ECUADORIAN JOURNAL OF PEDIATRICS
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ORIGINAL ARTICLE

Light-emitting diode (LED) versus fluorescent lamp phototherapy: A quasi-randomized clinical study.

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Received: January 9, 2020
Accepted: March 21, 2020
Published: Abril 30, 2020

Bibliographic letterhead:

Villarreal J, Vélez-Pinos P. Light-emitting diode (LED) versus fluorescent lamp phototherapy: A quasi-randomized clinical study. Rev. Ecuat. Pediatr. 2020;21(1). Article Number 2. Pages:1-10.

ABSTRACT

Introduction: It has been established that phototherapy with LED technology is more effective than conventional phototherapy to treat neonatal hyperbilirubinemia by reducing the number of hours of treatment required in term and preterm newborns. The objective of this study was to carry out a randomized clinical study with three types of lamps, including a prototype.

Methods: This was a clinical study with a parallel design of three groups, including newborns in need of treatment for hyperbilirubinemia, admitted to the Neonatology Unit of the "Homero Castanier Crespo" Hospital in Azogues-Ecuador. The newborns were divided into three groups: Phototherapy with a fluorescent lamp (Group 1, G1); commercialized LED phototherapy (Medix®, Mediled®) (Group 2, G2); and with prototype LED phototherapy (Group 3, G3). The bilirubin concentration and the mean difference of its reduction in each group were measured to demonstrate non-inferiority.

Results: The weight in G1 (n = 30) was 3050 ± 134 g, in G2 (n = 30) was 3200 ± 186 g, and in G3 (n = 30) was 3034 ± 234 g (P = 0.70). The gestational ages were 39 ± 1 weeks in G1, 39.1 ± 1.1 weeks in G2, and 39 ± 1.1 weeks in G3 (P = 0.80). Bilirubin levels were 15.8 ± 6.2 in G1, 14. 93 ± 5.9 in G2, and 15.62 ± 5.9 mg/dl in G3 (P = 0.60). The differences in bilirubin (Delta 1) pre-treatment and at 24 h of treatment were -2.4 mg/dl in G1, -2.4 mg/dl in G2, and -2.25 mg/dl in G3 (P = 0.60). Delta 2 at 48 h was -4.5 mg/dl in G1, -4.26 mg/dl in G2, and -4.42 mg/dl in G3 (P = 0.62).

Conclusion: The three treatments demonstrated non-inferiority in the treatment of neonatal hyperbilirubinemia.

Keywords: PUVA therapy, Phototherapy, Newborn, Neonatal Hyperbilirubinemia

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INTRODUCCTION

About 50% of full-term newborns and 80% of premature infants develop jaundice, which usually appears between 2 and 4 days of life. Jaundice is caused by the presence of bilirubin on the skin. High levels of unconjugated bilirubin can cause neurotoxicity with acute or chronic encephalopathy, manifesting clinically as developmental delay, deafness, and seizures[1].

Phototherapy is the treatment of choice to reduce the severity of neonatal hyperbilirubinemia, regardless of its etiology[2]. Phototherapy reduces bilirubin levels, transforming bilirubin into water-soluble isomers that can be eliminated in the urine unconjugated in the liver[3].

The implementation of a phototherapy system requires a technical framework that conforms to existing evidence-based guidelines that promote its safer and more effective use.

The optimal use of phototherapy has been defined by specific ranges of total serum bilirubin thresholds, adjusted for the age of the newborn (in hours) and the potential risk of neurotoxicity from bilirubin[2].

The efficacy of phototherapy in the treatment of hyperbilirubinemia might be influenced by the wavelength of light used, the intensity of the light source, and the total light dose received (phototherapy time, percentage of exposed skin)[3].

For effective phototherapy, it is recommended to use light in specific blue light wavelengths (maximum emission, 450 ± 20 nm) and emission spectrum (range, 400–520 nm), preferably in a narrow bandwidth that is administered at an irradiance of ≥30 μW/ cm^2/nm up to 80% of the child's body surface[2]. These recommendations, however, are often not feasible in clinical settings with limited resources. Therefore, phototherapies often use their own configuration. These, however, must meet established standards to achieve the ultimate goal: avoiding neurotoxicity.

