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TECHNICAL REPORT

Phototherapy to Prevent Severe Neonatal Hyperbilirubinemia in the Newborn Infant 35 or More Weeks of Gestation

abstract

FREE

OBJECTIVE: To standardize the use of phototherapy consistent with the American Academy of Pediatrics clinical practice guideline for the management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation.

METHODS: Relevant literature was reviewed. Phototherapy devices currently marketed in the United States that incorporate fluorescent, halogen, fiber-optic, or blue light-emitting diode light sources were assessed in the laboratory.

RESULTS: The efficacy of phototherapy units varies widely because of differences in light source and configuration. The following characteristics of a device contribute to its effectiveness: (1) emission of light in the blue-to-green range that overlaps the in vivo plasma bilirubin absorption spectrum (~460–490 nm); (2) irradiance of at least 30 $\mu W \cdot cm^{-2} \cdot nm^{-1}$ (confirmed with an appropriate irradiance meter calibrated over the appropriate wavelength range); (3) illumination of maximal body surface; and (4) demonstration of a decrease in total bilirubin concentrations during the first 4 to 6 hours of exposure.

RECOMMENDATIONS (SEE APPENDIX FOR GRADING DEFINITION): The intensity and spectral output of phototherapy devices is useful in predicting potential effectiveness in treating hyperbilirubinemia (group B recommendation). Clinical effectiveness should be evaluated before and monitored during use (group B recommendation). Blocking the light source or reducing exposed body surface should be avoided (group B recommendation). Standardization of irradiance meters, improvements in device design, and lower-upper limits of light intensity for phototherapy units merit further study. Comparing the in vivo performance of devices is not practical, in general, and alternative procedures need to be explored. *Pediatrics* 2011;128:e1046–e1052

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KEY WORDS
phototherapy, newborn jaundice, hyperbilirubinemia, light treatment

ABBREVIATION
LED—light-emitting diode

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INTRODUCTION

Clinical trials have validated the efficacy of phototherapy in reducing excessive unconjugated hyperbilirubinemia, and its implementation has drastically curtailed the use of exchange transfusions.[1] The initiation and duration of phototherapy is defined by a specific range of total bilirubin values based on an infant's postnatal age and the potential risk for bilirubin neurotoxicity.[1] Clinical response to phototherapy depends on the efficacy of the phototherapy device as well as the balance between an infant's rates of bilirubin production and elimination. The active agent in phototherapy is light delivered in measurable doses, which makes phototherapy conceptually similar to pharmacotherapy. This report standardizes the use of phototherapy consistent with the American Academy of Pediatrics clinical practice guideline for the management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation.

I. COMMERCIAL LIGHT SOURCES

A wide selection of commercial phototherapy devices is available in the United States. A complete discussion of devices is beyond the scope of this review; some are described in Tables 1 and 2. Phototherapy devices can be categorized according to their light source as follows: (1) fluorescent-tube devices that emit different colors (cool white daylight, blue [B], special blue [BB], turquoise, and green) and are straight (F20 T12, 60 cm, 20 W), U-shaped, or spiral-shaped; (2) metal halide bulbs, used in spotlights and incubator lights; (3) light-emitting diodes (LEDs) or metal halide bulbs, used with fiber-optic light guides in pads, blankets, or spotlights; and (4) high-intensity LEDs, used as over- and under-the-body devices.

TABLE 1 Phototherapy Devices Commonly Used in the United States and Their Performance Characteristics

