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Double versus Single Phototherapy in the Treatment of Neonatal Hyperbilirubinemia

*KZ Hossain[1], E Kabir[2], KK Biswas[3]

Abstract

Background: Hyperbilirubinemia is a common problem in full-term newborns. Since the 1950s, phototherapy has been the choice of treatment for lowering bilirubin concentration in neonates. **Objective:** To compare the effectiveness of single and double phototherapy and increasing spectral irradiance for decreasing serum bilirubin levels in neonates with indirect hyperbilirubinemia. **Methods:** An open-label, randomized controlled trial was conducted at Ad-din Sakina Women's Medical College, Jashore, from June to December 2022. Subjects were divided into two groups: those who received single phototherapy (n=35) and those who received double phototherapy (n=35). We included term newborns with neonatal jaundice in the first week of life. Serum bilirubin and average spectral irradiation levels were measured at baseline and after 12 hours and 24 hours of phototherapy treatment. **Results:** The mean total bilirubin levels of the single and double phototherapy groups at the beginning of therapy were 17.6±1.41 mg/dL and 17.5±1.32 mg/dL, respectively, with no significant difference between values. During the study period, the sum of average spectral irradiance by double phototherapy was significantly higher than that of single phototherapy ($P < 0.05$). A significantly greater decrease in bilirubin levels was observed in the double phototherapy group at 12 hours and 24 hours of phototherapy compared to the single phototherapy group ($P < 0.001$). **Conclusion:** Double phototherapy is more effective than single phototherapy in reducing bilirubin levels in jaundiced newborns.

Keywords: Neonatal Jaundice, Irradiation spectrum, Phototherapy, Bilirubin.

Introduction

Hyperbilirubinemia remains a common, important, and sometimes pathologic condition in newborns. Because of the risk of jaundice-associated neurotoxicity, management of neonatal hyperbilirubinemia is a subject of considerable discussion and debate among physicians.[1,2] Although all infants experience some degree of hyperbilirubinemia in the first few days of life and most have some physiologic jaundice, the extent and duration vary among populations of different racial compositions or geographic distributions.[3,4]

The jaundice in patients may be physiological or pathological. Hyperbilirubinemia is considered pathological if the time of appearance, duration, or serum bilirubin levels are determined to be significantly different from physiological jaundice.[5] Phototherapy, although slow in effect, is now the treatment of choice by most clinicians. It uses visible light to treat hyperbilirubinemia in newborns. Phototherapy systems that simultaneously irradiate the front and the back of the baby increase the dose by delivering the same amount of irradiance per square centimeter of skin to a larger skin surface area.[7]

Our study aimed to compare neonatal serum bilirubin levels and spectral irradiance for single and double phototherapy at 12 and 24 hours of treatment.

Materials and methods

We conducted a randomized, controlled, open trial in Addin Sakina Women's Medical College, Jashore, from June to December 2022. All babies admitted to the special care nursery for uncomplicated neonatal jaundice and requiring phototherapy were eligible for the study. The need for phototherapy was determined using the American Academy of Pediatrics guidelines for management of jaundice in healthy term newborns.

1. Dr. Kazi Zamir Hossain, Associate Professor, Department of Paediatrics, Ad-din Sakina Women's Medical College, Jashore, Bangladesh. Email: drzamiraddin@gmail.com ORCID: https://orcid.org/0009-0004-3255-0899
2. Dr. Ehsanul Kabir, Assistant Professor, Department of Paediatrics, Ad-din Sakina Women's Medical College, Jashore, Bangladesh.
3. Dr. Kishor Kumar Biswas, Associate Professor, Department of Paediatrics, Ad-din Sakina Women's Medical College, Jashore, Bangladesh.

We excluded infants with serum bilirubin levels close to the exchange transfusion limit, increased direct bilirubin, hemolytic diseases and congenital anomalies, sepsis & gestational age less than 37 weeks. This study was approved by the Medical Ethics Committee of our institution. [Out of 76 neonates with hyperbilirubinemia, 5 with direct hyperbilirubinemia were excluded, for a total of 71 subjects enrolled in our study. However, 1 subject dropped out due to blood sample damage.]