The costs of providing special neonatal care for newborns with jaundice could be prohibitive in low-resource countries. The World Health Organization maintains a valuable compendium of low-cost and innovative technologies, including recommended phototherapy devices for middle-income countries. Whatever the light source, the effectiveness of phototherapy devices can be compromised by erratic energy supply, inadequate skin exposure from overcrowding with multiple babies placed under a single device, suboptimal irradiance levels, and poor device maintenance[4]. However, the development of affordable and inexpensive phototherapy devices, as well as simple measures, such as monitoring light intensity, changing bulbs and cells regularly, and reducing the distance between the child and the lamps, can improve the effectiveness of phototherapy[5].

Fluorescent tubes or halogen lamps have been used as light sources for phototherapy for many years. A light-emitting diode (LED) is a newer type of light source that is energy efficient, has a longer life, is portable with low heat production, and is as effective as other light sources in lowering hyperbilirubinemia. The advantages of LEDs are especially relevant for low- and middle-income countries like Ecuador[6].

In several studies addressing the efficacy of LED phototherapy compared to conventional (non-LED) phototherapy, conventional LED phototherapy has been shown to be effective in reducing serum total bilirubin levels at rates similar to light source phototherapy[7].

A prospective study in term neonates comparing the effectiveness of conventional versus LED phototherapy showed that the mean duration of phototherapy in the LED group was significantly shorter than in the conventional phototherapy group (10 h). Similarly, the rate of fall in serum bilirubin levels at 6, 12, and 18 h was significantly higher in the LED group than in the conventional group. The need for exchange transfusion was lower in the LED group[8].

It has been established that phototherapy with LED technology is more effective than conventional phototherapy at reducing the number of hours of treatment required in term and preterm infants.1 In this regard, in a study conducted in preterm infants (between 33 and 36 weeks of pregnancy), LED light devices have been shown to be more effective than fluorescent tube phototherapy at reducing indirect hyperbilirubinemia. The lower frequency of adverse events, less energy consumption, and lower cost of therapy are also considered[9].

One of the ways to evaluate the effectiveness of phototherapy is to monitor the level of irradiance, an unusual practice in neonatology units. In a study conducted in 2016, irradiance levels (µW/cm2/nm) were measured weekly using the BiliBlanket (®) II Meter device in fluorescent tube phototherapies and LED phototherapies over a period of 19 weeks.

The LED fixtures showed stable irradiance levels that did not require changing any lamps. Of the conventional devices, all decreased their irradiance and required a complete lamp change in 5–6 weeks[10].

The phototherapy system constituted with LED technology originated due to the current needs of different health units with neonatal patients. At the moment, phototherapy lamps with blue fluorescent tubes are still used, which are not easily found on the market with the necessary technical characteristics. This situation led to the study and development of a phototherapy lamp that meets the demands of the treatment for jaundice.

Therefore, the final objective of this work was to develop a prototype of a phototherapy lamp with LED technology that complies with the irradiance standards established worldwide, that guarantees an effective treatment for neonatal hyperbilirubinemia, and that is of a lower cost than industrially commercialized LED devices. The hypothesis of the study was that the new prototype reduces bilirubin levels in the same intensity as the standard light in a group of neonates.

POPULATION AND METHODS

Study design

The present clinical study has a three-group parallel design, with an allocation ratio of 1:1:1.

There were no changes to the methods after the start of the trial.

Participants

The eligibility criteria were newborn patients admitted to the Neonatology Phototherapy Unit of the Homero Castanier Crespo Hospital in the city of Azogues, Ecuador, with a need for phototherapy treatment for neonatal hyperbilirubinemia. Premature, underweight patients or those with any concomitant pathology that conditions the elevation of bilirubins were excluded.

Interventions

Three types of interventions were carried out: Group 1 underwent fluorescent tube phototherapy; Group 2 underwent phototherapy with a commercialized LED lamp (Medix®, Mediled®); and Group 3 underwent prototype LED phototherapy.

