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A comparative study to determine intermittent versus continuous phototherapy for reducing neonatal hyperbilirubinemia at tertiary care hospital in Chennai, Tamil Nadu, India

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ABSTRACT

Background: Phototherapy is safe and effective in neonatal hyperbilirubinemia. Despite its worldwide application, questions regarding methods of optimizing efficacy remain unanswered, turning the infant is believed to be one of the methods to improve. Severe neonatal hyperbilirubinemia is associated with kernicterus, condition characterized by athetoid spasticity, gaze and visual abnormalities, and sensory-neural hearing loss. It may also be associated with mental retardation. Aim of this study was conducted to compare the efficacy of intermittent with continuous phototherapy.

Methods: Study was conducted in 100 neonates from February 2018 to July 2018 in Sree Balaji medical college and hospital. Inclusion criteria were weight >2000 grams, absence of other concomitant diseases, and hyperbilirubinemia not requiring exchange transfusion. The neonates were randomly divided into two groups. Continuous phototherapy group received phototherapy on and off for 2 hours and half an hour respectively and the intermittent phototherapy group on and then off for one hour. Serum total bilirubin levels were measured in every 36 hours.

Results: Mean age of the patients was 3.89±1.83 (p=0.91) days, mean baseline bilirubin was 17.56mg/dl±1.42 (p=0.36), while the mean follow-up bilirubin was 12.85mg/dl±1.65 (p=0.95), and the mean difference between the baseline and follow-up bilirubin was 4.7 mg/dl±1.19 (p=0.32). For group A and B babies, the mean difference between the baseline and follow-up bilirubin was 4.78 mg/dl±1.20 (p=0.32) and 4.63mg/dl±1.18(p=0.32) respectively. The difference between the mean age, mean baseline bilirubin, mean follow-up bilirubin, and the mean decrease in bilirubin for both the groups was statistically not significant.

Conclusions: Intermittent and continuous phototherapies were found to be equally effective for reducing neonatal hyperbilirubinemia.

Keywords: Continuous phototherapy, Hyperbilirubinemia, Intermittent phototherapy, Neonatal jaundice, Phototherapy, Term neonates

INTRODUCTION

Phototherapy has emerged as the widest form of therapy for the treatment and prophylaxis of neonatal unconjugated hyperbilirubinemia. In nearly all infants phototherapy reduces or blunts the rise of serum bilirubin concentrations, regardless of maturity, presence or absence of haemolysis, or degree of skin pigmentation.¹ Phototherapy appears to be safe given the decades of experience with its use in the United States and Europe

and the lack of reported serious long-term side effects of short-term phototherapy thus far.² The initial report from the Collaborative Study on the Effectiveness and Safety of Phototherapy, undertaken under the auspices of the National Institute of Child Health and Human Development, demonstrated that infants receiving phototherapy require significantly fewer exchange transfusions. Furthermore, subsequent follow-up studies revealed no adverse outcome in the neonates who received phototherapy in the neonatal period.

Phototherapy can be used either as therapy or as prophylaxis.³ Two different mechanisms have been proposed to explain the action of phototherapy in reducing serum bilirubin concentrations in newborn infants; photoisomerization and photooxidation.4 Compared with the photoisomerization pathway, the oxidation mechanism appears to play a very minor role in photocatabolism of unconjugated bilirubin in vivo. Clinical studies comparing intermittent to continuous phototherapy have yielded conflicting results. Several studies failed to show the effectiveness of intermittent therapy.⁵ These results may have resulted from prolonged light-on and light-off cycles, for example, 6- to 12-hour on-off schedules.6

Photoisomerization of bilirubin occurs primarily in skin layers and the restoration of the bilirubin pool in the skin takes approximately 1 to 3 hours. Thus a prolonged onoff schedule may not be as effective as continuous therapy, but an on-off cycle of less than one hour is apparently as effective as continuous treatment. Phototherapy lights should be shut off and eye patches removed during feeding and family visiting for up to one hour; this will not significantly reduce phototherapy effectiveness. Phototherapy is the mainstay of treatment of neonatal jaundice.

