

## Single vs. double phototherapy in the treatment of full-term newborns with nonhemolytic hyperbilirubinemia

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### Abstract

**Objectives:** To compare the effectiveness of single (1 panel) vs. double (2 panels) phototherapy in reducing nonhemolytic hyperbilirubinemia in term newborns.

**Methods:** Term newborns with hyperbilirubinemia were prospectively randomized to receive double or single phototherapy. Bilirubin levels were measured at admission and at 12-hour intervals, as well as at a follow-up 48 hours after discharge.

**Results:** Thirty-seven patients received single and 40 double phototherapy. The mean decrease in bilirubin level in the first 24 hours of treatment was greater in the double phototherapy group ( $5.1 \pm 2.2$  mg/dL vs.  $4.3 \pm 2.1$  mg/dL), but without statistical significance ( $p = 0.18$ ). Readmission rates were similar and no adverse effects were found in either group.

**Conclusions:** Double-surface was not more effective than single-surface phototherapy in the treatment of nonhemolytic hyperbilirubinemia in term newborns. However, our results suggest that double phototherapy may be more effective in those term newborns with higher bilirubin levels at admission.

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### Introduction

Over 60% of all term newborns develop jaundice in their first days of life.<sup>1</sup> A significant proportion of causes of hyperbilirubinemia in the term newborn are benign and reversible.<sup>2</sup> However, considering the potentially irreversible toxicity of bilirubin on the central nervous system (kernicterus), newborns must be evaluated to identify which ones will need treatment.<sup>3</sup> Since the 1950s, phototherapy has been the therapy of choice for the newborn with indirect hyperbilirubinemia.<sup>4,5</sup> The efficacy of phototherapy depends mainly on the intensity

and wavelength of the light and also on the proportion of skin area exposed to light. Single phototherapy (SP) is the most commonly used method, and, when bilirubin levels are close to the threshold for exchange transfusion, intensive phototherapy is indicated.<sup>6</sup> This can be obtained by increasing the surface area of the newborn exposed to light and the intensity of phototherapy using lateral panels, reflecting objects and fiber-optic blankets. Among them, a second lateral panel, also known as double phototherapy (DP), is frequently used.

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We did not find other studies comparing the efficacy between conventional phototherapy and phototherapy using a second lateral panel in the treatment of nonhemolytic hyperbilirubinemia in term newborns. Only a few small studies analyzing high-risk newborns and premature babies, but without post-discharge follow-up, were found.<sup>7</sup>

There is still a lack of consensus on the routine measurement of bilirubin levels after phototherapy discharge; nevertheless, it is well known that it usually rebounds after cessation of therapy.<sup>8,9</sup> It has been speculated that a more intensive treatment would induce greater or more frequent rebound.

The possible adverse effects associated with phototherapy are: skin rash, increased insensible losses, retinal damage, hyperthermia, and deposition alterations due to increased intestinal flow.<sup>10,11</sup>

The objective of the present study was to comparatively evaluate the efficacy of DP and SP in reducing bilirubin levels in term newborns with nonhemolytic hyperbilirubinemia, and to compare such response in relation to bilirubin levels at admission. Possible adverse effects and therapy readmissions were also analyzed.

## Methods

### Patients

All newborns admitted to our unit, between March and September 2007, for phototherapy with the diagnosis of hyperbilirubinemia were included in the study if they met the following inclusion criteria: 1) gestational age greater or equal to 37 weeks; 2) nonhemolytic hyperbilirubinemia (negative direct Coombs' test and no other sign of hemolysis); 3) more than 24 hours and less than 7 days of life; 4) no signs of sepsis or congenital malformations; 5) indication for phototherapy following criteria recommended by the American Academy of Pediatrics<sup>8</sup>; and 6) signed written consent form from one of the parents. The patients were assigned to each group by random numbers generated using the MINITAB 14 statistical software.

