The Efficacy of the In-House Light-Emitting Diode Phototherapy Equipment Compare to Conventional Phototherapy Equipment on the Treatment of Neonatal Hyperbilirubinemia

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Background: *From the empirical study, light-emitting diode (LED) phototherapy is effective for treatment of neonatal hyperbilirubinemia. However, commercial LED phototherapy equipment is still expensive. Thus, in-house LED phototherapy equipment has been developed.*
Objective: *To compare efficacy between in-house LED to conventional phototherapy equipment in the treatment of neonatal hyperbilirubinemia at Mae Sot Hospital.*
Material and Method: *This was a randomized controlled trial. Fifty newborns with hyperbilirubinemia were allocated to LED phototherapy group and conventional group. Baseline characteristics were compared and analyzed by descriptive statistics, exact probability and student t-test, and change in serum bilirubin level was analyzed by multilevel regression analysis.*
Results: *There were 25 patients in each of the two groups. The median duration of phototherapy in LED group was 25 hours, whereas the conventional group required 48 hours ($p<0.001$) and the average serum bilirubin level in LED group decreased more rapidly than in conventional group ($p = 0.007$). Hyperthermia were found in 22 infants from conventional group (88%) compared to 11 infants from LED group (44%) ($p = 0.002$).*
Conclusion: *In-house LED phototherapy equipment is more effective than conventional phototherapy in the reduction of serum bilirubin level and occurrence of hyperthermia during treatment is less.*

Keywords: *Light-emitting diode, Conventional phototherapy, Neonatal hyperbilirubinemia*

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Phototherapy is the standard treatment for neonatal unconjugated hyperbilirubinemia after the discovery in 1958 by Cremer et al[1]. It has a low adverse effect and is able to reduce the number of patients needed to be treated with blood exchange transfusion[2]. The factors affecting the efficacy of phototherapy included spectrum and irradiance of the source of light[3,4]. To date, light-emitting diode (LED) has been used as the light source of phototherapy. It provides a narrower spectrum of 450 to 480 nm. Its irradiance is higher than blue light and super-blue fluorescent bulb used in traditional phototherapy equipment[5].

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Since the clinical practice guideline on the management of hyperbilirubinemia in newborns established by the American Academy of Pediatrics has been implemented to our routine neonatal care, the number of newborns needing to be treated by phototherapy has increased substantially, hence the inadequacy in the phototherapy equipment.

American Academy of Pediatrics recommends using blue light from blue fluorescent bulb or LED to treat infants with neonatal hyperbilirubinemia[6]. Recent evidences showed empirically that LED phototherapy is effective in decreasing the bilirubin level and requires less time for treatment without rebound jaundice[11] compared with conventional phototherapy[7-12].

From aforementioned reasons, the use of LED phototherapy equipment to treat infants with neonatal hyperbilirubinemia was initiated. However, commercial

LED phototherapy equipment is expensive; therefore, the technical department developed an in-house LED phototherapy equipment for use in the treatment. The present study was conducted to examine the efficacy of the in-house LED phototherapy in comparison to the conventional phototherapy equipment.

Material and Method

Between June 1, 2012 and December 31, 2012, two-days-old newborns with 35 or more weeks' gestation that had neonatal hyperbilirubinemia requiring phototherapy were enrolled. Cases with congenital abnormality, birth asphyxia, or neonatal septicemia were excluded. The patients were oral fed, and were assigned to receive single phototherapy. Using a software package, the sample size was calculated under significant level of 0.05 and power of 0.9 to give at least 25 cases required to for each group of treatment. Randomized allocation into both treatment groups were done by using blinded envelope.

The American Academy of Pediatrics guidelines for phototherapy and exchange transfusion criteria[6] were used in this study. Blood sample was collected for the baseline serum bilirubin and other etiologic investigations. Serum bilirubin was then followed every 24 hours after phototherapy initiated. Either capillary blood from heel stick or peripheral venous blood from hand dorsum was collected in preheparinized micro-capillaries, centrifuged immediately at 12,000 rpm for 5 minutes and the total bilirubin was measured with a spectrophotometer (Apel dual wave length total bilirubin meter, Japan).

Phototherapy was discontinued whenever serum bilirubin level was 2 mg/dl below the threshold for phototherapy on age-specific bilirubin nomogram proposed by Bhutani and colleagues[13].

Body temperature was monitored via axillary route every 15 to 30 minutes in early of phototherapy for hyperthermia and hypothermia conditions and early alleviation. The duration was then extended to the routine measurement if the infant's body temperature was in a normal range for 3-consecutive measuring. The authors defined a case as with hypothermia if the body temperature ≤36.5°C on at least one occasion and a case as with hyperthermia if the body temperature >37.5°C on at least one occasion.

