

**OUTCOME OF INTERMITTENT VERSUS CONTINUOUS PHOTOTHERAPY IN  
TREATING NEONATAL JAUNDICE**

**Abstract**

**Aim**To compare the outcome of intermittent phototherapy versus continuous phototherapy in treatment of neonatal jaundice.

**Study Design:** Randomized clinical trial.

**Place and duration:** Department of pediatrics, neonatal ward, Liaquat university hospital Hyderabad/Jamshoro, 6 month from 8 January to 7 July 2020

**Methodology:** There were 222 neonate with jaundice, which were randomly allocated into two groups. One hundred and one neonates were in group A and received continuous phototherapy while 111 neonates were treated with intermittent phototherapy called group B. Phototherapy units were identical regarding manufacture and radiance with 5 blue light tubes at a distance of 15-20 cm above neonate that produced the irradiance of  $20\mu\text{W}/\text{cm}^2/\text{nm}$  at 420-470 nm. Serum bilirubin level was measured every 12 hourly after starting phototherapy up to 48 hours.

**Results:** - The average age of the neonates was  $2.23\pm 1.45$  days. In this study, the reduction of bilirubin level in both groups after 12, 24, 36, 48 hours of phototherapy and at the time taken for discharge was not different between groups.

**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 large scale RCTs.

**Key Words:** Intermittent phototherapy, Continuous phototherapy, Neonatal jaundice. Neonatal Ward,

## **Introduction:**

Yellow discoloration of skin and sclera that resulted from accumulation of un-conjugated bilirubin in underlying skin and mucosal membrane usually affects 60% of term and 80% of preterm neonates during the first week of life. It is a commonest clinical condition that require medical attention to prevent unusual consequences i.e. neurotoxicity [Error! Bookmark not defined.]. In a local report in 2010, about 39.7 babies per 1000 live birth had neonatal jaundice [3] Normally bilirubin production in neonates is 6-8 mg/kg i.e. two times higher than adults, but due to insufficiency of conjugate enzyme, the level of non-conjugate bilirubin becomes high over certain period of time, this level improves steadily. High levels of bilirubin can cause neurotoxicity i.e. kernicterus, cognitive impairment, muscle tone disorder, deafness and sometimes death. [4]

As for the prevention of neurotoxicity, there are several methods to treat hyper-bilirubinemia but phototherapy is widely used method. After being checked for jaundice and total bilirubin determination through clinical and laboratory investigation, one can go through phototherapy either continuous or intermittent approach [5].

Usually continuous phototherapy is routinely used but it causes separation of mother and infant, interference of breast feeds and increased risk of adverse effects i.e. skin rash, insensible losses, retinal damage, hyperthermia and increased intestinal flow.<sup>(6)</sup>

Beside the potential harms and concerns regarding phototherapy, intermittent approach can produce pleasant and ease, not only for parents and patients but even for hospital staff to accommodate more patients. Despite modification of phototherapy with decrement in light exposure without compromising the efficacy would certainly be advancement over conventional methods.<sup>(7)</sup>

The findings of this study may prove that the intermittent approach of phototherapy may provide benefit over continuous approach because it can help in reduction of hospital stay, staff burden and promotion of breast feeding, however for implementation, the evaluation of this intermittent approach need to be confirmed on large scale.

## **Methodology**

### **Operational Definitions:**

**Neonatal jaundice:** Neonates that presented after 24 hours of age and <10 days with jaundice but classified as well baby (vitaly stable, feeding well.) with their serum un-conjugated bilirubin to be 12.5mg/dl to 18mg/dl. Jaundice of <24 hours is considered pathological and need hospitalization. Jaundice appears for >10 days need further workup and hospitalization.

**Outcome of phototherapy:** It was measured in term of serum bilirubin level after starting phototherapy at 0 hours, 12, 24, 36, 48 hours and on discharge.

This Randomized clinical trial was done by Non-probability, consecutive sampling technique at Department of pediatrics, neonatal ward, Liaquat university hospital Hyderabad/Jamshoro from 8 January to 7 July 2020 (Total 6 month's duration). The sample size was calculated through openepi.com, sample size calculator with statistics of mean serum bilirubin at discharge in both study groups. Total sample size was 222 with 95% confidence of interval.

