Journal of Health and Rehabilitation Research 2791-156X JHRR

Original Article

Comparison of Intermittent Versus Continuous Phototherapy in Neonatal Hyperbilirubinaemia

Jaweria Zahid[1], Huzaifa Malik[2], Shakeel Ahmed[1], Ayesha Ali Shams[1], Ayesha Mustafa[1], Andaleeb Tariq[1], Muhammad Farrukh Habib*[3]

[1] Khyber Department of Paediatrics, Combined Military Hospital, Rawalpindi, Pakistan.

[2] Department of Ophthalmology, Pak-Emirates Military Hospital, Rawalpindi, Pakistan

[3] Shifa Tameer-e-Millat University, Islamabad, Pakistan.

Corresponding author: muhammadfarrukhhabib@gmail.com

Keywords: Neonatal Hyperbilirubinaemia, Intermittent Phototherapy, Continuous Phototherapy, Bilirubin Reduction, Neonatal Jaundice, Phototherapy Complications

Abstract

Background: Neonatal jaundice is a common condition characterized by elevated bilirubin levels, which, if untreated, can lead to severe complications such as kernicterus. Phototherapy is a widely used treatment modality, with two primary approaches: continuous and intermittent phototherapy. While both methods aim to reduce bilirubin levels, there is ongoing debate about their relative efficacy and safety.

Objective: This study aimed to compare the efficacy and safety of intermittent versus continuous phototherapy in the management of neonatal hyperbilirubinaemia in terms of bilirubin reduction, treatment duration, and associated complications.

Methods: A quasi-experimental study was conducted at the Department of Paediatrics, Combined Military Hospital, Rawalpindi, from January 2022 to December 2023. The study included 62 full-term neonates with indirect bilirubin levels >15.0 mg/dL but ≤20 mg/dL. Neonates were randomly assigned to receive either intermittent phototherapy (two hours on, two hours off) or continuous phototherapy. Serum indirect bilirubin levels were measured at 24 and 48 hours post-initiation of phototherapy. The total duration of phototherapy, volume of milk consumed, and complications such as hyperthermia and hypocalcaemia were recorded. Data were analyzed using SPSS version 25, with a p-value ≤ 0.05 considered statistically significant.

Results: At 24 hours post-treatment, the median indirect bilirubin level was 12.70 mg/dL (IQR: 1.20) in the intermittent group versus 12.50 mg/dL (IQR: 1.90) in the continuous group (p=0.893). At 48 hours, the levels were 6.40 mg/dL (IQR: 1.10) and 6.50 mg/dL (IQR: 1.10), respectively (p=0.821). The median total duration of phototherapy was significantly shorter in the intermittent group (22.0 hours, IQR: 2.0) compared to the continuous group (45.0 hours, IQR: 3.0; p<0.001). Neonates in the intermittent group consumed more milk (420.0 mL, IQR: 93.0) than those in the continuous group (397.0 mL, IQR: 57.0; p=0.014). Hyperthermia was less frequent in the intermittent group (3.2% vs. 25.8%, p=0.026), as was hypocalcaemia (16.1% vs. 45.2%, p=0.013).

Conclusion: Intermittent phototherapy is as effective as continuous phototherapy in reducing bilirubin levels and offers additional benefits, including a shorter treatment duration, improved feeding, and fewer complications. Intermittent phototherapy should be considered a preferred option for managing neonatal hyperbilirubinaemia in clinical practice.

1 Introduction

Neonatal jaundice, a common condition in the early days of life, manifests as a yellowish discoloration of the skin and eyes in newborns, resulting from elevated levels of bilirubin. While often benign and self-limiting, severe hyperbilirubinaemia can lead to significant neurological complications, including kernicterus, if not promptly managed (1). Phototherapy has long been established as a cornerstone in the treatment of neonatal hyperbilirubinaemia, leveraging light energy to convert unconjugated bilirubin into water-soluble isomers that can be easily excreted by the neonate's body (2). The clinical application of phototherapy has evolved over the decades, giving rise to two primary modalities: continuous and intermittent phototherapy (3, 4). Continuous phototherapy entails uninterrupted exposure to light, maximizing the cumulative effect of photodegradation and aiming for a rapid reduction in bilirubin levels. Proponents of this approach argue that continuous phototherapy can potentially shorten the duration of treatment and minimize the risk of rebound hyperbilirubinaemia, thereby reducing the likelihood of associated complications (5, 6). However, concerns regarding the continuous nature of this treatment include potential disruptions to the neonate's sleep-wake cycle, increased risks of dehydration, and adverse effects on parental bonding due to limited opportunities for maternal interaction during therapy (7).

