Comparison of Intermittent vs. Continuous Phototherapy in the treatment of Non-Haemolytic Neonatal Hyperbilirubinemia

IRFAN ULLAH¹, IRFAN KHAN², KHALIL AHMAD³, KHALID KHAN⁴, MUHAMMAD SHAFIQ⁵, SAEED ULLAH⁶

¹Senior Registrar Pediatric Medicine, Nowshera Medical College, Nowshera

²Assistant Professor Pediatric Medicine, Nowshera Medical College, Nowshera

³Assistant Professor Pediatric Medicine, Bacha Khan Medical College, Mardan

⁴Associate Professor Pediatric Medicine, Nowshera Medical College, Nowshera

⁵Senior Registrar Pediatric Medicine, Nowshera Medical College, Nowshera

⁶District Children Specialist, District Headquarter Hospital, Dir (Upper)

Corresponding author: Irfan Khan, Email: dr.irfankhan1984@gmail.com, Cell: +92 336 92058058

ABSTRACT

Introduction: Phototherapy is used in the treatment of hyperbilirubinemia in initial life-span of neonates. Our objective was the comparison of continuous vs intermittent phototherapy in the reduction of total serum bilirubin, bilirubin decrease rate, phototherapy time and hospital stay in non-haemolytic hyperbilirubinemia neonates.

Place and Duration: The study was conducted at department of Pediatric medicine in Qazi Hussain Ahmad Medical Complex, Nowshera for the duration of six months from 16th January 2021 to 15th July 2021.

Methods: The study involved 160 neonates with birth weight ≥2000 gm and age was above 34 weeks. They were randomly assigned to group A who were given continuous phototherapy for 3hrs and 50 mints and then rest for 45mints and group B who were given intermittent phototherapy for 3 hours and then rest for next 3 hours and so on. The levels of TSB were calculated in both groups and their comparison was made at every 12, 24 and 48 hrs after the start of phototherapy.

Results: The mean of total serum bilirubin on admission was $16.01 \pm 3.91 \text{ mg} / \text{dL}$ for the continuous group and $15.21 \pm 1.12 \text{ mg} / \text{dL}$ for the intermittent group. The TSB mean after 12, 24 and 48 hrs. for continuous phototherapy was $13.30 \pm 2.3 \text{ mg} / \text{dL}$, $11.1 \pm 2.01 \text{ mg} / \text{dL}$, $9.26 \pm 0.92 \text{ mg} / \text{dI}$ and $13.1 \pm 1.70 \text{ mg} / \text{dL}$, $9.54 \pm 1.7 \text{ mg} / \text{dL}$, $8.9 \pm 0.61 \text{ mg} / \text{dI}$ (p <0.05) for the intermittent group, respectively. The mean rate of decrease in serum concentration of bilirubin was $0.30 \pm 0.14 \text{ mg} / \text{dI} / \text{h}$ in group A and $0.19 \pm 0.07 \text{ mg} / \text{dI} / \text{h}$ in group B (p = 0.5). There was no big variance between the mean hospital stay in groups A and B (p = 0.550).

Conclusions: Intermittent phototherapy is a better choice than continuous phototherapy in the treatment of non-haemolytic hyperbilirubinemia, with added benefits such as less frequent disruption of the mother-child relationship and reduced radiation therapy.

Keywords: Intermittent phototherapy; Continuous phototherapy; Total serum bilirubin and Neonatal hyperbilirubinemia.

INTRODUCTION

Phototherapy has become the prophylaxis and main treatment of unconjugated neonatal hyperbilirubinemia and aids to decrease the serum bilirubin irrespective of the absence or presence of hemolysis, maturity, the degree of pigmentation in the skin1-2. Approximately 98% of preterm and full-term infants have physical hyperbilirubinemia (> 1 mg / dL of serum bilirubin) and approximately 67% have clinical jaundice³⁻⁴. It is the communal cause for re-hospitalization in the earlier life-span of neonatal life5 ⁶. The American Paediatrics Academy commends those new-borns discharged within 48 hours must have 48-72 hours later follow-up for any problems or jaundice. Phototherapy works by the principle of photoisomerization, which lowers the bilirubin level by breaking down bilirubin. The bilirubin photoisomerization mainly transpires in the skin layers, and it takes about one to three hours to restore the bilirubin levels in the skin7-8. Therefore, a long off and on follow-up may not be as operative as continuous therapy, but a shorter on and off sequence of <1 hr. appears to be as operative as continued therapy⁹⁻¹⁰. The phototherapy efficacy is correlated to the baseline bilirubin level and decreases as bilirubin levels of serum fall. A phototherapy reduction period of one to three hours will promote a more intense reflection of the bilirubin in the skin and hypothetically enhance the phototherapy effect by reducing the time of phototherapy from one to three hours allows time for nursing an infant, feeding, mother-kangaroo care, creating a bond between mother and child, saves nurses time and effort, and lowers phototherapy costs¹¹⁻¹². Our goal was the comparison of continuous vs intermittent phototherapy in the reduction of total serum bilirubin, bilirubin decrease rate, phototherapy time and hospital stay in non-haemolytic hyperbilirubinemia neonates.