The light sources of the in-house LED phototherapy equipment comprised of 156 superbright blue LEDs (Part No. TOL-80aBbCEa-B3H, Taiwan Oasis Company). The typical peak of the wavelength at 20 milliamps forward current is 470 nm with the range of 465 to 475 nm. The total spectral irradiance was 24 microwatts/cm^2/nm at 30 cm perpendicular distance from the light source whereas conventional phototherapy equipment comprised of four special blue fluorescent tubes ("Deep blue", Toshiba, 18 watts) plus four daylight fluorescent tubes (TL-D Super 80, Philips, 18 watts) had a total spectral irradiance of 10 microwatts/cm^2/nm when measured in the same manner. The LED phototherapy equipment developed by the hospital's technician was funded by the budget of hospital's medical equipment development project and was approved by the Research Ethics Committee to use in the research.

This research was approved by the Research Ethics Committee of Mae Sot Hospital. All patients were allowed to participate in the research by their parents.

The baseline characteristics of the infants including gender, gestational age, birth weight, delivery type, blood group of mother and infant, risk factors of neonatal hyperbilirubinemia, baseline serum bilirubin level following daily treatment, and body temperature of the infant were collected and analyzed using descriptive statistic, exact probability, and student t-test. The effects of the treatment were compared by multilevel regression analysis.

Results

Fifty two-days-old newborns with neonatal hyperbilirubinemia participating in the present study were randomized into a LED or a conventional phototherapy group. Each group consists of 25 patients, 13 males and 12 females. The blood group of the mother and child, reticulocyte count, and G6PD were not statistically different between the two groups. Most infants were spontaneous vaginal delivery. The average birth weight in the LED and conventional phototherapy were 3,143 and 2,945 grams respectively ($p = 0.080$). The average gestation of LED phototherapy was 39.5 weeks while the average gestation of conventional phototherapy group was 38.6 weeks, which were significantly different ($p = 0.023$; Table 1).

After phototherapy, fifteen infants (60%) treated with LED phototherapy were able to discontinue the treatment and were discharged from the hospital after only 24 hours of phototherapy. In comparison, only eight infants treated with conventional phototherapy only were able to discontinue the treatment after 24 hours of phototherapy (Table 2).

The average duration of phototherapy for the infants in LED phototherapy group and conventional phototherapy group were 25 and 48 hours respectively,

which was significantly different (p<0.001; Table 2). The effects of the baseline characteristic differences which may affect phototherapy efficacy; e.g. gestational age, birth weight, and baseline serum bilirubin level were controlled in the multilevel regression model so the authors found that the infants in the LED group had higher daily decreasing level of serum bilirubin than that of the conventional group, significantly on Wald method of post estimation (p = 0.007) (Table 2, Fig. 2).

On the aspect of harm and risks of treatment from this study, hypothermia was not found among

Table 1. Baseline characteristics of the infants

	LED (n = 25)		Conventional (n = 25)	
	Numbers	%	Numbers	%
Male	13	52.0	13	52.0
Gestational age (weeks)*				
≥38	24	96.0	21	84.0
Mean (±SD)	39.5 (±1.3)		38.6 (±1.4)	
Birth weight (grams)				
Mean (±SD)	3,143.6 (±387.7)		2,945.2 (±393.8)	
Delivery type				
Vaginal delivery	22	88.0	23	92.0
Cesarean section	3	12.0	2	8.0
High risk cases of ABO incompatibility**	3	12.0	5	20.0
G6PD deficiency	4	16.0	4	16.0
Reticulocyte count (%)				
≥6.5	6	24.0	4	16.0
Mean (±SD)	4.3 (±1.9)		4.5 (±2.1)	

* p = 0.023
** Maternal blood type was O, while fetal blood type was A, B, or AB
LED = light-emitting diode

Table 2. Result of phototherapy by treatment day and number of infants with abnormal body temperature

	LED (n = 25)		Conventional (n = 25)		p-value
	Numbers	%	Numbers	%	
Duration of phototherapy (hours)					
Median (IQR)	25 (21.5, 48)		48 (29, 51.8)		<0.001*
Serum bilirubin level (mg%): mean (± SD)					
Baseline	16.2 (±2.7)		15.8 (±1.5)		0.007**
After 24 hours	15.4 (±3.6)		15.2 (±2.6)		
After 48 hours	14.1 (±3.0)		15.1 (±3.1)		
After 72 hours	14.6 (±1.3)		15.3 (±3.3)		
Numbers of patient discontinued phototherapy					
After 24 hours	15	60.0	8	32.0	<0.001***
After 48 hours	6	24.0	10	40.0	
After 72 hours	4	16.0	7	28.0	
Body temperature					
Baseline (°C)					
Mean (±SD)	36.8 (±0.1)		36.9 (±0.1)		
Hypothermia (≤36.5°C)	1	4.0	0	0	0.317***
Hyperthermia (>37.5°C)	11	44.0	22	88.0	0.002***

