Prospective Randomized Controlled Study Comparing Low-Cost LED and Conventional Phototherapy for Treatment of Neonatal Hyperbilirubinemia

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Summary

Our objective was to carry out a prospective, randomized, single-blind study to evaluate whether light emitting diode (LED) phototherapy using a low-cost set of lights is as effective as conventional phototherapy in treating hyperbilirubinemia in neonates. The study included 45 pre-term neonates requiring phototherapy as per American Academy of Pediatrics guidelines; participants were randomized to receive phototherapy using LED-based lights, conventional fluorescent blue lights or conventional halogen lights. There were no statistically significant differences in the average bilirubin levels at the onset, at the maximum and at the end of treatment, nor in the duration of phototherapy treatment and the rate of decrease in bilirubin levels in the neonates receiving conventional fluorescent blue light, conventional halogen light and LED phototherapy. (Differences were considered significant at $p < 0.05$). The average rate of decrease of bilirubin levels was $0.047 \pm 0.037\,\mathrm{mg\,dl^{-1}\,h^{-1}}$, $0.055 \pm 0.056\,\mathrm{mg\,dl^{-1}\,h^{-1}}$ and $0.057 \pm 0.045\,\mathrm{mg\,dl^{-1}\,h^{-1}}$ in the groups receiving conventional fluorescent blue light, conventional halogen light and LED phototherapy, respectively. The average duration of phototherapy treatment in the three groups was 108.8 ± 85.9 h, 92.8 ± 38.1 h, 110.4 ± 42.6 h, respectively. In this pilot study, LED phototherapy using a simple, low-cost set of lights was as effective as conventional phototherapy in the treatment of neonatal hyperbilirubinemia. LED phototherapy lights that deliver 30–40 $\mu\mathrm{W\,cm^{-2}\,nm^{-1}}$ can be assembled in small quantities for <US$ 100 each using off-the-shelf parts; such lights may enable phototherapy to be safely and reliably delivered in low-resource settings.

Key words: phototherapy, neonatal jaundice, hyperbilirubinemia, LED phototherapy.

Introduction

Globally, 60% of the newborns develop jaundice in the first week of life [1]. Because bilirubin can be toxic to the central nervous system and can cause permanent neurological disability, it is important to identify newborn infants who might develop severe hyperbilirubinemia [2]. Phototherapy is the standard treatment for neonatal jaundice [2]. In the USA, it is estimated that between 1% and 8% of full-term infants receive phototherapy [1]. Phototherapy is considered a relatively safe procedure, especially when compared with the risks associated with blood transfusion [1]. Reports of significant clinical toxicity of phototherapy are rare, and include bronze baby syndrome, purpuric eruptions in patients with cholestatic hyperbilirubinemia and mild dehydration [1].

Phototherapy uses irradiation with blue light to photoisomerize bilirubin into products that can be excreted in bile or urine [1]. The light dosage for conventional phototherapy is typically 8–10 $\mu\mathrm{W\,cm^{-2}\,nm^{-1}}$ in the 430–490 nm band, while that required for intensive phototherapy is 30–40 $\mu\mathrm{W\,cm^{-2}\,nm^{-1}}$ [1]. Irradiance should be uniform

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over as much of the body surface as possible [3]. Phototherapy can be delivered using several types of conventional light sources, including daylight, white or blue fluorescent bulbs and filtered halogen bulbs [4]. The spectral output of blue fluorescent bulbs is well matched to the absorption spectrum of bilirubin, and these bulbs are recommended by the American Academy of Pediatrics (AAP) for intensive phototherapy [1]. Halogen systems offer a compact, lightweight alternative, which can reach acceptable levels of irradiance over smaller areas; however, halogen lights generate significant heat, increasing the risks of dehydration and burns [4].

