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ORIGINAL ARTICLE

Intermittent versus continuous phototherapy among term infants presenting with non-hemolytic moderate hyperbilirubinemia at a tertiary care hospital: a randomized controlled trial.

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ABSTRACT… Objective: To compare the effectiveness of intermittent versus continuous phototherapy among term infants presenting with non-hemolytic moderate hyperbilirubinemia at a tertiary care hospital. **Study Design:** Single Center, Open Label, Prospective Randomized Controlled Trial. **Setting:** Department of Neonatology, Sir Sadiq Abbasi Hospital, Bahawalpur, Pakistan. **Period:** January 2022 to December 2022. **Material & Methods:** A total of 38 neonates having maternal age between 18-35 years and gestational age at the time birth above or equal to 37 weeks presenting and admitted with non-haemolytic hyperbilirubinemia were included. These neonates (19 in each group) were randomized adopting lottery method to either continuous phototherapy group (CPT) or intermittent phototherapy group (IPT). At the time of enrollment, demographic characteristics like age (days), gender, birth weight (kg), mode of delivery, gestational age (weeks), maternal age (years), total serum bilirubin (mg/dl) in the neonates were noted. Total serum bilirubin levels were recorded after 24 hours of phototherapy. **Results:** In a total of 38 neonates, 20 (52.6%) were boys. The mean age was calculated to be 3.3±1.8 days. Mode of delivery was cesarean section in 24 (63.2%) neonates. The mean total serum bilirubin levels at baseline was recorded to be 15.5±1.7 mg/dl while comparison of baseline total serum bilirubin levels were not statistically significant different between both study groups (p=0.3715). The mean serum bilirubin levels after 24-hours were recorded to be 11.3±0.9 mg/dl in CPT group versus 11.0±1.1 mg/dl while the difference was noted to be statistically insignificant. (p=0.3637). **Conclusion:** The intermittent phototherapy yielded relatively similar reduction in total serum bilirubin when compared to continuous phototherapy among neonates with non-haemolytic moderate hyperbilirubinemia.

Key words: Bilirubin, Gestational Age, Hyperbilirubinemia, Non-haemolytic, Phototherapy.

INTRODUCTION

Phototherapy is known to impart reduction in the increase of serum bilirubin levels irrespective of the maturity or the existence and non-existence of hemolysis or the extent of skin pigmentation.[1] Phototherapy is considered to be the main approach towards treating neonates with unconjugated hyperbilirubinemia.[2] Around 97% of preterm neonates exhibit biochemical hyperbilirubinemia in terms of serum bilirubin above 1 mg/dl while approximately 65% of preterm neonates are estimated to have clinical jaundice.[3] Neonatal jaundice is considered to the most frequent reason for hospitalization among neonates.[4] The "American Academy of Paediatrics (AAP)", stated that neonates who are discharged with 48 hours need to be called for follow ups after 48-72 hours for the evaluation of jaundice and other related issues.[5]

The main mechanism behind phototherapy considered effective for neonatal hyperbilirubinemia is the photo-isomerization that imparts reduction in the levels of bilirubin through degradation of bilirubin.[6] The photo-isomerization of bilirubin transpires mainly in the layers of the skin whereas the reinstatement of the bilirubin levels in the skin layers might take about 1-3 hours.[7] Some

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researchers proposed that a relatively prolonged on and off routine of phototherapy might not be as efficient as continuous therapy. On the other hand, some propose that on-off cycles lasting lesser than 1 hour might provide relatively similar effectiveness as continuous phototherapy approach.[8] A study by Taheritafti R and Taheritaft M from Iran reported the baseline serum bilirubin levels among neonates presenting with non-hemolytic moderate hyperbilirubinemia to be 15.97±1.56 mg/dl and 16.14±1.58 mg/dl among neonates undergoing continuous and intermittent phototherapy respectively while the serum bilirubin levels fell down to 12.29±1.15 mg/dl and 13.36±1.18 mg/dl after 24-hour continuous and intermittent phototherapy respectively.[9] The effectiveness of phototherapy is said to be linked with the initial levels of bilirubin when the phototherapy starts while the effectiveness reduces as the levels of serum bilirubin decrease.[10] Theoretically, phototherapy duration of 1-3 hours may be favorable to rapid bilirubin recovery assisting effectiveness of phototherapy but this needs further verification.

