Annals of Neonatology

OPEN ACCESS
ISSN: 2636-3596

Original Article

The Effect of Phototherapy on The Number of Blood Eosinophils in Neonates. A Prospective Case Control Study

Abd El-Mageed Mohamed Bayomy[1], Hosny Abd El-kareem Ahmed[1], Abd El-Azeem El-sayed Ahmed[2], [1]Asmaa Gamal Abdallah Ismail[1*]

DOI: 10.21608/anj.2024.261357.1080

***Correspondence:** Department of Pediatrics, Faculty of Medicine, Al-Azhar University, Assiut, Egypt
Email: nadamali82@gmail.com

Abstract

Background: Neonatal hyperbilirubinemia is one of the most common caused for NICU admission and phototherapy is the main line of treatment in most cases with indirect hyperbilirubinemia either in fullterm or preterm neonates in NICU. The effect of phototherapy on the peripheral blood elements is still under evaluation.

Objective: To evaluate the effect of phototherapy used in treatment of neonatal indirect hyperbilirubinemia on the number of blood eosinophils.

Patients and Methods: This prospective case control study included 100 neonates with indirect hyperbilirubinemia treated with phototherapy in NICU. group 1 included 25 fullterm neonates treated with phototherapy while group 2 included 25 preterm neonates treated with phototherapy and group 3 and group 4 included 25 full term and 25 preterm with neonatal indirect hyperbilirubinemia who were not treated by phototherapy.

Results: Regarding eosinophils count, In full term neonates (group 1), there was no significant difference in eosinophils count after 24 hours compared to its level at admission ($p>0.05$) while in preterm neonates (group 2), there was significant increase in eosinophils levels after 24 hours compared to its levels at admission ($p=0.020$). Regarding lymphocytes, there was a significant decline in lymphocytes level after 24 hours compared its level at admission ($p=0.001$) in both fullterm and preterm neonates.

Conclusion: Increase in the level of peripheral eosinophils can occur in preterm neonates with neonatal hyperbilirubinemia treated by phototherapy while there was no significant difference in eosinophilic count after 24 hours after stoppage of phototherapy compared to its levels at admission in full-term neonates. This Increased eosinophilic count may predispose to allergic disease in the future.

Key words: Indirect hyperbilirubinemia, light-emitting diodes, eosinophiles, lymphocytes

Introduction

Neonatal hyperbilirubinemia results from a predisposition to the production of bilirubin in new-born infants and their limited ability to excrete it. Infants, especially preterm infants, have higher rates of bilirubin production than adults, because they have red blood cells with a higher turnover and a shorter life span. In newborn infants, unconjugated bilirubin is not readily excreted, and the ability to conjugate bilirubin is limited [1]**.** Together, these limitations lead to physiologic jaundice that is, high serum bilirubin concentrations in the first days of life in full- term infants (and up to the first week in preterm infants and in some full-term Asian infants), followed by a decline during the next several weeks to the values commonly found in adults [2].

The average full-term newborn infant has a peak serum bilirubin concentration of 5 to 6 mg per deciliter (86 to 103 pmol per liter). Exaggerated physiologic jaundice occurs at values above this threshold (7 to 17 mg per deciliter [104 to 291 pmol per liter]). Serum bilirubin concentrations higher than 17 mg per deciliter in full-term infants are no longer considered physiologic, and a cause of pathologic jaundice can usually be identified in such infants [3]. Even though neonatal jaundice is generally a temporary condition, it is the most common reason for hospitalization in the first week following delivery. Phototherapy (PT) is the most widespread method used in the treatment of indirect hyperbilirubinemia (IHB) in newborns. Phototherapy prevents increase of serum bilirubin concentrations and lowers them in nearly all newborns regardless of maturity, the extent of skin pigmentation and the presence of hemolysis and decreases the need for exchange transfusion (ET) [4].

Phototherapy is the use of visible light for the treatment of hyperbilirubinemia in the newborn. This relatively common therapy lowers the serum bilirubin level by transforming bilirubin into water-soluble isomers that can be eliminated without conjugation in the liver. The dose of

phototherapy largely determines how quickly it works; the dose, in turn, is determined by the wavelength of the light, the intensity of the light (irradiance), the distance between the light and the infant, and the body surface area exposed to the light [5].