Figure 1. Standard Nursery with Prototype Lamp

The patients were placed in standard 60 × 30 cm cribs, and the lamp was at a distance of 50 cm from the bed,

focusing in all cases on the entire newborn bed. All newborns wore eye protectors (**Figure 1**).

Prototype LED Phototherapy

The prototype LED lamp has an AC–DC power supply, a control system made up of a microcontroller, and as a light source, a plate with high-power LEDs, and blue color that emits a light spectrum between 440 and 500 nm that covers an exposure range of 140°.The adequate separation between each of the LEDs and their correct luminous flux distribution was calculated using the following equation:

$$E(\theta) = \frac{\Phi_{LED} \cos\theta}{\pi d^2}$$

To have a correct distribution of the luminous flux and in accordance with the calculations made, it was determined that our board requires 375 LEDs. The LEDs were distributed in a 25 × 15 matrix, and this, in turn, was divided into five sub-matrices of 5 × 15 for the correct control of the excitation of each of the LEDs, schematically represented in **Figure 2**.

The control of the prototype is commanded by the 16F628 microcontroller, and at each of its outputs, it feeds each sub-matrix of LEDs, made up of groups of controllers of the ZXLD1360 type. The control system is linked and calibrated with the five subarrays suppling 460-nm light.

At various distances, the prototype LED lamp emits optimal levels of irradiance (≥ 30 μW/cm2/nm) necessary for the reduction of bilirubin levels, thus complying with internationally established standards.

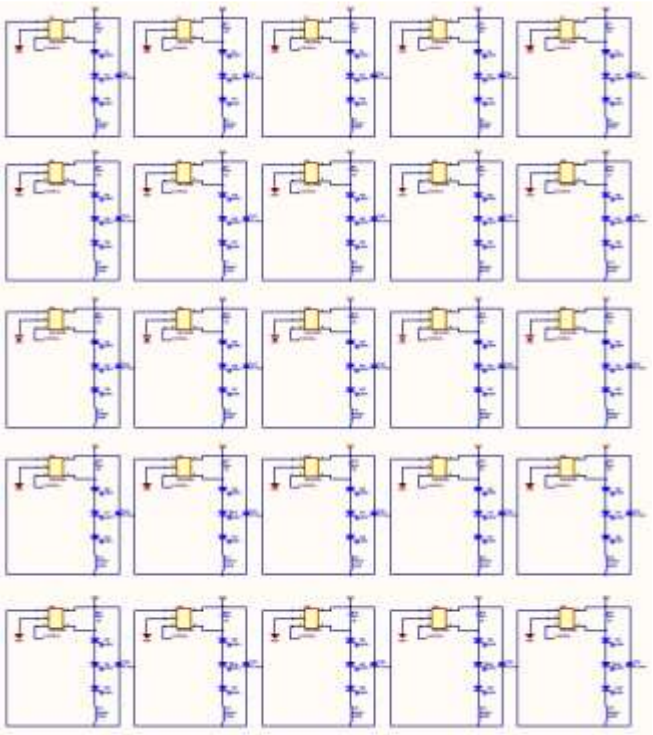
Prototype equipment calibration and safety

The equipment was calibrated by measuring its spectral irradiance. A photometer was used to measure the intensity of the light wave in each treatment. With this, it was ensured that the equipment provides > 30 micro W/cm² nm at any distance from the location of the lamp (table 1). The use in this study was 50 cm from the newborn's bed. The lamp does not emit heat from the LED light.

Table 1. Prototype equipment calibration measurement.

Source distance (cm)	Spectral irradiance (micro W / cm² nm)
20	95
30	74
40	55
50	40
60	33

Figure 2. Schematic representation of 5 x 15 matrix



Results measurement

The main results were the differences in bilirubin decrease pre-treatment and at 24 h (Delta 1) and the difference at 48 h (Delta 2) in each study group. To measure clinical efficacy, the time that patients required phototherapy to reduce their bilirubin levels to levels that did not cause the risk of neurotoxicity was additionally compared based on the recommendations of the American Academy of Pediatrics. Additionally, the adverse effects of the use of the lamps were recorded as skin lesions.