As per the best of our knowledge and literature search, there is scarcity of local data about the comparison in effectiveness of intermittent versus continuous phototherapy among term neonates presenting with moderate non-hemolytic hyperbilirubinemia so the present study was thought to provide much needed local evidence about the rate of reduction in bilirubin levels, reduction in total serum bilirubin levels, duration of phototherapy and hospitalization among these neonates. The aim of this study was to compare the effectiveness of intermittent versus continuous phototherapy among term infants presenting with non-hemolytic moderate hyperbilirubinemia at a tertiary care hospital.

MATERIAL & METHODS

This single center, open label, prospective randomized controlled trial was conducted at the department of neonatology, Sir Sadiq Abbasi Hospital, Bahawalpur, Pakistan from January 2022 to December 2022. Approval from "Institutional Ethical Committee (4805)" was acquired. With 95% confidence interval (2-sided), 80% power and ratio of sample in both study groups as 1:1, the sample size was calculated to be 38 (19 in each group) considering serum bilirubin levels as 12.29±1.15 mg/dl and 13.36±1.18 mg/dl after 24-hour continuous and intermittent phototherapy among term neonates presenting with non-hemolytic moderate hyperbilirubinemia.[9]

Inclusion criteria were neonates having maternal age between 18-35 years and gestational age at the time birth above or equal to 37 weeks presenting and admitted with non-haemolytic hyperbilirubinemia. Exclusion criteria were neonates who had haemolytic anaemia, premature birth, sepsis, severe hyperbilirubinemia (total bilirubin above 19 mg/dl), direct hyperbilirubinemia, congenital malformations or the occurrence of jaundice within first 24-hours after birth. A total of 39 children (19 in each group) were randomized adopting lottery method to either continuous phototherapy group (CPT) or intermittent phototherapy group (IPT). Informed and written consents were sought from parents/ legal guardians of all neonates.

At the time of enrollment, demographic characteristics like age (days), gender, birth weight (kg), mode of delivery, gestational age (weeks), maternal age (years), total serum bilirubin (mg/dl) in the neonates were noted. In the CPT group, phototherapy was given for 3 hours and then 45 minutes off while in IPT group, phototherapy was given for 3 hours than off for the next 3 hours. In both study groups, phototherapy was given adopting double surface phototherapy unit (Phoenix brilliance classic with 12 LED bulbs, LED intensity>45 microwatt/cm2/nm, wavelength 450-465 nm) and total serum bilirubin levels were recorded after 24 hours of phototherapy. Distance of 30-35 cm was ensured between the baby the bulb surface. A special proforma was designed to record all study data.

Data analysis was performed using "Statistical Package for Social Sciences (SPSS)", version 28.0. The qualitative data was highlighted as frequency and percentages while quantitate details were shown as mean and standard deviation (SD). Quantitative data were compared

using independent sample test while comparison of qualitative data were made using chi-square test. P value below 0.05 was considered as significant.

RESULTS

In a total of 38 neonates, 20 (52.6%) were boys and 18 (47.4%) girls. The mean age was 3.3±1.8 days (ranging between 2 to 6 days). The mean birth weight as per medical record was 2750±250 grams. Mode of delivery was cesarean section in 24 (63.2%) neonates. Table-I is showing comparison of baseline characteristics between neonates of both study groups.

The mean total serum bilirubin levels at baseline was recorded to be 15.5±1.7 mg/dl while comparison of baseline total serum bilirubin levels were not statistically significant different between both study groups (p=0.3715). The mean serum bilirubin levels after 24-hours were recorded to be 11.3±0.9 mg/dl in CPT group versus 11.0±1.1 mg/dl while the difference was noted to be statistically insignificant. (p=0.3637).

