Original Article

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Intermittent versus Continuous Phototherapy for Reducing Neonatal Hyperbilirubinemia

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Abstract

Objective: Clinical studies comparing intermittent versus continuous phototherapy for reducing neonatal hyperbilirubinemia have produced conflicting results. This study was conducted to compare the efficacy of intermittent with continuous phototherapy.

Methods: This study was performed on 114 neonates with indirect hyperbilirubinemia. Inclusion criteria were body weight above 2000 grams, absence of other concomitant diseases, and hyperbilirubinemia neither requiring intensive phototherapy nor exceeding the range of 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 off for one hour. The phototherapy units were identical and serum total bilirubin levels were measured every 12 hours after starting phototherapy.

Findings: Two groups were matched regarding weight and risk factors such as ABO and Rh incompatibility. The difference of total serum bilirubin levels between two groups was insignificant at the start of phototherapy and also after 12, 24, 36 and 48 hours (P>0.2).

Conclusion: Intermittent phototherapy defined as one hour on and one hour off is as effective as continuous phototherapy defined as 2 hours on and half an hour off, in reducing total serum bilirubin level in full term babies.

Key Words: Neonatal jaundice, Indirect hyperbilirubinemia, Phototherapy, Intermittent phototherapy, Continuous phototherapy

Introduction

Phototherapy has emerged as the most widely 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

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maturity, presence or absence of hemolysis, or degree of skin pigmentation. 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[1,2,3]. 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[4,5].

Phototherapy can be used either as therapy or as prophylaxis. Two different mechanisms have been proposed to explain the action of phototherapy in reducing serum bilirubin concentrations in newborn infants; photoisomerization and photooxidation. Compared with the photoisomerization pathway, the oxidation mechanism appears to play a very minor role in photocatabolism of unconjugated bilirubin in vivo[4,6,7].

Clinical studies comparing intermittent to continuous phototherapy have yielded conflicting results. Several studies failed to show effectiveness of the intermittent therapy. These results may have resulted from prolonged light-on and light-off cycles, for example 6- to 12-hour on-off schedules [4]. 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 on-off 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[4,8,9].

To find-out the optimal on-off schedule, we conducted a randomized clinical trial on 114 jaundiced neonates.

Subjects & Methods

A prospective randomized case-control study was performed on 114 neonates with indirect hyperbilirubinemia who were admitted to NICU in Afzalipour Medical Center in Kerman, Iran. Inclusion criteria were body weight above 2000 grams, absence of other concomitant diseases and hyperbilirubinemia neither exceeding the range of exchange transfusion nor requiring high intensity phototherapy. An approval letter from the ethics committee was obtained. Phototherapy units were equipped with 4 special blue tubes (XHZ-90, Ningbo David Medical Devices) placed 30 cm above the infant. This produced an average irradiance of 20 μW/cm2/nm at 425 to 475 nm, measured on a regular basis at the surface of the infant with a photometer (Minolta/Air-Shields, Japan).

The neonates (No. 114) were randomly divided into two groups, 57 neonates in continuous (Group I) and 57 in intermittent (Group II) phototherapy group. Continuous phototherapy group (Group I) received phototherapy for two hours and then half an hour off. Intermittent phototherapy group (Group II) received phototherapy for one hour and then one hour off intermittently. The phototherapy units were identical regarding the manufacture and the irradiance. Total serum bilirubin level was measured every 12 hours after starting phototherapy.

Data were analyzed by t-test and Repeated Analysis of Variance (Repeated ANOVA).

Findings

Among 114 neonates, 58 (50.9%) were female and 56 (49.1%) were male. The mean age of neonates at admission was 5.44 days with standard deviation of 2.69 (range 2-15 days) (Table 1). Mean weight of neonates at admission was 3072 gram with standard deviation of 558.2 (range 2000-4350 gr).

Mean weight of neonates in continuous group was 3070.1 gram with standard deviation of 579.0 and in intermittent group

Table 1. Age distribution of the neonates at the time of admission (No. 114)

Age (days)	Number	Cumulative percent
2	3 (2.6%)	**2.6%**
3	17 (14.9%)	**17.5%**
4	21 (18.4%)	**36.0%**
5	28 (24.6%)	**60.5%**
6	20 (17.5%)	**78.1%**
7	10 (8.8%)	**86.8%**
8	9 (7.9%)	**94.7%**
9	2 (1.8%)	**96.5%**
10	2 (1.8%)	**98.2%**
13	1 (0.9%)	**99.1%**
15	1 (0.9%)	**100%**
Total	**114 (100%)**	

was 3073.6 gram with standard deviation of 541.6. There was not any significant difference in the weight of neonates in two groups (*P*>0.9).