Sample size

The sample was probabilistic, and we used the annual admission data to the Neonatology Unit of 500 patients. For the sample calculation, the average annual admission of children to the Neonatology Unit was taken into account, considering that 10% of admissions of term neonates without concomitant pathology develop clinically significant jaundice, with a margin of error of 5% and with a level of 90% confidence. The study included 90 patients, with 30 patients distributed to each type of phototherapy.

Randomization

Sequence generation

Assignment blocks were established for a 3-arm study; the block size was six cases; equal numbers were included in each block for the assignment to treatments A, B, and C until 90 cases were completed. An online program (https://es.calcprofi.com/generador-de-numeros-aleatorios.html) was used to generate the sequence.

Sequence Concealment Mechanism

The mechanism used to hide the sequence was containers (folders) that contained the blocks until they were assigned to the interventions.

Implementation

The sequence was generated by the JVA investigator, PVP enrolled the participants and assigned the participants to the interventions.

Blinding

Blinding was partial because the members of the neonatology team (nurses and aides) knew which patient received each treatment. The participants' tutors did not know the type of treatment assigned.

Statistical methods

Means are compared between the groups; the differences in means are compared between the average days of stay and the average reduction of bilirubin in plasma at 24 and 48 h after admission (Deltas 1 and 2 respectively). The averages are compared with ANOVA. Differences (Deltas) of bilirubin decrease before and after treatment in each group were compared. The statistical intention is to demonstrate the non-inferiority of the treatment compared to the standard. The statistical package SPSS 20.0 for PC was used.

Ethics committee approval

The protocol was approved by the Institutional Ethics Committee, and prior approval of the protocol was given by the Headquarters of the Neonatology and Institutional Maintenance.

It was ensured that each patient received the appropriate treatment without affecting or impairing their physical integrity. Patients received standard additional treatment, such as oral nutrition, hydration, and antibiotic therapy (if required), which was not the object of the study.

RESULTS

The flow of participants is represented in **Figure 3**. Ninety cases were randomized into three groups. The patients were admitted to the study of the institution's neonatology unit. There were 30 neonates in each group.

Baseline data

Table 2 summarizes the clinical characteristics of the participants. In all groups, the average weight was 3000 to 3200 g, with a gestational age of 39 weeks. The hours of life upon admission to phototherapy were 60 to 70 h. The average stay was around 2 days in the three groups. No statistical differences were found between the baseline characteristics of the groups.

The phototherapy values with which the patients were admitted into the three groups are summarized in Figure 4. It shows that in the commercialized LED phototherapy group, the values are in the range of 22 to 7 mg/dl; in our self-made phototherapy, they are 22 to 10 mg/dl; and in the fluorescent tube lamps, they are 21 to 10 mg/dl.

Main results

The differences of bilirubin (Delta 1) pre-treatment to bilirubin concentration at 24 h of treatment were -2.4 mg/dl in Group 1, -2.4 mg/dl in Group 2, and -2.25 mg/dl in Group 3 (P = 0.60). The differences in bilirubin at 48 h of treatment (Delta 2) were -4.5 mg/dl in Group 1, -4.26 mg/dL in Group 2, and -4.42 mg/dl in Group 3 (P = 0.62). No light burn injuries were recorded in any of the groups (**Table 3 and Figure 4**).

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Figure 3. Flowchart of study participants.

