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# Efficacy of new microprocessed phototherapy system with five high intensity light emitting diodes (Super LED)

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**Abstract**

**Objectives:** To evaluate the efficacy of a microprocessed phototherapy (PT) system with five high intensity light emitting diodes (Super LED) for the treatment of neonatal hyperbilirubinemia of premature infants.

**Methods:** Randomized clinical trial using Super LED phototherapy in the study group and twin halogen spotlight phototherapy in the control group. A stratified blocked randomization, based on birth weight, was performed. The duration of phototherapy and the rate of decrease of total serum bilirubin (TSB) concentration in the first 24 hours of treatment were the main outcome measures.

**Results:** We studied 88 infants, 44 in the Super LED group and 44 in the halogen spotlight PT group. The demographic characteristics of the patients in both groups were similar. Infants in the Super LED group had a similar mean initial serum bilirubin level (10.1±2.4 mg%) to those receiving halogen spotlight treatment (10.9±2.0 mg%). After 24 hours of treatment, the decrease in total serum bilirubin levels was significantly greater in the Super LED group (27.9 vs. 10.7%, $p< 0.01$) and duration of phototherapy was significantly shorter in this group (36.8 h vs. 63.8 h, $p < 0.01$). After 24 hours of treatment, a significantly greater number of patients receiving Super LED phototherapy had reached serum bilirubin concentrations low enough to allow withdrawal of treatment (23 vs. 10, $p < 0.01$).

**Conclusions:** Our results demonstrate that the efficacy of Super LED phototherapy for treating hyperbilirubinemia in premature infants was significantly better than halogen phototherapy.

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## Introduction

Phototherapy is the most used therapeutic modality for the treatment of neonatal hyperbilirubinemia. Since it was first introduced, in 1958, clinical and laboratory investigations have concentrated on improving its efficacy.[1]

The therapeutic efficacy of phototherapy depends on the irradiance dose, spectrum of the light source employed and the body surface area exposed to the light.[2] The blue spectrum of visible light is considered most effective for the treatment of neonatal jaundice because it coincides with the absorption spectrum of bilirubin.[2,3]

There are a variety of phototherapy systems on the market, using different light sources: fluorescent tubes, halogen lamps and light emitting diodes (LED).[4-6]

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An LED is a special type of semiconductor diode that emits light when connected to an electrical circuit. The light is generally monochromatic and the color depends on the semiconductor material utilized. In general their dimensions are very small (0.5 to 1 cm in diameter) and they are used commercially in the displays of digital clocks, calculators and electronic message boards.

The use of LEDs in phototherapy equipment began in the 1990s. Some of those machines are already available on the international market and comprise from 100 to 300 LEDs with gallium nitrate as the semiconductor element.[7]

Recently, the Brazilian medical industry has developed a phototherapy system that employs a bank of LEDs with a different physical and chemical composition (indium gallium nitrate) and emitting high intensity blue light at wavelengths ranging from 420 to 500 nm, with a maximum peak at 450 nm. Adding indium to the semiconductor element confers significantly greater power to these LEDs than those using gallium nitrate alone. Furthermore, by means of nanotechnology, it was possible to group together many LEDs in small capsules of around 1 $cm^2$. These capsules have been named Super LEDs. This new phototherapy modality comprises five Super LED capsules, controlled by microprocessor technology and mounted in a small box measuring 11 cm wide by 23 cm long and 5 cm deep.

The objective of this study was to evaluate the therapeutic efficacy of this new phototherapy system and to compare it with halogen phototherapy.

## Methods

We studied 88 preterm newborn infants, with birth weight (BW) of more than 1,000 g, admitted consecutively to the neonatal intensive care unit (ICU) at the Clínica Perinatal Laranjeiras between June, 2005 and February, 2006. The criterion for indicating phototherapy was based on serum bilirubin concentrations for different BW ranges.[8] Newborn infants were excluded from the study if they exhibited direct bilirubin greater than 2 mg%, hemolytic jaundice (positive Coombs test), ecchymosis, malformations or congenital infection.

Sample size was defined based on a difference in serum total bilirubin (TB) of 25% between the experimental group and the control group after 24 hours of treatment with phototherapy, with a 5% significance level and 80% power. We performed stratified randomization (birth weight strata ≥ 1,500 g and < 1,500 g) and in blocks of four.[9]

The experimental group were given phototherapy with the Super LED system positioned 30 cm from the patient and illuminating an elliptical area of 38 cm x 27 cm diameter. The control group were given treatment using a halogen phototherapy system, equipped with a single quartz-halogen lamp with a dichroic reflector, positioned 50 cm from the patient and illuminating a circle of 18 cm diameter. Since the body surface area exposed to the light of the Super LEDs was almost double of that of patients receiving halogen phototherapy and bearing in mind that this is an important factor in the efficacy of treatment, we chose to use two halogen phototherapy systems for each patient in the control group in order to enhance the surface area exposed to light.

The irradiance emitted by the two types of phototherapy was determined with a FANEM 2620 model radiation monitor, which measures light in the wavelength range of 400 to 500 nm. Measurements were taken at the level of the infant's skin, on the anterior thoracic region, in the center of the phototherapy light's focus.