Cases with significant hyperbilirubinemia who were candidates to receive high intensive phototherapy including G6PD deficient neonates were excluded from the study.

There were 11 cases (19.3%) of ABO incompatibility (mother's blood group O and infant's A or B) in continuous group and 13 cases (22.8%) in intermittent group. There was not any significant difference in the ABO incompatibility in two groups (*P*>0.6). More severe cases of ABO hemolytic disease, who needed intensive phototherapy were excluded from the study.

There were 10 cases (17.5%) of Rh incompatibility (mother's Rh negative and infant's Rh positive) in continuous group and 6 cases (10.5%) in intermittent group. There was not any significant difference in the Rh incompatibility in two groups (*P*>0.2). All cases of Rh incompatibility were Coombs negative and did not need intensive phototherapy. Mean total serum bilirubin of neonates before phototherapy in continuous group was 16.60 mg/dL with standard deviation of 1.76 and in intermittent group was 16.33 mg/dL with standard deviation of 1.46. There was not any significant difference in mean total serum bilirubin of neonates before phototherapy in two groups.

Total serum bilirubin of the babies in two groups was also measured 12, 24, 36 and 48 hours after starting phototherapy. T-test was used to analyze the data and there was not any significant difference in total serum bilirubin levels 12, 24, 36, and 48 hours after starting phototherapy. In other words, the rate of decrease of total serum bilirubin was similar in both groups from the beginning to the end of phototherapy (Table 2). All the infants received phototherapy for 24 hours but 39 in group I and 30 in group II needed phototherapy for 36 hours and only 8 in group I and 7 in group II for 48 hours (Table 2).

Table 2– Comparison of mean total serum bilirubin (mg/dL) after 12, 24, 36 and 48 hours of phototherapy in two groups

Time (hour)	Group	Number	Mean (SD*) total bilirubin (mg/dL)	Result		
				t	*df*	*P*
12	**Continuous**	57	13.73 (1.89)	0.39	112	0.6
	Intermittent	57	13.57 (2.30)			
24	**Continuous**	57	11.06 (2.06)	0.49	108	0.6
	Intermittent	57	10.86 (2.13)			
36	**Continuous**	39	9.17 (1.83)	0.32	67	0.7
	Intermittent	30	9.02 (1.94)			
48	**Continuous**	8	8.93 (1.26)	0.52	13	0.6
	Intermittent	7	9.30 (1.43)			

* SD: Standard Deviation

Table 3– Comparison of mean total serum bilirubin (mg/dL) in the first 24 hours of phototherapy in two groups

Time	Group	Number	Mean (SD*) total bilirubin # (mg/dL)
12 hours	Continuous	57	13.82 (1.77)
	Intermittent	57	13.88 (1.86)
	Total	114	13.85 (1.81)
24 hours	Continuous	57	11.06 (2.06)
	Intermittent	57	10.86 (2.13)
	Total	114	10.96 (2.09)

* SD: Standard Deviation

Result: F=1.34, df=1, P=0.2

We also compared decrease of total serum bilirubin during the first 24 hours of treatment with Repeated Analysis Of Variance (Repeated ANOVA) test. Again, the difference of total serum bilirubin in two groups was insignificant (*P*> 0.2) (Table 3 and Fig. 1).

Discussion

Clinical studies comparing intermittent with continuous phototherapy have produced conflicting results. Because all light exposure increases bilirubin excretion (compared with darkness), continuous phototherapy should be more efficient than intermittent phototherapy.