Device	Manufacturer	Distance to Patient (cm)	Footprint Area (Length × Width, cm^2)	% Treatable BSA	Spectrum, Total (nm)	Bandwidth* (nm)	Peak (nm)	Footprint Irradiance ($\mu W/cm^2/nm$)		
								Min	Max	Mean ± SD
Light Emitting Diodes [LED]										
neoBLUE	Natus Medical, San Carlos, CA	30	1152 (48 × 24)	100	420–540	20	462	12	37	30 ± 7
PortaBed	Stanford University, Stanford, CA	≥5	1740 (30 × 58)	100	425–540	27	463	40	76	67 ± 8
Fluorescent										
BiliLite CW/BB	Olympic Medical, San Carlos, CA	45	2928 (48 × 61)	100	380–720	69	578	6	10	8 ± 1
BiliLite BB	Olympic Medical, San Carlos, CA	45	2928 (48 × 61)	100	400–550	35	445	11	22	17 ± 2
BiliLite TL52	Olympic Medical, San Carlos, CA	45	2928 (48 × 61)	100	400–626	69	437	13	23	19 ± 3
BiliBed	Medela, McHenry, IL	0	693 (21 × 33)	71	400–560	80	450	14	59	36 ± 2
Halogen										
MinBiliLite	Olympic Medical, San Carlos, CA	45	490 (25 diam)	54	350–800	190	580	<1	19	7 ± 5
Phototherapy Lite	Philips Inc, Andover, MA	45	490 (25 diam)	54	370–850	200	590	<1	17	5 ± 5
Halogen fiberoptic										
BiliBlanket	Ohmeda, Fairfield, CT	0	150 (10 × 15)	24	390–600	70	533	9	31	20 ± 6
Wallaby II Preterm	Philips, Inc, Andover, MA	0	117 (9 × 13)	19	400–560	45	513	8	30	16 ± 6
Wallaby II Term	Philips, Inc, Andover, MA	0	280 (8 × 35)	53	400–560	45	513	6	11	8 ± 1
SpotLight 1000	Philips, Inc, Andover, MA	45	490 (25 diam)	54	400–560	45	513	1	11	6 ± 3
PEP Model 2000	PEP, Fryeburg, ME	23	1530 (30 × 51)	100	400–717	63	445	12	49	28 ± 11
Bili Soft	GE Healthcare, Laurel, MD	0	825 (25 × 33)	71	400–670	40	453	1	52	25 ± 16

Data in Table 1 are expanded and updated from that previously reported by Vreman et al.[3] The definitions and standards for device assessment are explained below.

EMISSION SPECTRAL QUALITIES. Measured data of the light delivered by each of the light sources are presented as the minimum, maximum and range. Light source emission spectra within the range of 300–700 nm were recorded after the device had reached stable light emission, using a miniature fiberoptic radiometer (IRRAD2000, Ocean Optics, Inc, Dunedin, FL). For precision based device assessment, the spectral bandwidth (*), which is defined as the width of the emission spectrum in nm at 50% of peak light intensity, is the preferred method to distinguish and compare instead of the total range emission spectrum (data usually provided by manufacturers). Emission peak values are also used to characterize the quality of light emitted by a given light source.

IRRADIANCE. Measured data are presented as mean ± standard deviation (SD), representing the irradiance of blue light (including spectral bandwidth), for each device's light footprint at the manufacturer-recommended distance. To compare diverse devices, the spectral irradiance ($\mu W/cm2/nm$) measurements were made using calibrated BiliBlanket Meters I and II (Ohmeda, GE Healthcare, Fairfield, CT), which were found to yield identical results with stable output phototherapy devices. This type of meter was selected from the several devices with different photonic characteristics that are commercially available, because it has a wide sensitivity range (400–520 nm with peak sensitivity at 450 nm), which overlaps the bilirubin absorption spectrum and which renders it suitable for the evaluation of narrow and broad wavelength band light sources. The devices have been found exceptionally stable during several years of use and agree closely after each annual calibration.

FOOTPRINT. The minimum and maximum irradiance measured (at the intervals provided or defined) in the given irradiance footprint of the device (length × width). The footprint of a device is that area which is occupied by a patient to receive phototherapy. The irradiance footprint has greater dimensions than the emission surface, which is measured at the point where the light exits a phototherapy device. The minimum and maximum values are shown to indicate the range of irradiances encountered with a device and can be used as an indication of the uniformity of the emitted light. Most devices conform to an international standard to deliver a minimum/maximum footprint light ratio of no lower than 0.4.

