, Maulana Azad Medical College, 2- Bahadur Shah Zafar Marg, Delhi-110002, India
✉ Email: nidhijain.arain@gmail.com, https://orcid.org/0000-0003-1330-9595
Received: 22 August 2024, Revised: 17 February 2025, Accepted: 17 February 2025



Graphical abstract

threshold.[3] For infants born at or after 38 weeks' gestation, this "low threshold" corresponds to a TSB level of 14.7 mg/dL, aligning with the AAP's 1994 recommendation. The NICE guidelines thus provide a more flexible approach that can be used to assess whether discontinuing phototherapy at higher TSB levels increases the need for reinstitution of therapy.

Despite these advancements, the latest 2022 AAP guidelines, which recommend discontinuing phototherapy when TSB falls 2 mg/dL below the initial treatment threshold and suggest longer durations for those with risk factors for rebound hyperbilirubinemia, have not been incorporated into this study.[4] The omission of these updated guidelines limits the applicability of our findings to current practices and does not account for the most recent recommendations which may influence clinical decision-making regarding phototherapy cessation.

Methods

This randomized controlled trial was conducted in a referral neonatal unit of a tertiary care hospital in north India.

1. Inclusion criteria

All consecutive neonates with gestational age ≥35 weeks and postnatal age of ≥3 days with 2 TSB level 8–16 hours apart in the phototherapy range as per the NICE guidelines and second TSB value being less than or equal to the previous value were included in the study.

2. Exclusion criteria

Neonates with gross congenital malformation, babies who received phototherapy prior to admission, neonates requiring exchange transfusion prior to enrollment and those with encephalopathy were excluded from the study.

3. Outcomes

The occurrence of post phototherapy TSB rise measured at 12–24 hours after phototherapy discontinuation was taken as the primary outcome. The reinstitution and duration of phototherapy, neonates developing acute bilirubin encephalopathy (ABE) and babies developing brainstem evoked response audiometry (BERA) abnormality were the secondary outcomes.

4. Sample size

To detect occurrence of post phototherapy TSB rise in recommended threshold group of 15.3% as against a rise of 0.5% in low threshold group,[5] a sample of 128 neonates was required with 64 neonates in each group with a power of 80% and alpha error of 0.05. However, on interim analysis after recruiting 80 neonates, 41.5% and 53.9% of babies had post phototherapy serum bilirubin rise in the 2 groups respectively. Therefore, the present study had stopped enrolling subjects after including 80 neonates.

5. Randomization

Computer generated random number sequence after block randomization concealed in sealed opaque envelopes was used for randomization. Author AK generated the random allocation sequence, NJ enrolled and assigned participants to interventions.

6. Ethical clearance

Approval was taken from institutional ethical committee. Written informed consent was taken from parents. The trial is registered with CTRI (No. CTRI/2018/03/012882).

7. Intervention

The phototherapy was discontinued at TSB value of 3.0 mg/dL (50 μmol/L) and at 6.0 mg/dL (100 μmol/L) below phototherapy initiation threshold in recommended and low threshold groups respectively as per NICE guidelines as shown in Fig. 1. Subsequent TSB rise was estimated 6–12 hours apart. Babies with significant rebound defined as rise in TSB crossing phototherapy initiation threshold were reinstituted phototherapy. Babies were monitored for serum bilirubin level and clinical features of ABE 6–12 hours apart.

8. Follow-up

The babies were followed up till 28 days for any evidence of ABE and also underwent BERA screening on follow-up.

9. Data collection

Baseline neonatal characteristics like date and time of birth, age and anthropometry were recorded. Gestational age was calculated from last menstrual period or by first trimester ultrasound or by clinical Ballard score. Maternal characteristics like maternal age, parity, and illnesses were noted. During neonatal intensive care unit stay the details of mother and baby blood groups, Coomb test and hemogram were noted. Data about age and TSB at initiation and discontinuation of phototherapy was recorded. Details of neonatal illnesses and feeding were noted. The rise in serum bilirubin level was noted. During follow-up, enrolled babies were evaluated for ABE and jaundice till 4 weeks of age. Babies also underwent BERA during follow-up visit.