The issue is quite complicated, however, because the efficacy of phototherapy is related exponentially to the initial bilirubin concentration, efficacy will thus decrease as the bilirubin falls. Rebound into the skin probably takes place when there is an interruption of phototherapy but a question that remains unanswered is whether or not this brief elevation in skin bilirubin might improve efficiency when light therapy is restarted. In practice, however, short on-off cycles (less than one hour) complicate nursing care and are probably more trouble than they are worth[8,11,12]. There is no doubt; however, that phototherapy does not need to be continuous in the majority of circumstances. Phototherapy can and certainly should be

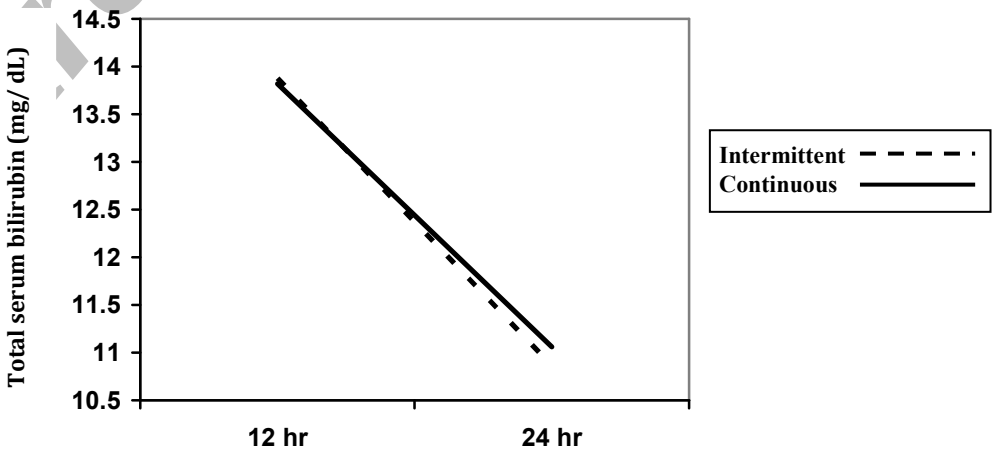

Fig 1- Comparison of decrease of total serum bilirubin (mg/dL) in the first 24 hours of phototherapy in two groups

continuous in the majority of circumstances. Phototherapy can and certainly should be interrupted during feeding or brief parental visits. On the other hand, when bilirubin levels are very high, intensive phototherapy should be administered continuously until a satisfactory decline in bilirubin level occurs or exchange transfusion is initiated.

In practice, however, it is not uncommon that the infant does not tolerate phototherapy and parents interrupt it for long periods of time[11,12].

To find-out the optimal on and off cycle, a study was conducted employing two groups of infants. The study, randomly assigned 114 jaundiced neonates receiving either continuous (Group I) or intermittent (Group II) light. The two groups, each consisting of 57 infants were matched regarding age, birth weight, the etiology of jaundice, bilirubin concentration at admission, and the circumstances of phototherapy. The difference of total serum bilirubin levels between two groups was insignificant at the start of phototherapy and also after 12, 24, 36 and 48 hours (P>0.2).

The results of this study showed that intermittent phototherapy defined as one hour on and one hour off is as effective as continuous phototherapy defined as two hours on and half-an-hour off in lowering total serum bilirubin level in full-term babies.

Lau and Fung showed that the difference in serum bilirubin kinetics between continuous and intermittent phototherapy was insignificant and a schedule of one in four hours of irradiation achieved the same treatment effect as continuous phototherapy[13]. In two other studies, Maurer and Vogl showed that intermittent phototherapy did not cause longer phototherapy periods[14,15].

However, with the realization that photoisomerization occurs within minutes and bilirubin slowly migrates to the skin over hours, intermittent phototherapy regimens were hypothesized to be effective and were tested. Regimens ranging from 15 minutes on/15 minutes off to 1 hour on/4 hours off have been employed and satisfactory results have been reported[6,7,15]. Short on-off cycles (15 minutes to less than one hour) necessitate very close observation and put the caregiver into embarrassment. On the other hand, prolonged on-off schedule mandates meticulous control of phototherapy units by a photometer regarding the irradiance of the lamps and also, elimination of many variables such as the surface area of the infant exposed to light, and distance from the light. However, individual judgment should be exercised and if the infant's bilirubin level is approaching the exchange transfusion zone, phototherapy should be administered continuously until a satisfactory decline in the serum bilirubin level occurs[9].

Conclusion

On the basis of this study, it is concluded that a phototherapy cycle of one hour on and one hour off is as effective as continuous phototherapy in the treatment of neonatal indirect hyperbilirubinemia in term infants. This method is more acceptable to the caregivers than the short cycle of less than one hour on-off and more cautiously than the prolonged cycle of one hour on, four hours off.

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