Effectiveness of Conventional Phototherapy versus Super Light-Emitting Diodes Phototherapy in Neonatal Hyperbilirubinemia

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Background: *Neonatal hyperbilirubinemia is very common. Phototherapy has been used for decades to prevent severe hyperbilirubinemia, which can cause kernicterus.*
Objective: *To compare the effectiveness of two phototherapy devices in reducing plasma bilirubin and duration of phototherapy in non-severe hyperbilirubinemia.*
Material and Method: *This was an open-label randomized controlled trial. Forty healthy infants aged between 1 and 5 days with non-severe hyperbilirubinemia, but to the level requiring phototherapy, were recruited. The phototherapy unit used in the "blue-light" group was the Siriraj Phototherapy Lamp with 6 special blue fluorescent tubes. The phototherapy unit used in the "light-emitting diodes (LEDs)" group was the Bilitron 3006 with 5 super LEDs.*
Results: *Twenty infants were included in each group. Demographic data and baseline clinical characteristics of infants in both groups were comparable. Median rate (25%, 75%tile) of plasma bilirubin decreasing during phototherapy in the "blue light" was significantly higher than in the "LEDs" group [0.16 (0.09, 0.25) and 0.10 (0.02, 0.17) mg/dL/hour, respectively; p = 0.03]. Duration of phototherapy in "blue light" group was shorter than in "LEDs" group but was not statistically significant.*
Conclusion: *A locally invented phototherapy device with special blue fluorescent tubes can be more effective than the more expensive commercial super LEDs phototherapy device in decreasing plasma bilirubin.*

Keywords: *Neonatal hyperbilirubinemia, Phototherapy, Blue light, LEDs*

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Incidence of neonatal hyperbilirubinemia varies between 25% and 50% in term newborn infants and higher in preterm infants[1]. The most devastating complication of hyperbilirubinemia is kernicterus, which has at least 10% mortality and at least 70% long-term morbidity[2]. In 35 term and near-term infants with kernicterus of unknown etiology, more than 90% had bilirubin level higher than 25 mg/dL and all of them had bilirubin level higher than 20 mg/dL[2]. Phototherapy has an absolute risk-reduction rate of 10% to 17% for prevention of hyperbilirubinemia to the level of more than 20 mg/dL[2]. Hence, appropriate bilirubin screening and effective phototherapy play important roles in preventing kernicterus.

Phototherapy lowers plasma bilirubin by photochemical reactions that occurred at the skin. Light energy, absorbed by bilirubin in the skin, alters their shape and structure to photoisomers, which can be excreted in bile and urine without conjugation[3]. The efficacy of phototherapy is highly dependent on wavelengths and intensity of the light used. The light photons are absorbed by the bilirubin molecules in the skin, which absorbs light most strongly in the blue region of the spectrum near 460 nm[3]. Blue light has been demonstrated as the most effective in decreasing bilirubin both in vitro and in vivo[4]. The American Academy of Pediatrics (AAP) recommends the use of special blue tubes or light-emitting diodes (LEDs) light source with output in blue-green spectrum for intensive phototherapy[5].

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There are many devices for delivering phototherapy with blue tubes used throughout Thailand and in other countries. At Siriraj Hospital, conventional intensive phototherapy device is the Siriraj Phototherapy Lamp (SPL) with six special blue fluorescent tubes invented by Jirapaet[6]. The super LEDs phototherapy device was introduced to our division in 2007. Recent studies reveal that the efficacy of the LEDs phototherapy device is superior to halogen conventional phototherapy[7] and is similar to a compact fluorescent tubes phototherapy[8]. The authors conducted the present study to compare the effectiveness between the authors' conventional phototherapy (SPL) and the super LEDs in reducing plasma bilirubin and duration of phototherapy in non-severe hyperbilirubinemia and to compare short-term side effects of these two phototherapy devices.