10. TSB estimation

Around 0.5-mL blood in a plain vial was used for estimation of total and direct serum bilirubin in the hospital's clinical biochemistry laboratory by modified Jendrassik method using Randox Kit (Randox Laboratories India Pvt Ltd.) adopted to clinical chemistry analyzer 'OLYMPUS AU480' (Beckman Coulter).[6]

11. Phototherapy

Enrolled subjects were started on continuous single surface intensive phototherapy (Flux>30 μW/cm²/nm) using LED (light emitting diode) Phototherapy (Bird Meditech Machine) approximately 10 cm from the baby to expose the maximum surface area. Eyes and genitalia were covered. Flux was checked once daily using standard flux meter.

12. BERA screening

The BERA test was performed in a dark quiet room in babies after sedationon GSI Audera Diagnostics Machine. Electrodes were applied in 10–20 system. Low (below 5 KOhms) and balanced impedance readings were necessary

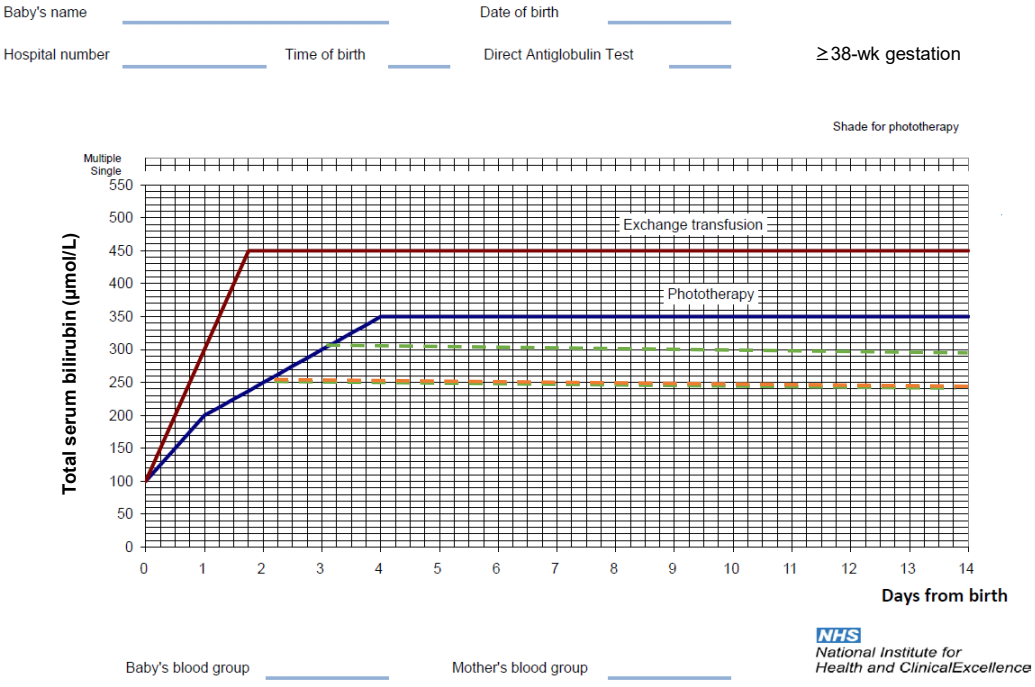


Fig. 1. The dashed green line indicates total serum bilirubin level for discontinuation of phototherapy in the recommended threshold group and dashed orange line in the low threshold group.

after applying electrodes for obtaining quality waveforms. Stimulus with frequency range from 1,000 to 4,000 Hz was given in the form of a click sound via an ear phone or head phone. Auditory brainstem response waves I, III and V were marked.

13. Statistical analysis

All the data recorded was entered in computer using Microsoft excel. Fisher exact test and chi-square test were applied for comparison of qualitative variables and Mann-Whitney test for quantitative variables. Logistic regression analysis to study the effect of various factors upon the need for a second course of phototherapy was used. A *P* value of less than 0.05 was considered significant.

Results

A total of 131 neonates were screened during the study period of 13 months from 1st May 2017 to 31 May 2018 as detailed in study flow chart (Fig. 2).

