The Role of Phototherapy as a Treatment of Full-Term Newborn with Neonatal Hyperbilirubinemia with Different Types of Infant Feeding

Shaimaa Khudair Abbas* HDFM**, Haider M Hussein**** CABP**, Mervat Abd Ali Abdul Whhab***** HDFM**, Shawq K Alashab***** FICMS

ABSTRACT

Background: Neonatal jaundice remains the most common and the most controversial problem in full-term newborns during the immediate postnatal period.

Objectives: To assess the association between types of feeding and response to phototherapy in full-term infants with indirect hyperbilirubinemia.

Methods: In the period from the 25th of January to the 22nd of July 2016, 120 full-term newborns admitted to the neonatal care unit in Tertiary Teaching Hospitals (children welfare Teaching Hospital in the Medical City, Al-Imamein AlKadhimein medical city and Child Center Teaching Hospital) were prospectively studied. The newborns diagnosed by pediatrician as cases of indirect hyperbilirubinemia and phototherapy started when TSB level >14.9 mg/dl. TSB was measured twice daily and phototherapy terminated when TSB level < 10.8 mg/dl. All infants were weighed at start and end of phototherapy. The duration of phototherapy had been recorded.

Results: The infants divided into three groups according to type of feeding; group 1, breast-fed infants (n=37); group 2, formula-fed infants (n=51); group 3, mixed-fed infants (n=32). Phototherapy was highly effective in reducing serum bilirubin concentration in all three groups but with a significant less efficacy for breast-fed neonates (mean duration of phototherapy 32.2 ± 2.1 hr.) in comparison to mix-fed neonates (30.4 ± 2.5 hr.) and formula-fed neonates (29.9± 2.7 hr.). There was a weight loss during phototherapy. There was significant difference in the weight loss in the three groups, more weight loss occurred in breast-fed neonates than mixed-fed and formula-fed neonates.

Conclusion: Phototherapy had effectively reduced bilirubin levels in breast-fed newborns with hyperbilirubinemia, but these patients showed a significantly slower response to this modality of treatment than mixed and formula-fed newborns.

Keywords: **Breastfeeding, Hyperbilirubinemia, Infants, Phototherapy.**

Iraqi Medical Journal Vol. 68, No. 1, Jan-June 2022; p. 7-14.

Almost all newborn infants develop a total serum bilirubin (TSB) level greater than 1 mg/dl, which is the upper limit of normal for neonates. As the TSB increases, it produces neonatal jaundice, the yellowish discoloration of the skin and/or sclerae caused by bilirubin deposition(1).

Neonatal hyperbilirubinemia, defined as a total serum bilirubin level above 5 mg/dl, is a frequently encountered problem. Neonatal jaundice becomes apparent at levels ranging from 5 to 7 mg/dl(1). Clinically apparent jaundice develops in approximately 50% of term infants. Jaundice is the most common condition requiring medical attention in newborns(2).

The yellow coloration of the skin and sclera in newborns with jaundice is the result of accumulation of unconjugated bilirubin. In most infants, unconjugated hyperbilirubinemia reflects a normal transitional phenomenon(3). However, in some infants, serum bilirubin levels may

*Al-Noor Primary Health Center, Baghdad.
**Al-Numania Hospital, Wasit.
***Al-Karkh Health Sector, Baghdad.

raise excessively, which can be the cause for concern because unconjugated bilirubin is neurotoxic and can cause death in newborns and lifelong neurologic sequelae in infants who survive (kernicterus). For these reasons the presence of neonatal jaundice frequently results in diagnostic evaluation[4]. In most cases, the level of bilirubin that causes jaundice is not harmful and does not require treatment[5].

Hyperbilirubinemia with a TSB > 25 to 32 mg/dl is associated with an increased risk for bilirubin-induced neurologic dysfunction (BIND), which occurs when bilirubin crosses the blood-brain barrier and binds to brain tissue. The term "acute bilirubin encephalopathy"(ABE) is used to describe the acute manifestations of BIND. The term "Kernicterus" is used to describe the chronic and permanent sequelae of BIND. Appropriate intervention is important to consider in every infant with severe hyperbilirubinemia. However, even if these infants are adequately treated, long-term neurologic sequelae (Kernicterus) can sometimes develop[6].