Material and Method

The present study was approved by the Ethics Committee of the Faculty of Medicine Siriraj Hospital, Mahidol University. Informed consents were obtained prior to the present study. This was an open-label randomized controlled trial. A web-based randomly permuted block was generated from http://www.randomization.com. Healthy infants aged between 1- and 5-days old with non-severe hyperbilirubinemia, but to a level requiring phototherapy, were recruited. Infants with severe hyperbilirubinemia, which was defined as phototherapy indicated within the first 24 hours of life or plasma bilirubin within 2 mg/dL less than the level of exchange transfusion, were excluded. The AAP guidelines for phototherapy and exchange transfusion criteria[5] were used. After phototherapy was started, plasma bilirubin was performed every 6 to 12 hours. In both groups, double phototherapy with two SPL units was indicated for those whose bilirubin still increased after single phototherapy but did not reach exchange transfusion criteria. Phototherapy was stopped when two consecutive plasma bilirubin specimens, measured 6 to 12 hours apart, were less than 14 mg/dL. Re-phototherapy was indicated when bilirubin, checked approximately 6 to 8 hours after phototherapy was stopped, rebounded to the level requiring phototherapy. Short-term complications of phototherapy, which included hyperthermia, rash, and frequent stooling, were recorded. Plasma bilirubin was measured by microbilirubin method at the same laboratory.

The phototherapy device used in the "blue-light" group was the SPL, with 6 special blue fluorescent tubes ("Deep blue", Thai Toshiba Electric Company, 18 watts) in a 33 x 61.5 x 12 cm unit, lined with white cloths. The phototherapy device used in the "LEDs" group was the Bilitron 3006 (Fanem, Sao Paulo, Brazil) with 5 super LEDs in a 11 x 23 x 5 cm unit. The distance between both devices and the infants was fixed at 30 cm. The spectral irradiance of the SPL and the Bilitron 3006 were 79 and 40 $\mu W/cm^2/nm$, respectively. The room temperature in the nursery was between 28°C and 29°C.

Sample size calculation was based on a pilot study, which showed rate of bilirubin decreasing of 0.2 ± 0.1 mg/dL per hour with blue-light fluorescent and 0.08 ± 0.1 mg/dL per hour with super LEDs. Type I and type II errors were 5% and 20%, respectively. This required 20 infants in each group. Continuous data with and without normal distribution were presented as mean ± standard deviation and median (25, 75 percentile (%tile)), respectively. Categorical data was presented as frequency (percentage). Continuous data with and without normal distribution were analyzed by student's t-test and Mann Whitney U test, respectively. Categorical data was analyzed by Chi-square test or Fisher exact test as appropriate. Level of significance was determined at p less than 0.05. The SPSS 17.0 (SPSS Inc, Chicago, IL, USA) was used for data entry and statistical analysis.

Results

The present study period was between February and April 2007. Forty healthy infants were recruited, 20 infants in each group. There were 26 male and 14 female infants with gestational age ranged from 36 to 42 weeks and mean gestational age of 38.0 ± 1.5 weeks gestation. All infants had phototherapy started between 40 and 98 hours of life. Causes of hyperbilirubinemia were non-hemolytic (72.5%), ABO incompatibility (12.5%) and glucose-6-phosphate dehydrogenase (G-6-PD) deficiency (15%). However, G-6-PD was not performed in 13 cases.

Demographic data and baseline clinical characteristics of infants in both groups were comparable (Table 1). Rate of plasma bilirubin decreasing during phototherapy in the "blue light" group was significantly higher than in the "LEDs" group ($p = 0.03$). Duration of phototherapy revealed a trend favoring the "blue light" but was not statistically significant (Table 2). Number of infants who required double phototherapy or re-phototherapy was not statistically different. None of the infants required total blood exchange transfusion.

Table 1. Demographic data and baseline characteristics

	Blue light (n = 20)	LEDs (n = 20)	p-value
Sex*			0.51
Male	14 (70%)	12 (60%)	
Female	6 (30%)	8 (40%)	
Gestational age** (wk)	38.1 ± 1.5	37.9 ± 1.6	0.68
Age at the beginning of phototherapy*** (h)	71.0 (58.3, 84.3)	67.0 (51.0, 71.0)	0.19
Plasma bilirubin at the beginning of phototherapy*** (mg/dL)	14.5 (14.0, 15.6)	14.2 (12.5, 15.0)	0.17
Reticulocyte count***	3.4 (3.0, 5.2)	4.6 (3.3, 5.7)	0.22
Infants with ABO incompatibility*	3 (15%)	2 (10%)	1.00
Infants with G-6-PD deficiency*	3 (21.4%)	3 (23.1%)	1.00

* Data is presented as frequency (percentage)
** Data is presented as mean ± SD
*** Data is presented as median (25, 75%tile)

