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ORIGINAL ARTICLE

# Randomized controlled trial of light-emitting diode phototherapy

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**Objective:** We wished to compare the efficacy of light-emitting diode (LED) phototherapy with special blue fluorescent (BB) tube phototherapy in the treatment of neonatal hyperbilirubinemia.

**Study design:** We randomly assigned 66 infants $\geqslant$35 weeks of gestation to receive phototherapy using an LED device or BB. In addition to phototherapy from above, all infants also received phototherapy from below using four BB tubes or a fiberoptic pad.

**Result:** After $15\pm5$ h of phototherapy, the rate of decline in the total serum bilirubin (TSB) was $0.35\pm0.25$ mg/dl/h in the LED group vs $0.27\pm0.25$ mg/dl/h in the BB group ($P=0.20$).

**Conclusion:** LED phototherapy is as effective as BB phototherapy in lowering serum bilirubin levels in term and near-term newborns.
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**Keywords:** phototherapy; light-emitting diode; hyperbilirubinemia; newborn infants

## Introduction

Phototherapy lamps with output in the blue to green part of the spectrum are most effective in lowering serum bilirubin levels.[1] At these wavelengths, light penetrates the skin well and is absorbed strongly by bilirubin.[1,2] Thus, special blue fluorescent (BB) tubes that have their output primarily in the blue spectrum (430 to 490 nm) are recommended by the American Academy of Pediatrics (AAP) as the most effective light source for lowering the serum bilirubin.[3] Prototype light-emitting diode (LED) lights have been developed and tested in clinical and laboratory studies,[4–6] and a commercially available LED device is being used, currently, in nurseries in the United States. The LED device consists of gallium nitride LEDs. These are power-efficient, durable light sources that provide high-intensity light in the blue portion of the visible spectrum. The LEDs emit light through a narrow wavelength band with a peak emission between 450 and 470 nm. The neoBLUE LED phototherapy device (Natus Medical Inc., San Carlos, CA, USA) is the only commercially available LED device in the United States, but there are no published studies documenting its efficacy.

The AAP defines intensive phototherapy as irradiance of at least 30 $\mu$W/cm$^2$/nm in the 430 to 490 nm band.[3] In our hospital, treatment with BB lights at this level of irradiance is the standard of care, and we compared it with LED phototherapy.

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## Methods

### *Sample size*

To show a difference of 0.15 mg/dl/h (2.6 $\mu$mol/l/h) in the rate at which the total serum bilirubin (TSB) declines under phototherapy, we calculated that 33 infants would be required in each group (two-sided, $\alpha=0.05$, $\beta=0.2$, 80% power). We analyzed continuous variables using Student's *t*-test and categorical variables with Fisher's exact test.

### *Patients*

We enrolled infants between January 2003 and October 2006 in two groups. Thirty infants received phototherapy during their birth hospitalization and before discharge from the nursery (newborn group). Thirty-six infants were discharged and readmitted for phototherapy (readmission group). The decision to use phototherapy was made by the attending pediatrician and well newborns $\geqslant$35 weeks of gestation were eligible for the study. The major reason for the exclusion was failure to obtain written informed consent.

### *Study design*

We used a computer-generated set of random numbers and sealed envelopes to assign infants to LED or standard BB-intensive phototherapy. After informed consent was obtained from one or both the parents, the envelope was opened and the infant assigned to a treatment group. The study was approved by the hospital's Human Investigation Committee. Figure 1 illustrates the design of the study.

*Newborn group (*n *= 30).* For the LED group, we used a prototype LED device provided by Natus Medical Inc. Infants receiving BB-intensive phototherapy were treated with a standard phototherapy light (Bili-Lite; Olympic Medical, Seattle, WA, USA) that contains eight 2-f long BB lamps (F20T12/BB). All infants remained in bassinettes, naked except for a diaper, and the BB phototherapy light was placed 15 to 20 cm above the infant. In both the LED and BB groups, a fiberoptic blanket, the Wallaby II phototherapy system (Fiberoptic Medical Products Inc., Allentown, PA, USA) was placed underneath the infant. The prototype LED device has the same characteristics of peak wavelength, wavelength distribution and light intensity as the neoBLUE device (see below).

*Readmission group (*n = *36).* LED phototherapy was provided by the neoBLUE device and BB phototherapy by the Bili-Bassinet (Olympic Medical) fitted throughout with BB tubes. Thus equipped, the Bili-Bassinet provides BB phototherapy from two units above the infant (each containing four BB lamps) and from four BB lamps contained in the transparent mattress underneath the infant. Infants receiving LED phototherapy were placed in the Bili-Bassinet and received BB phototherapy from below, but only LED phototherapy from the neoBLUE above. In all infants, the eyes were shielded with opaque patches.

On initiation of phototherapy, irradiance was measured using the Ohmeda BiliBlanket Meter II spectroradiometer (GE Ohmeda Medical, Laurel, MD, USA) placed on the infant's abdomen directly underneath the center of the phototherapy source. The distance between the lights and the infants was adjusted to provide an irradiance of approximately 40 $\mu$W/cm$^2$/nm.