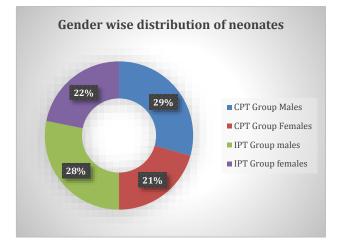
MATERIAL AND METHODS

This interventional and randomised study involved 160 neonates with birth weight \geq 2000 gm and ages were above 34 weeks. The study was conducted with agreement from the ethical committee at

the department of Pediatric medicine in Qazi Hussain Ahmad Medical Complex, Nowshera for the duration of six months from 16th January 2021 to 15th July 2021. The study included children over 34 weeks of age of both sexes who gave birth via normal vaginal delivery or lower segment cesarean delivery, with ≥2000 gm birth weight and > 7/10 of an APGAR score at 1 mint. ABO and Rh incompatibility, birth defects, neonatal sepsis, low birth weight babies and premature babies were exempted from the study. They were randomly assigned to group A who were given continuous phototherapy for 3hrs and 50 mints and then rest for 45mints and group B who were given intermittent phototherapy for 3 hours and then rest for next 3 hours and so on. The time lapse was given to the mother for infant feeding, breastfeeding and idle care. Demographic information such as gender, age, time and date of birth, APGAR scores, method of delivery, serum bilirubin levels and child and mother blood group were documented. Serum total bilirubin was estimated using a peripheral vein sample on admission, i.e., within 0 hours. Phototherapy was initiated according to the guidelines of the American Academy of Paediatrics in 2004. The levels of TSB were calculated in both groups and their comparison was made at every 12, 24 and 48 hrs. after the start of phototherapy.

A two-surface phototherapy unit was used in both groups (wavelength 450-465 nm and LED intensity> 45 microwatts / cm2 / nm with 12 LED bulbs). 30 to 35 cm of distance is kept between the bulb surface and baby. SPSS 23.0 was applied for statistical analysis. Categorical variables were articulated as proportions, and these variables analysis was done with Chi-square test. Continuous normally distributed variables were analyzed using measures like standard deviation and sample mean. The student's t-test was used for non-parametric data. Karl Pearson correlation analysis was done to determine the association between biochemical parameters. (p <0.05 was taken significant).

Amongst 160 neonates, the baseline features of the two groups were comparable. At admission; mean age in the CPT group was 77 hours and 78 hours in the IPT group, correspondingly.



There was no variance in mean APGAR scores and gestational age in the two groups. On admission; the mean body weight was 2600 grams in the CPT and 2700 grams in the IPT group, correspondingly (Table 1).

Table-1: shows the baseline characteristics of the neonates

Variables	CPT (n = 80)	IPT (n = 80)
# Gestational age (w)	38	38
Males	47 (58.8)	45 (56.3)
# APGAR	7	7
# Age at diagnosis	77	78
(hours)		
# Weight (g)	2600	2700
# TSB at admission	16.01 ± 3.91	15.21 ± 1.12
(mg/dl)		

The TSB mean after 12, 24 and 48 hrs. for continuous phototherapy was $13.30 \pm 2.3 \text{ mg}$ / dl, $11.1 \pm 2.01 \text{ mg}$ / dl, $9.26 \pm 0.92 \text{ mg}$ / dl and $13.1 \pm 1.70 \text{ mg}$ / dL, $9.54 \pm 1.7 \text{ mg}$ / dL, $8.9 \pm 0.61 \text{ mg}$ / dl (p <0.05) for the intermittent group, respectively. The mean rate of decrease in serum concentration of bilirubin was $0.30 \pm 0.14 \text{ mg}$ / dl / h in group A and $0.19 \pm 0.07 \text{ mg}$ / dl / h in group B (p = 0.5). There was no big variance between the mean hospital stay in groups A and B (p = 0.550) Table-2.