Intermittent phototherapy, in contrast, is characterized by periodic exposure to therapeutic light, interspersed with intervals of darkness. This approach is thought to reduce the risk of potential side effects such as skin irritation and dehydration, while allowing the neonate time for recovery and promoting opportunities for maternal bonding (8). Proponents of intermittent therapy suggest that it may offer comparable efficacy to continuous phototherapy, with the added benefits of improved neonatal comfort and maternal satisfaction. Despite these potential advantages, the clinical community remains divided over which method provides superior outcomes, particularly in terms of safety and the prevention of long-term complications (9).

The need for a direct comparison between these two phototherapy modalities is underscored by the ongoing debate regarding their respective efficacy and safety profiles. The present study seeks to fill this gap by conducting a rigorous comparative analysis of intermittent versus continuous phototherapy in the management of neonatal hyperbilirubinaemia. By evaluating serum bilirubin levels, total duration of phototherapy, and associated complications such as hyperthermia and hypocalcaemia, this research aims to provide clinicians with evidence-based guidance to inform clinical decision-making and optimize neonatal care (10, 11). The ultimate goal is to enhance the treatment outcomes for newborns with hyperbilirubinaemia, ensuring that therapeutic interventions not only effectively reduce bilirubin levels but also safeguard the overall well-being of the neonate.

2 Material and Methods

The study was a quasi-experimental research project conducted between January 2022 and December 2023 at the Department of Paediatrics, Combined Military Hospital, Rawalpindi. The primary objective was to compare the efficacy and safety of intermittent versus continuous phototherapy in the treatment of neonatal hyperbilirubinaemia. The study population comprised 62 full-term neonates diagnosed with hyperbilirubinaemia, defined as indirect bilirubin levels greater than 15.0 mg/dL but not exceeding 20 mg/dL. Inclusion criteria ensured the selection of full-term neonates, born between 37 and 42 weeks of gestation, of both genders. Neonates presenting with jaundice onset within 24 hours of delivery, an APGAR score below 7 at birth, sepsis, ABO and Rh incompatibility, birth defects, or those who had received an exchange transfusion or blood transfusion were excluded from the study. Additionally, neonates with hypocalcaemia or hypoalbuminemia at the time of enrollment or those born to mothers with diabetes mellitus or epilepsy were also excluded.

The study protocol was thoroughly explained to the parents or guardians of the neonates, who provided informed consent prior to enrollment. The research was conducted in accordance with the Declaration of Helsinki and adhered to the ethical guidelines established by the local institutional review board. Neonates meeting the inclusion criteria were selected using non-probability, consecutive sampling. The sample size was calculated using the WHO sample size calculator, with parameters derived from previous studies on serum total bilirubin levels with continuous and intermittent phototherapy (11).

Upon enrollment, each neonate underwent a detailed history-taking and clinical examination, during which demographic data were recorded. Peripheral venous blood samples were collected to measure baseline serum indirect bilirubin levels using an automated bilirubinometer (EasyBil-P, Micro Lab; Shenzhen, China). The neonates were then randomly assigned to receive either intermittent or continuous phototherapy through block randomization. Phototherapy was administered using light-emitting diode (LED) devices calibrated to deliver a total irradiance of 30 μW/cm2/nm within the wavelength range of 460 to 490 nm (KM-DSP, Korrida Medical Systems; Gujarat, India). Continuous phototherapy was provided without interruption, except during feeding, which was performed every two hours using expressed breast milk or formula. In the intermittent phototherapy group, neonates were exposed to light for two hours, followed by two hours of darkness, with feeding taking place during the dark intervals while the neonate was held in the mother's lap.

