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Comparison of light emitting diode phototherapy and double standard conventional phototherapy for nonhemolytic neonatal hyperbilirubinemia

Aim: To compare the efficacies and the rebound bilirubin levels of infants who received light emitting diode phototherapy and double standard conventional phototherapy.

Materials and Methods: One hundred twenty-three healthy term and near term (≥ 35 weeks) infants requiring phototherapy for non-hemolytic hyperbilirubinemia were enrolled in the study. All infants' gestational age, type of feeding, age at phototherapy, total serum bilirubin level at initiation and termination of phototherapy, duration of phototherapy, rebound TSB levels, and type of phototherapy were recorded. Fifty-four patients received double standard conventional phototherapy (Group I) and 69 patients received light emitting diode phototherapy (Group II). Rebound total serum bilirubin levels after 24-48 h were compared in both groups. Infants with rebound bilirubin values greater than or equal to concentrations before phototherapy was again exposed to phototherapy.

Results: Group I consisted of 54 patients whereas Group II included 69 patients. A decrease in bilirubin concentration occurred in all infants but was especially marked in the infants exposed to light emitting diode phototherapy. There was no significant difference in rebound total serum bilirubin levels between the groups.

Conclusions: Light emitting diode phototherapy was more effective than double standard conventional phototherapy in the treatment of non-hemolytic hyperbilirubinemia in newborns.

Key Words: Intensive phototherapy, newborn, rebound bilirubin, double conventional phototherapy

Neonatal hiperbilirübünemide yoğun fototerapi ile standart ikili konvansiyonel fototerapinin karşılaştırılması

Amaç: Yoğun fototerapi ile ikili standart konvansiyonel tedavinin etkinliğini ve rebound bilirubin düzeyine etkisini fototerapi alan yenidoğanlarda karşılaştırmak.

Yöntem ve Gereç: Hemolitik olmayan hiperbilirübünemisi olan ve gestasyonel yaşları 35 hafta ve üzerinde olan 123 bebek bu çalışmaya alındı. Bütün bebeklerin gestasyonel yaşları, beslenme şekilleri, fototerapi almaya başladıklarında kaç günlük oldukları, fototerapi başlangıcında ve bitiminde total bilirubin düzeyleri, fototerapi alma süreleri, rebound total serum bilirubin düzeyleri ve hangi fototerapi şeklini aldıkları kaydedildi. Bu hastaların 54'ü ikili standart konvansiyonel fototerapi (Grup I) almışken 69'u da yoğun fototerapi (Grup II) aldı. Her iki grupta da tedaviden 24-48 saat sonra rebound total serum bilirubin düzeyleri karşılaştırıldı. Eğer bebeklerin rebound serum bilirubin düzeyleri fototerapi öncesi bilirubin düzeylerine eşit ya da fazlaysa tekrar fototerapi verildi.

Bulgular: Grup I' de 54, Grup II' de 69 hasta vardı. Bütün bebeklerde serum bilirubin düzeyleri düşerken yoğun fototerapi alan hastalarda bu düşüş daha belirgindi. Her iki grupta da rebound serum bilirubin düzeyleri arasında fark yoktu.

Sonuç: Bu çalışmada non-hemolitik hiperbilirubinemisi olan yenidoğanlarda yoğun fototerapinin ikili standart konvansiyonel fototerapiye göre daha etkin olduğu bulunmuştur.

Anahtar Sözcükler: Yoğun fototerapi, yenidoğan, rebound bilirubin, ikili standart konvansiyonel fototerapi

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Introduction

Phototherapy is the accepted method of treating neonatal jaundice, its clinical efficacy having been confirmed in many studies (1,2). Although phototherapy is highly efficacious in the majority of infants presenting with neonatal jaundice, it is well known that phototherapy using daylight lamps is occasionally not effective, especially in cases of severe or rapidly increasing jaundice. In such situations, the use of high-intensity phototherapy to ensure greater effectiveness and a faster rate of decrement in bilirubin levels would be useful (1). Since this type of phototherapy produces a more rapid decline in the total serum bilirubin (TSB) level than conventional phototherapy, it is possible that a greater rebound might occur (3). Although intensive phototherapy has been used in Turkey since 2005, most centers do not have it. Therefore, double standard conventional phototherapy (DSCP) is the choice of treatment in severe hyperbilirubinemia in some centers to maximize the efficacy of phototherapy. However, no study in the literature has compared the efficacy of high-intensity phototherapy and DSCP. For this reason, in this study we aimed to compare efficacy in infants who received light emitting diode (LED) phototherapy and DSCP.

