A Prospective Randomized Controlled Study of Phototherapy Using Blue LED and Conventional Phototherapy in Neonatal Hyperbilirubinemia

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ABSTRACT:

BACKGROUND:

High intensity light emitting diodes (LEDs) are being studied as possible light sources for the phototherapy of neonatal jaundice, as they can emit high intensity light of narrow wavelength band in the blue region of the visible light spectrum corresponding to the spectrum of maximal bilirubin absorption. We used a new blue gallium nitride LED phototherapy unit with high intensity, and compared its efficacy to commercially used halogen quartz phototherapy device. The prototype device with two focused arrays, each with 20blue LEDs, generated greater irradiance than the conventional device tested.

OBJECTIVE:

To determine the efficacy of blue LED light versus conventional phototherapy lamp in treatment of neonatal jaundice.

PATIENTS AND METHODS:

A total of 101 jaundiced otherwise healthy, term and preterm neonate who had hyperbilirubinemia were prospectively randomized to either LED (n=57) or conventional phototherapy (n=44). Entry criteria to phototherapy followed the American Academy of Pediatrics' Practice Parameter.

RESULTS:

One hundred and one neonate were included in this study , the mean rate of TSB lowering increase with increase age was significant in LED group (p value =0.000), according to the maturity the mean rate of TSB lowering increase with increase age also was significant in LED group (p-value= 0.000), no significant correlation was found in regarding birth weight and rate of lowering of TSB (P=0.263),there where a significant correlation between mean rate of TSB lowering and initial TSB level in LED group(P-value= 0.000)and lastly there was a significant higher rate of lowering of TSB in LED group than those with conventional one.

CONCLUSION:

A blue LED phototherapy unit showed higher efficacy in bilirubin photodegradation compared to that of commercially used halogen quartz phototherapy device. And a significant correlation between the rate of lowering of TSB and each of (age, maturity , weight and initial TSB level) in the two groups. Additional studies will be necessary to prove its clinical efficacy.

***KEY WORDS*:** neonatal, jaundice, phototherapy.

INTRODUCTION:

Although phototherapy has been used for the treatment of neonatal jaundice for more than 4 decades, the most efficacious phototherapy method with the least side effects has not been developed yet [1,2,3].

Its efficacy is dependent on the color (wavelength) and intensity (irradiance) of the light emitted during phototherapy, the exposed body surface area, and the duration of exposure [2, 4,5,6].

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The currently available phototherapy devices such as fluorescent tubes, halogen spotlights and fiberoptic blankets have many disadvantages including high heat production and unstable broad wavelength light

In cases of severe or rapidly increasing neonatal jaundice, it is important to institute intensive phototherapy to decrease the bilirubin levels as soon as possible to reduce the need for exchange transfusion and the risk of kernicterus [9-11].

However, conventionally used phototherapy may be less effective, thereby increasing the risk of bilirubin-induced neurotoxicity [2, 4, 11].

Recently, high intensity gallium nitride light emitting diodes (LEDs) have been developed [12, 13], and studied as possible light sources for the phototherapy of neonatal jaundice[14].
Blue LEDs emit a high intensity narrow band of blue light overlapping the peak spectrum of bilirubin breakdown [14], resulting in potentially shorter treatment times [15, 16].
LEDs are also power efficient, light in weight, produce less heat, and have a longer lifetime [12,13,14].These unique characteristics of LEDs make them very optimal light sources for phototherapy devices.
Despite these potential benefits and substantial versatility of this device, two recent clinical trials of blue gallium nitride LED were not found to be of higher efficacy when applied using relatively low irradiances levels [17, 18].
These results suggest that besides the color (wavelength), the dose (irradiance) of light is also very important in determining the effectiveness of phototherapy [2,4,5,6,16].
As LED devices could generate significantly higher light irradiance levels compared to all currently available conventional phototherapy units [14], much higher irradiance levels are likely to be used clinically in the future.
So light therapy is used to treat cases of neonatal jaundice through isomerization of bilirubin and consequently transformation into compound that the newborn can excrete via urine and stools.
A common treatment of neonatal jaundice is the bili light

Figure:1

Anew born infant treated with white light phototherapy

Figure2 :

Blue LED phototherapy device.