Neonatal jaundice is due to an increased bilirubin load with a transient inefficiency of hepatic excretion resulting from decreased activity of glucuronyl transferase in the liver. There are additional factors. Some of the conjugated bilirubin excreted in the bile is normally deconjugated in small intestine and reabsorption is enhanced by the slower gut transit in the newborn who takes small volumes of milk. Bilirubin is absorbed from meconium and there is no intestinal flora to degrade bilirubin to urobilinogen[7] .

It is not a coincidence that majority of reported cases of kernicterus in the past two decades have involved breastfed infants, and numerous studies have reported an association between breastfeeding and increased incidence and severity of hyperbilirubinemia, both during the first few days of life and in the genesis of prolonged neonatal jaundice[8].

Breast-feeding is associated with more frequent and more severe jaundice, which is also of earlier onset and frequently of longer duration. Although bilirubin is an effective antioxidant and thus, may be beneficial, but in high concentrations it is harmful and it is capable of causing bilirubin encephalopathy. Hence, severe hyper-bilirubinemia in breast-fed infant requires treatment just as in other infants. Phototherapy is safe and effective in the management of neonatal hyper-bilirubinemia; its efficacy has been demonstrated in several studies. It is the standard method for the management of neonatal hyperbilirubinemia[9].

The aims of this study is to assess the association between types of feeding and the efficacy of phototherapy in healthy full-term infants with indirect hyperbilirubinemia and to know the relation between feeding type and TSB level. Also, to study the association between feeding types and weight loss during phototherapy exposure.

Methods

A cross-sectional study carried out at Tertiary Teaching Hospitals (Children Welfare Teaching Hospital in the Medical City, Al-Imamein Al-Kadhimein medical city, Child Center Teaching Hospital), during period from 25th of January to 22nd of July 2016.

One hundred twenty full term newborns with indirect hyperbilirubinemia from (2nd - 7th day) post-natal age admitted to the neonatal care units. Newborns presented with jaundice in the first 24 hours or after first week, blood group incompatibility, direct hyperbilirubinemia, excessive bruising or cephalhematoma, infection or any type of congenital malformation were excluded.

Full history was taken from their mothers including the sex, age of onset of jaundice, mode of delivery and type of feeding.

Three groups of infants were studied, Group 1: Breast-fed infants (n=37). Group 2: Formula-fed infants (n=51). Group 3: Mid-fed infants (n=32).

The study was conducted on neonates who diagnosed by pediatricians as

cases of indirect hyperbilirubinemia (not pathological) were treated by phototherapy. All cases were healthy and well before, during and after exposure to phototherapy.

Phototherapy was started when total serum bilirubin concentration rises more than 14.9 mg/dl, phototherapy was continuous except during feeding, providing nurse care and bathing of infants.

TSB was measured by direct spectrophotometry of the serum in a microhematocrit tube, it was measured twice daily.

Phototherapy was terminated when total serum bilirubin decreased to less than 10.8 mg/dl, the duration of phototherapy had been recorded. All infants were weighed at the start and the end of phototherapy.

Data collected were analyzed by using Microsoft Excel. Variables were expressed as percentage, range, mean, standard deviation and standard error. P-values (<0.05) were considered to indicate statistical significance. Student's t-test were used. The relationships between variables were assessed using linear correlation coefficient.

Results

The results based on the analysis of 120 cases with indirect hyperbilirubinemia (TSB >14.9 mg/ dl). Males constituted 50.8% and females constituted 49.2% of the study sample. All the neonates were full-term infants, those 37 weeks of gestation at birth were 34.2% of the sample, and those 38 weeks of gestation were 37.5% while those 39 to 40 weeks of gestation constituted 28.3% of cases.

The neonates were divided into three groups according to their type of feeding, group 1: Breast-fed group were 30.8% of subjects, group 2; Formula-fed group were 42.5% of infants and group 3: Mixed-fed group constituted the remaining 26.7%. More than half (55%) of neonates were delivered by Cesarean section, while the remaining (45%) were delivered by normal vaginal delivery.