Table-2: shows the comparison of Mean TSB at 12, 24 and 48 Hours of Phototherapy in two Groups

Time in hours	CPT TSB (mg/ dl) ± SD (No. of		IPT TSB (mg/ dl) Mean ± SD (No. of cases)	t value	p value
12 hrs	13.30 ± 2.3 (64)	13.1 ± 1.70 (75)	2.5	0.031
24 hrs	11.1 ± 2.01 (69)	9.54 ± 1.7 (71)	2.80	0.007
48 hrs	9.26 ± 0.92 (18)	8.9 ± 0.61 (10)	3.1	0.003

Compared to continuous phototherapy, the intermittent phototherapy duration was shorter, i.e., 28 hrs and 19 hrs with no statistically significant difference. Likewise, no significant variance in the mean hospital stays in the two groups (33.2 hours for IPT and 37 hours for CPT group). The cost of CPT was Rs 3,400, which is relatively greater than the IPT price, i.e. Rs 3,000.

DISCUSSION

The variance between the mean bilirubin and mean baseline value during the 12-, 24-, and 48-hour follow-up periods for the IPT and CPT groups was statistically substantial (p less than 0.05) (Table-

II). In the Niknafset et al study, no substantial differences were found in the mean serum level of bilirubin during the follow-up period in the IPT and CPT group¹³⁻¹⁴. This change might possibly be because of dissimilar descriptions of phototherapy duration in the continuous and intermittent groups. The time specified in our study for "with phototherapy and phototherapy" (three hours for the continuous group with 45 mints lapse, 3 hours for the intermittent group, 3 hours for the rest) could reduce enterohepatic bilirubin circulation (permitting additional spell for nursing in the intermittent group), which resulted in huge decline in serum level of bilirubin in comparison to the Niknafs et al study which used "two hours on, half an hour off" and "one hour off" in the CPT group and one hour on with one hour off, in the IPT group¹⁵⁻¹⁶. The phototherapy duration in the IPT group was shorter than in the continuous phototherapy group, as Monica et al¹⁷⁻¹⁸.

associating Preceding researches continuous and intermittent phototherapy have exhibited contradictory outcomes¹⁹. Since light exposure upsurges the bilirubin excretion, CPT will be more effective than IPT. Fung and Lau exhibited that the variance in serum levels of bilirubin, kinetics amid intermittent and continuous phototherapy was negligible, and that the four-hour irradiation program produced the similar therapeutic effect as CPT²⁰⁻²¹. In this research, we detected that the phototherapy duration was longer significantly in the CPT groups than in the IPT group. Our results are comparable to earlier researches published by Vogl and Maurer which presented that IPT does not lead to long-term phototherapy. This may be because photoisomerization transpires within mints and bilirubin migrates slowly to the skin in several hours. Since photoisomerization mainly takes place in the skin layers and it takes about one to three hours to rebuild the pool of bilirubin in the skin, IPT regimes be just as effective. Succeeding this supposition, several investigators have attempted to test the IPT effectiveness. Though, a long-term on-off program may not be as operative as CPT, while an on-off cycle of <1 hour apparently be as operative as CPT²²⁻²³. The concept of IPT is certainly more attractive than that of CPT. In addition to being simple to implement, it is also attractive economically to emerging republics where needs are greatest and resources limited. In addition, since new-borns are not confined to phototherapy throughout the duration of phototherapy, this mode makes it less disruptive to the mother-child relationship and breastfeeding.

We strained for comparing the effectiveness of CPT and IPT in our setting. Though, our results cannot be generalized to the whole populace as this is a single location study²⁴. Therefore, more researches are necessary in this area where more and more multicenter infants can be tested concurrently. This can have enduring consequences, particularly in a resource-constrained setup comparable to ours.

CONCLUSION

Intermittent phototherapy is a better choice than continuous phototherapy in the treatment of non-haemolytic hyperbilirubinemia, with added benefits such as less frequent disruption of the mother-child relationship and reduced radiation therapy.

REFERENCES

- Dani C, Becciani S, Pratesi S. Changes in total serum bilirubin during phototherapy in late preterm and term infants with non-haemolytic hyperbilirubinemia. Early Human Development. 2019 Apr 1;131:41-4.
- Patil MM, Gowthami GS, Bijapure HR, Sajjan AK, Kalyanshettar SS, Patil SV. Continuous Vs Intermittent Phototherapy In The Management Of Non-Hemolytic Neonatal Hyperbilirubinemia-A Randomized Non-Inferiority Study.
- Chang PW, Waite WM. Evaluation of home phototherapy for neonatal hyperbilirubinemia. The Journal of pediatrics. 2020 May 1;220:80-5.
- Mitra S, Rennie J. Neonatal jaundice: aetiology, diagnosis and treatment. British Journal of Hospital Medicine. 2017 Dec 2;78(12):699-704.