Treatment decision is based on the total serum bilirubin (TSB) level, birth weight, gestational week, postnatal age, and the presence of risk factors. According to the American Academy of Pediatrics (AAP) guidelines, intensive Phototherapy is defined as irradiance in the blue-green spectrum (wavelengths of approximately 430-490 nm) of 30 microwatts/cm2/nm, delivered to as much of the infant's surface as possible. High intensity gallium nitride light-emitting diodes (LEDs) with peak emissions of 460 nm have recently begun to be employed in Phototherapy and when compared with conventional phototherapy, LED lights are more effective in reducing serum unconjugated bilirubin levels [6]**.**

Commercially available phototherapy systems include those that deliver light via fluorescent bulbs, halogen quartz lamps, light- emitting diodes, and fiberoptic mattresses. Proper nursing care enhances the effectiveness of phototherapy and minimizes complications. Caregiver responsibilities include ensuring effective irradiance delivery, maximizing skin exposure, providing eye protection and eye care, carefully monitoring thermoregulation, maintaining adequate hydration, promoting elimination, and supporting parent-infant interaction [7].

Eosinophils are formed in the bone marrow and have a half- life of 6 to 10 hours. A normal eosinophil count within the circulating blood is 350 to 500/mm3.

Eosinophils are seen in the tracheobronchial tree, alimentary canal, exocrine glands, vagina, cervix, and connective tissue underneath the epithelium [8].

One of the issues discussed in the pathogenesis of allergic diseases is NH

and related neonatal PT. The tendency of the immune system is toward a Th-2 response in the neonatal period. There must be a transition from T-helper 2(Th-2) to T-helper 1(Th-1) response during the postnatal period to prevent allergy. An experimental study showed that bilirubin could restrict Th-1 cell response by disrupting this transformation [9]**.**

Aim of the study

To evaluate the effect of phototherapy used in treatment of neonatal hyperbilirubinemia on number of blood eosinophils.

Patients and Methods

This is a prospective study included 100 neonates with neonatal indirect hyperbilirubinemia in pediatric and neonatology department at Sohag Teaching Hospital.

Group (1) included 25 cases of fullterm neonatal patients with neonatal jaundice treated by phototherapy (CBC will be done before phototherapy and after phototherapy by 24 hours), group (2) included 25 cases of preterm neonatal patients with neonatal jaundice treated by phototherapy (CBC will be done before phototherapy and after phototherapy by 24 hours), group (3) included 25 cases of fullterm neonatal patients with neonatal jaundice without phototherapy (CBC will be done at the time of examinations) and group (4) included 25 cases of preterm neonatal patients with neonatal jaundice without phototherapy (CBC will be done at the time of examinations)

Ethical consideration: The privacy of all data collected will be assured. An approval of the study is obtained from Sohag teaching hospital and ethical committee, written consent will be obtained from parents of all cases prior to treatment plan, and benefits from participation in the research will be explained to parents of cases.

Inclusion criteria: Infants diagnosed to have indirect hyperbilirubinemia. Full term group: infants with a gestational age >36weeks. Preterm group: infants with a

gestational age >32 weeks and less than 36 weeks.

Exclusion criteria: Infants with direct hyperbilirubinemia. Infants with any disease other than indirect hyperbilirubinemia as neonatal liver diseases, cardiac disease, blood diseases and renal diseases. Infants with neonatal hyperbilirubinemia.

Methods:

All infants included in the study will be subjected to the following: complete history and physical examination and laboratory investigations included complete blood count (CBC) including esinophilic count. Total serum bilirubin, direct serum bilirubin and indirect serum bilirubin. Serum glutamate pyruvate transaminase (SGPT) and Serum glutamate oxaloacetate transaminase (SGOT). Renal function tests (blood urea and serum creatinine). Re-evaluation of investigations as complete blood count after stopping of phototherapy by 24 hours.

Ethical consideration

The privacy of all data collected will be assured. An approval of the study is obtained from Sohag teaching hospital and ethical committee, written consent will be obtained from parents of all cases prior to treatment plan, and benefits from participation in the research will be explained to parents of cases.

Statistical analysis

Data was collected, coded then entered as a spread sheet using Microsoft Excel 2016 for Windows, of the Microsoft Office bundle; 2016 of Microsoft Corporation, United States. Data was analyzed using IBM Statistical Package for Social Sciences software (SPSS), (IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp). The Kolmogorov-Smirnov test was used to verify the normality of distribution. Continuous data was expressed as mean ± standard deviation while categorical data as numbers and percentage. A statistical value <0.05 was considered as significant.