Table 2. Outcome of hyperbilirubinemia

	Blue light (n = 20)	LEDs (n = 20)	p-value
Rate of bilirubin decreasing** (mg/dL/h)	0.16 (0.09, 0.25)	0.10 (0.02, 0.17)	0.03***
Duration of phototherapy** (h)	23.0 (19.0, 30.8)	30.0 (22.3, 40.3)	0.11
Need for double phototherapy*	2 (10%)	4 (20%)	0.66
Need for re-phototherapy*	1 (5%)	0	1.00

* Data is presented as frequency (percentage)
** Data is presented as median (25, 75%tile)
*** Significant at p-value < 0.05

Table 3. Complications of phototherapy

	Blue light (n = 20)	LEDs (n = 20)	p-value
Hyperthermia*	0	0	NA
Hypothermia*	0	2 (1%)	0.49
Rash*	0	0	NA
Stool per day**	4.5 (3.1, 6.0)	5.1 (4.1, 6.0)	0.48

* Data is presented as frequency (percentage)
** Data is presented as median (25, 75%tile)

The only side effect of phototherapy found in the present study was hypothermia in 2 infants; both were in the "LEDs" group (Table 3).

Discussion

In the present study, rate of plasma bilirubin decreasing during phototherapy with special blue fluorescent tube is significantly higher than with super LEDs. The presented results are different from previous studies, which demonstrated that LEDs and blue light phototherapy have comparable effectiveness[8,9]. Both phototherapy devices used in Maisels' study have nearly equal spectral irradiance of approximately 40 μW/cm^2/nm, which is in the range of intensive phototherapy (higher than 30 μW/cm^2/nm) as recommended by AAP[5]. The SPL phototherapy device has spectral irradiance of 79 μW/cm^2/nm measured by Olympic Bilirubinometer by Natus Medical Incorp, CA, USA, which is approximately double the irradiance of the LEDs used, and which is

recommended by AAP[5]. This higher irradiance may explain the results. Earlier studies have demonstrated dose-response relationship of phototherapy irradiance and the decrease of bilirubin[10,11]. This response increases with increasing irradiance until a "saturation point" is reached, where further increase in irradiance does not give any significant benefit[12]. However, some experts believe that there may not be a saturation point because the conversion of bilirubin to excretable photoisomers is irreversible and follows first-order kinetics[5]. However, the maximum effective dose of phototherapy is not demonstrated.

In Kumar's study, the LED phototherapy device has higher irradiance than the compact blue light fluorescents tubes (47 and 28.7 μW/cm²/nm, respectively)[8]. The higher spectral irradiance of the LEDs phototherapy unit used in Kumar's study might be lessened by the smaller surface area illuminated by the phototherapy unit[8]. Area of skin exposed to the light also affects efficacy. The International Electrotechnical Commission defines the effective surface area as the intended treatment surface that is illuminated by the phototherapy light. The commission uses 60 x 30 cm as the standard-sized surface[5,13]. The use of LEDs allows the phototherapy unit to be smaller and produce less heat than fluorescent tubes. The possible drawback is the smaller area illuminated by the LEDs phototherapy unit. Moreover, the irradiance below the center is much greater than at the periphery of the phototherapy unit[5,6,14]. With smaller treatment surface area illuminated by the LEDs, the active healthy term and late preterm infants may be more often out of this focus area of light.

Rate of bilirubin decreasing under phototherapy also depends on plasma bilirubin level at the beginning of phototherapy[5]. Since the super LEDs phototherapy device was quite new to the authors at the time of the present study, the authors decided not to recruit severe hyperbilirubinemia for safety reasons. This may explain why the rate of plasma bilirubin reduction in the non-severe hyperbilirubinemia infants is lower than expected[5].

Phototherapy has been used for decades with exceptionally rare reports of significant complications[5]. Minor complications such as diarrhea and temperature instability have been reported[9,15]. Phototherapy-associated diarrhea is caused by increased bile salts during phototherapy[15]. The authors did not find a difference in stool character and frequency between the two groups. The lower heat production of the LEDs may be responsible for the 2 cases with hypothermia in the present study, which is similar to what was also observed in another study[9].

All of the fluorescent tubes used in the SPL device are special blue fluorescent tubes, which are used in order to get higher spectral irradiance. The blue light may cause headache, dizziness, and nausea in health care personnel work nearby this phototherapy unit. Lining the unit with white cloths or aluminum foils can relieve these side effects. This will also increase irradiance of the light. However, the drawback is the higher environmental temperature around the infant, which hence requires temperature monitoring. However, none of the infants in the "blue light" group had hyperthermia.

