Comparison of intensive light-emitting diode and intensive compact fluorescent phototherapy in non-hemolytic jaundice

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SUMMARY: Takcı Ş, Yiğit Ş, Bayram G, Korkmaz A, Yurdakök M. Comparison of intensive light-emitting diode and intensive compact fluorescent phototherapy in non-hemolytic jaundice. Turk J Pediatr 2013; 55: 29-34.

In severe and rapidly increasing jaundice, the use of intensive phototherapy provides greater effectiveness and a faster decrement in bilirubin levels compared to conventional phototherapy. The aim of this study was to compare the effectiveness of two types of intensive phototherapy: intensive compact fluorescent tube (CFT) and intensive light-emitting diode (LED) phototherapy. Forty-three infants over 35 weeks of gestation with severe non-hemolytic hyperbilirubinemia were enrolled in the prospective study. All infants received multidirectional (circular-shaped) intensive phototherapy. Of these, 20 infants received CFT while 23 infants received LED phototherapy. Bilirubin levels and body temperatures were measured periodically, and the rates of bilirubin decrement were calculated. Mean serum bilirubin level of the 43 infants was 20.5±1.5 mg/dl at the beginning of the therapy and mean duration of phototherapy was 20.6±1.1 hours. The rate of mean bilirubin decline was 47.2% and the decrease was more prominent in the first four hours (0.84 ± 0.41 mg/dl/h). The rates of bilirubin decrement were comparable between the LED and CFT groups. Slightly elevated mean body temperature (37.1°C) was determined in the CFT group ($p<0.05$). Intensive phototherapy units with both LED and CFT were effective, showing a decline of half the initial value of bilirubin during the study period in infants with non-hemolytic jaundice. This study shows that intensive phototherapy with either CFT or LED can provide rapid decrease in bilirubin levels in the first few hours. This rapid decline is important in cases that have high risk of bilirubin encephalopathy.

Key words: indirect hyperbilirubinemia, high intensive phototherapy, light-emitting diode, compact fluorescent tube.

In the first week of life, up to 60% of normal term infants have clinical jaundice[1]. Healthy newborns with jaundice need to be monitored because bilirubin is potentially toxic to the central nervous system. Excessive elevated levels of bilirubin can lead to bilirubin encephalopathy and subsequently kernicterus, with devastating, permanent neurodevelopmental handicaps[2].

Phototherapy has been accepted as the standard treatment for neonatal jaundice, and there are various methods of delivering phototherapy. The efficiency of phototherapy depends on the emission range, peak wavelength of the light source, irradiance, and exposed body surface area, apart from various clinical factors[3]. Irradiance is the light intensity, or number of photons, delivered per square centimeter of exposed body surface. Higher irradiance results in faster decline in serum bilirubin levels[3].

In the current guidelines of the American Academy of Pediatrics (AAP), intensive phototherapy is defined as the use of blue light (in the 430-490 nm band) delivered at 30 mw/ cm^2/nm or higher to the greatest body surface area as possible[4].

In severe and rapidly increasing jaundice, the use of high-intensity phototherapy provides greater effectiveness and a faster decrement in bilirubin levels[5]. Multiple phototherapy units are used to increase the light intensity and thus improve the efficiency of phototherapy[6]. Light intensity and the area of light-exposed skin can be increased by designated multidirectional

phototherapy devices, and thus, the increase in light-exposed surface area results in greater reduction in serum bilirubin levels[3].

The most commonly used light sources are fluorescent tubes, halogen bulbs and fiberoptic blankets. In addition to these sources, high-intensity gallium nitride light-emitting diodes (LEDs), which have significantly higher light irradiance levels when compared to current sources, have been developed[7].

There are a considerable number of reports comparing conventional and LED phototherapy; however, comparison of these units in higher irradiances is limited[8,9]. Therefore, we aimed to compare the effectiveness of intensive compact fluorescent tube (CFT) and intensive LED phototherapy using multidirectional phototherapy units.

Material and Methods

This study was carried out prospectively over 17 months (June 2010-December 2011) at Hacettepe University İhsan Doğramacı Children's Hospital, in the Neonatal Intensive Care Unit (NICU). The study was approved by our institution's ethics committee, and informed consent was obtained from all families before the infants were included in the study. Infants born after 35 weeks of gestation who developed significant hyperbilirubinemia requiring phototherapy were enrolled in the study. The decision to start phototherapy was made according to AAP guidelines[6]. The infants were not included in the study if they had any of the following: hemolysis (positive direct Coombs test), rhesus hemolytic disease, culture- positive or clinical sepsis, exchange transfusion, glucose-6-phosphate deficiency, pyruvate kinase deficiency, or severe dehydration.