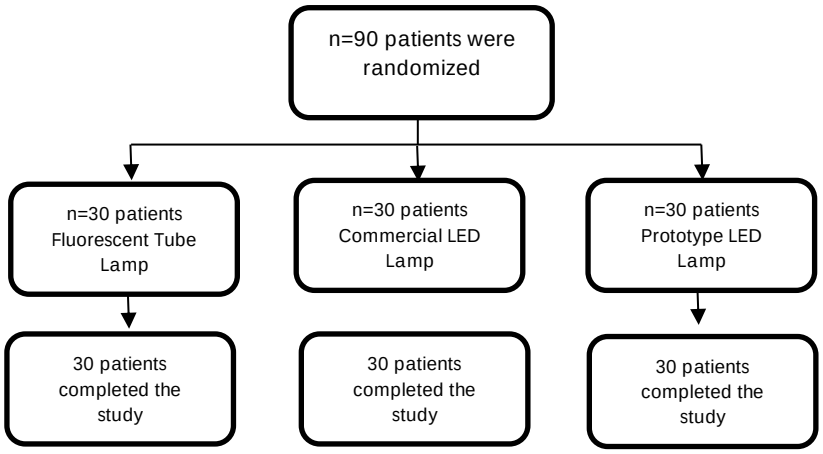

Table 2. Baseline data of the study group.

	Group 1 n = 30 Fluorescent Tube Lamp	Group 2 n = 30 Commercial LED Lamp	Group 3 n = 30 Prototype LED Lamp	P (ANOVA)
Weight (grams)	3050 ±134	3200 ±186	3034 ±234	0.70
Gestational Age (weeks)	39 ±1	39 ±1	39 ±1.1	0.80
Age of admission to Phototherapy (hours)	69.8 ±9	63.2 ±5	60 ±3	0.74
Basal bilirubin (mg/dL)	15.8 ±6.2	14.93 ±5.9	15.62 ±5.9	0.60

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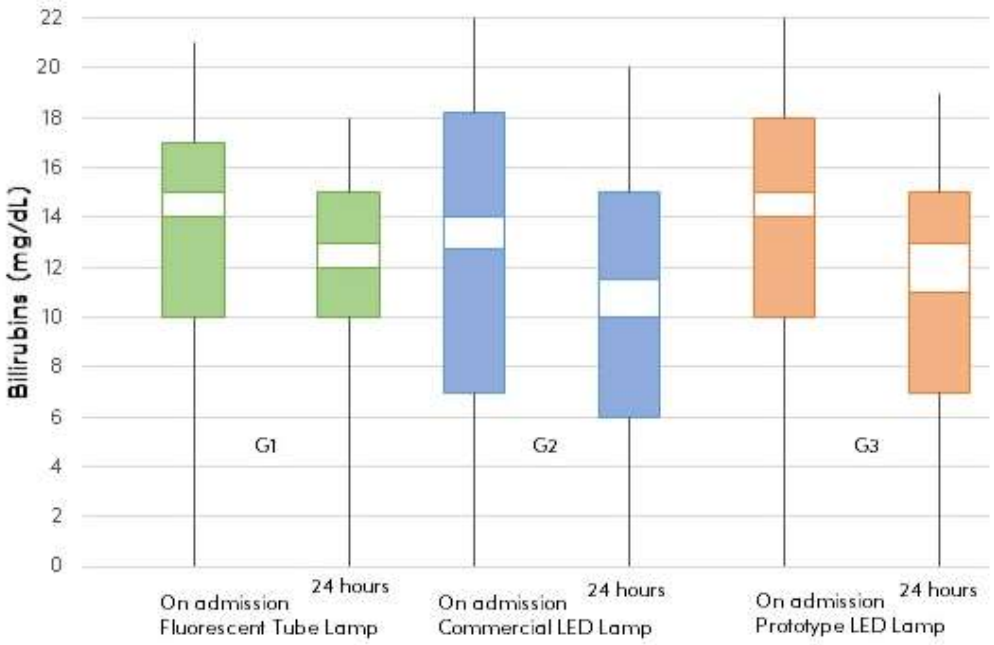
Table 3. Baseline levels and levels after 24 and 48 h of treatment.

	Group 1 n = 30 Fluorescent Tube Lamp	Group 2 n = 30 Commercial LED Lamp	Group 3 n = 30 Prototype LED Lamp	P (ANOVA)
Days of stay	1.83 ±0.18	2 ±0.2	2.1 ±0.2	0.76
Bilirubins on admission (mg / dL	15.8 ±6.2	14.93 ±5.9	15.62 ±5.9	0.60
Bilirubin after 24 hours of phototherapy	13.4 ±5.4	12.53 ±5.3	13.37 ±5.3	0.60
Bilirubins after 48 hours of phototherapy	11.3 ±4.1	10.67 ±4.8	11.2 ±4.17	0.62

Figure 4. Tukey's graph of serum bilirubin concentrations in the groups studied.