1. Baseline characteristics

Table 1 depicts baseline characteristics. Approximately 60% babies were <38 weeks in both groups. A total of 7 babies were small for gestational age as per Fenton growth charts.[7] Weight loss from birth till time of enrollment was approximately 7% in both the groups. Approximately 90% pregnancies were booked. While 2 mothers had diabetes in recommended threshold group, 3 had hypertension in low threshold group. Six mothers suffered from hypothyroidism and 2 had moderate anemia. Fifty percent babies were delivered in the study hospital and 40% were

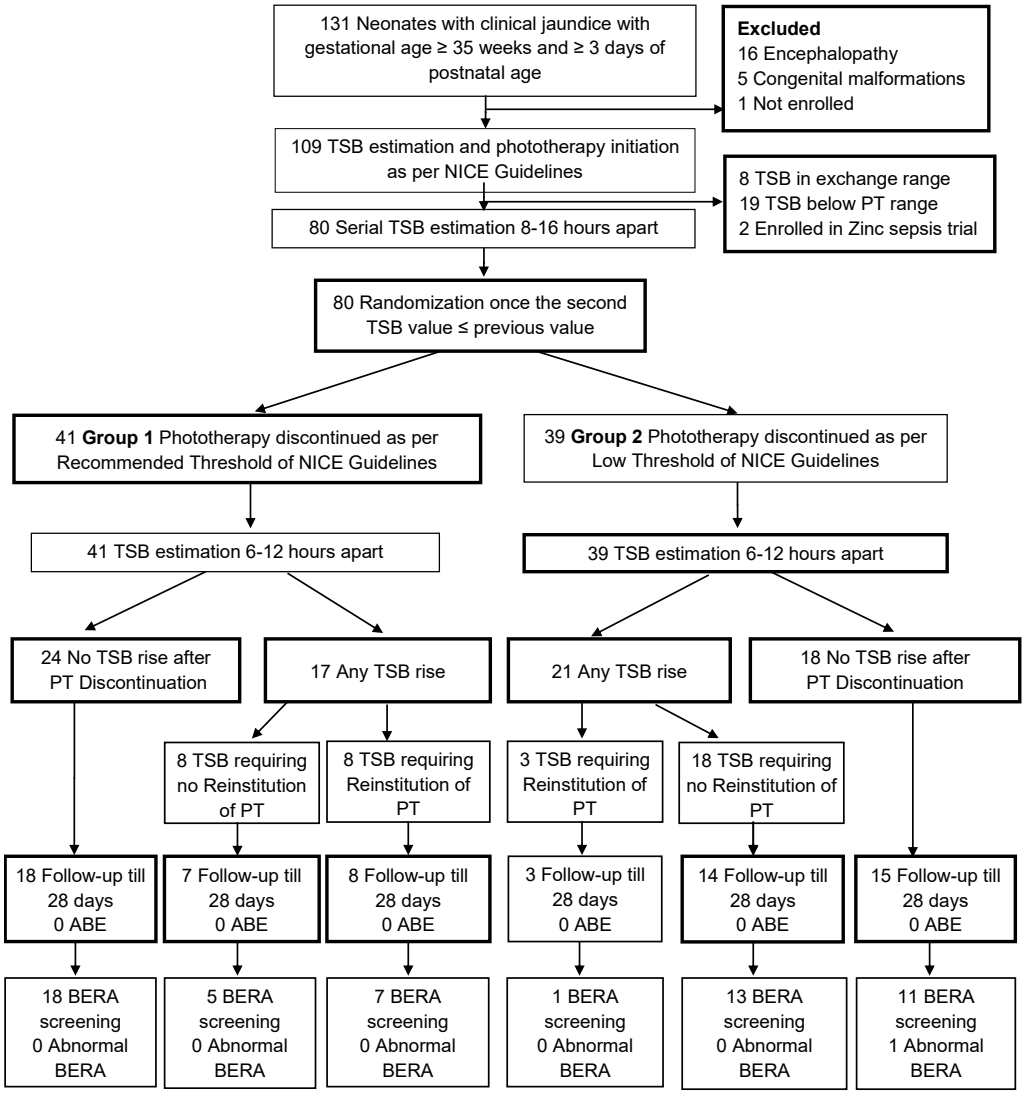


Fig. 2. Flowchart of study subject enrollment. TSB, total serum bilirubin; NICE, National Institute for Health and Clinical Excellence; PT, phototherapy; ABE, acute bilirubin encephalopathy; BERA, brainstem evoked response audiometry.