Figure 3: Conventional halogen phototherapy device

OBJECTIVE:

- to compare, at similar light intensities, through efficacy of narrow spectral band blue gallium nitride LED light versus conventional halogen quartz phototherapy lamps.
- to test the efficacy of using phototherapy devices with a very narrow wave length band.
-to find out any significant correlation between the rate of lowering of TSB and each of (age, maturity , weight and initial TSB level) in the two groups.

PATIENTS AND METHODS:

This study was conducted in the period from May 2011 through October 2012 at AL-Khansaa teaching hospitals in Mosul.
A total of 101 jaundiced otherwise healthy, term and preterm neonate who had hyperbilirubinemia were prospectively randomized to either LED (n=57) or conventional phototherapy (n=44). Entry criteria to phototherapy followed the American Academy of Pediatrics' Practice Parameter.(See below)
Phototherapy was discontinued when at least two consecutive total serum bilirubin (TSB) measurements showed no increase in TSB levels.
The gallium nitride LED phototherapy overhead device was developed with two focused arrays, each with 5 blue LEDs, generated an irradiance of >200 and had a peak wavelength at 450 nm and a half-spectral width of 22 nm with a 151 half-angle directivity.
Conventional phototherapy was administered to the control group according to our usual nursery protocol using standard phototherapy units
We placed the LED devices at a distance of 65 cm from the patients that provided light intensity within the measured limits of our conventional phototherapy device, that is, 5–8 mW/cm2/nm.
The neonate were weight and all investigated for TSB at start and after 4-6 hs, retics count, serial hematocrite measurements , blood group and Rh placed in open cribs and adequately hydrated with IV fluid and oral feeding unclothed except for a diaper, and with their eyes covered.
All infants were breast-fed, with only occasional formula supplementation. TSB was determined in heel stick capillary blood when the newborn appeared clinically jaundiced, and the test was repeated every 4 to 6 hours. The mean TSB at initiation of treatment did not differ between two groups.
The decision on discontinuation of treatment was made every 4 to 6
hours based on the TSB levels. The TSB was measured using a
Unistat Bilirubinometer (AO Scientific Instruments, Buffalo, NY) by
determining absorbancy at 460 nm.

RESULTS:

Table1: The ages of patients and mean rates of TSB lowering.

Age in days	No. patients	Conventional phototherapy Mean ±SD of TSB lowering(mg/dl/6hs)	No. of patient	LED phototherapy Mean ± SD of TSB lowering(mg/dl/6hs)
1day		-----------------	3	0.38± 0.002
2days	2	0.2± 0.05	7	0.34± 0.022
3days	6	o.28± 0.02	8	0.55± 0.07
4days	9	0.26± 0.03	10	0.53± 0.05
5days	7	0.179± 0.05	11	0.5± 0.09
6days	4	0.29± 0.016	6	0.78± 0.11
7days	4	0.13± 0.005	5	0.4± 0.06
>7days	12	0.16± 0.04	7	o.63± 0.1
Total	44		57	

t= -5.111 P= 0.000 significant

Table 2: The correlation between maturity and rate of lowering of TSB.

Age of patients in weeks	No. patients	Conventional phototherapy Mean ±SD of TSB lowering(mg/dl/6hs)	No. of patient	LED phototherapy Mean ± SD of TSB lowering(mg/dl/6hs)
28- 30	1	0.18± 0.045	4	0.38± 0.002
30 – 32	3	0.19± 0.05	7	0.34± 0.022
32 – 34	5	o.279± 0.02	8	0.54± 0.07
34 – 36	8	0.27± 0.03	10	0.53± 0.05
36 – 38	8	0.18± 0.05	11	0.49± 0.09
38 – 40	3	0.28± 0.016	6	0.78± 0.11
40- 42	5	0.14± 0.005	5	0.4± 0.06
>42	12	0.16± 0.04	6	o.63± 0.1
Total	45		56	

P- value = 0.000 significant

Table 3: Weight of neonates and mean TSB lowering.