DISCUSSION

Interpretation

In the present study, we compared three phototherapy devices (fluorescent tubes, commercialized LED lamps, and the prototype LED device). We detected no statistically significant differences in the reduction of bilirubin at 24 and 48 h, which confirms the non-inferiority of the device and the treatment carried out in this clinical study.

The use of phototherapy for the treatment of jaundice in neonatal patients is a treatment that has been used for more than 30 years as a safe method to decrease bilirubin levels, and its reduction rate is proportional to the intensity of the light applied. It has been shown that greater intensity of irradiance of phototherapy would increase its efficacy.

The phototherapy dose largely determines the rate of regression of bilirubin to normal values. When using high-intensity phototherapy, a drop between 0.5 mg

and 1 mg/dL per hour can be expected during the first 4–8 h of therapy.

With an irradiance standard considered effective, a decrease in bilirubin from 6% to 20% can be obtained in the first 24 h. Therefore, the higher the irradiance of the phototherapy device, the better and faster its success will be.

Several international guidelines have defined specific serum bilirubin thresholds for initiating phototherapy treatment. These guidelines also contain recommendations for the effective irradiance level of phototherapy that is strongly related to the decrease in serum bilirubin[11].

The spectrum of light effects for the degradation of bilirubin is between 400 and 520 nm, with a peak at 460 nm. The American Academy of Pediatrics recommends that effective phototherapy be performed with a minimum irradiance level of 8–10 $\mu W/cm^2/nm$[12].

Appropriate levels of irradiance are essential to achieve maximum bilirubin reduction rates. The American Academy of Pediatrics recommends that high-intensity phototherapy requires at least 30 μW/cm2/nm, and conventional phototherapy units generate a maximum of 10 $\mu W/cm^2/nm$. A positive relationship between irradiance and reduction in bilirubin levels has recently been demonstrated: when irradiance increased from 20 to 55 $\mu W/cm^2/nm$, the 24-h serum bilirubin reduction increased from 30% to 50%[13].

In the present study, the calibration measurements of the spectral irradiance prototype equipment showed that at different heights levels within the recommended for the effective treatment of neonatal hyperbilirubinemia was achieved, so that the three systems investigated by us can be used effectively for these patients.

The type of technology and the quality of the light source used in phototherapy influence this treatment. Traditional phototherapy lamps with fluorescent tubes do not emit a high degree of irradiance; there is energy loss due to heat dissipation and, at distances close to the patient, they can cause slight burns. In addition, this technology has a short useful life in relation to LED technology.

In LED technology lamps, the characteristics of the LEDs used must be taken into account, that is, the emission spectrum, its spectral width, and a transparent plastic encapsulation. At similar irradiance, LED devices have been found to be more effective than conventional phototherapy devices at reducing hyperbilirubinemia. Additionally, LED devices often emit higher irradiance (35 $\mu W/cm^2/nm$ or higher), are easier to place close to the baby (due to lower heat production), and age more slowly than conventional fluorescent and halogen lamps, so the original irradiance is maintained for a longer time[10].

Study limitations

The study has the limitations of randomization assignment since the service only has six phototherapy nurseries. The number of cases was limited due to the low annual casuistry compared to series from other institutions. Also, this was a single-center study.

Generalizability

The external validity of this study and the applicability of the findings can be replicated with the prototype design instructions (Materials and Methods).

CONCLUSIONS

The efficacy of the treatment of newborns with hyperbilirubinemia with the prototype phototherapy lamp described shows non-inferiority for the treatment of neonatal hyperbilirubinemia compared to treatments in newborns with therapies of commercial LED light lamps and fluorescent tube lamps.

ARTICLE ADMINISTRATIVE INFORMATION

Abbreviations

LED: Light Emitting Diode.

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Protection of people:

The authors declare that the procedures followed were in accordance with the ethical standards of the responsible human experimentation committee and in accordance with the World Medical Association and the Declaration of Helsinki.