delivered in other hospitals, rest were home delivered. Duration of labor (mean±standard deviation [SD]) was 10.4±8.8 hours (24% requiring induction) in recommended threshold group and 7.7±7.8 hours in low threshold group (36% requiring induction). Only one baby required instrumentation in each group. None of the baby required resuscitation. Three patients with sepsis had respiratory distress with radiographic evidence of pneumonia. Remaining 9 babies with respiratory distress at the time of admission were diagnosed with transient tachypnea of newborn and pneumonia in the absence of positive sepsis screen. One patient had meningitis in each group. In group 1, one baby had asymptomatic polycythaemia requiring hike in feed volume. Among all patients, hemolysis was evident in 5 cases (6.2%) based on peripheral smear results, with 2 in group 1 and 3 in group 2. A decrease in hemoglobin levels was observed in 22 patients (27.5%), while clinical pallor was noted in 15 patients (18.7%). The direct Coombs test returned positive results for 9 patients (11.2%), with 4 in group 1 and 5 in group 2. Glucose 6 phosphate dehydrogenase deficiency was detected in 3 patients (3.7%), consisting of 1 in group 1 and 2 in group 2. However, none of these findings were statistically significant.

Table 1. Baseline patient characteristics

Variable	Recommended threshold group (n=41)	Low threshold group (n=39)	*P* value
Gestational age (yr)	37.4±1.6	37.4±1.70	0.959
Gestational age < 38 wk	25 (60.9)	23 (58.9)	0.529
Female sex	14 (34.1)	14 (35.9)	0.87
Age at admission (hr)	97 (2.5–136.5)	84 (21–156)	0.807
Birth weight (g)	2,661±384 (n=36)	2,535±403 (n=33)	0.187
Enrollment weight (g)	2,466±417	2,363±423	0.274
Weight loss at enrollment (g)	223.31±201.22	154.09±224.37	0.18
Head circumference (cm)	32.8±1.6	32.8±1.8	0.991
Length (cm)	47.3±2.2	47.3±2.9	0.987
Maternal age (yr)	25.2±4.5	25.4±4	0.861
Primigravida	17 (41.4)	16 (41)	0.898
Multiplicity (singleton)	41 (100)	38 (97.4)	0.302
Vaginal delivery	30 (73.2)	31 (79.5)	0.552
Induction of labor with oxytocin	10 (24.3)	14 (35.8)	0.262
Meconium stained liquor	7 (17)	4 (10.2)	0.52
Breast feeding (adequate)	37 (90.2)	35 (89.7)	0.263
Sepsis (clinical + Sepsis screen +ve)	2 (4.8)	5 (12.8)	0.426
Diarrhoea±dehydration	2 (4.8)	4 (10.2)	0.353
Antibiotic usage	6 (14.6)	11 (28.2)	0.289

Values are presented as mean±standard deviation, number (%), or median (interquartile range).

2. Intervention

Table 2 shows effect of phototherapy discontinuation (intervention) on 2 study groups. TSB at the time of phototherapy discontinuation was 15.6 mg/dL and 13.1 mg/dLin babies >38 weeks and 11.9 mg/dL and 9.2 mg/dL in babies <38 weeks in the recommended and low threshold groups respectively.

3. Outcome variables

Table 3 shows post phototherapy TSB rise and reinstitution of phototherapyin the 2 study groups. A total of 17 babies had TSB rise in recommended threshold group and 21 babies in low threshold group. Twelve out of 80 babies required reinstitution of phototherapy with 9 babies in recommended threshold group and 3 babies in low threshold group. None of the 12 babies required exchange transfusion. Various factors were evaluated for reinstitution of phototherapy using logistic regression, but none of the factor came out be statistically significant as shown in Table 4.

Table 2. Effect of phototherapy discontinuation (intervention) on TSB by study group

Variable	Recommended threshold group (n=41)	Low threshold group (n=39)	*P* value
Age at PT initiation (hr)			0.996
Median (IQR)	113 (77–146)	108 (74–159)	
Mean±SD	119.58±66	121±66.5	
Age at PT discontinuation (hr)			0.636
Median (IQR)	142 (121.5–200.5)	178 (119–217)	
Mean±SD	168±78.3	175.5±68.2	
Duration of phototherapy (hr)			0.065
Median (IQR)	34 (25–55.5)	46 (33–60)	
Mean±SD	46.5±39.3	54.5±38.4	
Irradiance (μw/cm^2/nm), mean±SD	33.6±2.1	33.7±2.2	0.563
TSB at PT initiation (mg/dL), mean±SD	20.6±4.4	20±3.7	0.507
TSB at PT discontinuation (mg/dL), mean±SD	13.1±2.2	10.5±2.5	**<0.001**

TSB, total serum bilirubin; PT, phototherapy; IQR, interquartile range; SD, standard deviation.
Boldface indicates a statistically significant difference with $P<0.05$.