Total and direct serum bilirubin levels were measured in the clinical laboratory with a diazo method (Beckman Coulter, Fullerton, CA, USA).

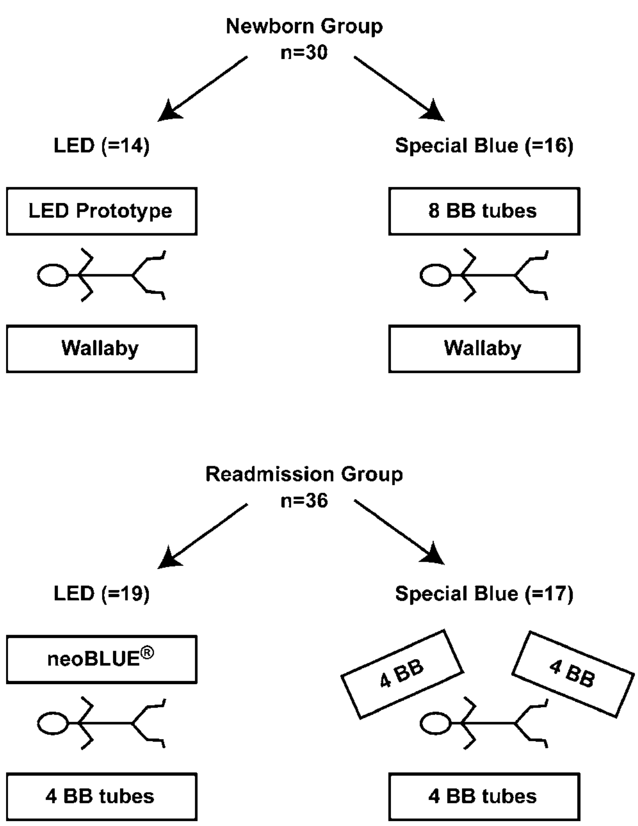


**Figure 1** Diagrammatic representation of the study groups and the phototherapy devices employed. See Methods for detailed description. NeoBLUE is an LED phototherapy device (Natus Medical Inc.). Wallaby is Wallaby II phototherapy system (Fiberoptic Medical Products). BB tubes, special blue fluorescent tubes; LED, light-emitting diode.

## Results

The results are shown in Tables 1 and 2. There were no differences between the two groups in birth weight, gestation, incidence of breast feeding, hemolytic disease, or other known causes of jaundice, initial TSB level or age at initiation of phototherapy. Average irradiance in the 400 to 520 nm range (peak sensitivity 450 nm) at the infant's abdomen was 41.4 ± 3.0 $\mu$W/cm$^2$/nm in the LED group and 40.6 ± 2.4 $\mu$W/cm$^2$/nm in the BB group ($P = 0.15$). Irradiance measured at the Bili-Bassinet mattress was 44 $\mu$W/cm$^2$/nm and at the Wallaby surface 7 $\mu$W/cm$^2$/nm. After approximately 14 to 15 h of phototherapy, the TSBs in the LED group and the BB group ($P = 0.18$) were 10.7 ± 4.0 and 11.8 ± 2.2 mg/dl, respectively. The TSB declined at a rate of

**Table 1** Demographic and clinical data

| | *BB* (n = *33)* | *LED* (n = *33)* | P-*value* |
|---|---|---|---|
| Birth weight (g) | 3425 ± 599 | 3227 ± 403 | 0.12 |
| Gestation (week) | 38.5 ± 1.45 | 38.7 ± 1.75 | 0.70 |
| Breastfed | 29 | 31 | 0.67 |
| Blood group and DAT measured | 26 | 31 | 0.15 |
| ABO hemolytic disease | 1 | 1 | 1.0 |
| Cephalhematoma/bruising | 6 | 5 | 1.0 |
| Previous sibling with hyperbilirubinemia | 1 | 0 | 1.0 |
| Breastfeeding-associated or unknown cause of jaundice | 24 | 26 | 0.78 |

Abbreviations: BB, special blue fluorescent; DAT, direct antibody test; LED, light-emitting diode.
Data shown are number or mean ± s.d.

**Table 2** Irradiance and bilirubin levels

| | *BB* (n = *33)* | *LED* (n = *33)* | P-*value* |
|---|---|---|---|
| Irradiance ($\mu$W/cm$^2$/nm) | 40.6 ± 2.4 | 41.4 ± 3.0 | 0.15 |
| Initial TSB (mg/dl) | 15.2 ± 4.2 | 15.5 ± 5.6 | 0.83 |
| F/U TSB (mg/dl) | 11.8 ± 2.2 | 10.7 ± 4.0 | 0.18 |
| Time to F/U TSB (h) | 14.2 ± 3.9 | 15.3 ± 3.6 | 0.23 |
| $\Delta$ TSB (mg/dl/h) | 0.27 ± 0.25 | 0.35 ± 0.25 | 0.20 |

Abbreviations: BB, special blue fluorescent; F/U, follow-up; LED, light-emitting diode. TSB, total serum bilirubin level.
Data shown as means ± s.d.