Materials and Methods

Patients

One hundred twenty-three healthy term and near term (≥ 35 weeks) infants requiring phototherapy for non-hemolytic hyperbilirubinemia were enrolled in the study. All infants were appropriate for gestational age (assumed to be the time measured from the first day of the mother's last menstrual cycle to the day of birth), with normal Apgar scores and normal findings on physical examination. Infants with normal blood counts and peripheral blood smears, no evidence of blood group iso-immunization, negative result of a direct Coombs test, normal reticulocyte count, and normal glucose-6-phosphate dehydrogenase activity were eligible for the study. Patients with any congenital malformation, direct hyperbilirubinemia, enclosed hemorrhage, positive

direct Coombs test, or infection were excluded. In every patient, clinical assessment of gestational age was performed using the Ballard scoring system.

Phototherapy

Criteria for phototherapy for healthy term and near-term neonates were based on those of the 1994 American Academy of Pediatrics Practice Parameter, as follows: <24 h: PTB 10 mg/dl (170 $\mu\text{mol/l}$); 24-48 h: 15 mg/dl (205 $\mu\text{mol/l}$); 49-72 h: 17 mg/dl (256 $\mu\text{mol/l}$); >72 h: 17 mg/dl (291-308 $\mu\text{mol/l}$) (4,5). All infants were exposed, completely unclothed with their eyes and genital regions covered, to continuous phototherapy, which was interrupted only for feeding, cleaning, and blood sampling. The infants' weights and temperatures were monitored. All infants' gestational age, type of feeding, age at phototherapy, TSB level at initiation and termination of phototherapy, duration of phototherapy, rebound TSB levels, and type of phototherapy were recorded. The type of phototherapy used was largely determined by the neonatal staff, who tended to prefer LED for those with rapidly increasing or with more severe jaundice and standard phototherapy for the more usual "standard" cases. Fifty-four patients received DSCP (Group I) and 69 patients received LED (Group II). In the DSCP group, 2 standard 25 W daylight fluorescent lamps and 2 special blue fluorescent lamps (Philips TL 20 W/52) were placed 35 cm over the infants and a phototherapy mattress was placed under the infants (Bilibed, Medela Medical Technology, Baar, Switzerland). Light intensity was measured by a Minolta 451 Fluoro-lite meter. The lamps were changed regularly after 2000 h of use, by which time the irradiance was 80% of the original. In the intensive phototherapy the LED system (Neoblu[®] LED phototherapy system, Natus Medical Inc. San Carlos, CA, USA, intensity: 35 $\mu\text{W/cm}^2/\text{nm}$, spectrum 450-470 nm) was used. The system was placed 30 cm over the infants. The intensity was checked every 6 months by Ohmeda Biliblanket.

Laboratory measurements

Venous blood sampling was performed at the start of phototherapy and 4 h thereafter, with the lights switched off. Phototherapy was stopped when bilirubin concentrations had decreased to <205

$\mu\text{mol/l}$ (12 mg/dl). The duration of phototherapy was recorded.

The rebound protocol included rebound bilirubin level determination 36 h (between 24 and 48 h) after the discontinuation of phototherapy. Those neonates whose post-phototherapy TSB concentrations were lower than those at the discontinuation of phototherapy were discharged from follow up. Rebound bilirubin level was measured in patients followed up for 24-48 h intervals until either stabilization or a decrease in the TSB concentrations, if repeat TSB levels $\geq 239 \mu\text{mol/l}$ ($\geq 14 \text{ mg/dl}$). Phototherapy was recommenced at the discretion of the attending neonatologist, but not usually at TSB values $< 256 \mu\text{mol/l}$ (15 mg/dl) (5). Infants with rebound bilirubin values greater than or equal to concentrations before phototherapy were again exposed to phototherapy, following the same guidelines as in the first exposure. Failure of phototherapy was defined as continued increase in bilirubin concentration in 2 consecutive determinations beyond the starting bilirubin value. The efficacy of phototherapy was assessed by the duration of phototherapy (h), and the overall decrease in bilirubin concentration related to the total exposure time.

Statistical analysis

Statistical analysis was carried out using Student's t-test and chi-square test and data are expressed as mean \pm SD.