Phototherapy and bilirubin measurements: SP was administered using standard phototherapy apparatus (Air-Shields Clinic Equip or ICR), with six to eight fluorescent tubes (two blue and four white 20-watt lamps in each tube). To DP patients a second lateral panel with similar characteristics was placed at 90 degrees to the first panel. In our unit all beds have 10-mm lateral bars with 85-mm spaces between them. The panels were positioned at 30-40 cm from the patients, who were unclothed but with diapers. In order to standardize therapies, light irradiance was measured at admission and every 12 hours with a portable radiometer (Fanem®, model 2620). The light spectrum was not measured.

For both groups nursing care was similar, with special emphasis on eye protection and temperature control. Phototherapy was administered continuously, being interrupted only for infant feeding and weighing, physical examination, and bilirubin measurements by photocolometric micromethod. In both groups, weight, temperature and bilirubin levels were controlled at admission and at 12-hour intervals. Hyperthermia, weight loss (in two or more control examinations) or significant skin rashes were considered as adverse effects of therapy. For discharge, bilirubin level should show a declining trend reaching a value less than or equal to 13.5 mg/dL. For all newborns included in the study a measurement of bilirubin level was performed at approximately 48 hours after discharge, and the readmission criterion was bilirubin level close to or above 20 mg/dL.

### Statistical analysis

The planned enrollment of 37 patients per group was based on the estimated percentage increase of 20 points in the velocity of bilirubin reduction in DP vs. SP, which, in turn, was based on a previous study with premature patients,<sup>10</sup> providing 80% statistical power, with an alpha of 0.05. The chi-square test and Student *t* test were used to compare the percentage changes.

This study was approved by the Research Ethics Committee of our institution.

## Results

Between March and September 2007, 37 patients were randomized for SP and 40 for DP. The groups were matched for clinical characteristics and mean bilirubin level at admission (Table 1). Conversely, the mean light intensity or irradiance was  $11.7 \pm 0.72 \mu\text{w}/\text{cm}^2/\text{nm}$  and  $9.4 \pm 1.94 \mu\text{w}/\text{cm}^2/\text{nm}$  in the DP and SP groups, respectively ( $p < 0.001$ ).

The mean decrease in bilirubin level after the first 24 hours of therapy was greater in the DP group ( $5.1 \pm 2.2 \text{ mg/dL}$  vs.  $4.3 \pm 2.1 \text{ mg/dL}$ ). However, this difference failed to reach statistical significance ( $p = 0.18$ ).

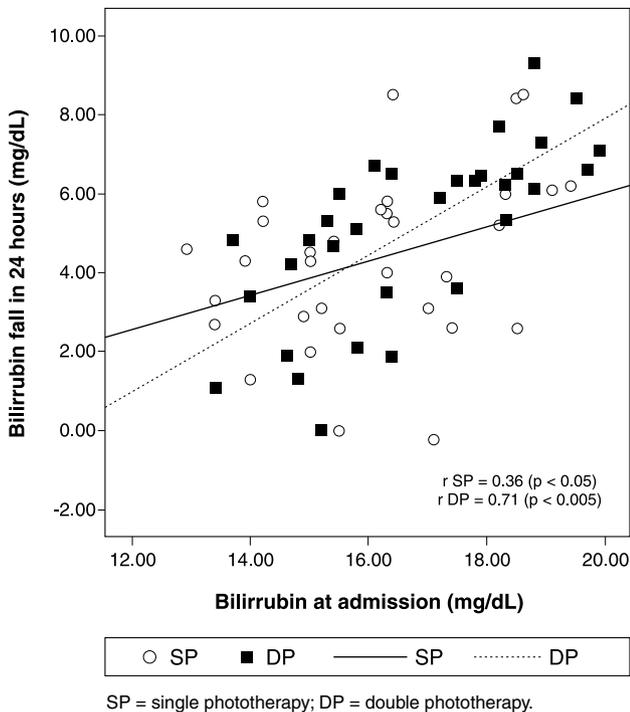
The correlation between bilirubin level at admission and velocity of bilirubin level decline was greater in the DP than in the SP group ( $r = 0.71$  vs.  $r = 0.36$ ), both associations being significant (Figure 1).