Weight in Kg	Conventional		LED	
	No.	Mean ±SD of TSB lowering(mg/dl/6hs)	No.	Mean ±SD of TSB lowering(mg/dl/6hs)
≤1	---	-----------	1	0.56
>1 to ≤1.5	6	0.19 ±0.006	2	0.46± 0.2
> 1.5 to ≤2	10	0.16± 0.006	1	0.8±
> 2 to ≤ 2.5	2	0.16± 0.001	9	0.5± 0.17
> 2.5 ≤3	10	0.21± 0.011	6	0.78± 0.074
> 3	18	0.19± 0.021	36	0.45± 0.048
Total No.	46		55	

t= 1.12 P= 0.26 not significant

Table 4: Initial TSB level and mean rate of lowering

Initial TSB(mg/dl)	Conventional		LED	
	No.	Mean ± SD of TSB lowering(mg/dl/6hs)	No.	Mean ±SD of TSB lowering(mg/dl/6hs)
≤ 10	9	0.2± 0.003)	4	0.33± =0.03
>10 to ≤15	15	0.19± 0.005	10	0.35± 0.033
>15 to ≤20	16	0.18± 0.004	25	0.42±0.04
>20	5	0.28± 0.03	17	0.72± 0.06
Total no.	45		56	

t = -6.92 P=0.000 significant

Table 5: The rate of lowering in both groups.

nventional Phototherapy		Blue LED Phototherapy	
No.	Mean ± SD of TSB lowering(mg/dl/6hs)	No.	Mean ±SD of TSB lowering(mg/dl/6hs)
45	0.19± 0.003)	56	0.52± =0.005

T= -3.087 p-value 0.003 significant

One hundred and one neonate were studied, the mean rate of lowering of TSB after 4 hrs from onset of phototherapy was 0.45 mg/dl in 4 hours
The rate of lowering was from 0.13to 0.9 mg/dl in 4 hours.
The percentage of lowering ranged from 13% to

53% of initial TSB in 4hrs with the mean being 45 % in 4hrs.
According to maturity the patients were divided into two groups full term and preterm(gestational age <37 wks
The full term were (70%) and preterm were (31%)
The mean rate of lowering of TSB in full term was 0.4mg /4hrs while in preterm baby it was 0.433mg/4hrs.
The mean ±SD gestational age (weeks)was 36.7±0.6 for the LED group,
36.33±0.9For conventional group.
The mean ±SD postnatal age at initiation of treatment was 5.7±0.8 for the LED group and 6.7±0.7 for the conventional group.
A statistical significant difference were found for characteristic of infant including birth weight and initial TSB as well.
As in table 1 there are 8 groups of patients according to the age with different mean rates of total serum bilirubin lowering , its shown that the mean rate of TSB lowering increase with increase age the p value 0.000 was significant.
In table 2 there are 8 groups of patients according to the maturity with different mean rates of total serum bilirubin lowering , its shown that the mean rate of TSB lowering increase with increase age the p- value= 0.000 was significant
In table 3 the patient were divided in to 6 group according to the weight. the mean rate of TSB lowering increase with increase weight but there is no significant correlation between these two variable .
P=0.263
In table 4 we divided patients into 4 groups according to the TSB level at the beginning of phototherapy, there were different mean rate of TSB lowering which were increasing with increase initial TSB, P-value= 0.000 significant.
Table 5 shows the rate of lowering in both group ,there were a difference in mean rate of lowering in which the rate of lowering in those group whose treated with LED phototherapy was much higher than those treated with conventional one ,p-value= 0.003 which is significant.
Regarding all characteristics; age , birth weight ,initial TSB level (table 1,2,3)
The blue LED phototherapy unit showed higher efficacy of bilirubin photodegradation compared to the conventional phototherapy device.
No side effects such as erythema ,were noted in any of newborns. the nurses who cared for the infants did not complain from dizzeness or nausea when caring for the babies under the blue LED light

DISCUSSION :

In the present study the new device (LED phototherapy)was more effective than conventional halogen phototherapy. LEDs achieved the greatest initial absolute reduction in TSB but were similar to hallogen in the other performance measures(weight) this is similar to that found by Morris BH[21]
More rapid break down of bilirubin with the use of more efficient LED phototherapy device would shorten the treatment time of neonatal jaundice[15 , 16] and ultimately improve the prognosis of sever neonatal hyperbilrubinemia by reducing the need for exchange transfusion and minimized the risk of neurotoxicity[2,4,11].however Kumar P and Tridente A found that LED light source phototherapy is efficacious in bringing down levels of serum total bilirubin at rates that are

similar to phototherapy with conventional (compact fluorescent lamp (CFL)
or halogen) light sources with haemolytic jaundice or in the presence of severe hyperbilirubinaemia (STB≥20 mg/dL) [22,23].
The color wave length and intensity of light emitted during phototherapy are two major factors determining its efficacy this was similar to was found by Bhutani VK were the intensity and spectral output of phototherapy devices is useful in predicting potential effectiveness in treating hyperbilirubinemia [2,4,6,24].
Blue LED's used for light sources of phototherapy in the present study would be more effective because they emit a high intensity narrow band of blue light corresponding to the peak absorption wave length at which bilirubin broken down [14].
Additional studies will be necessary to prove clinical efficacy