BSA: BODY SURFACE AREA refers to percent (%) exposure of either the ventral or dorsal planar surface exposed to light and Irradiance measurements are accurate to ±0.5.

All of the reported devices are marketed in the United States except the PortaBed, which is a non-licensed Stanford-developed research device and the Dutch Crigler-Najjar Association (used by Crigler-Najjar patients).

TABLE 2 Maximum Spectral Irradiance of Phototherapy Devices (Using Commercial Light Meters at Manufacturer Recommended Distances) Compared to Clear-Sky Sunlight

Light Meter [Range, Peak]	Footprint Irradiance, (μW/cm^2/nm[a])							
	Halogen/Fiberoptic			Fluorescent		LED		Sunlight
	BiliBlanket	Wallaby (Neo)		PEP Bed	Martin/Philips BB	neoBLUE	PortaBed	@ Zenith on 8/31/05
		II	III					
	@ Contact	@ Contact		@ 10 cm	@ 25 cm	@ 30 cm	@ 10 cm	Level Ground
BiliBlanket Meter II [400–520, 450 nm]	34	28	34	40	69	34	76	144
Bili-Meter, Model 22 [425–475, 460 nm]	29	16	32	49	100	25	86	65**
Joey Dosimeter, JD-100 [420–550, 470 nm]	53	51	60	88	174	84	195	304**
PMA-2123 Bilirubin Detector[a] (400–520, 460 nm)	24	24	37	35	70	38	73	81
GoldiLux UVA Photometer, GRP-1[b] [315–400, 365 nm]	<0.04	<0.04	<0.04	<0.04	<0.04	<0.04	<0.04	2489

Data in Table 2 were tested and compiled by Hendrik J. Vreman (June 2007 and reverified December 2010).

** Irradiance presented to this meter exceeded its range. Measurement was made through a stainless-steel screen that attenuated the measured irradiance to 57%, which was subsequently corrected by this factor.

[a] Solar Light Company, Inc., Glenside, PA 19038.

[b] Oriel Instruments, Stratford, CT 06615 and SmartMeter GRP-1 with UV-A probe. GRP-1 measures UV-A light as μW/cm^2. No artificial light source delivered significant (<0.04 μW/cm^2) UV-A radiation at the distances measured.

II. STANDARDS FOR PHOTOTHERAPY DEVICES

Methods for reporting and measuring phototherapy doses are not standardized. Comparisons of commercially available phototherapy devices that use in vitro photodegradation techniques may not accurately predict clinical efficacy.[2] A recent report explored an approach to standardizing and quantifying the magnitude of phototherapy delivered by various devices.[3] Table 1 lists technical data for some of the devices marketed in the United States.[3] Factors to consider in prescribing and implementing phototherapy are (1) emission range of the light source, (2) the light intensity (irradiance), (3) the exposed ("treatable") body surface area illuminated, and (4) the decrease in total bilirubin concentration. A measure of the effectiveness of phototherapy to rapidly configure the bilirubin molecule to less toxic photoisomers (measured in seconds) is not yet clinically available.

A. Light Wavelength

The visible white light spectrum ranges from approximately 350 to 800 nm. Bilirubin absorbs visible light most strongly in the blue region of the spectrum (~460 nm). Absorption of light transforms unconjugated bilirubin molecules bound to human serum albumin in solution into bilirubin photoproducts (predominantly isomers of bilirubin).[2,4,5] Because of the photophysical properties of skin, the most effective light in vivo is probably in the blue-to-green region (~460–490 nm).[2] The first prototype phototherapy device to result in a clinically significant rate of bilirubin decrease used a blue (B) fluorescent-tube light source with 420- to 480-nm emission.[6,7] More effective narrow-band special blue bulbs (F20T12/BB [General Electric, Westinghouse, Sylvania] or TL52/20W [Phillips]) were subsequently used.[8,9] Most recently, commercial compact fluorescent-tube light sources and devices that use LEDs of narrow spectral bandwidth have been used.[9–14] Unless specified otherwise, plastic covers or optical filters need to be used to remove potentially harmful ultraviolet light.