Neonate >34 week gestational age weighing 2.1kg to 3.5kg, age 24 hours to 10 days with jaundice were included in the study. Sick neonates with presumed sepsis, dysmorphic babies and neonates with co-morbidities (cardiac, skeletal, renal, etc) were excluded from the study. Neonates having the history of kernicterus and exchange transfusion in siblings or having hemolytic jaundice (Hb < 10 mg/dl or Retic count > 10 mg/dl) were also excluded from the study.

Data was collected through questionnaire based approach from babies admitted in neonatal ward, fulfilling the inclusion and exclusion criteria. An informed written consent was taken from parents before starting treatment. The neonates were divided into two groups by lottery methods. Group A received Continuous Phototherapy includes 2 hours on and half an hour off for whole day and was outlined as Control Group. Group B was received Intermittent Phototherapy includes 12 hours on and 12 hours off (breast feeding interval of 20-30 minutes is included in off phototherapy interval).

Phototherapy units were identical regarding manufacture and radiance with 5 blue light tubes at a distance of 15-20 cm above neonate that produced the irradiance of  $20\mu\text{W}/\text{cm}^2/\text{nm}$  at 420-470 nm. Serum bilirubin level was measured every 12 hourly after starting phototherapy up to 48 hours. Blood sample was sent to Liaquat university hospital laboratory and analyzed by lab authorized person working in lab since 3 years. Serum bilirubin level was measured in mg/dl collected by researcher and was noted down on proforma. Routine newborn care, eye pad care,

monitoring for sign of dehydration (decrease urinary output, dry oral mucosa, and decrease skin turgidity) and breast feeding counseling was done in every case as per recommended protocol.

The important concerns about personal contact information to be leaked was extremely low because the confidentiality of patient was the first priority, the information was shared only for health purposes, in concern with patient health. There was no medical interventions that could cause patient to be offensive.

After collection of data the analysis was conducted by using SPSS software version 23. Mean and standard deviation was calculated for quantitative variables like age, weight and serum bilirubin at start of phototherapy and serum bilirubin up to 48 hours. Qualitative measure like gender was presented as percentage and frequencies. Student t-test was applied to compare the serum bilirubin on different points. Effect modifiers age, weight, gender was controlled through stratification. Post stratification t-test was applied and p value  $<0.05$  was considered significant.

## **Results:**

There were 222 neonate with jaundice, which were randomly allocated into two groups. Most of the neonate's age were between 2 to 3 days in both groups. The average age of the neonates was  $2.56 \pm 1.77$  days and weight of the neonates was  $2.93 \pm 0.45$  kg. Mean age, weight and Serum bilirubin at start of phototherapy with respect to groups is reported in table 1. There were 130 (58.6%) male and 92 (41.4%) female.

In this study, the reduction of bilirubin level in both groups 12, 24, 36, 48 hour and at discharged after treatments were not significant. The mean bilirubin after 12, 24, 36 and 48 hours and at discharge in intermittent phototherapy group (group B) was  $14.77 \pm 1.35$ ,  $12.55 \pm 1.39$ ,  $11.15 \pm 1.62$ ,  $9.02 \pm 0.89$  and  $8.19 \pm 1.48$  respectively while in continuous phototherapy (group A) it

was  $14.71 \pm 1.37$ ,  $12.52 \pm 1.44$ ,  $11.05 \pm 1.46$ ,  $8.98 \pm 1.03$  and  $8.04 \pm 1.48$  respectively as presented in table 2.

Stratification analysis was performed to control the effect of age, gender and weight and observed that for above and equal 1 day, 2-3 days and above 3 days of neonate, there were insignificant difference between groups (table 3). Mean bilirubin level between groups overtime was also not statistically significant for male and female as shown in table 4. Mean bilirubin was also observed between group by weight of the neonates and found that effect of weight at 48 hours was significant in those neonates who had more than 2.9 kg as shown in table 5.