Table 3. Outcomes of 2 study groups

Variable	Recommended threshold group (n=17)	Low threshold group (n=21)	*P* value
TSB at PT discontinuation in the TSB rise group (mg/dL)	14.0±2.7	11.2±2.6	**0.002**
Peak TSB at rise (mg/dL)	17.1±3.8	13.5±4.05	**0.001**
TSB rise (mg/dL)	3.4 (0.9–5.5)/3.4±2.2	1.5 (0.6–3.3)/2.6±2.2	0.564
Age at TSB rise (hr)	157.0 (118.5–201.5)	214.0 (126.0–241.5)	0.141
Duration of TSB rise (hr)	24.0 (18.0–46.5)	18 (12–48)	0.175
Age at PT reinstitution (hr)	192.0 (155.5–212.5)	232 (171–449)	0.229
Age at discontinuation of PT reinstitution (hr)	218.0 (194.0–235.5)	291 (237–497)	0.052
Duration of PT reinstitution	31.0 (12.5–39.5)	59 (48–66)	**0.021**
Irradiance (μw/cm^2/nm)	33.0±2.5	33.4±2.3	0.165
Peak TSB at PT reinstitution (mg/dL)	18.5±4.0	19.5±4.2	0.853
TSB at PT discontinuation after reinstitution (mg/dL)	12.1±2.3	10.9±2.8	0.405
Duration of hospital stay (hr)	73.1±46.7	74.4±49.8	0.900

Values are presented as mean±standard deviation or median (interquartile range).
TSB, total serum bilirubin; PT, phototherapy.
Boldface indicates a statistically significant difference with $P<0.05$.

Table 4. Role of various factors in phototherapy reinstitution

Variable	Exp (B)	95% CI for Exp (B)	*P* value
Group (group 1 as reference)	0.249	0.057–1.084	0.064
Evidence for hemolysis (no hemolysis in reference)	2.919	0.524–16.248	0.221
Sex (female as reference)	2.977	0.581–15.248	0.190
Gestational age (<38 wk as reference)	1.357	0.352–5.228	0.657
Constant	0.097	-	0.244

CI, confidence interval.

4. ABE and BERA abnormalities

None of the babies developed ABE. Fifty-five babies (70%) underwent BERA evaluation at median (interquartile range) age of 38 days (30.5–44.5 days) and 39.5 days (29–53.3 days) in recommended and low threshold groups respectively. Only 1 patient in low threshold group had abnormal BERA.

Discussion

This randomized clinical trial assessed the rise in serum bilirubin levels and the need for reinstitution of phototherapy following discontinuation at TSB levels that were 3 mg/dL and 6 mg/dL below the phototherapy initiation threshold, as per NICE guidelines.[3] Out of 80 enrolled neonates, 17 and 21 babies in the recommended and low threshold groups, respectively, experienced TSB increases (mean±SD) of 3.4±2.2mg/dL and 2.6±2.2 mg/dL, P=0.564) at 180.8+90.5 and 196.6+84.1 hours postnatal age post phototherapy discontinuation. Significant bilirubin rebound requiring reinstitution of phototherapy was observed in 9 (22%) and 3 babies (7.7%). None of these infants required exchange transfusion.

There is a critical need for a study on phototherapy discontinuation due to inconsistencies in current guidelines and variability in clinical practice. Reinstitution rates vary widely from 4% to 25%,[8-11] with studies like Kaplan et al.[5] indicating that infants with hemolytic conditions may experience greater TSB rebounds. Niknafs et al.[12] found a higher reinstitution rate in the low threshold group, while Barak et al.[8] demonstrated that discontinuing phototherapy at 1 mg/dL below the threshold resulted in shorter treatment durations and hospital stays. Additionally, risk factors such as gestational age and timing of jaundice onset remain underexplored.

A recent study by Almohammadi et al.[13] found an 11% incidence of rebound hyperbilirubinemia in term and late preterm neonates. The relative TSB at the time of phototherapy termination was identified as the best predictor for postphototherapy rebound in neonates with a hemolytic etiology. A focused investigation can provide much-needed clarity and establish evidence-based recommendations, ultimately improving neonatal care and outcomes.