Confidentiality of the data:

The authors declare that they have followed the protocols of their work center on the publication of patient data.

Publication consent:

The authors have obtained the informed consent of the guardians of the patients who are part of the research. This document is in possession of the corresponding author. The authorization for publication of this case has been signed by the parents.

Conflicts of interest

The authors declare not to have any interest conflicts.

Financing

The authors provided funding for the research. The institution provided the funds for the purchase of the prototype parts..

Authors' contributions

JVA: Research idea, critical analysis, editorial corrections.

PVP, Data compilation, Bibliographic review, article writing.

All authors read and approved the final version of the manuscript.

Acknowledgments

We acknowledge the maintenance and pediatric service personnel of the Homero Castanier Crespo Hospital in the city of Azogues-Ecuador, who collaborated in the present study.

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BIBLIOGRAFÍA

1. Woodgate P, Jardine LA. Neonatal jaundice: phototherapy. BMJ Clin Evid. 2015;2015:0319. **PMID**: 25998618.
2. Bhutani VK, Cline BK, Donaldson KM, Vreman HJ. The need to implement effective phototherapy in resource-constrained settings. Semin Perinatol. 2011;35(3):192-7. **DOI**: 10.1053/j.semperi.2011.02.015.
3. Stokowski LA. Fundamentals of phototherapy for neonatal jaundice [published correction appears in Adv Neonatal Care. 2007 Apr;7(2):65]. Adv Neonatal Care. 2006;6(6):303-312. **DOI**: 10.1016/j.adnc.2006.08.004.
4. World Health Organization. Medical devices and eHealth solutions: compendium of innovative health technologies for low-resource settings 2011-2012. Geneva: WHO;2013.
5. Olusanya BO, Ogunlesi TA, Kumar P, Boo NY, Iskander I, B de Almeida M, et al. Management of late-preterm and term infants with hyperbilirubinaemia in resource-constrained settings. BMC Pediatr. 2015;15:39. **DOI**: 10.1186/s12887-015-0358-z.
6. 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(5):458-465. **DOI**: 10.1111/j.1651-2227.2011.02561.x
7. Bhat J, Qazi I, Ahangar A, Chroo B, Ahmed A, Ahmad I. Eficacy of different types of phototherapy devices: A 3 year prospective study from Northern India. J Clin Neonatol 2016;5:153-6 **SU**: t.ly/E1UN
8. Kumar P, Chawla D, Deorari A. Light-emitting diode phototherapy for unconjugated hyperbilirubinaemia in neonates. Cochrane Database Syst Rev. 2011;2011(12):CD007969. **DOI**: 10.1002/14651858.CD007969.pub29.
9. Mohammadizadeh M, Eliadarani FK, Badiei Z. Is the light-emitting diode a better light source than fluorescent tube for phototherapy of neonatal jaundice in preterm infants?. Adv Biomed Res. 2012;1:51. **DOI**: 10.4103/2277-9175.100158
10. Olusanya BO, Osibanjo FB, Emokpae AA, Slusher TM. Irradiance Decay in Fluorescent and Light-emitting Diode-based Phototherapy Devices: A Pilot Study. J Trop Pediatr. 2016 Oct;62(5):421-4. **DOI**: 10.1093/tropej/fmw022.
11. Schwartz HP, Haberman BE, Ruddy RM. Hyperbilirubinemia: current guidelines and emerging therapies. Pediatr Emerg Care. 2011;27(9):884-889. **DOI**: 10.1097/PEC.0b013e31822c9b4c
12. Maisels MJ. Phototherapy--traditional and nontraditional. J Perinatol. 2001;21 Suppl 1:S93-S107. **DOI**: 10.1038/sj.jp.7210642.
13. Hulzebos CV, Van't Klooster SJ, Lorenz K, Vreman HJ, Dijk PH. Irradiance levels of phototherapy devices: a national study in Dutch neonatal intensive care units. J Perinatol. 2017;37(7):839-842. **DOI**: 10.1038/jp.2017.13.

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