Intervention

All enrolled infants were randomly placed on circumferential CFTs and circumferential LEDs phototherapy. All infants were exposed to light completely unclothed; their eyes and diaper regions were protected. The demographic and clinical variables were recorded, including birth weight, gender, gestational age, and duration of phototherapy. The gestational age was calculated according to the mother's last menstrual period and dating ultrasonography. Bilirubin levels were measured and recorded at the fourth and eighth hours of the phototherapy and at the end of the treatment. The period that the infant could not receive phototherapy for various reasons (feeding, physical examination, blood sampling, etc.) was noted by the staff, and absolute phototherapy duration and rate of bilirubin decline were calculated for each sampling interval. Serum bilirubin levels were re-evaluated 24 hours after cessation of phototherapy. Body temperature of the babies was monitored during phototherapy. Body temperature was checked every hour with digital axillary thermometer (Filac 3000 EZ, Mansfield, MA). Hydration status of the infants was assessed with weight changes and physical examination. Skin rashes were also noted. Hearing screening was performed with otoacoustic emission and brainstem evoked response audiometry (BAER) at discharge.

Phototherapy

Circumferential phototherapy devices were produced by Novos Medical, Inc. (Ankara, Turkey); one was equipped with CFT and the other with LED. CFT units consisted of 16 circumferentially located special blue compact fluorescent bulbs (18 W, OSRAM special blue lamp). LED phototherapy units had multiple LED bulbs with 450 nm peak emission. The peak emission wavelengths of CFT units were in the range of 420-500 nm. CFT units delivered a spectral irradiance of 40-60 (max-min) mW/cm^2/nm, while LED units delivered 31.8-51 (max-min) mW/cm^2/nm, at a distance of 30 cm for both units. The intensity of light was checked periodically with Solar Light Co PMA 2100 (Glenside, PA) spectroradiometer.

Both of the devices had temperature regulation with integrated fan groups.

Statistical Analysis

All the variables were parametric. The significance of differences between the means of the two groups were determined by independent samples t test, with significance defined as $p<0.05$.

Results

Forty-three infants with indirect hyperbilirubinemia were included in the

study. All infants were put on intensive phototherapy. Of these, 20 infants received CFT phototherapy (Group I), while 23 infants received LED phototherapy (Group II). There were no significant differences in the clinical characteristics of the two groups (Table I).

Mean serum bilirubin level of the 43 infants was 20.5 ± 1.5 mg/dl at the beginning of the therapy, and mean duration of phototherapy was 20.6 ± 1.1 hours. Mean serum bilirubin level had decreased to 10.9 ± 2 mg/dl at the end of the phototherapy. The rate of mean bilirubin decline was 47.2 ± 9%. The rate of bilirubin decrease was 0.84 ± 0.41 mg/dl/h in the first four hours, and it was calculated as 0.47 ± 0.1 mg/dl/hr for 20.6 hours (Table I).

The mean initial serum bilirubin levels were 20.6 ± 1.6 mg/dl and 20.5 ± 1.5 mg/dl in the CFT and LED phototherapy groups, respectively ($p>0.05$). The phototherapy durations were comparable in each group ($p>0.05$). No phototherapy failure was observed during treatment, and phototherapy was effective in decreasing bilirubin levels in both groups. Four hours after phototherapy initiation, mean serum bilirubin level was 17.3 ± 1.9 mg/dl in the CFT and 17.8 ± 1.7 mg/dl in the LED groups. The rate of decrease in mean serum bilirubin levels per hour was 0.9 ± 0.4 mg/dl in the CFT group, while it was 0.78 ± 0.4 mg/dl in the LED group ($p>0.05$). At the end of the treatment, mean serum bilirubin levels were similar in both groups (10.4 ± 2.6 mg/dl for CFT versus 11.2 ± 1.5 for LED groups) ($p>0.05$) (Table I).