Study ethics

The study was approved by the Fatih University Ethics Committee and was conducted in accordance with the ethical principles described by the Declaration of Helsinki. Informed consent was obtained from the infants' parents before the study commenced.

Results

Group I consisted of 54 patients (32 male and 22 female), whereas Group II included 69 patients (39 male and 30 female). There was no significant difference in age distribution between the groups ($P > 0.05$). The Table lists the clinical data and results of the patients.

All the infants remained well during and after exposure. All the infants were able to maintain normothermia during phototherapy. Increased fluid intake was needed to ensure adequate hydration in Group II. During the study 3 newborns in the DSCP group, and 2 newborns in the LED group had

Table. Clinical and laboratory data of study groups.

	Group I n = 54	Group II n = 69	P value
Gestational age, weeks	37.7 \pm 1.48	37.4 \pm 4.1	NS
Birth weight, grams	3064 \pm 416	3011 \pm 453	NS
Age at phototherapy, hours	113 \pm 26	117 \pm 38	NS
Hematocrit, at the start of phototherapy	51 \pm 6.3	52 \pm 5	NS
Reticulocyte	2.1 \pm 1.6	2 \pm 1.1	NS
TSB level at initiate of phototherapy, $\mu\text{mol/l}$ (mg/dl)	317.9 \pm 20.4 (18.7 \pm 1.2)	340 \pm 52.7 (20 \pm 3.1)	.001
After 4 h of phototherapy, $\mu\text{mol/l}$ (mg/dl)	295.8 \pm 30.6 (17.4 \pm 1.8)	301 \pm 42.5 (17.7 \pm 2.5)	NS
TSB level at termination of phototherapy, $\mu\text{mol/l}$ (mg/dl)	222.7 \pm 22 (13.1 \pm 1.3)	207.4 \pm 27.2 (12.2 \pm 1.6)	.002
Duration of phototherapy	26.6 \pm 9.3	27.5 \pm 15	NS
Rebound TSB level, $\mu\text{mol/l}$ (mg/dl)	239.7 \pm 20.4 (14.1 \pm 1.2)	233 \pm 34 (13.7 \pm 2)	NS
Breastfed exclusively, number, (%)	37(69)	49(71)	NS
Breastfed plus formula, number, (%)	17(31)	20(29)	NS

NS: Nonsignificant

transient erythema, and 2 newborns in each group had mild watery defecation not leading to dehydration. No serious complications or side effects were observed during the study.

During the study period the average spectral irradiances in the DSCP group were $18.7 \pm 0.8 \mu\text{W}/\text{cm}^2/\text{nm}$ and $30.1 \pm 5.5 \mu\text{W}/\text{cm}^2/\text{nm}$ in the LED system.

No phototherapy failure was observed during treatment in either group and phototherapy was effective in decreasing bilirubin levels in both groups, but the response was greater to the LED ($P = 0.002$). Although TSB level at the initiation of phototherapy in Group II was higher than that in Group I, duration of phototherapy was similar in the groups ($P > 0.05$). TSB level at the initiation of phototherapy in Group I was lower than that in Group II, while it was higher in Group I than in Group II at the termination of phototherapy [at the initiation and $222.7 \pm 22.1 \mu\text{mol}/\text{l}$ ($13.1 \pm 1.3 \text{ mg}/\text{dl}$) and 207.4 ± 27.2 ($12.1 \pm 1.6 \text{ mg}/\text{dl}$) $\mu\text{mol}/\text{l}$ at the termination, respectively] ($P = 0.002$). However, there was no significant difference in rebound TSB levels between the 2 groups. A decrease in bilirubin concentration occurred in all infants but was especially marked in the infants exposed to LED (Figure); by the discontinuous of phototherapy the bilirubin concentration in Group II had decreased to below the bilirubin concentration of Group I [$71.4 \mu\text{mol}/\text{l}/24 \text{ h}$ ($4.2 \text{ mg}/\text{dl}/24 \text{ h}$), $118.32 \mu\text{mol}/\text{l}/24 \text{ h}$ ($6.9 \text{ mg}/\text{dl}/24 \text{ h}$), respectively] ($P < 0.05$).

After the termination of the phototherapy, 4 newborns in the conventional phototherapy group and 6 newborns in the LED group had increased rebound bilirubin values $\geq 256 \mu\text{mol}/\text{l}$ ($15 \text{ mg}/\text{dl}$). This difference was not statistically significant but the response was greater in the LED group ($P > 0.05$).