* Mann-Whitney test
** Post estimation test: Wald method
*** Chi-square test

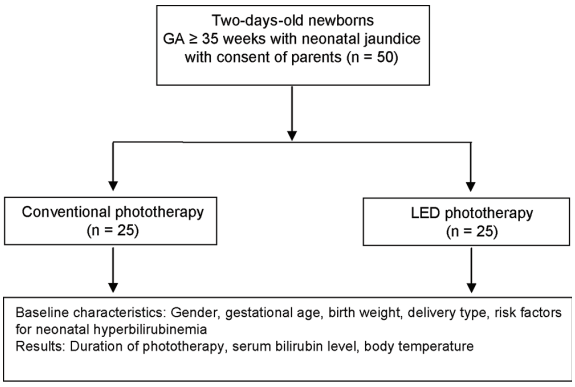

Fig. 1 Study flow.

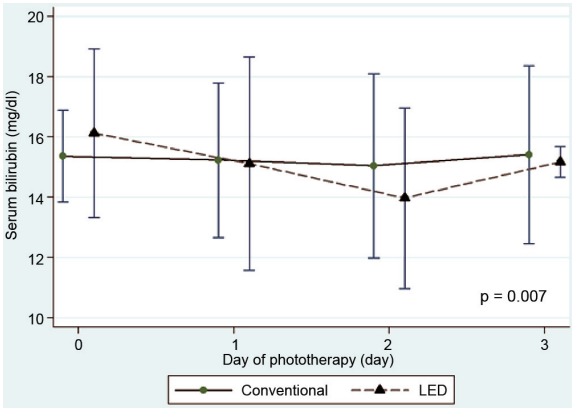

Fig. 2 The decrease of serum bilirubin level classified by type of phototherapy.

conventional group after the treatment but in one case (4%) among LED group. However, it was not significantly different (p = 0.317). Hyperthermia was found among infants in conventional group, which is equal to 88%. This is significantly higher than LED group, where only 44% of the cases were found (p = 0.002) (Table 2). No fatal complications including death and failure in phototherapy leading to total blood exchange transfusion in either groups.

Discussion

In the present study, it was found that the neonatal hyperbilirubinemia treatment using LED phototherapy equipment was more effective than conventional phototherapy. Median time of phototherapy among LED group was less than 23 hours. According to previous studies, it can provide more daily decrement of serum bilirubin[7-9,11,12]. Important factors that affect the decrease of bilirubin level are the intensity of light-emitted diode and a narrower and more specific spectrum[5,14-18].

In the case that the average serum bilirubin level increased after day 3 of phototherapy in both groups (Fig. 2), it was caused by the decreasing number of patients in the analysis, that is, there are four remaining patients in LED group and seven patients in conventional group that had high serum bilirubin level referred to age-specific threshold on the previous mentioned bilirubin nomogram.

Besides better efficacy in the neonatal hyperbilirubinemia treatment of such LED phototherapy equipment, LED phototherapy equipment had lower heat production and less increase the infants' body temperature. This allows a shorter distance between the lamp and the patient, providing more irradiance for the patient while causing no critical adverse effects such as hyperthermia or burn caused by conventional phototherapy. However, if the patient's environmental temperature is below the thermo-neutral zone, the infant being treated for neonatal hyperbilirubinemia using LED may have hypothermia[7,19]. Although the authors found one hypothermic infant in LED group with no significant difference when compared to conventional group, intensive temperature monitoring should be done particularly when LED phototherapy device was applied to the infant or patient with a low body weight in a cold climate, and additional warm measure e.g. using a heater should be considered.

The infants that phototherapy was discontinued, were discharged from the hospital and their mothers were taught to recognize the warning signs of severe hyperbilirubinemia at home. Karagol et al found that the infants treated with LED phototherapy equipment had less rebound jaundice than conventional group[11]. However, the present study did not follow-up on rebound jaundice after phototherapy, but there was no re-admission on OPD follows-up.

The population of the present study is term and late-preterm infants. This result may not be applicable to preterm infants. The present study also did not include the differences of etiologic of neonatal hyperbilirubinemia, spectral irradiance, and environmental temperature. These factors should be explored for their effects on the efficacy of phototherapy equipment.

Although in-house LED phototherapy of Mae Sot Hospital was cheap; unit price is around 4,000 Baht; its unit cost, lifetime, and the standardization are gaps of knowledge that should be examined in comparison with conventional phototherapy equipment and brand name LED phototherapy equipment in further study.

Conclusion

In-house LED phototherapy equipment developed by the cooperation between technicians and the department of pediatrics at Mae Sot Hospital has been more effective in reducing serum bilirubin levels in neonatal hyperbilirubinemia than the conventional phototherapy. The duration of phototherapy and occurrence of hyperthermia were lesser in LED phototherapy. In addition, it can be used as the demo of in-house LED phototherapy equipment among rural hospitals with limited resource.