Serum TB levels were measured at the start of treatment, and every 8 hours for the first 24 hours of treatment. After this period, measurements were taken every 12 hours until treatment was withdrawn. Blood samples were collected by heel prick, and serum total bilirubin was determined by micromethod (American Optical UNISTAT Bilirubinometer).

Phototherapy was withdrawn when serum TB levels reached values 30% below their initial levels, as this is a routine procedure in our unit. However, irrespective of serum bilirubin levels, the minimum length of treatment given to any patient was 24 hours.

Treatment was considered to have failed if serum TB levels continued to rise despite phototherapy, and reached values 20% lower than those that would indicate a need for exchange transfusion. If this happened, the infant would drop out of the study and the neonatologist would adopt whatever conduct was judged most appropriate. The criterion for indicating exchange transfusion was based on the relationship between TB and BW.[8]

The rate of decrease of serum TB concentration in the first 24 hours of treatment and duration of treatment (hours) were the main outcome measures considered for comparing the therapeutic efficacy of the study groups.

Possible adverse effects related to phototherapy (weight loss, temperature instability and skin rash) were monitored daily during the study period.

Results are expressed in terms of means and standard deviations (for quantitative characteristics) and in percentages (for qualitative characteristics). Student's *t* test (numerical variables) and the chi-square test (categorical variables) were used to verify the statistical significance of

observed differences. The statistical package SPSS version 13 was used to construct the database and to calculate results.

This study was approved by the Research Ethics Committee at Instituto Fernandes Figueiras (hearing nº 035/04), and all those responsible for the newborn infants involved in our study signed a free and informed consent form before randomization took place.

**Results**

The groups analyzed did not show statistically significant differences in terms of BW, gestational age (GA), number of newborn infants with 5 minute Apgar score below 7, sex or type of delivery (Table 1).

At the beginning of the study, the groups were also similar in terms of the number of patients on a zero diet (NPO) or ventilatory support (oxyhood, nasal CPAP or mechanical ventilation), and also in terms of hours of postnatal life and initial serum TB levels (Table 1).

Mean irradiance (μW/cm²/nm) emitted by the phototherapy device equipped with Super LED lamps was significantly greater than that emitted by the halogen phototherapy (37±9 μW/cm²/nm vs. 21±6 μW/cm²/nm, $p < 0.01$).

The decrease in serum TB concentration during the first 24 hours of treatment was significantly greater among patients receiving Super LED phototherapy than among those on halogen phototherapy (Table 2). After 24 hours of phototherapy, a significantly greater number of patients on Super LED phototherapy had achieved serum bilirubin levels that justified withdrawing treatment (23 vs. 10, $p < 0.01$).

The mean total treatment time was significantly shorter among patients receiving Super LED phototherapy than among those treated with halogen phototherapy (36.8±21 hours vs. 63.8±37 hours; $p< 0.01$).

After the first 24 hours, less patients in the Super LED group were still receiving phototherapy. After 36 hours of treatment, 21 patients in Super LED group were still receiving phototherapy, while the group on halogen phototherapy had 34 patients, resulting a difference of 38.2%. After 48 hours of treatment, this difference was 57.1%, with 12 newborn

**Table 1** - Demographic characteristics of the study population at birth and at the beginning of the study*

| | Super LED (n = 44) | Halogen (n = 44) |
|---|---|---|
| Birth weight (g) | 1,965±597 | 2,032±483 |
| GA (weeks) | 33.4±2.0 | 33.8±1.8 |
| Sex (M/F) | 28/16 | 30/14 |
| Caesarian delivery | 41/44 | 40/44 |
| Apgar 5 < 7 | 2/44 | 3/44 |
| NB < 1,500 g | 8/44 | 8/44 |
| NB on zero diet* | 19/44 | 14/44 |
| NB on MV* | 18/44 | 11/44 |
| Start of phototherapy (hours)* | 65.4±26 | 70.8±25 |
| Serum TB level (mg%)* | 10.1±2.4 | 10.9±2.0 |

F = female; GA = gestational age; M = male; MV = mechanical ventilation; NB= newborn infants; TB = total bilirubin.
Mean ± standard deviation. For all comparisons, $p > 0.05$.
* Data collected at the beginning of the study.

infants in the Super LED group and 28 in the halogen phototherapy group (Figure 1).

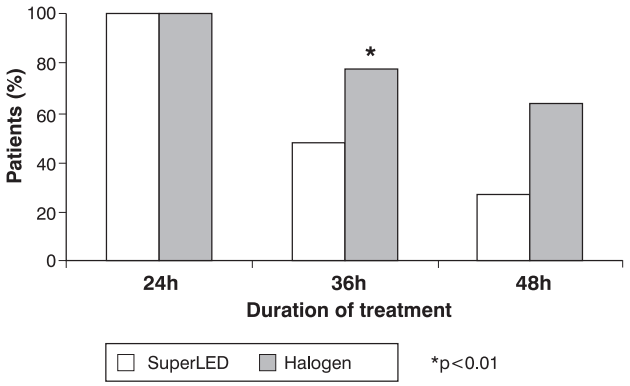


**Figure 1** - Number (%) of patients on phototherapy during the first 48 hours

A greater number of patients in the Super LED group relapsed with elevated TB levels and needed to go back on phototherapy, although this difference was not statistically significant (26.8 vs. 18.2%; p = 0.43).