REFERENCE:

1. McDonagh AF. :Phototherapy from ancient Egypt to the new millennium.J Perinatol 2001;21: S7-12.
2. Maisels MJ.: Phototherapy-traditional and nontraditional. J Perinatol 2001; 21: S93-97.
3. Hansen TW. :Phototherapy for neonatal jaundice- still in need of fine tuning. Acta Paediatr 2000; 89: 770-72.
4. Maisels MJ. :Why use homeopathic doses of phototherapy? Pediatrics1996; 98:283-87.
5. Tan KL. :The nature of the dose-response relationship of phototherapy for neonatal hyperbilirubinemia. J Pediatr 1977;90: 448-52.
6. Modi N, Keay AJ. :Phototherapy for neonatal hyperbilirubinemia:The importance of does. Arch Dis Child 1983;58:406-9.
7. Ente G, Klein SW. :Hazards of phototherapy. N Engl J Med 1970;283: 544-5 .
8. Christensen T, Reitan JB, Kinn G. :Single-strand breaks in the DNA of human cells exposed to visible light from phototherapy lamps in the presence and absence of bilirubin. J Photochem Photobiol B 1990;7:337-46.
9. Kang JH, Shankaran S. :Double phototherapy with high irradiance compared with single phototherapy in neonates with hyperbilirubinemia. Am J Perinatol 1995;12:178-80.
10. Hansen TW. :Acute management of extreme neonatal jaundice-the potential benefits of intensified phototherapy and interruption of enterohepatic.circulation. Acta Paediatr 1997; 86: 843-46.
11. Tan KL, Lim GC, Boey KW. :Efficacy of high intensity blue light andstandard daylight phototherapy for non-haemolytic hyperbilirubinemia.Acta Paediatr 1992; 81: 870-4.
12. Nakamura S, Fasol G. InGaN :single-quantum-well LEDs In The Blue Laser Diode. Berlin: Springer-Verlag, 1997; 201-21.
13. Fasol G. :Longer life for the blue laser. Science 1997;278:1902-3.
14. Vreman HJ, Wong RJ, Stevenson DK,et al. :Light-emitting diodes: A novel light source for phototherapy. Pediatr Res 1998;44:804-9.
15. Ennever JF, McDonagh AF, Speck WT. :Phototherapy for neonatal jaundice: Optimal wavelengths of light. J Pediatric1983;103:295-99.
16. Ennever J. Blue light, green light, white light, more light: Treatment of neonatal jaundice. Clin Perinatol 1990;17:467-81.
17. Seidman DS, Moise J, Ergaz Z, et al:A prospective randomized controlled study of phototherapy using blue and blue-green light-emitting devices, and conventional halogen-quartz phototherapy. J Perinatol 2003;23:123-27.
18. Seidman DS, Moise J, Ergaz Z, Laor A, Vreman HJ, Stevenson DK, Gale R. A new blue light-emitting phototherapy device: a prospective randomized controlled study. J Pediatric 2000;136: 771-74.
19. Tan KL. :The pattern of bilirubin response to phototherapy for neonatal hyperbilirubinaemia. Pediatric Res 1982;16: 670-74.
20. Newman TB ,Kuzniewic3 MW,Liljestrand P, :"Numbers needed to treat with phototherapy according to American Academy of pediatrics guidelines.pediatrics 2009;123:1352-59.
21. Morris BH, Tyson JE, Stevenson DK, et al. :Efficacy of phototherapy devices and outcomes among extremely low birth weight infants: multi-center observational study. J Perinatol 2013; 33:126.
22. Kumar P, Chawla D, Deorari A. :Light-emitting diode phototherapy for unconjugated hyperbilirubinaemia in neonates. Cochrane Database Syst Rev 2011:CD007969.
23. Tridente A, De Luca D. Efficacy of light-emitting diode versus other light sources for treatment of neonatal hyperbilirubinemia: a systematic review and meta-analysis. Acta Paediatr 2012; 101:458.

24. Bhutani VK, Committee on Fetus and Newborn, American Academy of Pediatrics. Phototherapy to prevent severe neonatal hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. Pediatrics 2011;128:e1046.