

## Original Research Article

# Double surface light emitting diode phototherapy versus double surface compact florescent light phototherapy in neonatal non-haemolytic hyperbilirubinemia: a randomized controlled trial

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## ABSTRACT

**Background:** The aim of the study was to evaluate whether light-emitting diode (LED) phototherapy is as efficacious as compact fluorescent tube (CFT) phototherapy for the treatment of non-hemolytic jaundice in healthy term and late preterm neonates.

**Methods:** Study design was open label randomized controlled trial conducted at tertiary care NICU. Healthy term and late preterm neonates with non-haemolytic jaundice included in the present study. Intervention was double-surface LED or CFT phototherapy. Primary outcome variable was duration of phototherapy.

**Results:** A total of 60 neonates were randomized to receive LED (n=30) or CFT (n=30) phototherapy. The baseline demographic and biochemical variables were similar in the two groups. The median duration of phototherapy (Mean±SD) in the two groups was comparable (26.7±7.0) h vs (24.8±6.05) h, P=0.0.241). The rate of fall of serum total bilirubin (STB) during phototherapy in initial 6 hours was significantly more LED group (n=30), 3.43±0.65 versus (n=30) 2.22±0.55 with P-value of <0.001.

**Conclusions:** LED and CFT phototherapy units were equally efficacious in the management of non-haemolytic hyperbilirubinemia in healthy term and late-preterm neonates. Side effects were rare, comparable in the two groups and included only rash.

**Keywords:** Compact fluorescent tube, Jaundice, Light emitting diode, Neonate, Phototherapy

## INTRODUCTION

Neonatal hyperbilirubinemia is one of the most common problems in newborns. Jaundice is observed during first week of life in approximately 50%-60%.<sup>1</sup> Newborns appear jaundiced when serum bilirubin is more than 7 mg/dl.<sup>2</sup> Hyperbilirubinemia encountered during neonatal period can be physiological or pathological. Pathological jaundice may be direct or indirect type while physiological is always indirect type. Some of the

common causes of pathological jaundice are Rhesus factor (Rh) incompatibility, ABO incompatibility, polycythaemia, galactosemia, sepsis, G6PD deficiency etc.<sup>3</sup> But in more than half of cases, no cause is identified.<sup>4</sup>

Phototherapy forms the mainstay of treatment, as it is easily available and devoid of any significant side effects.<sup>5,6</sup> It is most effective in lowering serum bilirubin when wavelength of light output is in blue to green

spectrum (420 to 490). Phototherapy causes bilirubin molecules in skin to undergo photochemical reactions to form nontoxic extractable isomers which can bypass the liver conjugating system and be extracted without further metabolism.

There are various types of phototherapy devices namely using, standard fluorescent light, fibreoptic light, compact fluorescent lamps (CFL) and light emitting diodes as the light source. However, there is no standard method of delivering phototherapy. Few factors affecting efficacy of phototherapy are irradiance or the energy output of the phototherapy light, distance, surface area of neonate exposed to light and spectrum of light delivered.<sup>7</sup> Since one way of improving effectiveness of phototherapy is by exposing more of the body surface area to it; double surface phototherapy came into practice and various hospitals worldwide including ours are using the same.

Gallium nitride derived light emitting diodes (LED) which emit high intensity light of narrow wavelength spectrum and produce minimal heat have recently been used as a light source in phototherapy units. These units can be placed very close to neonate without any untoward effects. They are also durable lights with an average life of 20000 hours low infrared emission and no ultraviolet emission. These unique characteristics of LED make them an attractive light source for the optimal phototherapy unit. Although LED devices have been shown to be effective in in-vitro studies, but comparison of double surface blue CFL with double surface LED phototherapy in treatment of Hyperbilirubinemia is still less reported. This prompted us to choose this as our study topic.

## METHODS

This randomized trial was done over a period of 1-year i.e. from November 2011 to October 2012 in tertiary care NICU of Jaipur Golden Hospital, Rohini, New Delhi, India. Study was conducted on neonates admitted with non-haemolytic Hyperbilirubinemia requiring phototherapy. Requirement of phototherapy was decided on the basis of total serum total bilirubin (STB) level as per AAP guidelines.