None of the patients studied exhibited treatment failure or required exchange transfusion.

None of the patients exhibited temperature instability or skin rash during the study period. There was not statistically significant difference in weight lost over the period during which patients were on phototherapy (1.89% of weight loss against initial weight for the Super LED group and 1.99% of initial weight in the halogen phototherapy group; p > 0.33).

## Discussion

Recent studies have suggested that LED phototherapy is effective for the treatment of neonatal hyperbilirubinemia.[7,10] Nevertheless, the majority of them were conducted *in vitro*, and only two involved newborn infants.[11,12]

Seidman et al., studied jaundiced full term newborns treated with LED (blue) phototherapy and conventional phototherapy, both adjusted to emit the same irradiance, and found no difference between the rate of decrease in serum bilirubin levels or in the duration of treatment.[11] The same authors, conducted a prospective study in 2003 comparing the therapeutic efficacy of LED (blue) vs. halogen phototherapy, both emitting similar irradiance, and did not observe a statistically significant difference in the rate of serum bilirubin concentration or in the duration of treatment.[12]

In our study, we analyzed premature newborn infants because they are more susceptible to the deleterious effects that high serum bilirubin concentrations have on the central nervous system and because they are the population that most often needs phototherapy in our neonatal ICU.

Since this was a study to test the efficacy of a new type of phototherapy, it was necessary to define serum bilirubin concentration limits, beyond which infants would be withdrawn from the trial and treated with measures known to be effective. We chose to test efficacy after 24 hours of treatment since this is a measure frequently described in the literature.[11,13-15]

**Table 2** - Total serum bilirubin level (mg%) during the first 24 hours of treatment

| | Initial TB | TB 8 h | TB 16 h | TB 24 h |
|---|---|---|---|---|
| Super LED | 10.1±2.4 | 9.3±2.5* | 8.1±2.7† | 7.2±2.5† |
| Halogen | 10.9±2.0 | 10.5±2.1 | 9.4±1.8 | 9.6±2.4 |

TB = total bilirubin.
Mean ± standard deviation.
* p < 0.05, † p < 0.01.

Our results demonstrate that the efficacy of Super LED phototherapy for the treatment of hyperbilirubinemia in premature newborn infants is superior to that of halogen phototherapy. Eight hours after the start of treatment, the decrease in serum TB levels was already significantly greater in the newborn infants treated with Super LED phototherapy than in those treated with halogen phototherapy (7.9 vs. 3.6%; p = 0.02). This difference becomes more accentuated as treatment continues and, after 24 hours of phototherapy, the percentage reduction in serum bilirubin levels of infants receiving Super LED phototherapy was more than double of those on halogen phototherapy (27.9 *vs.* 10.1%; p < 0.01).

The efficacy of a phototherapy system is principally influenced by the body surface area exposed to light and by the irradiance measured at the patient's skin.[2] The Super LED phototherapy lamp used in our study is capable of exposing a larger surface area to the light (an ellipse, 38 cm x 27 cm) than is the halogen phototherapy unit (a circle with 18 cm diameter). In order to minimize this difference we decided to treat newborn infants allocated to the halogen phototherapy group with two units focused tangentially.

In our study, irradiance was measured at the center of the focus of the light and was significantly greater for Super LED phototherapy than for the halogen phototherapy (37 vs. 21 μW/cm²/nm; p < 0.01). However, since the irradiance emitted by these systems is not uniformly distributed across the surface illuminated, a succession of measurements at a variety of points within the area illuminated would be more representative of the mean spectral irradiance of these phototherapy units.[16,17]

Another variable that may have contributed to the greater efficacy of Super LED phototherapy lies in the characteristics of the spectrum of the light emitted by the LEDs.

In our study, we only measured the irradiance emitted by the two phototherapy devices. Their light spectra were not analyzed. Nevertheless, a recent laboratory study conducted by Chang et al. in 2005 demonstrated differences in the spectra emitted by these two types of phototherapy.[10] Whereas the emission spectrum of the halogen lamp lays between 380 and 600 nm, that of the phototherapy LEDs is much narrower (420 to 500 nm) and coincides with the spectrum of light that is absorbed by the bilirubin molecule (400 to 500 nm). Therefore, all of the light emitted by the phototherapy is theoretically utilized in the isomerization of bilirubin, which is not the case with the halogen lamp, since part of its light spectrum lays outside the zone of interaction with bilirubin.[3,7]

In summary, our results demonstrate that LED phototherapy is more effective than halogen phototherapy for the treatment of hyperbilirubinemia in premature newborn infants. The irradiance and type of light spectrum emitted may be determinant factors of this superior efficacy.

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