Throughout the study period, neonates were closely monitored for changes in serum indirect bilirubin levels, which were measured again at 24 and 48 hours post-initiation of phototherapy. Additionally, total phototherapy duration was recorded, excluding any interruptions. The neonates' body temperature and serum calcium levels were regularly assessed to identify potential complications such as hyperthermia and hypocalcaemia. Hyperthermia was defined as a body temperature exceeding 37.0°C, while hypocalcaemia was diagnosed when serum calcium levels fell below 8.0 mg/dL. Treatment failure was defined as a sustained indirect bilirubin level above 20 mg/dL despite 24 hours of phototherapy.

Data collected during the study were entered into and analyzed using the Statistical Package for the Social Sciences (SPSS), version 25. Descriptive statistics, including mean and standard deviation for continuous variables, and frequencies and percentages for categorical variables, were calculated. The normality of the data was assessed using the Shapiro-Wilk test. Comparative analyses between the intermittent and continuous phototherapy groups were conducted using the independent samples t-test or Mann-Whitney U test for continuous variables and the Chi-square test or Fisher's exact test for categorical variables. A p-value of ≤ 0.05 was considered statistically significant in all analyses.

This rigorous methodological approach ensured that the study was conducted with a high degree of scientific integrity, providing robust data to inform clinical decision-making in the management of neonatal hyperbilirubinaemia.

3 Results

The study enrolled a total of 62 neonates, with 31 allocated to the intermittent phototherapy group and 31 to the continuous phototherapy group. The demographic and baseline clinical characteristics of the study population are summarized in Table 1. The median age of the neonates was 5.0 days (IQR: 3.0), with 36 (58.1%) of the participants being male. The median gestational age at delivery was 39.0 weeks (IQR: 2.0), and the median birth weight was 3274.5 grams (IQR: 622.0). The median pre-treatment indirect bilirubin level was 17.50 mg/dL (IQR: 2.20). No significant differences were observed between the two groups regarding gender, age, gestational age at birth, birth weight, or pre-treatment indirect bilirubin levels ($p > 0.05$ for all variables).

Table 1: Baseline Characteristics of Neonates by Phototherapy Group (n=62)

Variable	Intermittent (n=31)	Continuous (n=31)	p-value
Gender			
Male (%)	21 (67.7%)	15 (48.4%)	0.123
Female (%)	10 (32.3%)	16 (51.6%)	
Age (Days), Median (IQR)	4.0 (3.0)	5.0 (3.0)	0.256
Gestational Age (Weeks)	39.0 (2.0)	39.0 (3.0)	0.152
Birth Weight (g), Median (IQR)	3226.0 (697.0)	3345.0 (594.0)	0.849
Pre-treatment Indirect Bilirubin (mg/dL), Median (IQR)	17.50 (2.20)	17.50 (2.40)	0.805

The results of the study, including the primary and secondary outcomes, are presented in Table 2. At 24 hours post-initiation of phototherapy, the median indirect bilirubin level was 12.70 mg/dL (IQR: 1.20) in the intermittent group and 12.50 mg/dL (IQR: 1.90) in the continuous group, with no statistically significant difference between the two groups ($p = 0.893$). Similarly, at 48 hours post-initiation, the median indirect bilirubin levels were 6.40 mg/dL (IQR: 1.10) in the intermittent group and 6.50 mg/dL (IQR: 1.10) in the continuous group, with no significant difference observed ($p = 0.821$).

Table 2: Treatment Outcomes and Complications by Phototherapy Group (n=62)

Variable	Intermittent (n=31)	Continuous (n=31)	p-value
Indirect Bilirubin (mg/dL)			
Post-24 Hours, Median (IQR)	12.70 (1.20)	12.50 (1.90)	0.893
Post-48 Hours, Median (IQR)	6.40 (1.10)	6.50 (1.10)	0.821
Total Duration of Phototherapy (hours), Median (IQR)	22.0 (2.0)	45.0 (3.0)	<0.001
Volume of Milk Consumed (mL), Median (IQR)	420.0 (93.0)	397.0 (57.0)	0.014
Complications			
Hyperthermia, n (%)	1 (3.2%)	8 (25.8%)	0.026
Hypocalcaemia, n (%)	5 (16.1%)	14 (45.2%)	0.013
Treatment Failure, n (%)	-	-	-

The total duration of phototherapy was significantly shorter in the intermittent phototherapy group, with a median duration of 22.0 hours (IQR: 2.0) compared to 45.0 hours (IQR: 3.0) in the continuous phototherapy group ($p < 0.001$). Neonates in the intermittent group also consumed a significantly greater volume of milk, with a median intake of 420.0 mL (IQR: 93.0) compared to 397.0 mL (IQR: 57.0) in the continuous group ($p = 0.014$).