It acts by converting unconjugated bilirubin to more polar stereoisomer, which is less neurotoxic (cannot cross the blood-brain barrier) and can easily be excreted in bile and urine. The effectiveness of pho-therapy depends upon the light energy emitted in the effective range of wavelengths, the distance between the light source and the skin, and the surface area of the baby exposed to the light. Photoisomerization is a rapid process, in a study, it was found that a significant amount of 4Z, 15E photoisomers was formed in 15 minutes. The significant amount of 4Z, 15E photoisomers was formed in 15 minutes.

METHODS

This study was conducted in 100 neonates from February 2018 to July 2018. In Sree Balaji Medical College and Research Institute. The neonates were randomly divided into two groups. Continuous phototherapy group received phototherapy on and off for 2 hours and half an hour respectively and the intermittent phototherapy group on and off for one hour. The phototherapy units were identical, and serum total bilirubin levels were measured every 36 hours after starting phototherapy.

Inclusion criteria

Inclusion criteria were full-term neonates (\geq 37weeks) with age >24 hours and \leq 10days and serum indirect bilirubin level between 12 to 20mg/dl. APGAR at 5 minutes greater than 6 (as mentioned inpatient hospital record file).

Exclusion criteria

Patients on intensive care i.e. ventilator, endotracheal intubation, and peritoneal dialysis. Also, patients with major congenital malformation like cardiac, skeletal, renal, dysmorphism etc and sepsis i.e. positive blood culture, fit, reluctance to feed, platelets <50000. Babies who are having congenital abnormalities. Mothers those who are not willing.

Informed consents were taken from the parents, (father/mother, which one available) of those babies fulfilling the inclusion criterion, and which were enrolled in the study from the Neonatal unit of Children A Ward. We conducted this study by enrolling 100 babies, the male/female ratio, and mean baseline bilirubin level was matched between the two groups A and B. Group A received continuous phototherapy, while group B received intermittent phototherapy. Both the groups received phototherapy from apparatus of same manufacturer and same age. The height of the phototherapy light (distance between the light source and the infant) was kept similar for both groups. The follow-up bilirubin was measured at 36 hours. Group A patients received continuous phototherapy (2 hours on and 20 minutes off) while Group B patients received intermittent phototherapy (one hour on and 30 minutes off). The on-off timing, of phototherapy, was observed by the researcher. Blood samples were taken and sent to hospital labs, (on arrival before starting phototherapy, every 8 hourly while on phototherapy, and at the 36th hour), by the researcher, to look for serum bilirubin levels. The results were collect-ed from the lab by the researcher and the serum bilirubin levels were noted down in the Proforma. Exclusion criteria were followed, strictly, to control confounders and bias in the study results. All the laboratory investigations were done from hospital laboratory.

Standard tools for analysis

Bilirubin assessment scale

Normal level: Below 5mg/dl
Mild jaundice: 5 to 10mg/dl
Moderate jaundice: 10 to 15mg/dl

• Severe jaundice: Above 15mg/dl

Cramer's dermal zones index of neonatal jaundice

• Zone I face: 5mg/dl

• Zone II chest and upper abdomen: 10mg/dl

• Zone III thighs and upper arms: 12mg/dl

• Zone IV legs and forearm 15mg/dl

• Zone V palms and soles: 15mg/dl

Statistical analysis

Data were analysed a using SPS version 16. Quantitative variables such as age, serum bilirubin at the start of phototherapy and serum bilirubin at 36th hour was presented as Mean±SD. Qualitative variables such as gender were presented as %age and frequencies. To compare the mean of a decrease in serum bilirubin between the two groups, a t-test was applied and p-value ≤0.05 was considered statistically significant. All results were presented as tables.

RESULTS

There were 100 patients in our study. Gender wise the difference between the two groups, A and B, was statistically not significant (Table 1).