Approach to indirect hyperbilirubinemia in healthy term infants without hemolysis*

Treatment Strategies

(Indirect serum bilirubin mg/dl)

Age in hours	Phototherapy	Intensive Phototherapy *If failed exchange transfusion	Exchange Transfusion: If phototherapy fails
<24	†	†	†
24-48	≥ 15-18	≥ 25	≥ 20
49-72	≥ 18-20	≥ 30	≥ 25
>72	≥ 20	≥ 30	≥ 25
>2week	≠	≠	≠

* With hemolysis, exchange transfusion is initiated with an indirect bilirubin level of ≥20 mg/dl at any age.

† Jaundice appearing in the 1st 24 hours of life is not seen in healthy infants. If jaundice appears in 1st 24 hours, require further evaluation.

* Intensive phototherapy should produce a decline of TSB of 1-2 mg/dl within 4-6 hours, and the TSB level should continue to fall and remain below the threshold level for exchange transfusion. If this does not occur, it is considered a "failure of phototherapy".

†Jaundice appearing in the 2nd week of life or continuing beyond the 2nd week of life is probably due to a serious underlying cause such as biliary atresia, galactocemia, hypothyroidism, or neonatal hepatitis.

The sample size needed was estimated to be 35 neonates per group. Sample sizes were designed according to clinical characteristics and mean bilirubin level at admission. In total, 70 babies were included. Demographic and laboratory data were obtained, including age, gender, and hemoglobin levels. The babies included in the study were randomized to receive either single phototherapy (control group) or double phototherapy. Subjects remained in their assigned group until after 24 hours of phototherapy. Light intensity was measured as spectral irradiance (μ W/cm^2/ nm) using a Dale 40 light intensity meter (USA).

Phototherapy units used were manufactured by Tessna, USA. The phototherapy units utilized five compact blue fluorescent lamps (Toshiba 20WT52), with irradiation of 6.6 μW/cm^2 by a radiometer. For double phototherapy patients, a 2nd lateral panel with similar characteristics was placed at a 90-degree angle to the 1st panel. The distance between the phototherapy unit and the baby was standardized at 45 cm above and 10 cm below the baby. We used blue light photo lights (Toshiba 20WT52) with irradiation of 6.6 μW/cm^2 by radiometer (Dale). 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 Photo-colorimetric micro method.

Primary outcome measures were the mean differences in serum bilirubin levels at baseline, 12 hours and 24 hours. Secondary outcome measures were spectral irradiance of single phototherapy (control group) and double phototherapy. At baseline and 12 and 24 hours of phototherapy, serum bilirubin levels and spectral irradiance were measured.

The safety of both methods was assessed and compared by monitoring body temperature, hydration status (monitored clinically and by weight measurement), skin problems (such as rashes) and gastrointestinal problems (such as loose stools or feeding intolerance).

Associations between phototherapy types and serum bilirubin levels were analyzed by Student's t-test. We analyzed data with SPSS version 15.0. Statistical significance was accepted as $P < 0.05$ with a 95% confidence interval.

Results

Subjects were divided into two groups of 35 each. One group received single phototherapy and the other group received double phototherapy. Infants' characteristics, including gender, age, initial bilirubin levels before phototherapy and hemoglobin levels, are shown in Table 01.

Table 01: Baseline characteristics of the subjects

Characteristic	Single phototherapy (n=30)	Double phototherapy (n=30)
Gender, male/female	19/16	18/17
Age at phototherapy (days)	4.5 ± 1.5	5 ± 1.3
Weight (grams)	3124 ± 442	3032 ± 324
Initial bilirubin level (mg/dL)	16.5 ± 1.30	17.6 ± 1.62
Hemoglobin (g/dL)	14.0 ± 1.42	14.0 ± 1.23

Bilirubin profile

There were significant decreases from the initial bilirubin levels to those measured after 12 and 24 hours in the double phototherapy group. For the single phototherapy group, a significant decrease was observed from the initial to the 24-hour bilirubin level only, but not in the 12-hour measurement (Table 02).