The following tests were used: Chi-square test; used to study the association between two qualitative variables. Analysis of variance (ANOVA or F test): was used for continuous data to test for significant difference between more than two normally distributed groups. Kruskal-Wallis test: It is a non-parametric equivalent to ANOVA and used when ANOVA assumptions were violated to compare between more than two groups of skewed data. Post Hoc tests: Tukey honestly significant difference (Tukey-HSD) test was used as a post hoc test to adjust for multiple comparisons after significant ANOVA test to indicate which significant difference between pairs of groups whereas Bonferroni post hoc test was used after significant Kruskal- Wallis test.

Results

Table 1: Demographic characteristics among the studied groups.

Item		Group (1) (n.= 25)		Group (2) (n.= 25)		Group (3) (n.= 25)		Group (4) (n.= 25)		Test value	P- value
		No	%	No.	%	No.	%	No.	%		
Sex	Male	18	72.0%	17	68.0%	20	80.0%	21	84.0%	X = 2.193	0.533 (NS)
	Female	7	28.0%	8	32.0%	5	20.0%	4	16.0%		
Gestational age (Weeks)	Mean± SD	38.04±1.62		33.68± 1.14		37.92± 1.98		33.04± 0.84		KW= 37.7	<0.001 (HS)
	Median	38.0		34.0		38.0		33.0			
	Range	37.0- 41.0		32.0- 35.0		37.0- 42.0		32.0- 34.0			
Postnatal age (days)	Mean± SD	4.76± 1.45		5.84± 2.15		4.84± 0.99		5.08± 1.29		KW = 2.127	0.248 (NS)
	Median	5.0		5.0		5.0		5.0			
	Range	3.0- 8.0		3.0- 11.0		3.0- 6.0		3.0- 8.0			

p≤0.05 is considered statistically significant, p≤0.01 is considered highly statistically significant, SD: standard deviation, analysis done by X2: Chi-Square Test& KW: Kruskal Wallis Test.

Table 2: Comparison between the studied groups regarding clinical history.

Item		Group (1) (n.= 25)		Group (2) (n.= 25)		Group (3) (n.= 25)		Group (4) (n.= 25)		Test value	P- value
		No	%	No.	%	No	%	N.	%		
Maternal history during pregnancy	No	25	100.0%	25	100.0%	23	92.0%	23	92.0%	X 4.167	0.244 (NS)
	HTN	0	0.0%	0	0.0%	2	8.0%	2	8.0%		
Type of delivery	CS	18	72.0%	14	56.0%	13	52.0%	15	60.0%	X=2.33	0.506 (NS)
	NVD	7	28.0%	11	44.0%	12	48.0%	10	40.0%		
Gross congenital anomaly	No	25	100.0%	25	100.0%	25	100.0%	25	100.0%	-	-

p≤0.05 is considered statistically significant, p≤0.01 is considered highly statistically significant,, analysis done by X2: Chi-Square Test.

Table 3: Comparison between the studied groups regarding anthropometric measurements.

Item		Mean	SD	Median	Range		Test value	P-value
Head circumference (cm)	**Group (1)**	37.14	.21	36.80	34.7	38.3	F= 0.427	0.536 (NS)
	Group (2)	35.54	.45	35.60	34.7	36.3		
	Group (3)	36.11	.32	35.90	34.7	37.4		
	Group (4)	34.61	.30	34.50	34.7	35.7		
Weight (gm)	**Group (1)**	2828.00	391.33	2800.0	2300.0	3700.0	KW= 21.62	<0.001 (HS) p1-2=0.063 p1-3= 0.001 p1-4<0.001 p2-3= 0.158 p2-4= 0.009 p3-4= 0.235
	Group (2)	2175.00	452.11	2150.0	1500.0	2700.0		
	Group (3)	2940.00	645.15	2800.0	2500.0	3700.0		
	Group (4)	2196.00	262.96	2200.0	1500.0	3000.0		

p≤0.05 is considered statistically significant, p≤0.01 is considered highly statistically significant, analysis done by F: One-way ANOVA Test, KW: Kruskal Wallis Test..

Table 4: Comparison between the studied groups regarding CBC at admission.