Mean age of the patients was 3.89 ± 1.83 (p=0.91), the mean baseline bilirubin of patients was 17.56mg/dl ±1.42 (p=0.36), while the mean follow-up bilirubin was 12.85mg/dl ±1.65 (p=0.95), and the mean difference between the baseline and follow-up bilirubin was 4.7 mg/dl ±1.19 (p=0.32) (Table 2).

Table 1: Gender distribution.

Gender	Group-A (n=50)		Group-B (n=50)	
	No. of patients	%	No. of patients	%
Male	35	66.5	30	54.3
Female	15	33.5	20	45.7
Total	50	100	50	100

For the group A babies, who received continuous phototherapy, the mean age on admission was 3.91 ± 1.82 (p=0.91), the mean baseline bilirubin of patients was 17.64 mg/dl \pm 1.37 (p=0.36), the mean follow-up bilirubin was 12.86mg/dl \pm 1.53 (p=0.95) and the mean difference between the baseline and follow-up bilirubin was 4.78mg/dl \pm 1.20 (p=0.32) (Table 3).

For the group B babies who received intermittent phototherapy, the mean age on admission was 3.88 ± 1.84 (p=0.91), the mean baseline bilirubin was $17.48\,\text{mg/dl}\pm1.47$ (p=.36), the mean follow-up bilirubin was $12.85\,\text{mg/dl}\pm1.76$ (p=0.95), and the mean difference between the baseline and follow-up bilirubin was $4.63\,\text{mg/dl}\pm1.18$ (p=0.32) (Table 4).

Table 2: Age of patient, baseline bilirubin, follow-up bilirubin, and the difference b/w baseline and follow-up bilirubin for total 100 patients.

Total patients	Age of patients in days	Baseline bilirubin	Follow up bilirubin after 36 hours	The difference between baseline and follow-up bilirubin
Mean	3.8983	17.5624	12.8539	4.7081
N	258	258	258	258
Std. Deviation	1.8279	1.42354	1.65106	1.19463
% Of total sum	100.0%	100.0%	100.0%	100.0%

Table 3: Group A (continuous phototherapy)-age of patient, baseline bilirubin, follow-up bilirubin, and the difference b/w baseline and follow-up bilirubin.

Continuous Phototherapy	Age of patients in days	Baseline bilirubin	Follow up bilirubin after 36 hours	The difference between baseline and follow-up bilirubin
Mean	3.9109	17.6434	12.8605	4.7822
N	129	129	129	129
Std. Deviation	1.8234	1.37238	1.53279	1.20231
% Of total sum	50.2%	50.2%	50.0%	50.8%

Table 4: Group B (intermittent phototherapy)-age of patient, baseline bilirubin, follow-up bilirubin, and the difference b/w baseline and follow-up bilirubin.

Intermittent Phototherapy	Age of patients in days	Baseline bilirubin	Follow up bilirubin after 36 hours	The difference between baseline and follow-up bilirubin
Mean	3.8857	17.4814	12.8473	4.6341
N	129	129	129	129
Std. Deviation	1.8395	1.47382	1.76742	1.18694
% Of total sum	49.8%	49.8%	50.0%	49.2%

Table 5: Comparision between group A and B.

Mean	Age of patients in days		Follow up bilirubin after 36 hours	The difference between baseline and follow-up bilirubin
Continuous Phototherapy	3.9109	17.6434	12.8605	4.7822
Intermittent Phototherapy	3.8857	17.4814	12.8473	4.6341