A significantly greater decrease in bilirubin levels was observed in the double phototherapy group at 12 hours and 24 hours of phototherapy compared to the single phototherapy group (P 0.001) (Table 03).

We observed the adverse effect of hyperthermia (T> 37.5°C) in 8 (13.3% of total) subjects from both the single and double phototherapy groups, 3 and 5 subjects, respectively. Other potential side effects, such as diarrhea and dehydration, were not found during monitoring.

Table 02: Mean decreases in serum total bilirubin levels between initial and 12 hours, and between initial and 24 hours in the double and single phototherapy groups

Type of phototherapy	Mean±SD	95% CI	P
Double phototherapy			
Decrease in bilirubin from baseline to 12 hours (mg/dL)	6.5±0.63	6.3 to 6.7	0.001
Decrease in bilirubin from baseline to 24 hours (mg/dL)	10.1±1.05	9.7 to 10.4*	0.001
Single phototherapy			
Decrease in bilirubin from baseline to 12 hours (mg/dL)	0.1±0.25	0.0 to 0.1	0.059
Decrease in bilirubin from baseline to 24 hours (mg/dL)	3.8±1.32	3.5 to 4.5	0.001

(* The significant P values and CIs)

Table 03: Bilirubin levels at baseline, and after 12 and 24 hours of phototherapy

Traits	Double phototherapy Mean (±SD)	Single phototherapy Mean (±SD)	95% CI	P
Initial bilirubin	17.5±1.32	17.6±1.41	-5.8 to 0.8	0.694
Bilirubin after 12 hours	11.0±1.43	17.6±1.44	5.8 to 7.3	0.001
Bilirubin after 24 hours	7.4±1.61	13.8±1.84	7.4 to 9.0	0.001

[Figure 01 shows significant differences in irradiance between single and double phototherapy (P < 0.05) at initial, 12 hours and 24 hours of phototherapy. The total irradiation 45 cm above and 10 cm below the neonate's body in the double phototherapy group was approximately 29.2 μW/cm2/nm.]

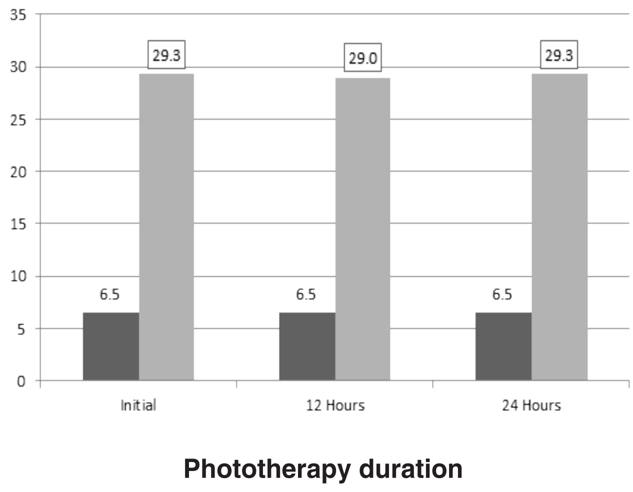

Figure 01: Comparison of spectral irradiance in single and double phototherapy at initial, 12 hours and 24 hours of phototherapy

Discussion

The average age of subjects in our study was 4 to 5 days. It is known that elevated bilirubin levels often peak in the first week of life.[3] Hyperbilirubinemia is a serious and potentially life-threatening condition. This condition is the main reason for hospital revisits by full-term infants in their first week of life.[8]

A significant decrease of bilirubin level between baseline and 12 hours and between baseline and 24 hours was seen in the double phototherapy group, with an average decrement of 6.5 mg/dl (P=0.001) and 10.1 mg/dL (P=0.001), respectively. For the single phototherapy group, a significant decrease in bilirubin level was observed only between baseline and 24 hours, with an average decrement of 3.8 mg/dL (P= 0.001).