Phototherapy was well-tolerated overall, with no evidence of adverse effects in either group.

Bilirubin levels 48 hours after discharge were similar between groups (mean of 13.5 mg/dL in the SP group vs. 12.9 mg/dL in the DP group;  $p = 0.39$ ). Readmission rate was also similar between groups (8.1% in the SP group vs. and 7.5% in the DP group;  $p = 0.92$ ). The mean bilirubin

**Table 1** - Biodemographic characteristics of both groups

Characteristics	Single phototherapy (n = 37)	Double phototherapy (n = 40)
Sex (% male)	54	65
Gestational age (weeks)	38.4±0.8	38.4±0.9
Birth weight (g)	3,424±511	3,324±350
Weight at admission (g)	3,211±448	3,096±334
Age at admission (hours)	63.5±23.5	80.4±45.3
Bilirubin at admission (mg/dL)	16.7±1.7	16.5±1.9



**Figure 1** - Bilirubin fall in the first 24 hours of therapy in relation to bilirubin level at admission

levels at readmission were 19.6 mg/dL in the SP group and 20.1 mg/dL in the DP group.

**Discussion**

In our study, double phototherapy with an additional lateral panel produced a greater decrease (although without statistical significance) in the bilirubin level at 24 hours of treatment in term newborns with nonhemolytic hyperbilirubinemia. A similar comparative study showed

a higher decrease in bilirubin level with DP, but patients were low birth weight neonates or with hemolytic hyperbilirubinemia.<sup>7</sup> Additionally, in that study, the authors did not mention differences in the light intensity employed. This is an important factor concerning treatment response. In a study comparing high (12 μw/cm<sup>2</sup>/nm) vs. low intensity phototherapy (6 μw/cm<sup>2</sup>/nm) in low birth weight neonates, the authors described a significant higher proportion of structural photoisomers in the high intensity group.<sup>12</sup> In our study, light intensity was significantly different between groups; nevertheless, we did not find a significant difference in treatment efficacy. A possible explanation for this result is that the difference in light intensity should be greater in order to promote significant biological differences in effectiveness. On the other hand, our sample size estimation was based on a possible increase of 20% in the velocity of bilirubin fall; however, we detected only a 18.7% increase in our study. We could assume that by including more patients in the study this difference would gain significance. Another consideration is that the effect of phototherapy also depends on the bilirubin level at admission. A greater fall in bilirubin level has been described in association with a higher level at admission.<sup>10,13</sup> In agreement with such investigations, the present study showed a stronger association between decrease in bilirubin after 24 hours of therapy and bilirubin level at admission in the DP group when compared to the SP group. This finding suggests that at higher levels of bilirubin DP could be more effective than SP. A limitation of the present study is that most patients had only moderate hyperbilirubinemia. However, the strength of this study is that it is based on common clinical practice with little evidence in clinical trials.

Phototherapy has little adverse effects with an appropriate nursing care.<sup>14</sup> Consequently, it was not surprising that no adverse effects were observed in our patients.

In agreement with published data, it seems unnecessary to maintain newborns hospitalized after treatment with

phototherapy for possible rebound in bilirubin levels.<sup>3,15</sup> In the present study, both groups had similar bilirubin levels after 48 hours of discharge. Likewise, both therapies had the same rate of readmissions. Therefore, it does not seem necessary to change treatment from DP to SP before discharge.

Considering the readmission rates found in the present study, at least in our center, we would recommend measurement of bilirubin level from 24 to 48 hours after discharge. However, different recommendations might apply if other discharge criteria are used.

In conclusion, double phototherapy did not prove to be more effective than single phototherapy in the treatment of term newborns with nonhemolytic hyperbilirubinemia in this study. Thus, for most newborns with this condition, single phototherapy is sufficient. Our results suggest that double phototherapy may be more effective in treating term newborns with higher bilirubin levels at admission, but further investigation is warranted to clarify this possibility. Readmission rates were similar and no adverse effects were found in either group.

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