Clinical Context

Devices with maximum emission within the 460- to 490-nm (blue-green) region of the visible spectrum are probably the most effective for treating hyperbilirubinemia.[2,4] Lights with broader emission also will work, although not as effectively. Special blue (BB) fluorescent lights are effective but should not be confused with white lights painted blue or covered with blue plastic sheaths, which should not be used. Devices that contain high-intensity gallium nitride LEDs with emission within the 460- to 490-nm regions are also effective and have a longer lifetime (>20 000 hours), lower heat output, low infrared emission, and no ultraviolet emission.

B. Measuring Light Irradiance

Light intensity or energy output is defined by irradiance and refers to the number of photons (spectral energy) that are delivered per unit area (cm^2) of exposed skin.[1] The dose of phototherapy is a measure of the irradiance delivered for a specific duration and adjusted to the exposed body surface area. Determination of an in vivo dose-response relationship is confounded by the optical properties of skin and the rates of bilirubin production and elimination.[1] Irradiance is measured with a radiometer (W·cm^{-2}) or spectroradiometer (μW·cm^{-2}·nm^{-1}) over a given wavelength band. Table 2 compares the spectral irradiance of some of the devices in the US market, as measured with different brands of me-

ters. Often, radiometers measure wavelengths that do not penetrate skin well or that are far from optimal for phototherapy and, therefore, may be of little value for predicting the clinical efficacy of phototherapy units. A direct relationship between irradiance and the rate of in vivo total bilirubin concentration decrease was described in the report of a study of term "healthy" infants with nonhemolytic hyperbilirubinemia (peak values: 15–18 mg/dL) using fluorescent Philips daylight (TL20W/54, TL20W/52) and special blue (TLAK 40W/03) lamps.[15,16] The American Academy of Pediatrics has recommended that the irradiance for intensive phototherapy be at least 30 $\mu W \cdot cm^{-2} \cdot nm^{-1}$ over the waveband interval 460 to 490 nm.[1] Devices that emit lower irradiance may be supplemented with auxiliary devices. Much higher doses (>65 $\mu W \cdot cm^{-2} \cdot nm^{-1}$) might have (as-yet-unidentified) adverse effects. Currently, no single method is in general use for measuring phototherapy dosages. In addition, the calibration methods, wavelength responses, and geometries of instruments are not standardized. Consequently, different radiometers may show different values for the same light source.[2]

Clinical Context

For routine measurements, clinicians are limited by reliance on irradiance meters supplied or recommended by the manufacturer. Visual estimations of brightness and use of ordinary photometric or colorimetric light meters are inappropriate.[1,2] Maximal irradiance can be achieved by bringing the light source close to the infant[1]; however, this should not be done with halogen or tungsten lights, because the heat generated can cause a burn. Furthermore, with some fixtures, increasing the proximity may reduce the exposed body surface area. Irradiance distribution in the illuminated area (footprint) is rarely uniform; measurements at the center of the footprint may greatly exceed those at the periphery and are variable among phototherapy devices.[1] Thus, irradiance should be measured at several sites on the infant's body surface. The ideal distance and orientation of the light source should be maintained according to the manufacturer's recommendations. The irradiance of all lamps decreases with use; manufacturers may provide useful-lifetime estimates, which should not be exceeded.

C. Optimal Body Surface Area

An infant's total body surface area[17] can be influenced by the disproportionate head size, especially in the more preterm infant. Complete (100%) exposure of the total body surface to light is impractical and limited by use of eye masks and diapers. Circumferential illumination (total body surface exposure from multiple directions) achieves exposure of approximately 80% of the total body surface. In clinical practice, exposure is usually planar: ventral with overhead light sources and dorsal with lighted mattresses. Approximately 35% of the total body surface (ventral or dorsal) is exposed with either method. Changing the infant's posture every 2 to 3 hours may maximize the area exposed to light. Exposed body surface area treated rather than the number of devices (double, triple, etc) used is clinically more important. Maximal skin surface illumination allows for a more intensive exposure and may require combined use of more than 1 phototherapy device.[1]