Double phototherapy using blue light wavelength 430-490 nm and spectral irradiance of ≥ 30 μ W/cm^2/nm (measured with radiometer or estimated by placing the baby directly under the light or widening the exposed surface) is effective for reducing bilirubin levels.[9,10] Double phototherapy was more effective than single phototherapy in our study. Newborns receiving double phototherapy had a larger surface area exposed to constant irradiance, thereby increasing their total dose of phototherapy, compared to those undergoing single phototherapy. This increased dose causes the production of more bilirubin.[11] However, merely increasing the surface area exposed, while maintaining the same total energy output to the skin, does not improve the efficacy of phototherapy.[12,13] A randomized, clinical trial in Thailand showed that double phototherapy was safer and more effective in reducing bilirubin levels compared to single phototherapy.[14] Double phototherapy is an alternative mode of intensive phototherapy that is effective, economical and easy to use.

A study in Brazil compared the effectiveness of double phototherapy with total irradiance 75.6 μW/cm^2/nm and pharmacotherapy, and found that double phototherapy was better and safer in reducing bilirubin levels with minimal side effects.[15] Similar studies, including one in Saudi Arabia, also showed that double phototherapy with blue light was more effective than single phototherapy, with minimal side effects.[16-18]

Light intensity is the factor that determines the effectiveness of phototherapy. Higher light intensity reduced bilirubin levels faster. A study in England showed that phototherapy with maximum irradiance and wide exposure shortened the duration of phototherapy.[22]

In our study, the nearest light source was 10 cm from the neonates' bodies. During phototherapy, the eyes and genitalia were covered to avoid damage from exposure to high light intensity.[19-21]

Blue light of wavelength 425-475 nm is the best light type to reduce indirect bilirubin levels.[23,24] Blue light is very effective because it has a shorter wavelength compared to other visible light, except for purple. Wavelength is inversely proportional to energy level; the shorter the wavelength, the greater the energy produced.[24]

In our study, we used blue light. Light intensity was measured at baseline, 12, and 24 hours of phototherapy. There was a significant difference in spectral irradiance between the two groups at all time points (P = 0.001). To increase photo light intensity for both groups, we placed the neonates supine and varied positions every 3 hours during phototherapy. However, a clinical trial in Israel comparing 14 neonates in alternating positions to 16 others in a supine position while using single phototherapy showed a significantly greater decrease in bilirubin levels in the supine group after 24 hours of phototherapy.[25]

Neonates treated for high bilirubin levels can also suffer from dehydration and may require additional fluid intake.[26] Neonatal maturity, adequate caloric intake, photo light unit temperature, distance between the neonate and photo light, and incubator rate of heat loss are all potential factors in increasing neonatal body temperature, environmental temperature, insensible water loss, as well as respiratory rate and blood flow to the skin. Increased peripheral blood flow can increase fluid loss, requiring adjustment by administration of intravenous fluids.[26,27] Changes in skin, such as rash, darker skin colour and burning, can be seen if infants are overexposed to fluorescent light. A study in the Netherlands found that during intensive phototherapy, a 20% increment of total fluid requirement may prevent increased body temperature.[28]

Body temperature and fluid administration were strictly monitored. Fluid intake was given every 2 hours and was increased by 10-20% of the total fluid requirement. In breastfed neonates, phototherapy was withheld during breastfeeding.[29,30] In our study, we found hyperthermia (T > 37.5 °C) in 3 (5% of total) neonates in the single phototherapy group and 5 (8.3% of total) in the double phototherapy group.

Limitations

A limitation of our study was not including maternal characteristic data associated with hyper- bilirubinemia in neonates. Most patients had only moderate hyperbilirubinemia. However the strength of this study is that it is base on common clinical practice with little evidence in clinical trials.

Conclusion

In conclusion, we found a significantly greater decrease in bilirubin levels in the double phototherapy group at 12 hours and 24 hours of phototherapy compared to the single phototherapy group. Double phototherapy is more effective than single phototherapy in reducing bilirubin levels in neonatal hyperbilirubinemia.

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