Regarding complications, hyperthermia was significantly less frequent in the intermittent group, occurring in only 1 neonate (3.2%) compared to 8 neonates (25.8%) in the continuous group ($p = 0.026$). Similarly, hypocalcaemia was observed less frequently in the intermittent group, with 5 cases (16.1%) compared to 14 cases (45.2%) in the continuous group ($p = 0.013$). No cases of treatment failure, defined as a persistent rise in indirect bilirubin levels above 20 mg/dL despite phototherapy, were reported in either group.These findings highlight that while both phototherapy modalities are equally effective in reducing bilirubin levels, intermittent phototherapy offers advantages in terms of shorter treatment duration, improved feeding outcomes, and a lower incidence of complications such as hyperthermia and hypocalcaemia.

4 Discussion

The findings of this study provide important insights into the management of neonatal hyperbilirubinaemia, particularly when comparing intermittent and continuous phototherapy. The results demonstrated that both phototherapy modalities were equally effective in reducing serum indirect bilirubin levels at 24 and 48 hours post-initiation of treatment. This outcome aligns with previous research, which has shown that intermittent phototherapy can achieve a similar degree of bilirubin reduction as continuous phototherapy, challenging the assumption that continuous light exposure is inherently superior (12, 13).

The rationale for the comparable efficacy of intermittent phototherapy lies in the two-stage process of phototherapy, where photons rapidly convert bilirubin in the dermis to water-soluble photoisomers, followed by the slower movement of bilirubin from the bloodstream into the dermis. This process suggests that intermittent light exposure, allowing periods of darkness, may be sufficient for effective phototherapy, as the rate-limiting step is not continuous light exposure but the bilirubin clearance from the bloodstream (14).

Beyond efficacy, this study highlighted several advantages of intermittent phototherapy. Notably, neonates in the intermittent group had a significantly shorter duration of phototherapy, which is clinically relevant as it minimizes the total time the newborn is exposed to phototherapy, reducing potential discomfort and allowing for more opportunities for maternal bonding and feeding. The increased volume of milk consumed by neonates in the intermittent group further underscores the benefits of this approach, as phototherapy is known to disrupt feeding patterns. The ability to maintain regular feeding intervals during periods of darkness may enhance neonatal nutrition and hydration, contributing to better overall outcomes (15, 16).

The study also demonstrated a lower incidence of complications such as hyperthermia and hypocalcaemia in the intermittent phototherapy group. Hyperthermia has been a known complication of continuous phototherapy due to the prolonged exposure to light, which can increase the neonate's body temperature. The reduced risk of hyperthermia with intermittent phototherapy is consistent with previous studies that have suggested intermittent phototherapy allows for better thermoregulation and reduced adverse effects (17-19). Similarly, hypocalcaemia, which has been associated with prolonged phototherapy due to its impact on calcium metabolism via the suppression of melatonin and cortisol pathways, was less frequent in the intermittent group, further supporting the safety profile of this modality (20, 21).

Despite these strengths, the study had some limitations. The research was conducted within a single-center setting, and the study population was restricted to neonates from a specific demographic, potentially limiting the generalizability of the findings to broader populations. Moreover, the study focused primarily on short-term outcomes, such as bilirubin levels and complications within the first 48 hours of treatment. While these are critical markers of treatment efficacy and safety, the study did not assess long-term outcomes, such as neurodevelopmental status or the incidence of rebound hyperbilirubinaemia, which would provide a more comprehensive understanding of the long-term benefits and risks associated with each phototherapy modality.