TABLE 1

## DESCRIPTIVE STATISTICS OF CHARACTERISTICS OF PATIENTS BY GROUPS

Variables	Group A n=111		Group B n=111	
	Mean	Std. Deviation	Mean	Std. Deviation
Age (days4	2.56	1.77	2.16	1.27
Weight (kg)	2.93	0.45	2.91	0.50
Serum bilirubin at start of phototherapy	17.22	0.93	17.2	0.84

TABLE 2

## COMPARISON OF SERUM BILIRUBIN BETWEEN GROUPS OVERTIME

Serum bilirubin	Group A n=111		Group B n=111		P-Value
	Mean	Std. Deviation	Mean	Std. Deviation	
	At start of phototherapy	17.22	0.93	17.22	
12h	14.71	1.37	14.77	1.35	0.77
24h	12.52	1.44	12.55	1.39	0.89
36h	11.05	1.46	11.15	1.62	0.63
48h	8.98	1.03	9.02	0.89	0.74
At discharged	8.04	1.48	8.19	1.48	0.46

TABLE 3

COMPARISON OF SERUM BILIRUBIN BETWEEN GROUPS OVERTIME FOR  
NEONATES AGE ABOVE AND  
EQUAL  $\geq 1$  DAYS

Serum bilirubin	Group A n=30		Group B n=33		P-Value
	Mean	Std. Deviation	Mean	Std. Deviation	
At start of phototherapy	16.52	1.03	16.80	0.67	0.204
12h	13.28	0.88	13.49	0.62	0.286
24h	11.26	0.84	11.49	0.58	0.200
36h	10.07	0.88	10.35	0.52	0.136
48h	9.04	1.16	9.34	0.41	0.174
At discharged	8.20	1.73	8.59	1.26	0.308

TABLE 4

COMPARISON OF SERUM BILIRUBIN BETWEEN GROUPS OVERTIME FOR  
NEONATES AGE 2 TO 3 DAYS

Serum bilirubin	Group A n=61		Group B n=65		P-Value
	Mean	Std. Deviation	Mean	Std. Deviation	
At start of phototherapy	17.55	0.63	17.41	0.82	0.270
12h	15.20	0.90	15.31	1.11	0.557
24h	12.87	0.94	12.97	1.19	0.592
36h	11.44	0.96	11.67	1.57	0.343
48h	9.07	0.72	9.03	0.91	0.821
At discharged	8.30	1.21	8.29	1.44	0.977

TABLE 5

COMPARISON OF SERUM BILIRUBIN BETWEEN GROUPS OVERTIME FOR  
NEONATES AGE ABOVE 3 DAYS

Serum bilirubin	Group A n=20		Group B n=13		P-Value
	Mean	Std. Deviation	Mean	Std. Deviation	
At start of phototherapy	17.26	0.99	17.35	1.03	0.801
12h	15.37	1.64	15.29	1.67	0.902
24h	13.37	2.12	13.11	2.23	0.741
36h	11.32	2.47	10.62	2.57	0.438
48h	8.61	1.49	8.14	1.14	0.346
At discharged	7.01	1.43	6.62	1.25	0.427

## DISCUSSION

Jaundice becomes detectable to the naked eye when the total serum bilirubin level exceeds about  $85\mu\text{mo}$  ( $5\text{mg}/100\text{ml}$ ) and most babies become visibly jaundiced in the first week of life. Jaundice is only really 'actionable' in the otherwise healthy term baby when the level exceeds  $340\mu\text{mo}$  ( $20\text{mg}/100\text{ml}$ ) and potentially dangerous when it exceeds  $43\mu\text{mo}$  ( $25\text{mg}/100\text{ml}$ ). Approximately 60% of full-term infants and 80% of premature infants develop jaundice due to hyperbilirubinemia during neonatal period. Also 5-10% of them require treatment by phototherapy<sup>(8)</sup>

In this study the average age of the neonates was  $2.56\pm 1.77$  days and weight of the neonates was  $2.93\pm 0.45$  kg. The difference between the mean decreases in serum bilirubin of both groups was statistically not significant. In this study, the reduction of bilirubin level in both groups 12, 24, 36, 48 hour and at discharged after treatments were not significant. The results of this study were similar to a systemic review and meta-analysis study in which intermittent phototherapy and continuous phototherapy were equally effective in reducing the total serum bilirubin<sup>(9)</sup>. In another international study there was no significant difference in serum bilirubin levels between continuous and intermittent phototherapy groups at 24, 48 and 72 h after treatment ( $P>0.050$ )<sup>(10)</sup>

A randomized controlled trial was done in Iran that showed that, intermittent phototherapy was as effective as continuous phototherapy to treat icteric full-term neonates. . The rate of serum bilirubin cessation in the two groups was similar after 36 hours<sup>(11)</sup>. In an Indian study the intermittent phototherapy was as efficacious as the continuous phototherapy, the mean age on admission was 76 hours and 77 hours in continuous phototherapy group and intermittent phototherapy groups respectively. Mean TSB at 12, 24, 48 hours were  $13.26 \pm 2.4$  mg/dl,  $10.8 \pm$

1.72 mg/dl,  $10.16 \pm 0.95$  mg/dl respectively for continuous and  $12.6 \pm 1.65$  mg/dl,  $10.04 \pm 1.8$  mg/dl,  $9.1 \pm 0.66$  mg/dl respectively for intermittent group ( $p < 0.05$ )<sup>(12)</sup>. In another similar Indian study 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<sup>(13)</sup>.