Neonatal jaundice is an important cause of morbidity in the developing world. For example, in the Pediatric Department of Hospital Roosevelt, Guatemala City, Guatemala, neonatal jaundice is the fifth leading cause of morbidity, with 281 cases reported in 2007 [5]. However phototherapy lights are often not available in the developing world because the devices and replacement bulbs are too expensive [6]. Malkin noted that the phototherapy systems most commonly donated to hospitals in the developing world cost between US$ 3000 and $5000 [6]. Fluorescent and halogen bulbs for phototherapy systems have a recommended lifespan of between 1000 and 1500 h, corresponding to 2–3 months of continuous usage. A set of replacement fluorescent bulbs typically cost several hundred dollars [6]. Unfortunately, most hospitals in rural Guatemala do not have phototherapy services. As a result, jaundiced neonates must be transferred to major hospitals in Guatemala City for treatment; average travel times are between 2 and 12 h.

Recently, a number of phototherapy devices based on blue light emitting diode (LED) lights have been reported [7–12]. These devices offer several advantages, including long bulb life (>10 000 h), low heat production and potential low cost. Recent studies have suggested that LED phototherapy is as effective as conventional phototherapy [8, 10, 11].

Materials and Methods

We developed low-cost LED phototherapy lights that can be built in several hours using off-the-shelf parts, a printed circuit board and a wood frame. The cost of the parts is <US$ 100. LED-based phototherapy lights were built using eighty 10 mm blue LEDs that emit a dominant wavelength of 470 nm. The LEDs had a half-spectral width of 20 nm with a 20° half-angle directivity. The LEDs were arranged in eight strips of 10 LEDs each. If a single LED fails, the remaining LEDs still light. The LEDs illuminated an area of about 350 cm^2 at a distance of 25 cm from the lights. The peak irradiance measured at the center of the illuminated area was 25 $\mu W\,cm^{-2}\,nm^{-1}$. The average irradiance across the regions of the light spot that were > 8 $\mu W\,cm^{-2}\,nm^{-1}$ was 14 $\mu W\,cm^{-2}\,nm^{-1}$. Figure 1 shows the system in use.

The objective of this study was to compare the efficacy of phototherapy using this LED system with that of standard phototherapy using blue fluorescent light and halogen light. A pilot study with a random distribution of subjects into groups was completed at the low-risk neonatal ward of Roosevelt Hospital in Guatemala City, Guatemala. Forty-five pre-term neonates with neonatal hyperbilirubinemia and indication for phototherapy according to AAP criteria were recruited to participate. Neonates were eligible to participate if their total bilirubin serum concentration was above the cutoff line for their age group, according to their hours of life. Informed consent was obtained from the legal guardian of the newborn and the study was reviewed and approved by the Institutional Review Boards at Roosevelt Hospital and Rice University. Patients with the following characteristics were excluded: gestational age <32 weeks or >38 weeks; birth weight <1000 g or >2500 g;

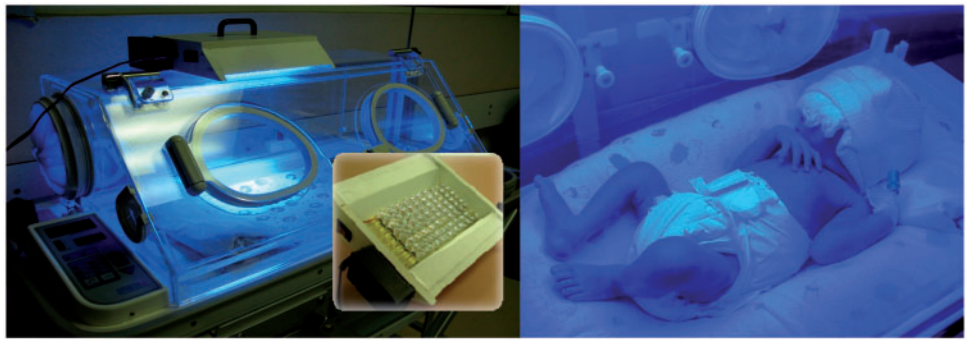

FIG. 1. (Left) Photographs of LED system used to deliver phototherapy. (Right) Photograph of study participant receiving phototherapy; note the large diaper and eye cover which cover a significant fraction of the abdominal surface and face.

cholestatic jaundice, defined as direct bilirubin >20% of total bilirubin levels; with other diagnosis, such as sepsis, or requiring ventilation; lack of informed consent.