Group	Hemoglobin (g/dl)					Kruskal Wallis Test	
	Mean	± SD	Median	Range		Test value	e
Group (1)	16.36	±1.08	16.00	15.00	19.00	KW= 2.530	0.470 (NS)
Group (2)	16.44	±0.88	16.10	15.10	18.00		
Group (3)	16.45	±1.04	16.20	15.00	18.30		
Group (4)	16.70	±0.82	16.80	15.00	18.00		
	WBCs × 10^3/ mm^3						
	Mean	± SD	Median	Range		Test value	P-value
Group (1)	11.14×10^3	±2313.20	11×10^3	8×10^3	17.1×10^3	KW= 27.11	<0.001 (HS), p1-2<0.001, p1-3<0.001, p1-4<0.001, p2-3= 0.940, p2-4= 0.942, p3-4=0.998
Group (2)	14.96×10^3	±3131.54	15×10^3	8×10^3	19.5×10^3		
Group (3)	15.04×10^3	±2921.61	14.7×10^3	10×10^3	20×10^3		
Group (4)	15.01×10^3	±2738.11	14.5×10^3	10×10^3	19.5×20^3		
	Platelets count × 10^3/mm^3						
	Mean	± SD	Median	Range		Test value	P-value
Group (1)	330×10^3	±63.38	350×10^3	230×10^3	450×10^3	KW= 0.391	0.942 (NS)
Group (2)	328.4×10^3	±66.88	340×10^3	240×10^3	430×10^3		
Group (3)	337.6×10^3	±67.86	330×10^3	250×10^3	450×10^3		
Group (4)	332.80×10^3	±73.47	320×10^3	230×10^3	460×10^3		
	Eosinophils%						
	Mean	± SD	Median	Range		Test value	P-value
Group (1)	0.68	±0.80	0.00	0.00	2.00	KW= 1.350	0.717 (NS)
Group (2)	0.60	±0.71	0.00	0.00	2.00		
Group (3)	0.48	±0.51	0.00	0.00	1.00		
Group (4)	0.68	±0.56	1.00	0.00	2.00		
	Lymphocytes%						
	Mean	± SD	Median	Range		Test value	P-value
Group (1)	50.36	±2.93	50.0	46.0	56.0	KW= 5.601	0.133 (NS)
Group (2)	49.80	±4.41	51.0	40.0	56.0		
Group (3)	48.64	±4.18	48.0	41.0	56.0		
Group (4)	48.40	±3.19	48.0	41.0	55.0		

p≤0.05 is considered statistically significant, p≤0.01 is considered highly statistically significant, SD: standard deviation, analysis done by KW: Kruskal-Wallis Test.

Table 5: Comparison between the studied groups regarding liver and renal function tests before phototherapy.

	SGPT (ALT)(U/l)					Test value	P-value
	Mean	**± SD**	**Median**	**Range**			
Group (1)	23.52	±7.22	23.00	11.00	35.00	KW= 4.803	0.187 (NS)
Group (2)	21.84	±7.50	21.00	10.00	38.00		
Group (3)	26.00	±8.39	24.00	12.00	39.00		
Group (4)	26.08	±7.91	27.00	11.00	37.00		
	SGOT (AST)(U/l)					**Test value**	**P-value**
	Mean	**± SD**	**Median**	**Range**			
Group (1)	20.24	±6.13	19.0	12.0	31.0	KW= 0.039	0.998 (NS)
Group (2)	20.28	±6.07	19.0	10.0	32.0		
Group (3)	20.48	±5.89	20.0	10.0	30.0		
Group (4)	20.16	±6.33	21.0	10.0	30.0		
	Serum creatinine (mg /dl)						
	Mean	**± SD**	**Median**	**Range**		**Test value**	**P-value**
Group (1)	0.41	±0.15	0.40	0.20	0.80	KW= 10.87	0.012 (S)
Group (2)	0.43	±0.18	0.40	0.20	0.80		p1-2=0.783, p1-3=0.013
Group (3)	0.57	±0.23	0.60	0.20	0.90		p1-4=0.015, p2-3=0.027
Group (4)	0.58	±0.25	0.60	0.20	0.90		p2-4=0.031, p3-4=0.953
	Blood Urea (mg /dl)						
	Mean	**± SD**	**Median**	**Range**		**Test value**	**P-value**
Group (1)	6.03	±2.50	5.5	3.2	13.0	KW= 15.72	0.001 (HS)
Group (2)	8.86	±2.33	9.2	4.5	12.4		p1-2=0.001, p1-3=0.002
Group (3)	8.60	±3.19	9.3	3.0	13.0		p1-4=0.182, p2-3=0.726
Group (4)	7.08	±2.68	6.9	3.0	12.0		p2-4=0.033, p3-4=0.074

$p \leq 0.05$ is considered statistically significant, $p \leq 0.01$ is considered highly statistically significant, SD: standard deviation, analysis done by KW: Kruskal-Wallis Test.