In an international study the length of hospital stay was  $2.3 \pm 0.60$  and  $2.46 \pm 0.93$  days in the continuous and intermittent groups, respectively ( $P=0.516$ ) and there was no significant differences between them in respect of decrease in serum bilirubin<sup>(14)</sup>.

## CONCLUSION

Our study concluded that Intermittent and continuous phototherapies are found to be equally effective. So because of additional benefits as it can help in reduction of hospital stay, staff burden and promotion of breast feeding, intermittent phototherapy can be adopted as a routine procedure instead of continuous phototherapy in neonatal care units, however, it needs to be confirmed by large scale Randomized Control Trials.

## References

1. Stoicescu M. General Medical Semiology Guide Part I. Academic Press; 2019 Nov 22.
2. Mitra S, Rennie J. Neonatal jaundice: aetiology, diagnosis and treatment. British Journal of Hospital Medicine. 2017 Dec 2; 78(12):699-704.
3. Tikmani SS, Warraich HJ, Abbasi F, Rizvi A, Darmstadt GL, Zaidi AK. Incidence of neonatal hyperbilirubinemia: a population-based prospective study in Pakistan. Tropical Medicine & International Health. 2010; 15(5):502-7.
4. Tripathi N, Jialal I. Conjugated Hyperbilirubinemia. StatPearls [Internet]. 2020 Aug 25.

5. Watchko JF. Neonatal indirect hyperbilirubinemia and kernicterus. In *Avery's Diseases of the Newborn* 2018 Jan 1 (pp. 1198-1218). Elsevier.
6. Anand P, Gopalakrishnan S, Sachdeva A, Sahoo T, Sivanandan S. Screening, prevention, and management of neonatal hyperbilirubinemia. *Journal of Neonatology*. 2020; 34(3):153-69.
7. Raikes AC, Killgore WD. Potential for the development of light therapies in mild traumatic brain injury. *Concussion*. 2018; 3(3):CNC57.
8. Shaw D. Neonatal jaundice. In *Pharm: The Comprehensive Pharmacology Reference* 2007 (pp. 1-4). Elsevier Inc...
9. Chu L, Xue X, Qiao J. Efficacy of Intermittent Phototherapy versus Continuous Phototherapy for Treatment of Neonatal Hyperbilirubinaemia: A Systematic Review and Meta-analysis. *Journal of Advanced Nursing*. 2021; 77(1):12-22.
10. Zhou S, Wu X, Ma A, Zhang M, Liu Y. Analysis of therapeutic effect of intermittent and continuous phototherapy on neonatal hemolytic jaundice. *Experimental and therapeutic medicine*. 2019; 17(5):4007-12.
11. Taheritafti R, Taheritafti M. Comparison of Intermittent and Continuous Phototherapy to Treat Non-hemolytic Moderate Hyperbilirubinemia in Term Infants-A Randomized, Controlled Trial. *Biomedical Journal of Scientific & Technical Research*. 2020; 24(2):18065-70.
12. Patil MM, Gowthami GS, Bijapure HR, Sajjan AK, Kalyanshetkar SS, Patil SV. Continuous vs Intermittent Phototherapy in the Management of Non-Haemolytic Neonatal Hyperbilirubinemia-A Randomised Non-Inferiority Study. *Journal of Nepal Paediatric Society*. 2020; 40(3):185-9.

13. Suri D, 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 ContempPediatr.* 2019;6(6):2287-2291
14. Taheritafti R, Taheritafti M. Intermittent versus continuous phototherapy for the treatment of nonhemolytic moderate hyperbilirubinemia in term infants: a randomized controlled trial. *TUMJ.* 2019; 76(10): 686-91

UNDER PEER REVIEW