Conclusion

There is no standardized method for delivering phototherapy recommended. A locally invented phototherapy device with special blue fluorescents tubes can be more effective than a more expensive commercial super LEDs phototherapy device in decreasing plasma bilirubin.

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Potential conflicts of interest

None.

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ประสิทธิผลของเครื่องส่องไฟรักษาตัวเหลืองชนิดมาตรฐานเปรียบเทียบกับชนิดซูเปอร์ไลท์อีมิททิ่งไดโอดส์ (Super Light-emitting Diodes) ในการรักษาภาวะตัวเหลืองในทารกแรกเกิด

โสภาพรรณ เงินฉ่ำ, เกรียงศักดิ์ จีระแพทย์, รัตนาพันธ์ สุวรรณชัย, เรณู ฉวีรัตน์, พิมล วงศ์ศิริเดช, ธราธิป โคละทัต

ภูมิหลัง: *ภาวะตัวเหลืองในทารกแรกเกิดพบได้บ่อยมาก การรักษาที่ใช้กันมานานนับสิบปีแล้วคือ การส่องไฟเพื่อป้องกันภาวะตัวเหลืองรุนแรงซึ่งอาจทำให้เกิดภาวะ kernicterus ได้*

วัตถุประสงค์: *เพื่อเปรียบเทียบประสิทธิผลของเครื่องส่องไฟรักษาตัวเหลือง 2 ชนิดในการลดระดับของสารบิลิรูบินในพลาสมาและระยะเวลาที่ใช้ในการส่องไฟรักษาในทารกแรกเกิดที่มีภาวะตัวเหลืองชนิดไม่รุนแรง*

วัสดุและวิธีการ: *เป็นการศึกษาแบบสุ่มและมีกลุ่มควบคุม ทารกที่เข้าร่วมในการศึกษาเป็นทารกที่มีภาวะตัวเหลืองชนิดไม่รุนแรงแต่เหลืองถึงเกณฑ์ที่ต้องได้รับการรักษาจำนวน 40 ราย อายุตั้งแต่ 1 ถึง 5 วัน เครื่องส่องไฟรักษาตัวเหลืองชนิดมาตรฐานที่ใช้ในกลุ่ม "หลอดไฟสีฟ้า" คือ เครื่องส่องไฟ-ศิริราช ซึ่งประกอบด้วย หลอดฟลูออเรสเซนต์แสงสีฟ้าพิเศษ จำนวน 6 หลอด เครื่องส่องไฟรักษาตัวเหลืองชนิดซูเปอร์ไลท์อีมิททิ่งไดโอดส์ ที่ใช้ในกลุ่ม "ไลท์อีมิททิ่งไดโอดส์ (แอลอีดี)" คือ Bilitron 3006 ซึ่งประกอบด้วย หลอดไฟซูเปอร์แอลอีดี จำนวน 5 หลอด*

ผลการศึกษา: *ในแต่ละกลุ่มมีทารกจำนวน 20 ราย ข้อมูลพื้นฐานและลักษณะทางคลินิกก่อนเริ่มการรักษาด้วยการส่องไฟของทารกทั้งสองกลุ่มสามารถเทียบเคียงกันได้ ค่ากลาง (25 เปอร์เซ็นต์ไทล์, 75 เปอร์เซ็นต์ไทล์) ของการลดลงของสารบิลิรูบินในพลาสมาของกลุ่ม "หลอดไฟสีฟ้า" มีค่ามากกว่าของกลุ่ม "แอลอีดี" อย่างมีนัยสำคัญทางสถิติ [0.16 (0.09, 0.25) และ 0.10 (0.02, 0.17) มิลลิกรัม/เดซิลิตร/ชั่วโมง ตามลำดับ; p = 0.03] ระยะเวลาในการส่องไฟรักษาตัวเหลืองของกลุ่ม "หลอดไฟสีฟ้า" สั้นกว่าของกลุ่ม "แอลอีดี" แต่ไม่มีนัยสำคัญทางสถิติ*

สรุป: *เครื่องส่องไฟรักษาตัวเหลืองชนิดมาตรฐานที่ผลิตขึ้นเองมีประสิทธิผลในการลดระดับสารบิลิรูบินในพลาสมาได้ดีกว่าเครื่องส่องไฟชนิดซูเปอร์แอลอีดี ซึ่งมีราคาแพงกว่ามาก*