By use of closed envelopes, the patients were randomized to receive phototherapy from one of three systems. A consort diagram illustrating the study can be found in Figure 2. Halogen light phototherapy was administered with an Air Shields Micro-lite model PPT 68-1, series 2. This system has three EXZ halogens lamps, of high intensity quartz. The blue fluorescent light phototherapy was administered with a Medix phototherapy lamp, model LU-6 T (S|N 568-06), which uses six blue fluorescent tubes. The conventional systems were used according to manufacturer's directions. Finally, LED phototherapy was administered with the system described above.

After obtaining informed consent, the weight, length, gestational age, baseline bilirubin level, serum albumin, direct Coomb's test, blood type and other medical conditions, were recorded. The patients were placed in incubators, in supine position and fully exposed to the light except for the diaper area and eye region. The phototherapy devices were placed at a distance specified by the manufacturers, with the LED device placed at a distance of 22–25 cm away from the infant. Total serum bilirubin levels were obtained every 12 h, using peripheral venipuncture. Bilirubin levels were analyzed in the Roosevelt Hospital Laboratory using a BIL-T analyzer, Roche/Hitachi model 911 ACN 269, with an analytic sensitivity of 0.1 mg dl^{-1}. This procedure was done until phototherapy was stopped, per clinical criteria. Twenty-four hours after completing phototherapy a last bilirubin level was measured.

The rate of decrease of bilirubin (mg dl^{-1} h^{-1}) was calculated using the following formula:

$$\text{Rate of decrease} = [(\text{initial bilirubin concentration} - \text{final bilirubin concentration}) / \text{total treatment time}]$$

Results

Eleven female neonates and four male neonates received fluorescent blue light phototherapy; all were blood type O Rh positive and had negative direct Coombs tests. In the halogen light phototherapy group, eight patients were female and seven were male. In this group, 13 patients were blood type O Rh positive, 1 was A Rh positive and 1 was B Rh positive; all had a negative direct Coombs test. In the

