Procedures in Family Practice

Phototherapy

Avrum L. Katcher, MD
Flemington, New Jersey

Phototherapy is a widely used and efficient method of reducing and preventing hyperbilirubinemia both in term and in premature infants. Although a number of complications from its use are recognized, few serious long-term consequences have been described. Indications, technique, and dosage are generally agreed upon. When thoughtfully used, with full understanding of potential dangers and after careful diagnostic study, it is a safe procedure.

In 1958 Cremer and associates[1] demonstrated that light alters unconjugated bilirubin to colorless products and that light treatment of newborn infants lowered the intensity of jaundice. Not until 10 years had passed and phototherapy was widely practiced abroad did the well-controlled study of Lucey and associates[2] on the prevention of jaundice in premature infants bring about widespread use of light treatment. A consensus was soon achieved that phototherapy was efficacious for treatment as well as prevention of hyperbilirubinemia, but uncertainty as to how it works has persisted, and doubt concerning its safety has lingered. This paper outlines (1) current understanding of the mechanism of action, (2) indications and contraindications, (3) methods of use and precautions to be observed, and (4) side effects of phototherapy.

Mechanism of Action of Phototherapy

Although an unequivocal description of the products of light-induced bilirubin breakdown is not yet available, recent studies[3,4] suggest that a rapid and reversible isomeric rearrangement of bilirubin IXα is the most likely mechanism. The traditional explanation of a light-induced oxygenation reaction is incompatible with the speed of the reaction and its consistency in almost any solvent. Instead, "photochemical excitation of bilirubin near the skin surface yields an excited state species that decays to . . . bilirubin or after isomerization to . . . photobilirubin."[4] Photobilirubin is the name applied to a mixture of four isomers with overlapping light absorption bands. Photobilirubin in the extravascular compartment migrates through the plasma membrane into blood. Because it is more polarized, thereby being more soluble in water, photobilirubin is more quickly extracted by the hepatocyte and excreted in the bile. The shift from the extravascular compartment to the blood is probably by passive diffusion. The excretion from the hepatocyte to the bile probably does not require enzymatic conjugation. Along the way, much of the photobilirubin reverts to bilirubin, since the photoisomerization is a readily reversible process. The entire process causes bilirubin to be transported from skin to blood to bile.[4]

Since all babies are exposed to light, typically 24 hours a day in a newborn nursery, all babies are in effect subjected to phototherapy. Almost all babies are jaundiced to some extent; therefore, photobilirubin is a normal metabolite of newborn infants. The ready reversibility of the photobilirubin $\rightleftharpoons$ bilirubin reaction results in the dominant product in the bile becoming bilirubin again. As a result, factors governing the enterohepatic circulation will influence the equilibrium level of unconjugated bilirubin in the blood.

From the Pediatric Service, Hunterdon Medical Center, Flemington, and the Department of Pediatrics, Rutgers Medical School, Piscataway, New Jersey. Requests for reprints should be addressed to Dr. Avrum L. Katcher, Hunterdon Medical Center, Flemington, NJ 08822.

0094-3509/82/061123-05$01.25

Indications

The essential indication for phototherapy is hyperbilirubinemia. There do not exist well-defined or consistent guidelines for the onset of therapy. For the term infant less than four days old, it might be suggested to start when the bilirubin level reaches 12 mg/100 mL. For premature or small infants, phototherapy might be used prophylactically for infants weighing less than 1,500 g, and therapeutically at serum levels of 8 mg/100 mL or above in infants weighing between 1,500 g and 2,500 g. Other indications might be as an adjunct after exchange transfusion or when multiple exchange transfusions are indicated. Sick babies with sepsis, hemolytic disorders, respiratory distress, or other complications of the neonatal period must be evaluated on an individual basis after appropriate consultation with the neonatologist or the pediatrician knowledgeable about the newborn.

Contraindications

Porphyria

Since some patients with porphyria suffer exacerbations from light, inquiry should be made about the family history before commencing phototherapy.

Elevated Direct Reacting Bilirubin

This may indicate liver disease, with cholestasis. Accumulation of unexcreted photobilirubin products may produce the bronze baby syndrome. Although it is unclear if there is any major hazard, phototherapy in such instances should be undertaken only after careful comparison of possible benefits with risks.

Erythroblastosis

If the infant suffers from a form of maternal-fetal blood incompatibility, there is the risk of being lulled into a false sense of security and delaying or even failing to offer exchange transfusion. Phototherapy in such instances, therefore, should only be commenced after full consideration of other alternative therapies.