The mean TSB of all neonates at start of phototherapy was (16.1 ± 0.6 mg/dl). This mean value showed a gradual decline to reach its minimum (9.8 ± 0.8 mg/dl) after 36 hours of starting phototherapy. On average the study sample showed a statistically significant mean reduction of 6.3 mg/dl during 36 hours of phototherapy, (Table 1).

The mean reduction in body weight after phototherapy compared to its pretreatment value was highest (mean reduction of 41 g) for breast-fed infants and lowest for formula-fed infants (mean reduction of 17 g). The mixed type of feeding was associated with a mean reduction in body weight of 33 g. The differences observed with type of feeding were statistically significant. Similarly, a longer duration of phototherapy was associated with a statistically significant higher reduction in body weight.

The reduction in body weight was lowest (1 g mean reduction) for infants with the shortest duration of phototherapy (< 28 hours) and increase in magnitude to reach its highest mean reduction (44 g) among infants with the longest duration of phototherapy (33+ hours).

There was a statistically significant moderately strong positive linear correlation between duration of phototherapy and changes in body weight at the end of phototherapy (r=-0.617).

There was no significant difference in the mean of change in weight at end of phototherapy according to sex, gestational age and mode of delivery, (Table 2).

The mean of duration of phototherapy was highest (mean of duration of 32.2 h) for breast-fed infants and lowest duration for formula fed infants (mean of duration of 29.9 h), the mixed type of feeding was associated with (mean of duration of 30.4 h). The differences observed with type of feeding were statistically significant. There were no significant differences in the mean of duration of phototherapy according to sex, gestational age and mode of delivery, (Table 3).

The mean change in TSB after terminating phototherapy compared to pretreatment level was highest (mean of 6.6 mg/dl) for formula-fed infants and lowest for breast-fed infants (mean of5.8 mg/dl), the mixed type of feeding was associated with (mean of 6.4mg /dl). The differences observed with types of feeding were statistically significant.

There were no significant differences in the mean change in TSB after terminating phototherapy according to sex, gestational age and mode of delivery, (Table 4).

The mean of TSB reduction rate was highest (mean of TSB reduction of 0.22 mg/dl per h) in formula-fed infants and lowest for breast-fed infants (mean of TSB reduction of 0.18 mg/dl per h), the mixed-fed infants was associated with (mean of TSB reduction of 0.21 mg/dl per h).

The differences observed with types of feeding were statistically significant. There was no significant difference in the mean of TSB reduction rate according to sex, gestational age and mode of delivery, (Table 5).

Table 1: The mean serum TSB at baseline (start of phototherapy) and at successive 12 hours intervals.

	TSB at start of phototherapy (mg/dl)	TSB after 12 hours of phototherapy (mg/dl)	TSB after 24 hours of phototherapy (mg/dl)	TSB after terminating phototherapy (mg/dl)	Change in TSB after terminating phototherapy (mg/dl)
Mean	16.1	13.9	12.5	9.8	-6.3
SD	0.6	0.8	0.5	0.8	0.7
N	120	120	120	120	120
P (Paired t-test)					**< 0.001**

Table 2: The mean change in body weight at the end of phototherapy by selected independent (explanatory) variables.

	Change in weight at the end of phototherapy (g)					
	Range	Mean	SD	SE	N	P
Gender						0.05 [NS]
Male	(-70 to 0)	-24	25	3	61	
Female	(-110 to 0)	-34	27	4	59	
Gestational age (weeks)-categories						0.65 [NS]
37 weeks	(-110 to 0)	-30	25	4	41	
38 weeks	(-100 to 0)	-31	28	4	45	
39-40 weeks	(-80 to 0)	-25	26	4	34	
r=0.053						0.56 [NS]
Type of feeding						
Breast feeding	(-110 to 0)	-41	29	5	37	
Bottle feeding	(-60 to 0)	-17	22	3	51	
Mixed feeding	(-70 to 0)	-33	23	4	32	<0.001
Mode of delivery	0.34[NS]					
NVD	(-80 to 0)	-26	24	3	54	
Caesarean Delivery	(-110 to 0)	-31	28	3	66	
Duration of photo-therapy (hours)						
<28 hours	(-10 to 0)	-1	2	1	18	
28-32 hour	(-110 to 0)	-28	25	3	67	
33+ hours	(-100 to 0)	-44	24	4	35	0.001
r=-0.617						P < 0.001

Table 3: The mean of duration of phototherapy (hours) by selected independent (explanatory) variables.