The strength of this study lies in its prospective, randomized design and its evaluation of hyperbilirubinemia at 2 different TSB targets for phototherapy discontinuation. It is among the few to compare the older AAP and NICE guidelines directly. A limitation of the study is its relatively small sample size, as recruitment was halted early, and the lack of blinding of the clinicians may affect the results. Importantly, the study does not address the most recent 2022 AAP guidelines, which might influence the generalizability of the findings.[4]

Discontinuing phototherapy for infants with stable or decreasing TSB trends at 3 mg/dL below the initiation threshold, as per NICE guidelines, led to a 14.3% increase in the need for reinstituting treatment. The average dura-

tion for this reinstitution was 28.11 hours. Importantly, there were no adverse outcomes reported, such as ABE or abnormal BERA.

In conclusion, discontinuing phototherapy in neonates can lead to increased TSB levels, with a 14.3% reinstitution rate observed. While adherence to NICE guidelines is important, careful posttreatment monitoring is essential. Incorporating the 2022 AAP guidelines in future research could provide a more comprehensive understanding of safe practices in this area.

Footnotes

Conflicts of interest: No potential conflict of interest relevant to this article was reported.

Funding: This study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Author contribution: Conceptualization: AK; Data curation: NJ; Formal analysis: NJ; Methodology: Ak; Project administration: AK; Visualization: AK; Writing-original draft: NJ; Writing - review & editing: NJ & AK

ORCID:
Nidhi Jain https://orcid.org/0000-0003-1330-9595

References

1. Practice parameter: management of hyperbilirubinemia in the healthy term newborn. American Academy of Pediatrics. Provisional Committee for Quality Improvement and Subcommittee on Hyperbilirubinemia. Pediatrics 1994;94(4 Pt 1):558-65. Erratum in: Pediatrics 1995;95:458-61.
2. American Academy of Pediatrics Subcommittee on Hyperbilirubinemia. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. Pediatrics 2004;114:297-316. Erratum in: Pediatrics 2004;114:1138.
3. National Collaborating Centre for Women's and Children's Health (UK). Neonatal Jaundice. London: RCOG Press; 2010 May.
4. Kemper AR, Newman TB, Slaughter JL, Maisels MJ, Watchko JF, Downs SM, et al. Clinical practice guideline revision: management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. Pediatrics 2022;150: e2022058859.
5. Kaplan M, Kaplan E, Hammerman C, Algur N, Bromiker R, Schimmel MS, et al. Post-phototherapy neonatal bilirubin rebound: a potential cause of significant hyperbilirubinaemia. Arch Dis Child 2006;91:31-4.
6. Jendrassik L, Grof P. Simplified photometric methods for the determination of bilirubin. Biochem J 1938;297:81-9.
7. Fenton TR, Kim JH. A systematic review and meta-analysis to revise the Fenton growth chart for preterm infants. BMC Pediatr 2013;13:59.
8. Barak M, Berger I, Dollberg S, Mimouni FB, Mandel D. When should phototherapy be stopped? A pilot study comparing two targets of serum bilirubin concentration. Acta Pediatrica 2009;98:277-81.
9. Berkwitt A, Osborn R, Grossman M. The utility of inpatient rebound bilirubin levels in infants readmitted after birth hospitalization for hyperbilirubinemia. Hosp Paediatr 2015; 5:74-8.
10. Elhawary IM, Abdel Ghany EAG, Aboelhamed WA, Ibrahim SGE. Incidence and risk factors of post-phototherapy neonatal rebound hyperbilirubinemia. World J Pediatr 2018;14:350-6.
11. Chang PW, Kuzniewicz MW, McCulloch CE, Newman TB. A clinical prediction rule for rebound hyperbilirubinemia following inpatient phototherapy. Pediatrics 2017;139: e20162896.
12. Niknafs N, Nili F, Dalili H, Nayeri F, Esmaeilnia T, Amini E. A comparison of significant bilirubin rebound after discontinuation of phototherapy in two groups of neonates in Valiasr Hospital: a randomized clinical trial. Iran J Neonatol 2014;4:17-21.
13. Almohammadi H, Nasef N, Al-Harbi A, Saidy K, Nour I. Risk factors and predictors of rebound hyperbilirubinemia in a term and late-preterm infant with hemolysis. Am J Perinatol 2022;39:836-43.

How to cite this article: Kumar A, Jain N. Evaluation of total serum bilirubin thresholds for discontinuing phototherapy in jaundiced neonates: a randomized study. Clin Exp Pediatr 2025;68:539-45.