Preparation

The decision to administer phototherapy can be made only after appropriate consideration of the condition of the infant, the cause of the jaundice, the need for intervention, and the usefulness of phototherapy vis-a-vis alternative methods for lowering serum bilirubin levels.

In a term infant, development of a serum bilirubin level of 12 mg/100 mL or over indicates that a search should be made for systemic, hematologic, or hepatic disease producing hyperbilirubinemia. Such a search should include the following steps:

1. Review the history of the mother, the pregnancy, labor and delivery, and the condition of the infant up to the present time. In particular, look for the following complications known to be associated with hyperbilirubinemia: (1) mother with diabetes, (2) prior family history of icteric newborn infants, (3) known blood incompatibility: Rh negative or type O mother, (4) toxemia of pregnancy, (5) rubella-susceptible mother, (6) premature delivery, (7) perinatal stress or hypoxia at delivery, and (8) mother with positive serology.

2. Examine the infant, with particular attention to the following: (1) evidence of serious sickness, pallor, petechiae, or other signs of hemorrhagic disorder, (2) enlargement of liver or spleen, (3) respiratory distress, (4) central nervous system depression, (5) cataracts or chorioretinitis, (6) fetal age less than 38 weeks, (7) infant small for dates, and (8) plethora.

3. If the infant appears sick, obtain blood, urine, and spinal fluid cultures, and institute appropriate therapy for sepsis or meningitis. Pediatric consultation is appropriate for a sick infant.

4. Perform ABO and Rh typing and Coombs' tests. It may be necessary to test for rare blood types if Coombs' test is positive but there is no ABO or Rh incompatibility. Only a type O mother will form antibodies against a type A or B infant.

5. Even if there is no clinical evidence suggesting hepatitis, such as enlargement of the liver or spleen, screen for hepatic disease by measuring both conjugated and unconjugated bilirubin and some representative enzymes such as serum glutamic-pyruvic transaminase or gamma glutamyl transpeptidase.

6. Evaluate for other causes of hemolysis by a complete blood count, including platelet count, reticulocyte count, percentage of nucleated red blood cells, and red blood cell morphology on smear.

7. Measure serum albumin as an indication of bilirubin-binding capacity.

8. If clinically indicated, obtain blood specimen from infant and mother for measurement of immuno-

Table 1. Irradiance of Fluorescent Lamps (nm)

Type of Light	Range of Wavelength Emitted	Peak Irradiance
Daylight (GE F20T12-D)	350-700	450-600
Blue (GE F20T12-B)	350-600	425-475
Cool White (GE F20T12-CW)	375-700	550-600
Special Blue (Westinghouse) (F20T12-BB)	425-480	425-480

Source: Olympic Bililite instruction manual, Olympic Medical Corp, Seattle, Washington

globulin M antibodies to detect antenatal infection with TORCHS (toxoplasmosis, rubella, cytomegalic inclusion body disease, herpes, syphilis).

9. Discuss the infant's condition with parents in order to obtain their informed agreement for proposed therapy and to assure that no additional information of diagnostic value will be overlooked.

10. Consult with pediatrician or neonatologist on care of newborn who appears sick or in whom findings suggest serious disorder.

Dosage and Administration

In planning dosage of light, three relevant characteristics are of importance[5]: The spectral characteristics of the lights used, the irradiance, and the duration.

Although light in the blue range (420 to 500 nm)* is most efficiently absorbed by bilirubin, some fluorescent lamps used in phototherapy units emit electromagnetic radiation beyond either end of the visible range; others emit radiation in more restricted ranges. The maximal absorption peak for albumin-bound bilirubin is 460 nm; for free bilirubin it is 440 nm. Lights that emit radiation confined to the most active wavelengths should be of greater effectiveness and safety.

In addition to wavelength, the amount of light energy emitted by a lamp must be determined in order to determine the exposure of an infant under that lamp. Such measurements are often performed with light meters, which do not provide the information desired. A light meter measures illuminance, which is the density of electromagnetic radiation spectrally weighted to the response of the human eye. Light meters function with maximal sensitivity between 500 and 600 nm, but with diminishing sensitivity in the 400 to 500 range, where bilirubin is most effectively changed to photobilirubin. Behrman et al[5] have prepared diagrams showing the magnitude of error created when illuminance (what is measured by a light meter) is confused with irradiance (actual radiant energy).

The latter can only be measured by a spectroradiometer, expressed in watts per square centimeter per unit wavelength ($w/cm^2/U$) over the entire spectral range incident on the patient.

Table 1 is derived from charts presented in the instruction manual for the Olympic Bililite, a commercial mount for fluorescent lights for phototherapy, showing typical ranges of irradiance in some commonly used fluorescent lamps.

