ARTICLE

Rebound in Serum Bilirubin Level Following Intensive Phototherapy

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Objectives: To document the need for repeated phototherapy (as an index of significant rebound in serum bilirubin levels) following the discontinuation of intensive phototherapy and to compare the use of repeated phototherapy in infants who first received phototherapy during their birth hospitalization with the use of first-time phototherapy on readmission after infants were discharged from their birth hospitalization.

Design: A retrospective review of the medical records of 303 term and near-term newborns treated between January 1996 and December 1998, who received phototherapy in our well-baby nursery during their birth hospitalization (group 1, n=158) or who had been discharged from the nursery and were readmitted for phototherapy (group 2, n=144). All infants received intensive phototherapy but were managed by individual attending pediatricians. Rebound measurements were included if a bilirubin level was obtained between 4 and 48 hours after discontinuing phototherapy.

Setting: Newborn nursery and pediatric ward of a large community hospital.

Main Outcome Measures: The number of infants who received repeated phototherapy and the magnitude of the bilirubin-level rebound.

Results: Thirteen (8.2%) of 158 (95% confidence interval [CI], 3.9-12.4) infants treated with phototherapy before discharge from the nursery (group 1) and only 1 (0.7%) of 144 (95% CI, 0-2.0) infants who first received phototherapy on readmission (group 2) received repeated phototherapy (P=.002). Phototherapy was discontinued when mean±SD total serum bilirubin levels were, 10.4±1.8 mg/dL (178±31 µmol/L) in group 1 and 12.3±1.3 mg/dL (210±22 µmol/L) in group 2. The mean±SD increase in the total serum bilirubin levels following rebound was 1.3±2.0 mg/dL (22±34 µmol/L) in group 1 and 0.27±1.46 mg/dL (4.6±25 µmol/L) in group 2 (P<.001).

Conclusions: It is not necessary to keep infants in the hospital to check for rebound. However, for infants who require phototherapy during their birth hospitalization and for those with significant hemolytic disease, we recommend obtaining a follow-up bilirubin level 24 hours after discharge. This is probably not necessary in those who are readmitted for phototherapy but, because rare instances of significant rebound have occurred in these infants, additional clinical follow-up is appropriate, particularly if phototherapy is discontinued at higher total serum bilirubin levels than used in this study.

Arch Pediatr Adolesc Med. 2002;156:669-672

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DECREASING hospital length of stay is an objective sought by physicians and administrators alike, and the American Academy of Pediatrics has recommended that infants need not be kept in the hospital to measure rebound bilirubin levels following the discontinuation of phototherapy.[1] Nevertheless, many physicians keep infants in the hospital for several hours to obtain a rebound bilirubin level after phototherapy has been discontinued. Only 2 observational studies have specifically addressed this issue.[2,3] These studies included both term and preterm infants and concluded that the measurement of rebound bilirubin levels following phototherapy was probably unnecessary. Examination of other published data suggests that significant rebound following discontinuation of phototherapy is rare.[4,5] The infants in all of these studies were treated during their birth hospitalization (as opposed to having been readmitted for phototherapy). Infants who are discharged following birth and readmitted with hyperbilirubinemia have significantly higher total serum bilirubin (TSB) levels than those who are treated before they are discharged from the nursery.

Since 1995, we have used intensive phototherapy[6] to treat all infants with hyperbilirubinemia who require photo-

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SUBJECTS AND METHODS

We reviewed the medical records of 2 groups of infants treated between January 1996 and December 1998. Group 1 consisted of 158 term and near-term (gestational age, 33-37 weeks) newborns who received phototherapy in our well-baby nursery during their birth hospitalization. Infants who received phototherapy in the special-care or intensive-care nurseries were excluded. Group 2 consisted of 144 infants who had been discharged from the well-baby nursery and had not received phototherapy during their initial hospital stay but were subsequently readmitted for phototherapy. All infants were treated in bassinets, not incubators, and phototherapy was administered with 8 special blue fluorescent tubes (F20T12/BB; General Electric, Milwaukee, Wis) placed 10 cm above the infant. This produced an average irradiance of 43 $\mu W/cm^2$ per nanometer, at 425 to 475 nm, measured at the surface of the infant with an Olympic Bilimeter Mark II (Olympic Medical Corp, Seattle, Wash). In addition, all infants lay on a fiberoptic blanket (Ohmeda Biliblanket; Ohmada Inc, Columbia, Md, or Fiberoptic Medical Wallaby; Fiberoptic Medical Products Inc, Allentown, Pa) and the mean irradiance of the blanket was 18 to 21 $\mu W/cm^2$ per nanometer.