	Duration of phototherapy (hours)					
	Range	**Mean**	**SD**	**SE**	**N**	**P**
Gender						0.58 [NS]
Male	(25 to 35)	30.6	2.6	0.34	61	
Female	(26 to 35)	30.8	2.7	0.35	59	
Gestational age (weeks)-categories						0.68 [NS]
37 weeks	(26 to 35)	31	2.9	0.45	41	
38 weeks	(26 to 35)	30.7	2.5	0.38	45	
39-40 weeks	(25 to 34)	30.4	2.6	0.45	34	
r= - 0.067						P=0.47 [NS]
Type of feeding						
Breast feeding	(28 to 35)	32.2	2.1	0.35	37	0.001
Bottle feeding	(25 to 34)	29.9	2.7	0.38	51	
Mixed feeding	(27 to 35)	30.4	2.5	0.45	32	
Mode of delivery						0.4 [NS]
NVD	(25 to 35)	30.5	2.8	0.39	54	
Caesarean Delivery	(26 to 35)	30.9	2.5	0.31	66	

Table 4: The mean of change in TSB after terminating phototherapy compared to pre-treatment level (mg/dl) by selected independent (explanatory) variables.

	Change in TSB after terminating phototherapy compared to pre-treatment level (mg/dl)					
	Range	**Mean**	**SD**	**SE**	**N**	**P**
Gender						0.24[NS]
Male	(-8.2 to -4.9)	-6.2	0.7	0.09	61	
Female	(-7.9 to -4.7)	-6.4	0.8	0.1	59	
Gestational age (weeks)-categories						0.12[NS]
37 weeks	(-7.4 to -4.7)	-6.2	0.7	0.11	41	
38 weeks	(-8.2 to -4.9)	-6.5	0.8	0.12	45	
39-40 weeks	(-7.6 to -4.9)	-6.2	0.7	0.13	34	
r = 0.027						0.77 [NS]
Type of feeding						
Breast feeding	(-7.5 to -4.7)	-5.8	0.7	0.12	37	0.001
Bottle feeding	(-8.2 to -5.7)	-6.6	0.6	0.08	51	
Mixed feeding	(-7.7 to -5)	-6.4	0.7	0.12	32	
Mode of delivery						0.72 [NS]
NVD	(-7.9 to -4.7)	-6.3	0.8	0.11	54	
Caesarean Delivery	(-8.2 to -4.9)	-6.3	0.7	0.09	66	

Table 5: The mean of TSB reduction rate (mg/dl per hour) by selected independent (explanatory) variables.

	TSB Reduction rate (mg/dl per hour)					
	Range	**Mean**	**SD**	**SE**	**N**	**P**
Gender						0.57 [NS]
Male	(-0.27 to -0.15)	-0.21	0.03	0.004	61	
Female	(-0.29 to -0.14)	-0.21	0.04	0.005	59	
Gestational age (weeks)-categories						0.35 [NS]
37 weeks	(-0.27 to -0.15)	-0.2	0.03	0.005	41	
38 weeks	(-0.28 to -0.14)	-0.21	0.03	0.005	45	
39-40 weeks	(-0.29 to -0.15)	-0.2	0.04	0.006	34	
r = -0.009						0.92 [NS]
Type of feeding						
Breast feeding	(-0.23 to -0.14)	-0.18	0.02	0.004	37	0.001
Bottle feeding	(-0.29 to -0.17)	-0.22	0.03	0.004	51	
Mixed feeding	(-0.27 to -0.16)	-0.21	0.03	0.005	32	
Mode of delivery						0.45 [NS]
NVD	(-0.28 to -0.14)	-0.21	0.04	0.005	54	
Caesarean Delivery	(-0.29 to -0.15)	-0.21	0.03	0.004	66	