0.35±0.25 mg/dl/h in the LED group and 0.27±0.25 mg/dl/h in the BB group ($P = 0.20$).

When analyzed separately, the newborn and readmission groups showed no significant differences in LED vs BB in TSB levels or rate of decline of TSB. In the newborn nursery, in the LED group, the TSB declined at a rate of 0.13±0.12 vs 0.07±0.12 mg/dl/h under BB phototherapy ($P = 0.23$). In the readmission group, the rate was 0.52±0.17 (LED) vs 0.47±0.17 mg/dl/h (BB, $P = 0.34$).

## Discussion

When used as described, the neoBLUE was as effective as our special blue intensive phototherapy. The device was easy to use and well accepted by the nursing staff. LED lights have several advantages.[4] The irradiance can be adjusted to almost any intensity, the intensity remains stable and the lights have a very long life (more than 1 year of continuous use). They have a high-energy efficiency, do not emit significant infrared or ultraviolet radiation and produce minimal radiant heat. The virtual absence of heat when delivering overhead neoBLUE phototherapy to a naked infant might be a disadvantage, however. An occasional infant had a mild fall in temperature (to 36°C) during LED phototherapy. In our experience, BB bulbs when placed 15 to 20 cm above a term or near-term infant provide enough warmth to maintain excellent thermal stability. Although some fluorescent bulbs do emit some UVA light (315 to 400 nm) and a small amount of UVB light below 320 nm, most of the higher energy (shorter wavelength) is blocked by the phosphor and glass envelope as well as the polycarbonate shield that covers the lamps. If properly used with a polycarbonate shield, all radiation below about 350 nm will be removed.[7] BB lamps, however, emit almost no UVA or UVB radiation (AF McDonagh, personal communication, 2007). A limitation of this study is the complexity of the design, and the use of different types of LED and BB units.

We recognize, for example, that there are differences in the way in which the overhead phototherapy was delivered — a single neoBLUE vs two overhead units in the Bili-Bassinet. Nevertheless, the irradiance delivered to the baby was similar in both groups, and these were the only units available to us.

Within-group comparisons showed that the rate of decline in the readmission LED group was 0.52±0.17 mg/dl/h and in the newborn LED group 0.13±0.12 mg/dl/h. In the readmission BB group, the rate of decline was 0.47±0.14 mg/dl/h and in the newborn BB group 0.07±0.12 mg/dl/h. These groups, however, should not be compared. First, the readmission groups received significantly more irradiance to a greater surface area from underneath the baby (four BB tubes vs the Wallaby), and second, pre-phototherapy TSB levels in the readmission groups were significantly higher than the newborn groups (18.9±2.9 vs 10.7±3.1 mg/dl, $P = 0.000$). Because the rate of TSB decline under phototherapy is directly related to the pre-phototherapy TSB level,[8] we would expect the decline to be more rapid in the readmitted infants.

We conclude that, with similar irradiance and surface area exposure, LED phototherapy is as effective as BB phototherapy in lowering serum bilirubin levels in term and near-term newborns. The small size, high luminous intensity and narrow wavelength band light of LED phototherapy makes this a useful method for delivering intensive phototherapy to newborn infants.

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## References

1 Ennever JF. Blue light, green light, white light, more light: treatment of neonatal jaundice. *Clin Perinatol* 1990; **17**: 467–481.
2 McDonagh AF, Agati G, Fusi F, Pratesi R. Quantum yields for laser photocyclization of bilirubin in the presence of human serum albumin. Dependence of quantum yield on excitation wavelength. *Photochem Photobiol* 1989; **50**: 305–319.
3 Maisels MJ, Baltz RD, Bhutani V, Newman TB, Palmer H, Rosenfeld W *et al.* Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. *Pediatrics* 2004; **114**: 297–316.
4 Vreman HJ, Wong RJ, Stevenson DK. Light-emitting diodes: a novel light source for phototherapy. *Pediatr Res* 1998; **44**: 804–809.
5 Seidman DS, Moise J, Ergaz Z, Laor A, Vreman HJ, Stevenson DK *et al.* A prospective randomized controlled study of phototherapy using blue and blue-green light-emitting devices, and conventional halogen-quartz phototherapy. *J Perinatol* 2003; **23**: 123–127.
6 Seidman DS, Moise J, Ergaz Z. A new blue light-emitting phototherapy device: a prospective randomized controlled study. *J Pediatr* 2000; **136**: 771–774.
7 McDonagh AF, Nguyen ML. Spectacles, ultraviolet radiation, and formation of cataracts. *N Engl J Med* 1989; **321**: 1478–1479.
8 Jährig K, Jährig D, Meisel P. Dependence of the efficiency of phototherapy on plasma bilirubin concentration. *Acta Paediatr Scand* 1982; **71**(2): 293–299.