DISCUSSION

Jaundice becomes detectable to the naked eye when the total serum bilirubin level exceeds about 85µmo (5mg/100ml) and most babies become visibly jaundiced in the first week of life. Unfortunately, the terminology used in many texts Talks of jaundice being 'moderate' when it exceeds 200µmo and 'severe' when it exceeds 250 mmo on any such definition 'severe' jaundice develops in a third of all breastfed babies in the first week of life. Jaundice is only really 'actionable' in the otherwise healthy term baby when the level exceeds 340µmo (20mg/100ml) and potentially dangerous when it exceeds 43µmo (25mg/100ml).11 Phototherapy would not need to be given so often if it were administered more effectively when given. The graph shown here documents how the bilirubin level varied over time in a large group of mature exclusive breastfed babies-most other 'normative' charts document the levels seen in a population where at least a third of the babies were bottle fed. 12 The investigator investigates the prevalence the rate of hyperbilirubinemia is high. The phototherapy plays a significant role in the reduction of bilirubin in babies with hyperbilirubinemia. So, the researcher has the interest to determine the effectiveness between continuous and intermittent phototherapy to find the rapid recovery from hyperbilirubinemia.¹³ Gender wise the difference between the two groups, A and B, was statistically not significant (Table 1). The difference between the mean decreases in serum bilirubin of both groups was statistically not significant.¹⁴ The difference between the mean age on admission, mean baseline bilirubin, mean follow-up bilirubin, and the mean decrease in serum bilirubin for both the groups A and B was statistically not significant (Table 5). 15 This results of this study were similar to those of Tikmani SS et al. in that there was statistically no significant difference in the effectiveness (mean decrease in serum bilirubin) of both types of phototherapy. 16 Although we applied phototherapy for prolonged duration (2 hours on and 20 minutes off for continuous, and one hour on and 30 minutes off for intermittent group) compared to the above-mentioned study (2 hours on and 30 minutes off for continuous and one hour on and one hour off for intermittent group). In this study the mean serum bilirubin level before the start of phototherapy was 16.60mg/dl±1.67 for continuous and 16.33mg/dl±1.46 for intermittent group, and the mean serum bilirubin at 36 hours was 9.17mg/dl±1.83 for continuous and 9.02±1.94 for intermittent group, while in our study the mean serum bilirubin before the start of phototherapy was 17.64mg/dl±1.37 for continuous and 17.48mg/dl±1.47 for intermittent group, and the mean serum bilirubin at 36 was 12.86mg/dl±1.53 for continuous and 12.85mg/dl±1.76.¹⁷ In other words, in this study, the mean decrease in serum bilirubin was far less than theirs. This may be because of the difference in the apparatus. In intermittent phototherapy group, we applied the phototherapy for one hour and observed 30 mints off, because we consider thirty minutes time is sufficient for baby cleaning, feeding, and other helpful interventions if needed.¹⁸ The study was conducted on "Serum bilirubin kinetics in intermittent phototherapy of physiological jaundice" at Japan with the objectives of to treat the babies in the easiest way to minimize hospital duration Thirty-four term babies with physiological jaundice were subjected to continuous phototherapy and to two regimens of intermittent phototherapy.¹⁹ The difference in serum bilirubin kinetics between the three groups of treated babies was insignificant; a schedule of one in four hours of irradiation achieved the same treatment effect as continuous phototherapy. study was conducted on Regardless of different protocols of phototherapy, the Number-Needed-to-Treat (NNT) for prevention of serum bilirubin level exceeding 20 mg/dL ranged from six to 10 in infants of at least 34 weeks gestation at America.²⁰ This implies that one needs to treat six to 10 jaundiced neonates with TSB ≥15 mg/dL by phototherapy in order to prevent the TSB in one infant from rising above 20 mg/dL. Phototherapy combined with cessation of breastfeeding and substitution with formula was the most effective treatment protocol for infants of at least 34 weeks gestation with jaundice.²¹ Eight studies examined the effect of bilirubin reduction on brainstem auditory evoked response (BAER). All consistently showed treatments for neonatal hyperbilirubinemia significantly improved abnormal BAER's in both healthy jaundiced infants and jaundiced infants with hemolytic disease.²² Three studies evaluated the effect of phototherapy on visual outcomes. All showed no short- or long-term (up to 36 months) effect on vision as a result of phototherapy when infants' eyes were properly protected during treatment. 23-25

CONCLUSION

Intermittent and continuous phototherapies were found to be equally effective. Because of its additional benefits, intermittent phototherapy can be adopted as a routine procedure instead of continuous phototherapy in neonatal care units, however, it needs to be confirmed by largescale RCTs.

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Institutional Ethics Committee

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