There is insufficient information available to determine whether it is wiser to utilize blue lights (greater specificity) or the ordinary fluorescent light (greater ease of detecting cyanosis). The blue lights, however, do provide two or three times the irradiance of other lamps. There are no good data on the effects of irradiation out of the visual range. Very short wavelengths below 380 nm are filtered out by the commonly used Plexiglas shields. There are no good data to indicate how long an infant should be under the light in each 24-hour day or whether lights along the side or even underside of a transport mattress would be more effective.

The time of therapy should be whenever the infant is not being fed, cared for, or given other treatments. This might amount to a total of 12 to 16 hours out of each 24-hour cycle for a term baby, allowing time for nursing care, medical inspections, and feeding and loving with the infant's mother. In the care of the premature infant, greater proportions of time might be allotted to the

*1 nanometer (nm) = millimicron = 10 angstrom units

Continued on page 1128

Continued from page 1125

phototherapy if such an infant were in a special care nursery.

Finally, it has been shown that serum bilirubin concentrations correlate inversely with caloric intake in infants receiving phototherapy, perhaps because there is increased transit through the gut, thereby facilitating excretion of bilirubin. Intakes of greater than 60 cal/kg/d are sufficient.[6]

Precautions

Eyes should be covered with a black shield to prevent radiation from reaching the cornea or retina. This should be of such a design that will not slip down over the infant's nose.[7] The shield should be removed as soon as the infant is taken from under the light in order to allow the infant to maintain eye contact with the parents during feeding and play periods for early bonding and early developmental stimulation.

Temperature should be monitored every four to six hours to avoid both overheating and underheating, and appropriate adjustments should be made in ambient temperature or sources of radiant heat.

A Plexiglas shield should be used in every instance to prevent light of less than 320 nm from reaching the infant.

Weights should be measured daily (twice daily in the small infant) and fluid intake, breast-feedings, urine, and stools charted to avoid inadvertent dehydration from water loss. Provision should be made for additional fluid intake as indicated in the range of 10 to 15 mL/kg/d.

The hours of therapy should be charted for each infant. Follow-up measurements of serum bilirubin should be performed every eight hours initially, less often when rate of rise is known, but at least daily and more often as indicated.

The infant should be examined at least twice daily to review clinical progress and verify the absence of any complications of therapy or of the cause of the jaundice. Estimates of jaundice based on skin appearance are very inaccurate. Although instruments are available that reliably measure bilirubin through skin, they are *not* reliable during phototherapy.[8]

Riboflavin at a dose of 3 mg/kg/d as an adjunct to increase formation of photobilirubin[9] is theoretically indicated but not widely used.

Records should be kept of the hours of use of light bulbs. They should be replaced according to recommendations of the manufacturer.

Discontinuing Therapy

When the bilirubin is falling progressively and is below 12 to 14 mg/100 mL in the term infant, a trial on discontinuing therapy may be made. In the small infant the bilirubin should be at or less than 8 mg/100 mL.

Side Effects of Phototherapy

Although a large variety of side effects of irradiation have been postulated, there is little direct evidence of untoward consequences from phototherapy.[3] Radiant energy is known to produce many kinds of injury in a large number of species. Light may produce death or mutation in microorganisms, particularly in the presence of oxygen. Chemicals are known to photosensitize living organisms to light injury, resulting in mutation, death, or production of neoplasms. The lamps used for phototherapy produce radiation of many wavelengths, both longer and shorter than that which is visible. The light from a sunny window, however, may provide more radiant energy exposure than the much less intense light of phototherapy.

Complications may be divided into those resulting directly from irradiation, those resulting from the circumstances of irradiation (infant nearly naked, eyes covered), and those resulting from secondary effects of irradiation on metabolism. To date no major irreversible short-term side effects have been observed, and long-term unwanted effects are, thus far, undocumented.[3] A list might include the following complications.

Erythema. A "flea bite" rash may be noticed, more on the trunk. It is transient, and there is no report of any permanent change when phototherapy is discontinued.

Bronze Baby Syndrome. The serum, urine, and skin become brownish black in color following onset of phototherapy in association with elevation of the conjugated bilirubin fraction in infants with cholestasis. These infants show normal development and no neurological impairment after the syndrome subsides. It is rare, 0.3 percent in one series.[10]

Late Skin Changes. There could be potential long-term effects on the skin in the form of increased mutations, increased pigmentation, and incidence of neoplasms. No such consequences have been reported.

Loose Stools. Probably 25 percent of infants

Continued on page 1133

Continued from page 1128

under phototherapy may have increased intestinal transit time, perhaps from lactase deficiency, leading to loose stools and an increased loss of body water. This may, together with the complications of increased heat and insensible loss, require replenishment of water.