The decisions to initiate and discontinue phototherapy and to obtain a rebound TSB level were made by the responsible attending pediatrician. Of those infants readmitted for phototherapy, 64 (44.4%) of 144 had been born at other hospitals. The data extracted from the medical records included the gestational age, type of feeding, age, and TSB level at initiation of phototherapy and at termination of phototherapy, duration of phototherapy, rebound TSB level measurement, maternal and infant blood types, and direct Coombs test result when available. Rebound measurements were included if a TSB level was obtained between 4 and 48 hours after discontinuing phototherapy. We compared continuous data using the 2-sample *t* test (unless otherwise indicated) and categorical data using the Fisher exact test. Unless otherwise indicated, data are expressed as mean±SD. The study was approved by the hospital human investigation committee.

therapy. Since this type of phototherapy produces a more rapid decline in the TSB level than does conventional phototherapy, it is possible that a greater rebound might occur. Our objective was to document the incidence of rebound of TSB levels after termination of phototherapy and to compare the rebound in a group of infants who received phototherapy during their birth hospitalization with those treated after discharge and readmission to the hospital.

RESULTS

The clinical data and results are presented in the **Table**. One hundred nineteen (75.3%) of 158 infants in group 1 and 115 (79%) of 144 infants in group 2 had rebound TSB levels measured at 17.6±11 (range, 4-48) hours and 16.5±10.5 (range, 4-43) hours, respectively, following the termination of phototherapy. The mean increase in TSB level following rebound was 1.3±2.0 mg/dL (22±34 µmol/L) in group 1 and 0.27±1.46 mg/dL (4.6±25 µmol/L) in group 2 ($P<.001$). In group 1, phototherapy was initiated at 47.5±22.3 (range, 1-106) hours. In this group, 13 (8.2%) of 158 infants (95% confidence interval [CI], 3.9-12.4) received repeated phototherapy, which was initiated at a mean age of 107.3+41.4 hours and at a mean TSB level of 17.2±3.9 mg/dL (294±67 µmol/L). Five were exclusively breastfed and 8 received breast milk and formula. Eight of these 13 mothers had type O blood and direct Coombs tests were performed in 7 infants. Only 2 of these infants had a positive Coombs test result (1 ABO incompatibility, 1 anti C) and 6 had bruising. No cause for the hyperbilirubinemia was found in the remaining 5. Six infants received repeated phototherapy before discharge and 7 were discharged and readmitted 24 to 124 hours later. There were no differences between the infants in group 1 who did or did not receive repeated phototherapy except that all 13 infants who received repeated phototherapy were fully or partially breastfed vs 51.0% of those who did not receive repeated phototherapy ($P<.001$). In 3 infants who received a repeated course of phototherapy while still in the nursery, the TSB level before the repeated course was lower than the level at which phototherapy had been started originally, calling into question the need for repeated phototherapy.

In group 2, phototherapy was initiated at a mean age of 4.6±1.8 days. (Because 44% of these infants were born at other hospitals, the exact time of birth was not available from the hospital record and thus precluded precise calculation of the age in hours.) Only 1 (0.7%) of 144 infants (95% CI, 0-2.0) in this group received repeated phototherapy. This 5436-g male had O Rh-positive blood type, was formula-fed, and his TSB level on admission on day 4 was 23.1 mg/dL (395 µmol/L). His TSB level decreased to 13.2 mg/dL (226 µmol/L) after 31 hours of phototherapy (a decrease of 0.32 mg/dL [5.5 µmol/L] per hour). Nine hours after stopping phototherapy, his TSB level was 17.4 mg/dL (298 µmol/L) and phototherapy was reinstituted.