Clinical Context

Physical obstruction of light by equipment, such as radiant warmers, head covers, large diapers, eye masks that enclose large areas of the scalp, tape, electrode patches, and insulating plastic covers, decrease the exposed skin surface area. Circumferential phototherapy maximizes the exposed area. Combining several devices, such as fluorescent tubes with fiber-optic pads or LED mattresses placed below the infant or bassinet, will increase the surface area exposed. If the infant is in an incubator, the light rays should be perpendicular to the surface of the incubator to minimize reflectance and loss of efficacy.[1,2]

D. Rate of Response Measured by Decrease in Serum Bilirubin Concentration

The clinical impact of phototherapy should be evident within 4 to 6 hours of initiation with an anticipated decrease of more than 2 mg/dL (34 μmol/L) in serum bilirubin concentration.[1] The clinical response depends on the rates of bilirubin production, enterohepatic circulation, and bilirubin elimination; the degree of tissue bilirubin deposition[15,16,18]; and the rates of the photochemical reactions of bilirubin. Aggressive implementation of phototherapy for excessive hyperbilirubinemia, sometimes referred to as the "crash-cart" approach,[19,20] has been reported to reduce the need for exchange transfusion and possibly reduce the severity of bilirubin neurotoxicity.

Clinical Context

Serial measurements of bilirubin concentration are used to monitor the effectiveness of phototherapy, but the value of these measurements can be confounded by changes in bilirubin production or elimination and by a sudden increase in bilirubin concentration (rebound) if phototherapy is stopped. Periodicity of serial measurements is based on clinical judgment.

III. EVIDENCE FOR EFFECTIVE PHOTOTHERAPY

Light-emission characteristics of phototherapy devices help in predicting

TABLE 3 Practice Considerations for Optimal Administration of Phototherapy

Checklist	Recommendation	Implementation
Light source (nm)	Wavelength spectrum in ~460- 490-nm blue-green light region	Know the spectral output of the light source
Light irradiance ($\mu W \cdot cm^{-2} \cdot nm^{-1}$)	Use optimal irradiance: >30 $\mu W \cdot cm^{-2} \cdot nm^{-1}$ within the 460- to 490-nm waveband	Ensure uniformity over the light footprint area
Body surface area (cm^2)	Expose maximal skin area	Reduce blocking of light
Timeliness of implementation	Urgent or "crash-cart" intervention for excessive hyperbilirubinemia	May conduct procedures while infant is on phototherapy
Continuity of therapy	Briefly interrupt for feeding, parental bonding, nursing care	After confirmation of adequate bilirubin concentration decrease
Efficacy of intervention	Periodically measure rate of response in bilirubin load reduction	Degree of total serum/plasma bilirubin concentration decrease
Duration of therapy	Discontinue at desired bilirubin threshold; be aware of possible rebound increase	Serial bilirubin measurements based on rate of decrease

their effectiveness (group B recommendation) (see Appendix). The clinical effectiveness of the device should be known before and monitored during clinical application (group B recommendation). Local guidelines (instructions) for routine clinical use should be available. Important factors that need to be considered are listed in Table 3. Obstructing the light source and reducing the exposed body surface area must be avoided (group B recommendation).

These recommendations are appropriate for clinical care in high-resource settings. In low-resource settings the use of improvised technologies and affordable phototherapy device choices need to meet minimum efficacy and safety standards.

IV. SAFETY AND PROTECTIVE MEASURES

A clinician skilled in newborn care should assess the neonate's clinical status during phototherapy to ensure adequate hydration, nutrition, and temperature control. Clinical improvement or progression of jaundice should also be assessed, including signs suggestive of early bilirubin encephalopathy such as changes in sleeping pattern, deteriorating feeding pattern, or inability to be consoled while crying.[1] Staff should be educated regarding the importance of safely minimizing the distance of the phototherapy device from the infant. They should be aware that the intensity of light decreases at the outer perimeter of the light footprint and recognize the effects of physical factors that could impede or obstruct light exposure. Staff should be aware that phototherapy does not use ultraviolet light and that exposure to the lights is mostly harmless. Four decades of neonatal phototherapy use has revealed no serious adverse clinical effects in newborn infants 35 or more weeks of gestation. For more preterm infants, who are usually treated with prophylactic rather than therapeutic phototherapy, this may not be true. Informed staff should educate parents regarding the care of their newborn infant undergoing phototherapy. Devices must comply with general safety standards listed by the International Electrotechnical Commission.[21] Other clinical considerations include:

a. Interruption of phototherapy: After a documented decrease in bilirubin concentration, continuous exposure to the light source may be interrupted and the eye mask removed to allow for feeding and maternal-infant bonding.[1]
b. Use of eye masks: Eye masks to prevent retinal damage are used routinely, although there is no evidence to support this recommendation. Retinal damage has been documented in the unpatched eyes of newborn monkeys exposed to phototherapy, but there are no similar data available from human newborns, because eye patches have always been used.[22–24] Purulent eye discharge and conjunctivitis in term infants have been reported with prolonged use of eye patches.[25,26]
c. Use of diapers: Concerns for the long-term effects of continuous phototherapy exposure of the reproductive system have been raised but not substantiated.[27–29] Diapers may be used for hygiene but are not essential.
d. Other protective considerations: Devices used in environments with high humidity and oxygen must meet electrical and fire hazard safety standards.[21] Phototherapy is contraindicated in infants with congenital porphyria or those treated with photosensitizing drugs.[1] Prolonged phototherapy has been associated with increased oxidant stress and lipid peroxidation[30] and riboflavin deficiency.[31] Recent clinical reports of other adverse outcomes (eg, malignant melanoma, DNA damage, and skin changes) have yet to be validated.[1,2,32,33] Phototherapy does not exacerbate hemolysis.[34]

V. RESEARCH NEEDS

Among the gaps in knowledge that remain regarding the use of phototherapy to prevent severe neonatal hyperbilirubinemia, the following are among the most important:

1. The ability to measure the actual wavelength and irradiance delivered by a phototherapy device is urgently needed to assess the efficiency of

phototherapy in reducing total serum bilirubin concentrations.

2. The safety and efficacy of home phototherapy remains a research priority.
3. Further delineation of the short- and long-term consequences of exposing infants with conjugated and unconjugated hyperbilirubinemia to phototherapy is needed.
4. Whether use of phototherapy reduces the risk of bilirubin neurotoxicity in a timely and effective manner needs further exploration.

SUMMARY

Clinicians and hospitals should ensure that the phototherapy devices they use fully illuminate the patient's body surface area, have an irradiance level of $\geq 30\ \mu W \cdot cm^{-2} \cdot nm^{-1}$ (confirmed with accuracy with an appropriate spectral radiometer) over the waveband of approximately 460 to 490 nm, and are implemented in a timely manner. Standard procedures should be documented for their safe deployment.

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APPENDIX Definition of Grades for Recommendation and Suggestion for Practice

Grade	Definition	Suggestion for Practice
A	This intervention is recommended. There is a high certainty that the net benefit is substantial	Offer and administer this intervention
B	This intervention is recommended. There is a moderate certainty that the net benefit is moderate to substantial	Offer and administer this intervention
C	This intervention is recommended. There may be considerations that support the use of this intervention in an individual patient. There is a moderate to high certainty that the net benefit is small	Offer and administer this intervention only if other considerations support this intervention in an individual patient
D	This intervention is not recommended. There is a moderate to high certainty that the intervention has no net benefit and that the harms outweigh the benefits	Discourage use of this intervention
I	The current evidence is insufficient to assess the balance of benefits against and harms of this intervention. There is a moderate to high certainty that the intervention has no net benefit and that the harms outweigh the benefits. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined	If this intervention is conducted, the patient should understand the uncertainty about the balance of benefits and harms

US Preventive Services Task Force Grade definitions, May, 2008 (available at www.uspreventiveservicestaskforce.org/3rduspstf/ratings.htm).