- Snook J. Is home phototherapy in the term neonate with physiological jaundice a feasible practice? A systematic literature review. Journal of Neonatal Nursing. 2017 Feb 1;23(1):28-39.
- Slusher TM, Vaucher YE. Management of neonatal jaundice in lowand middle-income countries. Paediatrics and International Child Health. 2020 Jan 2;40(1):7-10.
- Hamed AM, Younis MM, Mohammed SM. Efficacy of intensive phototherapy as a treatment modality for neonatal hyperbilirubinemia. The Egyptian Journal of Hospital Medicine. 2020 Jul 1;80(3):971-6.
- Choo YM, Springer S, Yip KX, Kamar AA, Wong EH, Lee SW, Lai NM. High-versus low-dose conventional phototherapy for neonatal jaundice. Cochrane Database of Systematic Reviews. 2020(4).
- Patil A, Pawar JM, Kshirsagar VY. Effect of fluid supplementation with phototherapy in reducing the serum bilirubin levels in severe hyperbilirubinemia. International Journal of Research in Pharmaceutical Sciences. 2020 Jul 10;11(3):3279-83.
- Onianwa PO, Adubi IO, Alonge TO, Otegbayo AJ, Yaya OS, Ojo OV, Ola FT, Layemo BO, Emiola OR, Mosebolatan AO. Super LED lamps and compact fluorescent lamps in the management of neonatal jaundice. Africa Journal of Nursing and Midwifery. 2018 Oct 10;20(2):14-pages.
- 11. Swain A, Mishra S, Mishra A, Behera S. A STUDY OF REBOUND HYPERBILIRUBINEMIA IN POST PHOTOTHERAPY NEONATES.
- Phyu KL, Zaw K, Soe HH, Than NN, Lwin H, Limkittikul K. A Retrospective Study on Clinical Features of Early Neonatal Jaundice in Term Babies at Ratchaburi Hospital, Thailand.
- Al-Lawama M, Al-Rimawi E, Al-Shibi R, Badran E. Adoption of the American Academy of Pediatrics' neonatal hyperbilirubinemia guidelines and its effect on blood exchange transfusion rate in a tertiary care center in Amman, Jordan. Journal of Blood Medicine. 2018;9:61.
- Lohiya SB, Jindal T. Double surface light emitting diode phototherapy versus double surface compact florescent light phototherapy in neonatal non-haemolytic hyperbilirubinemia: a randomized controlled trial.
- Chu L, Qiao J, Xu C. Home-Based phototherapy versus hospitalbased phototherapy for treatment of neonatal hyperbilirubinemia: a

systematic review and meta-analysis. Clinical Pediatrics. 2020 Jun;59(6):588-95.

- Biswas ŔK, Munian D, Mukherjee R. A Randomized Controlled Trial Comparing the Duration of Phototherapy Following NICE and AAP Guidelines in Neonatal Hyperbilirubinemia.
- Capasso L, Palma M, Coppola C, Salomè S, Esposito V, Grappone L, Raimondi F. Neonatal Hyperbilirubinemia: An Updated Appraisal of National Guidelines. Current Pediatric Reviews. 2020 Nov 1;16(4):298-306.
- Akefi R, Hashemi SM, Alinejad S, Almasi-Hashiani A. The effect of ursodeoxycholic acid on indirect hyperbilirubinemia in neonates treated with phototherapy: a randomized clinical trial. The Journal of Maternal-Fetal & Neonatal Medicine. 2020 Nov 10:1-6.
- Van Rostenberghe H, Ho JJ, Lim CH, Abd Hamid IJ. Use of reflective materials during phototherapy for newborn infants with unconjugated hyperbilirubinaemia. Cochrane Database of Systematic Reviews. 2020(7).
- Picó MJ, Maciá MS, Soler LM. Variability of neonatal hyperbilirubinemia of non-immune cause in the clinical practice. Journal of Neonatal Nursing. 2018 Jun 1;24(3):126-33.
- Bhardwaj K, Locke T, Biringer A, Booth A, K Darling E, Dougan S, Harrison J, Hill S, Johnson A, Makin S, Potter B. Newborn bilirubin screening for preventing severe hyperbilirubinemia and bilirubin encephalopathy: a rapid review. Current Pediatric Reviews. 2017 Feb 1;13(1):67-90.
- 22. Sinha A, Pradhan A, Thumburu KK, Gupta N. Probiotics for the prevention or treatment of hyperbilirubinaemia in late preterm and term neonates. The Cochrane Database of Systematic Reviews. 2017 Aug;2017(8).
- Tsao PC, Yeh HL, Shiau YS, Chang YC, Chiang SH, Soong WJ, Jeng MJ, Hsiao KJ, Chiang PH. Long-term neurodevelopmental outcomes of significant neonatal jaundice in Taiwan from 2000–2003: A nationwide, population-based cohort study. Scientific Reports. 2020 Jul 9;10(1):1-8.
- Sroufe NS, Vredeveld JL, Levy M, Little SH, Schumacher RE, Seagull FJ, Skoczylas MS. Management of indirect neonatal hyperbilirubinemia.