COMMENT

Two observational studies have specifically addressed the question of rebound,[2,3] but data on rebound of TSB level are provided in other studies.[4,5] The infants in all of these studies were treated during their birth hospitalization only; ours is the first, to our knowledge, to examine TSB level rebound in a population readmitted for phototherapy and to compare these infants with those treated during their birth hospitalization. Our data confirm the previous observations dealing with TSB level rebound after phototherapy. In the study by Lazar et al,[2] none of 58 infants weighing more than 1500 g had a TSB level rebound that required additional phototherapy. Yetman et al[3] studied 264 infants, all of whom were treated during their birth hospitalization. Repeated phototherapy was required in 11 infants but 9 of these infants weighed less than

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Clinical Data*

	Group 1 Phototherapy Before Discharge (n = 158)	Group 2 Phototherapy on Readmission (n = 144)	*P* Value
Gestation, wk	38.1 ± 2.0 (33 5/7-42)	37.9 ± 1.7 (32 6/7-42)	.38
Gestation ≤37 wk, No. (%)	76 (48)	64 (44)	.65
Blood type and Coombs test result obtained, No. (%)	109 (69)	109 (76)	.2
ABO incompatible with positive direct Coombs test result, No. (%)	35 (22.0)	5 (3.5)	<.001
Breastfed exclusively, No. (%)	47 (29.7)	99 (68.8)	<.001
Breastfed plus formula, No. (%)	80 (51)	36 (25)	<.001
Formula-fed, No. (%)	31 (19.6)	9 (6.3)	.001
Born at WBH, No. (%)	158 (100)	80 (55.6)	<.001
TSB level start, mg/dL†	12.7 ± 2.7 (5.6-19.4)	20.1 ± 2.3 (15.0-29.3)	<.001
TSB level end, mg/dL†	10.4 ± 1.8 (6.0-15.7)	12.3 ± 1.3 (9.5-15.9)	<.001
Δ TSB level, mg/dL‡	2.3 ± 2.3 (–4.9 to 7.8)	7.8 ± 2.6 (0.6-18.1)	<.001
Duration of phototherapy, h	26.2 ± 14.3 (5.1-87.3)	25.7 ± 10.4 (8.8-67.0)	.83
Δ TSB level, mg/dL per h‡	0.11 ± 0.1 (–.25 to 0.54)	0.3 ± 1.3 (0.03-0.97)	<.001
Received repeated phototherapy, No. (%)	13 (8.2)	1 (0.7)	.002

*Data are given as mean ± SD (range) unless otherwise indicated. To convert TSB (total serum bilirubin) values to micromoles per liter, multiply by 17.1. WBH indicates William Beaumont Hospital (Royal Oak, Mich).

†Total serum bilirubin levels at initiation and termination of phototherapy.

‡Δ TSB indicates decline in total serum bilirubin from start of phototherapy.

1800 g. In the other 2 infants, the authors considered the reinstitution of phototherapy to be unnecessary. Tan et al[5] studied 3802 infants who received phototherapy for nonhemolytic jaundice. Of 2879 full-term infants receiving standard white light phototherapy, only 24 (0.66%) required a second dose of phototherapy following rebound compared with 4 (2.8%) of 141 term infants receiving intensive phototherapy with special blue lights ($P<.001$).

In the 1974-1976 collaborative phototherapy study of the National Institutes of Child Health and Human Development (Bethesda, Md), 672 infants received phototherapy.[4] Those with birth weights less than 2000 g were treated "prophylactically" starting at age 24±12 hours. The authors report a rebound in serum TSB level "usually less than 1.0 mg/dL" that occurred within 24 hours after discontinuing phototherapy. Seventy infants with birth weights of 2000 to 2499 g in this study were treated with phototherapy when their TSB values reached 10 mg/dL (171 µmol/L), and 140 infants with birth weights greater than or equal to 2500 g received phototherapy at a mean TSB level of 15.7±2.5 mg/dL (269±43 µmol/L) at age 62.5 hours. In both groups of infants, mean TSB levels continued to decline once phototherapy was discontinued.