Table 6: Comparison between CBC at admission and after 24hrs of phototherapy in groups 1& 2

Item		Hemoglobin (g/dl)					Wilcoxon Signed Rank Test	
		Mean	± SD	Median	Range		Test value	P-value
Group(1)	At admission	16.36	1.08	16.00	15.00	19.00	4.382	<0.001 (HS)
	After 24 hrs	15.36	0.93	15.20	13.90	17.50		
Group(2)	At admission	16.44	0.88	16.10	15.10	18.00	4.368	<0.001 (HS)
	After 24 hrs	15.55	0.78	15.50	14.20	16.90		
		WBCs ×10^3/mm^3						
		Mean	± SD	Median	Range		Test value	P-value
Group(1)	At admission	11.1×10^3	±2313.20	11×10^3	8×10^3	17.1×10^3	0.810	0.418 (NS)
	After 24 hrs	11×10^3	±2205.35	11×10^3	8×10^3	17×10^3		
Group(2)	At admission	14.96×10^3	±3131.54	15×10^3	8×10^3	19.5×10^3	4.408	<0.001 (HS)
	After 24 hrs	14.17×10^3	±3069.51	14.3×10^3	7.9×10^3	18.5×10^3		
		Platelets ×10^3/mm^3						
		Mean	± SD	Median	Range		Test value	P-value
Group(1)	At admission	330×10^3	±63.38	350×10^3	230×10^3	450×10^3	4.47	<0.001 (HS)
	After 24 hrs	315×10^3	±64.37	325×10^3	200×10^3	430×10^3	7	
Group(2)	At admission	328×10^3	±66.88	340×10^3	240×10^3	430×10^3	4.451	<0.001 (HS)
	After 24 hrs	311×10^3	±68.42	320×10^3	210×10^3	420×10^3		
		Eosinophils%						
		Mean	± SD	Median	Range		Test value	P-value
Group(1)	At admission	0.68	±0.80	0.0	0.0	2.0	0.832	0.405 (NS)
	After 24 hrs	0.56	±0.51	1.0	0.0	1.0		
Group(2)	At admission	0.60	±0.71	0.0	0.0	2.0	2.33	< 0.001 (HS)
	After 24 hrs	1.47	±0.92	0.8	0.5	1.7		
		Basophils%						
		Mean	± SD	Median	Range		Test value	P-value
Group(1)	At admission	0.80	±0.71	1.0	0.0	2.0	1.732	0.083 (NS)
	After 24 hrs	0.56	±0.51	1.0	0.0	1.0		
Group(2)	At admission	0.64	±0.57	1.0	0.0	2.0	1.00	0.317 (NS)
	After 24 hrs	0.56	±0.51	1.0	0.0	1.0		
		Lymphocytes %						
		Mean	± SD	Median	Range		Test value	P-value
Group(1)	At admission	50.36	±2.93	50.0	46.0	56.0	3.43	0.
	After 24 hrs	46.32	±4.14	46.0	39.0	54.0	8	001 (HS)
Group(2)	At admission	49.80	±4.41	51.0	40.0	56.0	3.903	<0.001 (HS)
	After 24 hrs	46.72	±5.40	47.0	39.0	54.0		

$p \leq 0.05$ is considered statistically significant, $p \leq 0.01$ is considered highly statistically significant, SD: standard deviation, analysis done by Wilcoxon Signed Rank Test.

Discussion

Neonatal Jaundice is the most common neonatal illness and is the most common cause of hospitalization. In about 8 to 11 percent of cases, bilirubin levels elevate up to 95th percentile of the normal range and need to be followed and treated [10]. In the absence of proper treatment, dangerous complications such as kernicterus can cause life-long disability. Care, support, and lactation training before and after birth are important to prevent pathologic and life-threatening jaundice. Also, early detection and appropriate treatment reduce complications of jaundice [11].