### Technical specifications

#### CFL phototherapy

- Wavelength; 420-480 nm
- Effective surface area; 500 x 300 mm
- Lamps; 4 blue CFL (18 W) and 2 white CFL (15W) Philips
- Electrical supply- 190-240 v
- Make of bassinet; Medicaid ISO 13485:2003

#### LED phototherapy

- Effective surface area 500 x 400 mm
- Electrical supply; 220-240 v
- Lamps- 15 LED bulbs
- Make of bassinet; Medicaid.

Total of sixty neonates included thirty as study group A and thirty as study group B.

#### Inclusion criteria

Neonate who is  $\geq 35$  weeks of gestation presenting with hyperbilirubinemia.

#### Exclusion criteria

- Infants with perinatal asphyxia (Apgar score  $< 4$  at 1 minute or  $< 7$  at 5 minute),
- Onset of jaundice within 24 hours of age,
- Evidence of haemolysis (positive direct Coombs test),
- Rhesus haemolytic disease,
- Culture-positive or clinical sepsis,
- Need for exchange transfusion at the time of enrolment,
- Major congenital malformations were excluded.

Babies in study group A received double surface LED phototherapy while in neonates in group B received double surface CFL phototherapy. eyes and genitals were kept covered when under phototherapy. Repeat serum bilirubin was done after 6 hours of initiation of phototherapy and then repeated every 12 hourly. Phototherapy was stopped when two consecutive STB levels, measured 12 hours apart were less than 15 mg/dL.

Every neonate was checked for rebound bilirubin 12 hours after stopping of phototherapy. Other parameters monitored were irradiance of phototherapy units at surface of babies at the level of xiphoid by photo radiometer. Gestational age was assessed based on accurate last menstrual period and in absence of reliable records it was done with modified Ballard's score.

Enrolled infants were randomized to receive double surface LED or CFL phototherapy. Simple random table was used for randomization. The CFL lamps were replaced during the study period as and when they were visibly discoloured or were producing less light or when the irradiance fell to less than  $15 \mu\text{W}/\text{cm}^2/\text{nm}$ . The LED lamps were not changed during the study period. In both the groups, each enrolled neonate received phototherapy using double surface phototherapy units.

A distance of 25-30 cm was maintained between the baby and the bulb/lamp surface for both types of units.

### Outcome variables

The duration of phototherapy was the primary outcome. It was calculated by subtracting age at start of phototherapy from age at end of phototherapy in hours. Brief periods of discontinuation of phototherapy for feeding the baby or changing nappy were not excluded while calculating total duration of phototherapy. The secondary outcomes were failure of phototherapy, rate of fall of STB. Failure of phototherapy was defined as STB rising or becoming more than 20 mg/dL during phototherapy or exchange transfusion.

### Statistical analysis

Statistical analysis was conducted with the statistical package for social sciences system version SPSS 17.0 (Chicago, IL, USA). Continuous variables are presented as Mean±SD and categorical variables are presented as absolute numbers and percentage. The comparison of

continuous variables between the groups was performed using student's T test. Nominal categorical data between the groups were compared using Chi-squared test or fisher's exact test as appropriate. Repeated measurements (serum bilirubin) were analysed by repeated measures ANNOVA. P <0.05 was considered statistically significant.

It was decided a priori that LED will be considered equally efficacious if the difference in duration of phototherapy between two groups is less than 6 hours without any increase in adverse effects.

### RESULTS

The birth weight, gestation and other demographic variables were similar in the neonates enrolled in LED or CFL groups (Table 1). P value was not significant for any baseline characters.

**Table 1: Baseline characters of two groups.**

Parameters	LED ( n=30)	CFL (n=30)	P
Birth weight (g) (mean±sd)	2.72±0.34	2.81±0.81	0.369
Gestation (wk) (mean±sd)	37.07±1.48	37.4±1.27	0.355
Apgar at 1 min			
6	1 (3.3%)	0 (0%)	0.313
7	17 (56.7%)	17 (56.%)	1.000
8	12 (40%)	13 (43.3%)	0.793
Apgar at 5 min			
7	2 (6.7%)	3 (10%)	0.640
8	18 (60%)	19 (63.3%)	0.791
Frequency (%)			
Male sex	15 (50%)	17 (56.7%)	0.865
Gestational diabetes in mother	2 (6.7%)	0 (0%)	0.15
Mode of delivery			
Vaginal	9 (30%)	9 (30)	1.000
Cesarean	21 (70%)	21(70%)	1.000
Setting of ABO incompatibility	11 (36.6%)	9 (30%)	0.26
Exclusive breastfeeding	20 (66.6%)	21 (70%)	0.74