The rate of mean bilirubin decrement was not

Table I. Clinical and Laboratory Parameters of the Two Groups

	Total (CFT + LED)n = 43	Group I(CFT)n = 23	Group II(LED)n = 20	P values
Gestational age, weeks	38.1 ± 1.5	38.2 ± 1.6	37.9 ± 1.5	0.59
Birth weight, grams	3175± 409	3166 ± 325	3183 ± 478	0.89
Age at phototherapy, hours	124 ± 51	129 ± 50	120 ± 52	0.54
Hematocrit % (at the beginning of phototherapy)	53.2 ± 6.5	53.4 ± 7.2	53 ± 5.9	0.84
Absolute duration of phototherapy (hour)	20.6 ± 1.1	20.8 ± 1.1	20.3 ± 1	0.38
Baseline TSB level, mg/dl (mmol/L)	20.5 ± 1.5 (350.5 ± 25.7)	20.6 ± 1.6 (352.3 ± 27.4)	20.5 ± 1.5 (350.5 ± 25.7)	0.80
After 4 h of phototherapy mg/dl (mmol/L)	17.6 ± 1.8 (300.1 ± 30.8)	17.3 ± 1.9 (295.8 ± 32.5)	17.8 ± 1.7 (304.4 ± 29.1)	0.39
After 8 h of phototherapy mg/dl (mmol/L)	15.2 ± 2 (259.9 ± 34.2)	14.9 ± 2 (254.8 ± 34.2)	15.4 ± 2 (263.3 ± 34.2)	0.38
TSB level at termination of phototherapy mg/dl (mmol/L)	10.9 ± 2 (186.4 ± 34.2)	10.4 ± 2.6 (177.8 ± 44.5)	11.2 ± 1.5 (191.5 ± 25.7)	0.19
TSB change per hour in first 4 hours mg/dl/hour (mmol/L/hour)	0.84 ± 0.41 (14.4 ± 7)	0.9 ± 0.4 (15.4 ± 6.8)	0.78 ± 0.4 (13.3 ± 6.8)	0.32
TSB change per hour in first 8 hours, mg/dl/hour (mmol/L/hour)	0.74 ± 0.28 (12.7 ± 4.8)	0.78 ± 0.3 (13.3 ± 5.1)	0.72 ± 0.26 (12.3 ± 4.4)	0.49
TSB change per hour during study period, mg/dl/hour (mmol/L/hour)	0.47 ± 0.1 (8 ± 1.7)	0.49 ± 0.07 (8.4 ± 1.2)	0.45 ± 0.06 (7.7 ± 1)	0.15
The rate of bilirubin decrement at termination of phototherapy (%)	47.2 ± 9	49.6 ± 11.8	45 ± 6.1	0.11

CFT: Compact fluorescent tube. LED: Light-emitting diode. TSB: Total serum bilirubin.

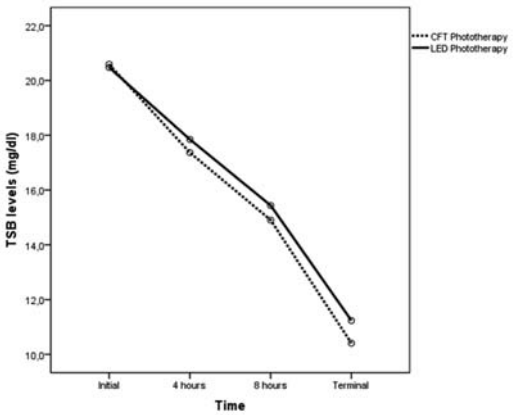

Figure.1 Total serum bilirubin levels under LED and CFT phototherapy.

statistically different between the CFT and LED groups (49.6 ± 11.8% versus 45 ± 6.1%, p>0.05) at the end of the treatment. The rates of bilirubin decrement per hour were 0.49 ± 0.07 mg/dl and 0.45 ± 0.06 mg/dl in the LED and CFT groups, respectively (p>0.05) (Table I). The decrease in mean serum bilirubin levels in response to CFT and LED phototherapy are seen in Figure 1.

After termination of treatment, none of the infants required another course of phototherapy. Hypothermia was not observed during phototherapy, while hyperthermia (³37.5ºC) was noted in three infants in the CFT and two infants in the LED group. Mean body temperature was higher in the CFT group (37.1 ± 0.3ºC) than the LED group (36.8 ± 0.4ºC) during the treatment period (p<0.05) (Table II). None of infants had received intravenous fluid and none of them had significant weight loss. Skin rashes due to phototherapy were noted in one infant receiving CFT phototherapy. Otoacoustic emission and BAER tests were normal in all infants at discharge from the hospital.

Discussion

Phototherapy is an important treatment of choice to prevent the complications of unconjugated hyperbilirubinemia. The duration of exposure to elevated total bilirubin level is an important risk factor for acute bilirubin encephalopathy or kernicterus. Effective phototherapy decreasing total bilirubin to safe levels quickly can minimize the risk of bilirubin neurotoxicity.

Different phototherapy devices are being used worldwide, and there is no standard recommended method of administering phototherapy. In the present study, we used two circumferential phototherapy units, which both generate high light intensity using either LED or conventional light sources. The units were designed to give circular illumination in order to improve the efficiency of phototherapy by maximizing light-exposed body surface area. Ventral- or dorsal-placed phototherapy units can illuminate approximately 35% of the total body surface, while the illuminated body surface area can be increased up to approximately 80% using multidirectional devices[3].