Discussion

In the present study, phototherapy with daylight fluorescent lamps was highly effective on all the 120 infants with non-hemolytic hyperbilirubinemia, the failure rate was zero. Phototherapy remained highly effective in controlling the hyperbilirubinemia, but with significantly slower efficacy for breast-fed neonates compared with the formula-fed and mixed-fed neonates when the duration of exposure to phototherapy was longer in breast-fed neonates (mean = 32.2 h) than formula-fed and mixed-fed neonates (mean = 29.9 h), (mean = 30.4 h), respectively. The results were agreed with the results of Abeer study[8], and Gulcan et al[10].

Breast-feeding was probably the main reason for the reduced response to phototherapy, so exclusively breast-fed infants with jaundice that requires phototherapy, the addition of formula feeding might enhance the response to phototherapy, this also agreed with Gulcan et al[10] that showed breast milk continues to be strongly recommended as the preferred food for newborns, with rare exceptions. Although, supplementation of breastfeeding with formula was shown to enhance the response to phototherapy and shorten the exposure time period, increasing the frequency of breast-feeding to ensure adequate fluid intake would be a rather appropriate recommendation in breast-fed newborns with excessive weight loss.

The effectiveness of phototherapy was best assessed by relating the proportionate decrease in concentration during the whole period of exposure to the duration of phototherapy, expressed as TSB decline/hour. This reduction was significantly different between the groups where the breast-fed neonates was lesser in reduction in the rate of TSB (mean = 0.18mg/dl per h) than formula-fed and mixed-fed neonates (mean = 0.22 mg/dl per h), (mean = 0.21 mg/dl per h), respectively. These results were agreed with Basil M[11] and Gulcan et al[10] who found that the overall rate of decrease in the bilirubin

concentration during the duration of exposure to phototherapy in breast-fed neonates was significantly lower than formula-fed and mixed-fed neonates.

Regarding types of feeding and weight loss, the breast-fed neonates had weight loss (mean = 41 g) more than weight loss in formula-fed and mixed-fed neonates (mean = 17 g), (mean = 33 g), respectively, so formula-fed neonates had lesser weight loss due to the easier bottle feeding techniques and the large amount of milk that can be given by a bottle. Whereas, more weight loss had be seen with poor breast feeding practice and inadequacy of milk intake. This was consistent with the study of Miasels[12] who suggested that even mild degree of dehydration in conjunction with breastfeeding has impacts on the severity of hyperbilirubinemia. Some studies showed that frequent breastfeeding of at least 11 times per day starting with the first day have been associated with the lowest serum bilirubin concentrations on the third to sixth day of life[13,14]. This result agreed with Abeer[8] who noticed that breast-fed neonates still had the greatest weight deficit at the end of exposure; this relative dehydration, although mild, might be a contributing factor in reducing the response to phototherapy.

There was a study conducted among 200 (100 early initiators and 100 late initiators) healthy term neonates and screening of jaundice was done on day 3 and day 7 using the transcutaneous bilirubinometry (JM 120), they conclude the early breast-feeding initiation had strong association with severe jaundice[15].

In the present study, there was no significant relationship between mode of delivery and hyperbilirubinemia and this results were agreed with Boskabadi[16], Agarwal[17] who showed that there was no significant relationship between mode of delivery and hyperbilirubinemia. But the results were disagreed with Tamook[18] that showed that there was positive relationship between mode of delivery and hyperbilirubinemia.

The conflicting results regarding the relationship between mode of delivery and hyperbilirubinemia may be due to differences between the selected variables, study conditions and sample size, which may affect the results.

There was no significant effect of the sex of the newborns, this may be due to sample size in the present study. This was disagreed with Tamook that notice there was positive relationship between sex of newborns and jaundice.

In fact, male newborns are more susceptible to neonatal jaundice than females, although the cause remains unknown[18].

In conclusion; Phototherapy is highly effective in reducing the serum bilirubin concentration in variables feeding patterns. Breast-fed neonates require longer duration of phototherapy to decrease the bilirubin to safe levels. Breastfeeding is associated with decreased response to phototherapy.