**Table 2: Age at onset of jaundice.**

Onset of jaundice day	Frequency	LED (N=30), %	CFL (N=30), frequency	%	P value
2	21	70	18	60	0.419
3	7	23.3	12	40	0.165
4	1	3.3	0	0	0.313
5	1	3.3	0	0	0.313
Total	30	100	30	100	
Mean ± SD	2.40±0.72		2.40± 0.50		1.000

Other baseline characters which can affect onset and degree of jaundice in neonate were considered like mode

of delivery, gestational diabetes in mother, ABO incompatibility setting, exclusive breast feeding.

All characters were comparable in both groups. out of 60 babies, 10 were low birth weight but not IUGR (<10<sup>th</sup>

centile). Out of these 7 low birth weight babies were in CFL group. Low birth was considered as below 2.5 kg.

**Table 3: Duration of phototherapy.**

	LED		CFL		P value
	Mean±sd	Min- max	Mean±sd	Min-max	
Phototherapy duration	26.7± 7.0	18-42	24.8± 6.05	18-42	0.241

**Table 4: Rate of fall serum bilirubin.**

Time for starting of phototherapy	Fall in serum bilirubin LED	Fall in serum bilirubin CFL	P value
0-6 hours	(n=30) 3.43±0.65	(n=30) 2.22±0.55	<0.001
6-18 hours	(n=30) 2.01±0.55	(n=30) 2.01±0.76	0.967
18-30 hours	(n=16) 1.73±0.31	(n=19) 2.04±0.64	0.071
30-42 hours	(n=5) 1.1±0.42	(n=4) 1.85±0.74	0.096

Age of onset of jaundice was similar in both groups as seen in table 2. Maximum babies had onset of jaundice on day 2 of life, 70% in LED group 60% in CFL group. In LED group babies mean age at which jaundice appeared was 2.4 while in CFL group it was again 2.4 days.

Mean duration of phototherapy was not statistically different in both LED and CFL group. It was 26.7±7 hours in LED group while in CFL group it was 24.8±6.05 hours with a p value of 0.241. So, LED phototherapy can be considered equally efficacious as CFL phototherapy in terms of total duration of phototherapy. As in table 4, after 6 hours of initiation of phototherapy fall in serum bilirubin was significantly more in LED group as compared to CFL group with p value<0.001. That means, this finding was not by chance and is very important

when we have to treat neonates with serum bilirubin dangerously high reaching exchange transfusion level. But it is comparable in both groups in other time slabs after first 6 hours of phototherapy.

Rebound serum total bilirubin checked after 12 hours of stopping phototherapy was similar in both groups. It was statistically also not significantly different. It was out of range of phototherapy. There was no case of failure of phototherapy. Irradiance was measured using a photo radiometer kept at the site or area on the bassinet parallel to xiphisternum of the neonate. Old lights were replaced in CFL phototherapy before stating this trial. Daily monitoring of irradiance was done to keep a check on the fall in the irradiance. The distance between light source and baby was kept same in all cases, it was about 25 cms above and 30 cms below.

**Table 5: Rebound serum bilirubin in two groups after 12 hours of stopping phototherapy.**

	LED (N=30), Mean±SD	Min-max	CFL (N=30), Mean±SD	Min-max	P value
Rebound serum bilirubin (mg/dl)	12.7±0.73	11.0-14.2	13.0±1.16	10.7-15.3	0.246

**Table 6: Irradiance of phototherapy in both groups.**

	LED (N=30), Mean± SD	Min- Max	CFL (N=30), Mean± SD	Min- Max
Irradiance (µW/cm <sup>2</sup> / nm)	68.88± 3.29	65-73	41.49±1.88	33- 44

As irradiance was significantly more in LED group with P value <0.01. This is proposed as the main reason for a faster fall in serum bilirubin in first 6 hours in LED group. Five neonates in LED group had rash and 4 in CFL group, no baby had diarrhoea or any other side effects.