Additionally, the study's reliance on biochemical markers to evaluate treatment efficacy may have overlooked other important aspects, such as parental satisfaction or the quality of mother-infant bonding, which are increasingly recognized as important outcomes in neonatal care (22,23). Future research should aim to include these parameters, as well as explore the impact of phototherapy modalities on long-term developmental outcomes.

In conclusion, this study supports the use of intermittent phototherapy as a viable alternative to continuous phototherapy in the management of neonatal hyperbilirubinaemia. Intermittent phototherapy not only offers comparable efficacy in bilirubin reduction but also presents a superior safety profile with fewer complications, shorter treatment duration, and better feeding outcomes. These findings suggest that intermittent phototherapy should be considered in clinical practice as a preferred treatment option for managing neonatal hyperbilirubinaemia. However, further research is warranted to confirm these findings in larger, multi-center trials and to explore the long-term effects of phototherapy modalities on neonatal health and development.

5 Conclusion

In The study concludes that intermittent phototherapy is as effective as continuous phototherapy in reducing serum bilirubin levels in neonates with hyperbilirubinaemia. Additionally, intermittent phototherapy offers significant advantages, including a shorter treatment duration, improved feeding outcomes, and a lower incidence of complications such as hyperthermia and hypocalcaemia. These findings suggest that intermittent phototherapy should be considered a preferred treatment option in clinical practice for managing neonatal hyperbilirubinaemia. Further research is recommended to confirm these results and explore long-term outcomes associated with different phototherapy modalities.

6 References

1. Ansong-Assoku B, Shah SD, Adnan M, Ankola PA. Neonatal Jaundice. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK532930/.
2. Alkén J, Håkansson S, Ekéus C, Gustafson P, Norman M. Rates of Extreme Neonatal Hyperbilirubinemia and Kernicterus in Children and Adherence to National Guidelines for Screening, Diagnosis, and Treatment in Sweden. JAMA Netw Open. 2019 Mar 1;2(3)
3. . doi: 10.1001/jamanetworkopen.2019.0858.