Our data and the data from these studies show that it is unnecessary to keep an infant in the hospital after phototherapy has been discontinued to check for a rebound of the TSB level. This applies to infants with Coombs-positive ABO incompatibility as well. Yetman et al[2] found no rebound in any of 57 infants who had positive direct Coombs test results and received phototherapy. An important difference between our study and that of Yetman et al[3] is that our infants received phototherapy for an average of only 25.8 hours (and some as little as 5 hours), while the average duration of phototherapy in their study was 121 hours.

The differences in the apparent cause of hyperbilirubinemia between the 2 groups of infants are instructive. ABO incompatibility with a positive direct Coombs test result occurred in 22% of infants (in whom blood type and Coombs test results were obtained) in group 1 but only 3.5% of those in group 2. Even in the absence of blood group incompatibility, there is evidence that increased bilirubin production (including bruising) is the most likely cause of early hyperbilirubinemia and rebound in the infants in group 1.[7] We measured end-tidal carbon monoxide concentrations, corrected for ambient carbon monoxide (an index of heme catabolism and bilirubin production)[8] in infants in our nursery who developed significant jaundice (TSB >75th percentile for age in hours).[7] In 89%, the end-tidal carbon monoxide concentration corrected for ambient carbon monoxide was above the 50th percentile and in 55% it was above the 75th percentile compared with controls. This suggests that most infants who develop early jaundice have an increase in their rate of bilirubin production.[7] On the other hand (and not surprisingly), breastfeeding seemed to play a much more significant role in those infants readmitted for hyperbilirubinemia than in those who developed early hyperbilirubinemia.

The differences between groups 1 and 2 probably reflect both the causes of hyperbilirubinemia and the natural history of neonatal jaundice. As discussed, far fewer infants in group 2 (than in group 1) had evidence of hemolysis. Furthermore, in group 2, because phototherapy was started at an average age of 4.6±1.8 days, it is likely that the TSB level was approaching, or had reached its peak, so that rebound was much less likely. The above reasons also account, in part, for the differences in the efficacy of phototherapy in the 2 groups. In group 1, phototherapy produced a much slower decline in TSB levels (0.11±0.1 mg/dL [1.9±1.7 µmol/L] per hour) than in group 2 (0.3±0.13 mg/dL [5.1±2.2 µmol/L] per hour) ($P<.001$). Perhaps the most important reason for this, however, is the difference in the mean TSB level at the start of phototherapy: 12.7 mg/dL (217 µmol/L) in group 1 vs 20.1 mg/dL (344 µmol/L) in group 2. It is well known

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What This Study Adds

Many physicians keep infants hospitalized for measurement of rebound TSB levels following the discontinuation of phototherapy, even though published data have suggested that this is not necessary. The studies to date have been limited to infants who received phototherapy during the birth hospitalization and there are very limited data on infants who have received intensive (vs standard) phototherapy. To our knowledge, this study is the first to provide data on the rebound of TSB levels that occurs in infants who have been discharged following birth and then readmitted for intensive phototherapy and the first to compare infants who are treated during their birth hospitalization with those treated after discharge and readmission to the hospital. We provide guidelines for the physician regarding the follow-up of infants after phototherapy is discontinued.

that the higher the initial TSB level, the better the response to phototherapy.[9]

Weaknesses in this study include its design (a retrospective survey) and the fact that decisions to measure rebound TSB levels or to initiate or restart phototherapy were not established prior to the study and were made by individual attending pediatricians. Thus, the need for repeated phototherapy in some infants could be questioned. On the other hand, follow-up was inconsistent, so we do not know if significant rebound was missed in some infants who might have required additional phototherapy. Nevertheless, when measured, the rebound in both groups was small. This confirms our conclusion that infants need not remain in the hospital to have rebound TSB levels measured. Clinical follow-up and/or an outpatient TSB level should identify infants who need additional treatment.

Accepted for publication April 3, 2002.

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