**DISCUSSION**

In 2004 AAP published guidelines for the use of phototherapy. these guidelines take into consideration not only level of serum bilirubin but also the gestational age of the infant, time since birth and presence or absence of

risk factors, including iso immune haemolytic anemia, asphyxia, lethargy, temperature, instability, sepsis, acidosis and hypoalbuminemia.

In this study authors selected patients who did not have most of the above-mentioned risk factors and were of gestational age  $\geq 35$  weeks. It was done to minimize the bias in the result regarding efficacy of phototherapy as haemolytic jaundice could have resulted in failure of phototherapy. Neonates were similarly selected in study by Kumar P et al, the mean birth weight and gestation enrolled and excluded neonates were comparable.<sup>8</sup>

Clinical studies have shown that five major factors influence the dose and efficacy of phototherapy. these are spectrum of light emitted, irradiance of light source, design of phototherapy unit, surface area of infant exposed to light, distance of infant from light source.<sup>9</sup>

Ennever et al, compared different phototherapies emitting light in different spectra and found that blue light have maximum effect in vitro, by measuring the production of lumirubin, the structural isomer of bilirubin and rate of fall of bilirubin was greatest with the special blue lamps which he attributed to intensity of irradiation falling within bilirubin absorption band.<sup>10</sup>

Shankaran S in USA, Sarici et al, in Turkey, Nuntnarumit P in Thailand, Bonnyaritpong P in Thailand all concluded in their studies that double surface phototherapy is more effective than the single surface phototherapy and found no side effects of the same, except increase in body temperature after 24 hours of double surface phototherapy by Boonyarittipong P.<sup>11-14</sup>

There is no 'standard' recommended method of administering phototherapy and a variety of strategies have been followed by different researchers.

Meisels et al, did a randomized controlled trial in neonates  $\geq 35$  weeks gestation for Hyperbilirubinemia using a LED prototype device. In this study, they in control and treatment group distance between phototherapy and neonate was adjusted to provide an irradiance of approximately  $40 \mu\text{W}/\text{cm}^2/\text{nm}$ , similar in both groups. Rate of fall in serum bilirubin and duration of phototherapy was same in both groups.<sup>15</sup>

In our study distance between phototherapy units and neonate was kept similar but irradiance differed significantly. It was statistically more in LED group. But it was in intensive phototherapy range in both groups ( $>30 \mu\text{W}/\text{cm}^2/\text{nm}$ ).

In study by Kumar P et al, which compared single surface LED versus single surface CFL phototherapy in a similar population as ours, rate of fall in serum bilirubin and duration of phototherapy didn't differ significantly.<sup>8</sup> While in our study, rate of fall of serum bilirubin in first 6 hours was significantly more in LED group though

duration of phototherapy was similar in both groups. This can be attributed to more irradiance in LED group and also use of double surface phototherapy while Kumar P et al, used single surface. Significantly more rate of fall in serum bilirubin in first 6 hours of initiation of phototherapy in LED group can be explained by the fact that because phototherapy works on bilirubin present in skin and superficial subcutaneous tissue, the more bilirubin present at those sites (i.e. the higher the serum bilirubin level), the more effective phototherapy will be. So as the bilirubin levels were high in both the groups, there is more rapid fall in initial hours in both the groups with LED group showing statistically better fall in serum bilirubin when compared to CFL group due to higher irradiance.

Phototherapy is associate with side effects like dehydration, loose stools, rash and temperature instability. Apart from rash no other side effect was observed in this study. It also was comparable in both groups. There was no significant rebound in serum bilirubin in our study and no case of failure of phototherapy too. Since authors were using a relatively new LED system, we enrolled relatively low risk population. Whether LED will be similarly effective in haemolytic jaundice is not known. The efficacy of phototherapy is affected by initial serum bilirubin level, body area exposed and spectral irradiance. Authors kept LED light source at relatively large distance to match with CFL. As LED lights do not produce heat, they can be kept much closer to body without causing hyperthermia. Limitations of study was the sample size was small and population of study didn't cover haemolytic jaundice.

### **Recommendation**

LED phototherapy is as good as CFL phototherapy when kept at same distance. LED phototherapy causes faster fall in serum bilirubin in initial hours, hence can be used as first choice when serum bilirubin is dangerously approaching exchange transfusion level.

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