The rate of mean bilirubin decrease per hour was 0.45 ± 1 mg/dl at the end of the phototherapy in the present study. Furthermore, serum bilirubin rate of decline was more prominent within the first four hours of phototherapy. On average, we achieved a 47% decrement in bilirubin levels with intensive LED and CFT phototherapy at the end of the treatment (absolute phototherapy duration was approximately 20.6 hours). It was shown that with standard phototherapy systems, 6% to 20% decreases are usually obtained in the first 24 hours[10]. Tan[11] and de Carvalho et al.[12] achieved an average 50% decrement in bilirubin levels with a high-intensity phototherapy at the end of 24 hours. The reduction rate in bilirubin levels was more rapid within the first few hours of the treatment. The present study

Table II. Mean Body Temperatures in the Two Groups

	Group I (CFT) n = 23	Group II (LED) n = 20	P values
Mean initiation temperature (ºC)	36.6 ± 0.32	36.7 ± 0.35	0.40
Mean temperature during study (ºC)	37.1 ± 0.3	36.8 ± 0.4	0.00

CFT: Compact fluorescent tube. LED: Light-emitting diode.

is in line with these reports, supporting the effectiveness of high-intensive phototherapy in the treatment of severe non-hemolytic jaundice.

Tan[11] showed that there is a dose-response relationship with increased intensity of phototherapy, but the rate of decline progressively decreases while reaching a saturation point. No further decline was provided with further increase in radiance. In the present study, we used a slightly higher dose of irradiance and obtained nearly the same rate of decrement as in Tan's study[11]. This result shows that higher doses of irradiance are unnecessary and may be harmful for infants, even though we observed no adverse effects in the short term[3]. A number of adverse effects of phototherapy have been noted in the literature, such as water loss, electrolyte disturbances, disorder of circadian rhythms, bronze baby syndrome, and interference with maternal-infant interaction. Other possible side effects of phototherapy are allergic disorders, melanotic nevus, skin cancer, patent ductus arteriosus, and retinopathy of prematurity[13]. Furthermore, in some studies, it was shown that phototherapy increases DNA damage, but the amount of DNA damage was not affected with increasing irradiance[14,15]. Theoretically, the side effects of phototherapy may be related to the intensity of irradiance; however, this fact could not be clearly established.

One of the new types of light sources is LED, which emits blue light with a peak emission between 450 and 470 nm and which overlaps the peak spectrum of bilirubin breakdown[1,16]. LED phototherapy that employs gallium nitride LEDs has been developed and is being used as an effective light source in the management of neonatal jaundice[9,17]. LED light sources are power-efficient, have a longer life (more than one year of continuous use), and are portable, with low heat production. They can be placed very close to the skin of the infants without any apparent untoward effects, and LED phototherapy has been shown to be as effective as CFT phototherapy in lowering serum bilirubin levels in infants with jaundice[18]. In a Cochrane database review[18] evaluating six randomized trials comparing the efficiency of LED and conventional phototherapy, serum bilirubin decrement rates were reported as 0.13-0.35 mg/dl/h for LED and as 0.12-0.27 mg/dl/h for non-LED phototherapy units. However, there are limited data evaluating the efficiencies of intensive LED and intensive CFT phototherapy using multidirectional units.

In the present study, no significant side effect of phototherapy was observed, and phototherapy was effective in decreasing bilirubin levels in both groups. The rate of bilirubin decline was similar at the end of the treatment. Although irradiance in CFT phototherapy was slightly higher than in LED phototherapy in this study, it did not show any effect on the rate of bilirubin decrement, as expected.

We did not observe any rebound increase in bilirubin levels requiring re-treatment in the groups in spite of the short treatment period and rapid bilirubin decrement. This data shows that intensive phototherapy for 24 hours can be used reliably in the cases of non-hemolytic jaundice.

One of the aims of this study was to compare the differences in heat production of intensive CFT and LED phototherapy. Mean body temperature in the LED group was in the normal range in the present study. A slightly elevated mean body temperature, which could not be defined as hyperthermia, was determined in the CFT group ($p<0.05$). The main advantage of LED phototherapy compared to CFT is less heat production. CFT phototherapy did not cause hyperthermia in spite of use of high irradiance. This favorable outcome may be explained by the effective fan system of the devices.

In conclusion, the results of this study suggest that intensive phototherapy is effective, showing a decline of half the initial value of bilirubin during the study period in infants with non-hemolytic jaundice. LED phototherapy is as effective as CFT. Intensive phototherapy, using either CFT or LED, can provide a rapid decrease in bilirubin levels in the first few hours. This rapid decline is important in cases that have a high risk of bilirubin encephalopathy.

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