4. Sampurna MT, Pratama DC, Visuddho V, Oktaviana N, Putra AJ, Zakiyah R, et al. A Review of Existing Neonatal Hyperbilirubinemia Guidelines in Indonesia. F1000Res. 2023 Nov 13;11:1534. doi: 10.12688/f1000research.110550.2.
5. Wang J, Guo G, Li A, Cai WQ, Wang X. Challenges of Phototherapy for Neonatal Hyperbilirubinemia: Review. Exp Ther Med. 2021 Mar;21(3):231. doi: 10.3892/etm.2021.9662.
6. Par EJ, Hughes CA, DeRico P. Neonatal Hyperbilirubinemia: Evaluation and Treatment. Am Fam Physician. 2023 May;107(5):525-534.
7. So V, Khurshid F. Treatment Practices and Implementation of Guidelines for Hyperbilirubinemia and Rebound Hyperbilirubinemia. J Neonatal Perinatal Med. 2022;15(2):335-343. doi: 10.3233/NPM-210781.
8. Shoris I, Gover A, Toropine A, Iofe A, Zoabi-Safadi R, Tsuprun S, et al. "Light" on Phototherapy-Complications and Strategies for Shortening Its Duration: A Review of the Literature. Children (Basel). 2023 Oct 17;10(10):1699. doi: 10.3390/children10101699.
9. Thomas N, Abiramalatha T. Phototherapy for Neonatal Hyperbilirubinaemia: Unresolved Aspects & Future Directions. Indian J Med Res. 2021 Apr;153(4):409-412. doi: 10.4103/ijmr.IJMR_1628_20.
10. Arnold C, Tyson JE. Phototherapy for Preterm Newborns—Historical Controversies and RCT Evidence. Pediatr Med. 2021;4(1):35. doi: 10.21037/pm-21-42.
11. Kemper AR, Newman TB, Slaughter JL, Maisels MJ, Watchko JF, Downs SM, et al. Clinical Practice Guideline Revision: Management of Hyperbilirubinemia in the Newborn Infant 35 or More Weeks of Gestation. Pediatrics. 2022 Sep 1;150(3)
12. . doi: 10.1542/peds.2022-058859.
13. Ullah I, Khan I, Ahmad K, Khan K, Shafiq M, Ullah S. Comparison of Intermittent Vs. Continuous Phototherapy in the Treatment of Non-Haemolytic Neonatal Hyperbilirubinemia. Pak J Med Health Sci. 2022;16(4):1168-1170. doi: 10.53350/pjmhs221641168.
14. Gottimukkala SB, Sethuraman G, Kitchanan S, Pathak S. Comparison of Efficacy, Safety & Satisfaction of Intermittent Versus Continuous Phototherapy in Hyperbilirubinaemic Newborns ≥35 Week Gestation: A Randomized Controlled Trial. Indian J Med Res. 2021 Apr;153(4):446-452. doi: 10.4103/ijmr.IJMR_2156_18.
15. Suri D, Krithika AP, Somasekar R. A Comparative Study to Determine Intermittent Versus Continuous Phototherapy for Reducing Neonatal Hyperbilirubinemia at Tertiary Care Hospital in Chennai, Tamil Nadu, India. Int J Contemp Pediatr. 2019 Nov;6(6):2287-2291. doi: 10.18203/2349-3291.ijcp20194536.
16. Thomas N, Abiramalatha T. Phototherapy for Neonatal Hyperbilirubinaemia: Unresolved Aspects & Future Directions. Indian J Med Res. 2021 Apr;153(4):409-412. doi: 10.4103/ijmr.IJMR_1628_20.
17. Wang J, Guo G, Li A, Cai WQ, Wang X. Challenges of Phototherapy for Neonatal Hyperbilirubinemia: Review. Exp Ther Med. 2021 Mar;21(3):231. doi: 10.3892/etm.2021.9662.
18. Lori-Kenari R, Aziznejadroshan P, Haghshenas-Mojaveri M, Hajian-Tilaki K. Comparing the Effect of Kangaroo Mother Care and Field Massage on Serum Bilirubin Level of Term Neonates With Hyperbilirubinemia Under Phototherapy in the Neonatal Ward. Caspian J Intern Med. 2020 Winter;11(1):34-40. doi: 10.22088/cjim.11.1.34.
19. Waite WM, Taylor JA. Phototherapy for the Treatment of Neonatal Jaundice and Breastfeeding Duration and Exclusivity Breastfeed Med. 2016 May;11:180-185. doi: 10.1089/bfm.2015.0170.
20. Zhou S, Wu X, Ma A, Zhang M, Liu Y. Analysis of Therapeutic Effect of Intermittent and Continuous Phototherapy on Neonatal Hemolytic Jaundice. Exp Ther Med. 2019;17(1):4007-4012. doi: 10.3892/etm.2019.7432.
21. Zhang XR, Zeng CM, Liu J. Effect and Safety of Intensive Phototherapy in Treatment of Neonatal Hyperbilirubinemia. Zhongguo Dang Dai Er Ke Za Zhi. 2016 Mar;18(3):195-200. doi: 10.7499/j.issn.1008-8830.2016.03.001.
22. Alizadeh-Taheri P, Sajjadian N, Eivazzadeh B. Prevalence of Phototherapy-Induced Hypocalcemia in Term Neonates. Iran J Pediatr. 2013 Dec;23(6):710-711.
23. Khan M, Malik KA, Bai R. Hypocalcemia in Jaundiced Neonates Receiving Phototherapy. Pak J Med Sci. 2016 Nov-Dec;32(6):1449-1452. doi: 10.12669/pjms.326.10849.

Disclaimers	
Author Contributions	All authors contributed significantly to this work. Jaweria Zahid designed the study and conducted the experiments, while Dr. Huzaifa Malik analyzed the data and wrote the manuscript. Shakeel Ahmed, Ayesha Ali Shams, Ayesha Mustafa, and Andaleeb Tariq assisted in data collection and interpretation. Muhammad Farrukh Habib provided critical revisions and guidance throughout the research process. All authors reviewed and approved the final manuscript.
Conflict of Interest	The authors declare that there are no conflicts of interest.
Data Availability	Data and supplements available on request to the corresponding author.
Funding	NA
Ethical Approval	Institutional Review Board (IRB) Combined Military Hospital, Rawalpindi, Pakistan.
Trial Registration	NA
Acknowledgments	NA

~ JHRR, ISSN: 2791-156X ~