Insensible Water Loss. The exposure of the infants for phototherapy results in increased blood flow and thereby increased insensible loss from the skin, up to three times that seen in the normal infant. Small babies, who have less mass per unit skin surface, and infants in open warmers or in low humidity environments are at greater risk.

Thermal Balance. Most phototherapy units throw radiant heat on the infants. If the infant is also in a heated environment, there will be increased blood flow and respiratory rate and a rise in skin temperature, producing greater water loss. In an open crib, radiant heat loss from the naked infant may be greater than that absorbed, and the net result will be loss of body heat. Oxygen consumption has been shown to increase if a speedup to metabolic processes is required in order to compensate for increased heat loss.

Blood Changes. Decreased platelet counts have been documented during phototherapy, perhaps as a result of membrane changes from direct phototoxicity. Red blood cells might also hemolyze at an increased rate as a result of loss of enzymes necessary for energy metabolism or membrane function, but there is no solid evidence that red blood cells suffer from light or oxidative damage under usual clinical conditions. There is debate whether peripheral blood lymphocytes undergo chromatid damage.[3] The answer to this question may have to wait on long-term studies of the incidence of lymphocytic malignancies in infants who have received phototherapy.

Miscellaneous Changes. Hypocalcemia, decreased levels of prostaglandin A, decreased levels of serum nonesterified fatty acids, and changes in tryptophan metabolism have all been reported. Cohen and Ostrow[3] have extensively discussed direct and indirect phototoxicity.

Riboflavin. Levels of riboflavin in blood are lowered by as much as one third after 18 to 24 hours of phototherapy. The mechanism is unclear. The fall can be prevented by daily supplementation with at least 0.3 mg of riboflavin.

Abdominal Distention. This has been reported in some instances.

Eye Injury. Since phototherapy has been first utilized, there has been concern for possible radiation injury to eye structures. Experimental animals have shown extensive photoreceptor damage after exposure to comparable intensities of illumination. No long-term reports of injury have appeared thus far in the literature, although it should be noted that the use of protective eye covering is and should be universal. Phototherapy should not be conducted without appropriate protection for the eyes.

Obstructive Apnea. The most serious complication reported[7] is cyanosis and apnea resulting from an eye shield slipping down over the nose of a premature infant, causing respiratory obstruction.

Behavior. Exposure to light itself has been shown to alter behavior: infants exposed to continuous room light show poorer regulation of sleep states and decreased total daily sleep. Some studies suggest that phototherapy produces disorders of circadian rhythms lasting for several days. Telzrow's group have observed decreased orienting on the Brazelton scale[11] but were unable to distinguish the effect of separation from the mother from that of the jaundice or the phototherapy.

Growth. During phototherapy growth is slowed, but there is a prompt catch-up immediately afterward. This may be related to metabolic alterations described above.

References

1. Cremer RJ, Perryman PW, Richards DH: Influence of light on the hyperbilirubinemia of infants. Lancet 1:1094, 1958
2. Lucey J, Ferreiro M, Hewitt J: Prevention of hyperbilirubinemia of prematurity by phototherapy. Pediatrics 41:1047, 1968
3. Cohen AN, Ostrow JD: New concepts in phototherapy: Photoisomerization of bilirubin IXα and potential toxic effects of light. Pediatrics 65:740, 1980
4. McDonagh AF, Palma LA, Lightner DA: Blue light and bilirubin excretion. Science 208:145, 1980
5. Behrman RE, Brown AK, Currie MR, et al: Preliminary report of the committee on phototherapy in the newborn infant. J Pediatr 84:135, 1974
6. Brown A, Wu CPK: Efficacy of phototherapy in prevention of hyperbilirubinemia. Pediatr Res 13:277, 1979
7. Kang H, Mazzi E: Apnea resulting from obstruction of the nares by an eye shield. J Pediatr 89:652, 1976
8. Hegyi T, Hiatt IM, Indyk L: Transcutaneous bilirubinometry I: Correlations in term infants. J Pediatr, in press
9. Pascale JA, Mims LC, Greenberg MH, et al: Riboflavin and bilirubin response during phototherapy. Pediatr Res 10:854, 1976
10. Drew JH, Marriage KJ, Bayle VU, et al: Phototherapy: Short and long-term consequences. Arch Dis Child 51: 454, 1976
11. Telzrow RW, Snyder DM, Tronich, et al: The behavior of jaundiced infants undergoing phototherapy. Dev Med Child Neurol 22:317, 1980