The infants tolerated the blue light well and no behavioral difference was observed between the infants exposed to white or blue light. Feeding was well tolerated and no vomiting or irritability was observed in either group.

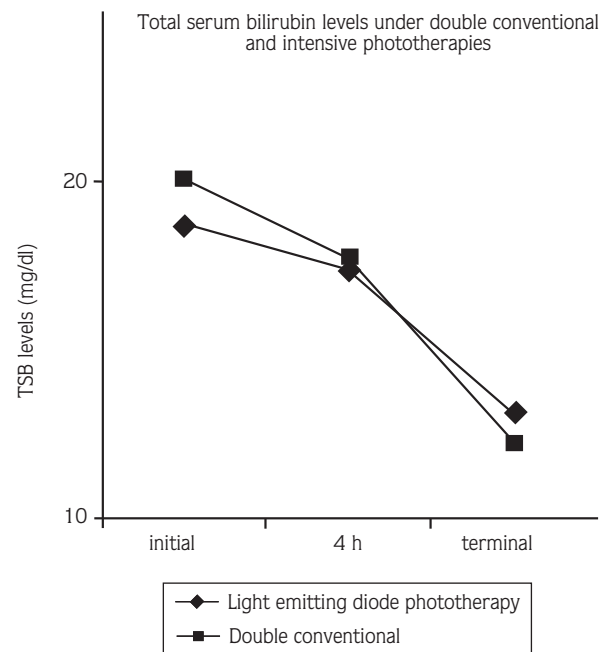


Figure. Total serum bilirubin levels under double conventional and intensive phototherapies.

Discussion

In this study of 123 infants LED was more effective than DSCP in the treatment of nonhemolytic hyperbilirubinemia. This occurred despite lower initial bilirubin levels in the DSCP group. Moreover, rebound bilirubin levels were similar in the 2 groups. There is no previously reported study that has specifically compared LED phototherapy and DSCP in the clinical setting.

The DSCP system used in our study was similar to the one used by Sarici et al. (6). They used a combination of fiberoptic phototherapy plus conventional phototherapy with a special blue light that was found to be more effective in reducing serum bilirubin levels than single conventional phototherapy. Tan et al. found DSCP very efficacious in preterm babies, and claimed that this resulted from the skin properties of preterm babies (7).

Tan et al. also demonstrated that the maximum average spectral irradiance level required to eliminate bilirubin effectively by reaching a saturation point occurs at doses of $40 \mu\text{W}/\text{cm}^2/\text{nm}$ or higher (8). Although the total average spectral irradiance of LED

was 30 $\mu\text{W}/\text{cm}^2/\text{nm}$ in our LED group, which was below the reported level, we obtained a satisfactory and safe bilirubin reduction in the given time period. Although DSCP was applied to a wider surface area, LED was more effective. The greater efficacy of phototherapy in this group was due to increases in average spectral irradiance. As the average spectral power increased consequently, it must have provided effective bilirubin elimination by causing much more lumirubin production (9).

More rebound was observed after LED, resulting in a need for re-phototherapy that was about 5 times more frequent than that in the daylight group (8). This phenomenon is probably due to the duration of LED being significantly shorter, with cessation of phototherapy occurring at a period when the rate of bilirubin accumulation was still appreciable; a level still capable of reducing the efficacy of standard daylight phototherapy ensured cessation at a later stage when the rate of bilirubin accumulation was probably already declining; hence the lower rebound and need for a second exposure. Our study showed that the post-phototherapy rebound was also mild in LED; repeat treatment for those few needing a second exposure was equally effective compared with the conventional phototherapy.

In our clinic we often prefer LED for those with rapidly increasing or more severe jaundice and standard phototherapy for the more usual "standard" cases. Therefore there was a significant difference between initial TSB levels.

There was no phototherapy failure in this study. This may be due to the non-hemolytic nature of the hyperbilirubinemia of our patients and the greater efficacy of LED lamps in this study (1,10).

We observed no acute and severe side-effects, or complications with LED. This was in agreement with the study reported by Granati et al. (11). They investigated whether high-dose phototherapy given to newborns during the neonatal period would cause any long-term negative effects on visual functions, hearing, growth, and neurological developments of patients at 6 year of age, and reported no difference between the patients receiving high-dose phototherapy and the control group receiving no phototherapy (11).

In conclusion, light emitting diode phototherapy should be considered for infants with especially severe hyperbilirubinemia. This should also be the case for those infants not responding to conventional phototherapy lamps.

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