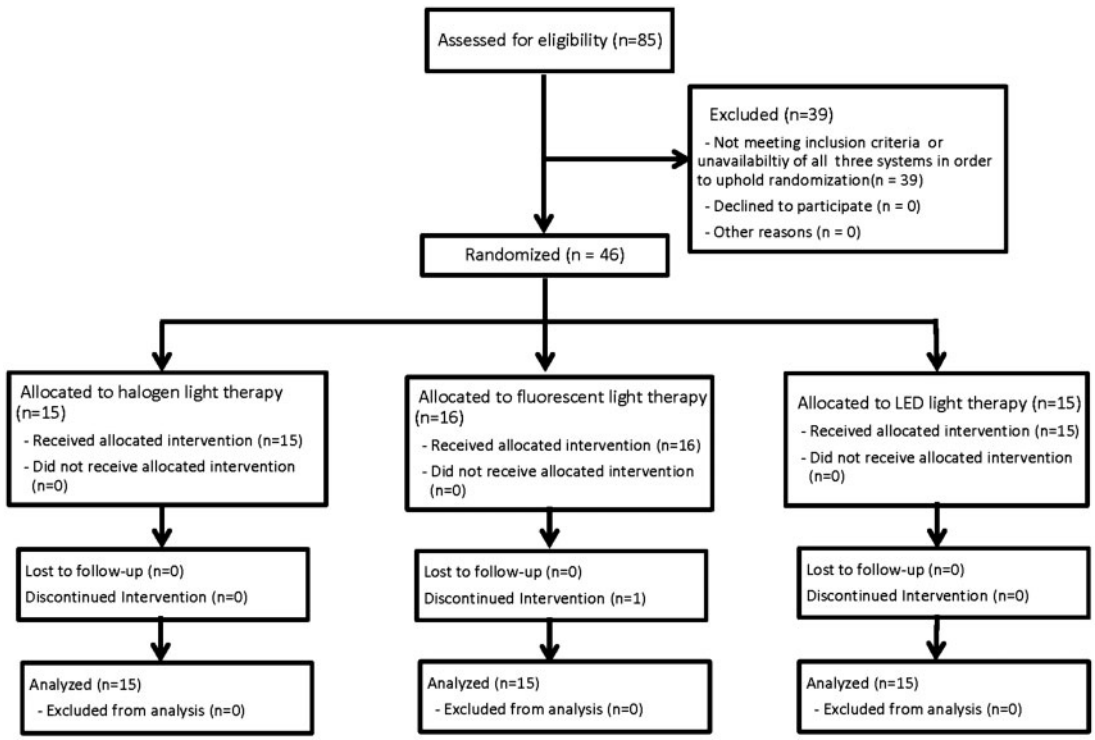

FIG. 2. Consort diagram of the randomized clinical study.

group receiving LED phototherapy, seven patients were female and eight were male; all were blood type O Rh positive, and all had negative direct Coombs tests. All patients in this group had the same blood type as their mothers. Other patient characteristics are summarized in Table 1.

There were no statistically significant differences in the cohorts with regard to average values of gestational age and albumin levels, but differences in the average body surface area of the group treated with blue fluorescent light were statistically significant. Figure 3 shows the average initial, maximum, final and post-therapy serum bilirubin concentrations for the three groups; differences in the mean values were not statistically different for the three groups. Figure 4a shows the average duration of phototherapy, and Figure 4(b) shows the average rate of decrease of bilirubin concentration for the three groups; differences between groups were not statistically significant.

In the group receiving phototherapy with the LED light system, one patient developed exanthema from the treatment on the last day. This resolved without further intervention and without short-term sequelae. There were no other adverse events in the other 44 patients.

Discussion

In this pilot study, phototherapy using low-cost LED lights was found to be as effective as conventional therapy using blue fluorescent lights or halogen lights. While differences in the mean duration of phototherapy in each of the three groups were not significantly different, the mean duration of phototherapy in this study was two to three times longer than that reported in other studies [8, 9, 11]. There are many possible explanations for this difference. First, this study did not take into account the time that patients were removed from phototherapy for hygiene, feeding and administration of medicines. It is possible

TABLE 1
Patient characteristics

Light system	Gestational age (weeks)	Albumin (gdl^{-1})	Body surface area (m^2)
Blue fluorescent	34.8 ± 1.7	3.41 ± 0.29	0.121 ± 0.015
Halogen	35.7 ± 1.4	3.46 ± 0.34	0.134 ± 0.020
LED	35.3 ± 1.2	3.54 ± 0.31	0.136 ± 0.008

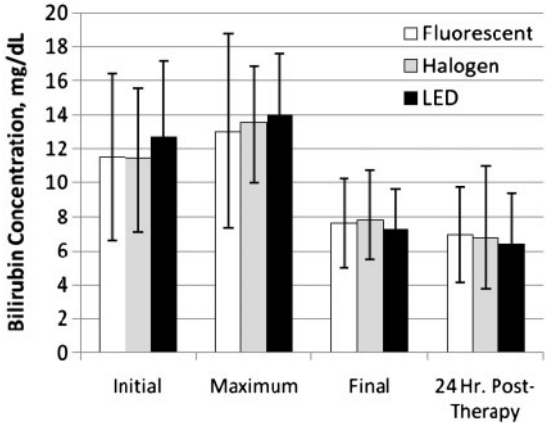

FIG. 3. The average initial, maximum, final and post-therapy serum bilirubin concentrations for the three groups; differences in the mean values were not statistically different for the three groups. Error bars represent ±1 SD.