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What is already known on this topic?

Blue light both from special blue fluorescent bulb and LED have the effectiveness in reducing plasma unconjugated bilirubin in the treatment of neonatal hyperbilirubinemia.

Commercial LED phototherapy equipment can provide a narrower and a more specific spectral light source compared to conventional fluorescent phototherapy equipment.

Efficacy in treatment of neonatal hyperbilirubinemia by using commercial LED and conventional phototherapy equipment are comparable.

What this study adds?

In-house LED phototherapy equipment is safe and more effective than conventional phototherapy for the treatment of neonatal hyperbilirubinemia in healthy term and late-preterm infants with non-hemolytic jaundice and the occurrence of hyperthermia during treatment is less.

Potential conflicts of interest

None.

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ประสิทธิภาพของเครื่องส่องไฟชนิด light-emitting diode ที่ประดิษฐ์ขึ้นเปรียบเทียบกับเครื่องส่องไฟชนิดมาตรฐานในการรักษาทารกแรกเกิดที่มีภาวะตัวเหลือง

รัฐเขตต์ เอกอิสริยาภรณ์, รัตติกาล มณีนุตร์, จิราภรณ์ กาศเรือนแก้ว, วลีรัตน์ ขอบคุณ, สุนารี แสนพรหม

ภูมิหลัง: *จากการศึกษาหลักฐานเชิงประจักษ์พบว่าเครื่องส่องไฟชนิด light-emitting diode (LED) มีประสิทธิภาพสูงในการลดระดับบิลิรูบินในพลาสมา แต่ปัจจุบันเครื่องส่องไฟชนิดดังกล่าวยังคงมีราคาแพง งานช่างโรงพยาบาลแม่สอดจึงได้ประดิษฐ์และพัฒนาเครื่องส่องไฟชนิดดังกล่าวขึ้นเพื่อใช้ในโรงพยาบาล*

วัตถุประสงค์: *เพื่อศึกษาเปรียบเทียบประสิทธิภาพของเครื่องส่องไฟชนิด LED ที่ประดิษฐ์ขึ้นเปรียบเทียบกับเครื่องส่องไฟชนิดมาตรฐานในการรักษาทารกแรกเกิดที่มีภาวะตัวเหลืองในโรงพยาบาลแม่สอด*

วัสดุและวิธีการ: *เป็นการศึกษาแบบสุ่มและมีกลุ่มควบคุม ทารกแรกเกิดที่มีภาวะตัวเหลืองซึ่งได้รับการรักษาด้วยการส่องไฟจำนวน 50 ราย จะถูกสุ่มเข้ากลุ่มศึกษาสองกลุ่ม ประกอบด้วยกลุ่มที่ใช้เครื่องส่องไฟชนิด LED และกลุ่มที่ใช้เครื่องส่องไฟชนิดมาตรฐาน รวบรวมและวิเคราะห์ข้อมูลลักษณะพื้นฐานด้วยสถิติเชิงพรรณนา, exact probability และ student t-test วิเคราะห์เปรียบเทียบประสิทธิภาพของเครื่องส่องไฟในการลดระดับบิลิรูบินในพลาสมาด้วย multilevel regression analysis*

ผลการศึกษา: *ผู้ป่วยกลุ่มละ 25 ราย พบกลุ่มเครื่องส่องไฟชนิด LED ใช้ระยะเวลาเฉลี่ยในการส่องไฟ 25 ชั่วโมง น้อยกว่ากลุ่มเครื่องส่องไฟชนิดมาตรฐานที่ใช้ระยะเวลาเฉลี่ย 48 ชั่วโมง ($p<0.001$) นอกจากนี้กลุ่มเครื่องส่องไฟชนิด LED ยังมีการลดลงของระดับบิลิรูบินในพลาสมามากกว่ากลุ่มเครื่องส่องไฟชนิดมาตรฐานอย่างมีนัยสำคัญทางสถิติ ($p = 0.007$) ทารกที่ได้รับการรักษาด้วยเครื่องส่องไฟชนิดมาตรฐานพบภาวะ hyperthermia ร้อยละ 88 มากกว่ากลุ่มที่ได้รับการรักษาด้วยเครื่องส่องไฟชนิด LED ซึ่งพบเพียงร้อยละ 44 อย่างมีนัยสำคัญทางสถิติ ($p = 0.002$)*

สรุป: *เครื่องส่องไฟชนิด LED ที่ประดิษฐ์และพัฒนาขึ้นมีประสิทธิภาพในการลดระดับบิลิรูบินในพลาสมาได้มากกว่าเครื่องส่องไฟชนิดมาตรฐาน ตลอดจนเกิดภาวะ hyperthermia น้อยกว่า*