DISCUSSION

Around 60% full term and 80% pre term neonates develop jaundice because of hyperbilirubinemia.[11] Furthermore, it is estimated that between 5-10% of these neonates require phototherapy.[11,12] The literature exhibits that "ABO-incompatibility" is the commonest reason behind hemolytic disorders in the neonatal period.[13,14]

In this study, the mean serum bilirubin levels after 24-hours were recorded to be 11.3±0.9 mg/dl in CPT group versus 11.0±1.1 mg/dl while the difference was noted to be statistically insignificant. (p=0.3637). Our findings are consistent with a study done by Zhou et al from China reported that continuous phototherapy approach in neonatal jaundice was effective in 89.7% neonates in comparison to 88.7% adopting intermittent phototherapy approach (p=0.786).[15] Another study done by Monica Sachdeva et al compared IPT based on the 12:12 hours on-off schedule versus 24-hour CPT. The researchers found that IPT was more effective in comparison to CPT among neonates with non-hemolytic moderate hyperbilirubinemia.[16] Published literature gives conflicting evidence regarding effectiveness of IPT versus CPT in non-hemolytic moderate hyperbilirubinemia. Theoretically, when the exposure to light is increased, it should increase the excretion of bilirubin, so CPT should be more efficient in comparison to CPT but its not always the case.[16] A study proved CPT and IPT (1 in 4 hours) were comparable with regards to serum bilirubin kinetics.[17] The findings of this study stands comparable to previously published data where authors exhibited that longer duration of phototherapy was not required among neonates who underwent IPT.[18,19] It is known that photo-isomerization happens inside minutes while migration of bilirubin occurs slowly which takes hours.

Characteristics		CPT Group (n=19)	IPT Group (n=19)	P-Value
Gender	Boys	9 (47.4%)	11 (57.9%)	0.5158
	Girls	10 (52.6%)	8 (42.1%)	
Age (days)		3.2±1.9	3.4±1.8	0.7410
Birth weight (kg)		2700±200	2800±250	0.1818
Mode of delivery	Normal vaginal delivery	6 (31.6%)	8 (42.1%)	0.5012
	Cesarean section	13 (68.4%)	11 (57.9%)	
Maternal age (years)		26.5±3.2	25.4±3.8	0.3409
Gestational age (weeks)		38.2±0.8	37.9±0.7	0.2266

Table-I. Characteristics of neonates with non-haemolytic moderate hyperbilirubinemia (N=38)

Total Serum Bilirubin	CPT Group (n=19)	IPT Group (n=19)	P-Value
At baseline (mg/dl)	15.3±1.8	15.8±1.6	0.3715
After 24-hours (mg/dl)	11.3±0.9	11.0±1.1	0.3637

Table-II. Comparison of mean total serum bilirubin at baseline and after 24-Hours (N=38)

As photo-isomerization happens mainly in the skin, the restoration of the bilirubin pool might be taking 1 to 3 hours in the skin layers so, IPT should be providing equal effectiveness in comparison to CPT.

The IPT approach seems to be more simple and doable, on the other hand, it is more economical as well which provides more interest for adopting it in routine care in a country like Pakistan where most of the healthcare facilities are resource limited. Furthermore, IPT causes less interruption between mother-and-infant which might help in improving the bonding between the two as the affected infants are not limited to phototherapy in case of CPT until the completion of the full course. The IPT can further assist in continuation of the routine nursing and maternal care which is more important in resource limited settings as the extent of neonatal care is distributed between the mother and nursing staff. Theoretically, IPT might be reducing the maternal stress and anxiety as they can spend relatively more time with their babies when compared to CPT.

The present study adds important insights about the role of IPT versus CPT in neonatal non-haemolytic moderate hyperbilirubinemia. Being an single center study conducted on relatively small number of babies, further trials should be conducted to add what is already known about the role of IPT and CPT among neonates.

CONCLUSION

The intermittent phototherapy yielded relatively similar reduction in total serum bilirubin when compared to continuous phototherapy among neonates with non-haemolytic moderate hyperbilirubinemia. Additional benefits of intermittent phototherapy could be less interruption between mother and the infants which could improve their bonding and may promote exclusive breast feeding and less burden on healthcare facilities.

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3	Afaq Hussain	Data Collection, Data analysis.	
4	Asif Javeed	Literature review, Discussion.	