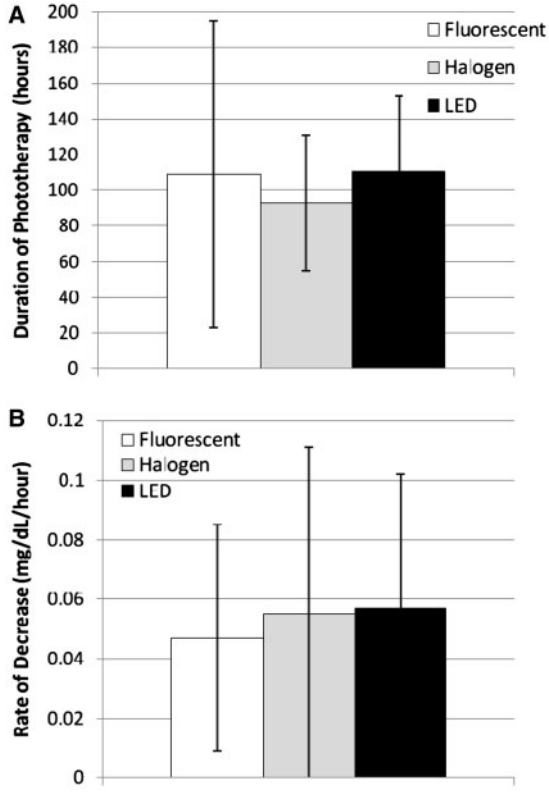

FIG. 4. (**A**) The average duration of phototherapy for the three groups and (**B**) the average rate of decrease of bilirubin concentration for the three groups; differences between groups were not statistically significant. Error bars represent ±1 SD.

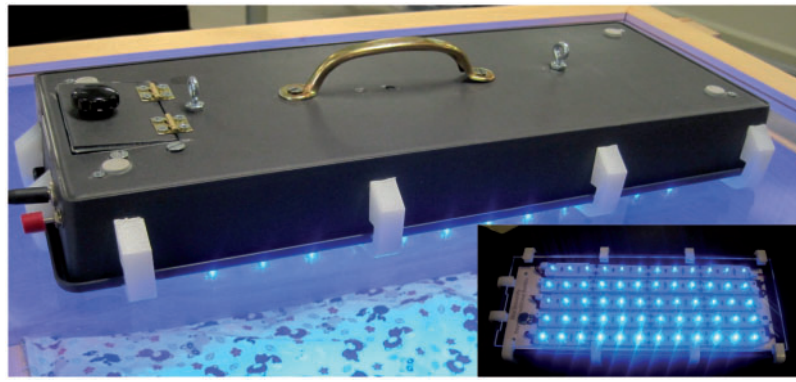

FIG. 5. Photographs of the modified LED phototherapy system.

that this was insignificant, but the data to affirm that are not available. Second, premature-sized diapers were not available for the participants; the standard-sized diapers covered a significant fraction of the abdominal surface area (Fig. 1) and this may have reduced light exposure. Finally, conservative guidelines were used in making decisions about when to discontinue phototherapy. There is no consensus standard for discontinuing phototherapy [2]; in this setting, phototherapy was typically discontinued when serum bilirubin concentrations dropped below 7.6–8.0 mg dl^{-1}. Other studies have discontinued therapy at higher levels of 12–15 mg dl^{-1} [8, 10, 11]. None of the neonates from the study required restarting the phototherapy after 24 h of having finished the treatment. Other studies have shown up to 10% of significant bilirubin rebound 24 h after phototherapy has been discontinued, especially in patients with gestational ages <35 weeks and/or weight <2000 g [13].

Based on feedback from clinicians who have used the LED-based phototherapy system in low-resource settings, we have developed a modified system that is easy to repair and manufacture, costs less, can be used with a variety of cribs, and includes a dimming option to adjust the phototherapy dose.

The modified LED-based phototherapy lamps were built using 84 3-mm high flux blue LEDs that emit a dominant wavelength of 470 nm. The LEDs had a half-spectral width of 30 nm with a 45° half angle directivity. The LEDs were arranged in seven strips of 12 LEDs each. Power is supplied so that if a single LED fails, the remaining LEDs still light. The peak irradiance at the center, 25 cm from the lights is 21 μW cm^{-2} nm^{-1}. The illuminated area is 1500 cm^2 at a distance of 25 cm from the lights. This system contains a dimmer to allow adjustment of the phototherapy dose. This dimmer is placed so that it is unlikely to be accidentally altered by a caregiver. The system is made entirely of off-the-shelf components costing <US$ 110 and takes <1 h to build. Figure 5 shows a picture of this new system. Instructions and bill of materials for this system are available at: http://cohesion.rice.edu/collaborations/btb/emplibrary/Assembly%20Instructions%20Final.pdf.

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