Recommendations; Encouragement of early initiation of breast feeding within the first few hours of life. Provide good lactation support to all mothers to increase successful breastfeeding at least 8-12 times a day. Breast feeding strongly recommended as the preferred food for newborns, with rare exceptions. In breast-fed infants with severe jaundice that requires phototherapy, continue breastfeeding with addition of formula to enhance the response to phototherapy without interruption of breast feeding, even temporary, would be necessary.

References

1. Wong RJ, Stevenson DK. Clinical manifestations of unconjugated hyperbilirubinemia in term and near-term infants. Up To Date 2007. Online article available at http://www.iptodate.com/.
2. Ujaddughe MO, Eigbedion EO, Ujaddughe ME, Okhiai O, Eigiacheyi MA. An overview of neonatal jaundice: The burden and the way forward. Int Res Med Sci 2016; 4(4): 60-2.
3. American Academy of Pediatrics. Breastfeeding and the use of human milk. Pediatrics 2012; 129: e827-e41.
4. Hansen TW. Neonatal jaundice. eMedicine neonatology 2006; 238-54.

5. Huang A, Tai BC, Wong LY, Lee J, Yong EL. Differential risk for early breastfeeding jaundice in a multi-ethnic Asian cohort. Ann Acad Med Singapore 2009; 38: 217-22.
6. Bansal A, Jain S, Parmar VR, Chawla D. Bilirubin rebound after intensive phototherapy for neonatal jaundice. Indian Pediatr 2010; 47: 607-9.
7. Watchko JF. Vigintiphobia Revisited. Pediatrics 2005; 115: 1747-53.
8. Abeer El Sakka, Safaa S Imam, Mohamed El Barbary, Wafaa Ibrahium. Does type of infant feeding affect phototherapy for neonatal hyperbilirubinemia? D ICAN: Infant, Child, & Adolescent Nutrition 2012; 4(6): 334-9.
9. Behrman RE, Kliegman RM, Jenson HB. Jaundice in the newborns. Nelson Textbook of Pediatrics, 17th ed., Philadelphia. Saunders. 2004. P. 592-9.
10. Gulcan H, Tiker F, Kilicdag H. Effect of feeding type on the efficacy of phototherapy. Indian Pediatrics 2007; 44: 32-36.
11. Basil M Hanoudi. Effect of feeding type on efficacy of phototherapy in neonatal non-haemolytic hyperbilirubinaemia. Am J Med Medi Sci 2013, 3(4): 91-95.
12. Maisels MJ, Bhutani VK, Bogen D, Newman TB, Stark AR, Watchko JF. Hyperbilirubinemia in the newborn infant ≥ 35 weeks' gestation: an update with clarifications. Pediatr 2009;124(4):1193-8.
13. Chowdhury AD, Hussey MH, Shortland DB. Critical overview of the management of neonatal jaundice in the UK. Public Health 2007;121:137-43.
14. Ennever JF, Sobel, M, McDonagh AF, Speck WT. Phototherapy for neonatal jaundice: in vitro comparison of light sources. Pediatr Res 2010;18 (7) :667-70.
15. Gladys Mugadza, Mathilda Zvinavashe, Zvanyadza Gumbo, Babill Stray-Pedersen. Early breastfeeding initiation and incidence of severe neonatal jaundice in Chipinge district Zimbabwe. Intern J Contemporary Pediatrics 2017; 6(4):19-22.
16. Boskabadi H, Navaei M. Relationship between delivery type and jaundice severity among newborns referred to Ghaem Hospital within a 6-year period in Mashhad. Iran J Obstet Gynecol Infertil 2011; 14(4): 15-21.
17. Agarwal V, Singh V, Goel SP, Gupta B. Maternal and neonatal factors affecting physiological jaundice in western U.P. Ind J Physiol Pharmacol 2007; 51(2): 203-6.
18. Tamook A, Salehzadeh F, Aminisani N, Etiology of neonatal hyperbilirubinemia at Ardabil Sabalan hospital, 2003. J Ardabil Univ Med Sci 2005; 5(4): 316-20.

IMJ 2022; 68(1): 7-14.