Therapeutic interventions in hyperbilirubinemia newborns include phototherapy and blood exchange transfusion. Currently, the most effective and commonly used treatment for neonatal jaundice is phototherapy, which is a safe treatment in term and preterm infants [12]. Phototherapy reduces the risk of blood exchange by decreasing total bilirubin concentration, the complications of phototherapy can be categorized as follows: Short-term complications include: separation between mother and baby, ambient temperature imbalance, water loss, electrolyte disorders (especially hypocalcemia), conjunctivitis, sleep disturbances, tanning child syndrome and long-term complications include allergic disease (such as allergic rhinitis and asthma), melanocytic macular degeneration, melanoma, and skin cancers, open ductus arteriosus (PDA) and retinal damage [13].

Eosinophils are white blood cells of the immune system, which are responsible for parasite defense reactions, allergic response, tissue inflammation and immune modulation [14]. In term of neonates, the mean value for eosinophils is reported to be 550/uL, ranged between 140 to 1300/uL. Eosinophils have role in the pathogenesis of asthmatics patients with persistent airways eosinophilia. Eosinophils are differentiated bone marrow-derived granulocytes that play an

essential role in the pathogenesis of asthma [15,16].

We aimed to evaluate the effect of phototherapy in neonatal hyperbilirubinemia on number of blood eosinophils. We found a significant difference between the four studied groups regarding gestational age ($p<0.001$) as groups (1) & (3) had significant higher gestational age compared to groups (2) and (4). No significant difference was found between the four studied groups regarding sex and post-natal age ($p >0.05$).

Khan et al. [17] who investigated 100 newborns babies with hyperbilirubinemia and found that mean gestational age of term babies was 38.9±1.22 weeks and of preterm babies was 34.64±1.05 weeks with significant difference between both groups.

Bebars et al. [18] observed that neonates have a gestational age ranged 37–41 weeks with a mean ± SD (38.85 ± 1.49) for the full-term group and for the preterm group 31–36 weeks with a mean ± SD (34.95 ± 2.1) which was significantly different ($P = 0.001$).

In the present study, there was no statistically significant difference between the four studied groups regarding maternal history during pregnancy and type of delivery.

Regarding weight and head circumference we found that there was statistically significant difference between the four studied groups in weight ($p<0.001$) and statistically significant difference between the four studied groups regarding head circumference ($p>0.05$). *Khan et al.* [18] who observed that mean ±SD weight of the term babies was 2.96 (±0.23) kg and of the preterm babies was 1.89 (±0.2) kg found that birth weight was significantly different between both group. *Mengesha et al.* [19] who found that birth weight was significantly different between both groups.

Our findings showed that general examination and systematic examination

including chest, cardiac, abdominal and neurological examinations were normal in all.

In the present study, No statistically significant difference between the four studied groups regarding hemoglobin, HCT and RBC count ($p > 0.05$).

A statistically significant difference between the four studied groups was observed regarding WBCs ($p<0.001$) as WBCs was significantly lower in group (1) when compared to groups (2, 3 & 4). No statistically significant difference between the four studied groups regarding Platelets count eosinophils and lymphocytes.

In our study, in group (1) and group (2) there was significant decline in hemoglobin level after 24 hours compared its level at admission ($p<0.001$).

Regarding WBCs, in group (1), there was no significant difference in WBCs level after 24 hours compared its level at admission ($p>0.05$). In group (2), there was significant decline in WBCs level after 24 hours compared its level at admission ($p<0.001$). Regarding platelets, In group (1), there was significant decline in platelets level after 24 hours compared its level at admission, ($p<0.001$). In group (2), there was significant decline in platelets level after 24 hours compared its level at admission ($p<0.001$).

Erduran et al. [20] showed a significant decrease in WBCs' count after exposure to Ultravilot radiation. *Saber et al.* [21] observed no statistically significant difference in WBCs' count before and after phototherapy.

Mrkaic et al. [22] studied the effects of phototherapy on the immune system of neonates without signs of infection, anoxia, and birth injury. Their results showed a raise in the amount of peripheral WBCs, polymorphonuclears, lymphocytes, and monocytes as well as a delay in the response of the peripheral blood phagocytes.

Jahanshahifard et al. [23] demonstrated that phototherapy might increase the

peripheral WBCs' count. Their results were against ours. They reported that this increase was unspecific and might be because of admission stress or beginning of infection.

Regarding basophils, in group (1) and group (2), there was no significant difference in basophils level after 24 hours compared its level at admission (p>0.05).

Regarding lymphocytes, in group (1) and group (2), there was significant decline in lymphocytes level after 24 hours compared its level at admission p=0.001).

Hart et al [24], suggested that the mechanism of action of phototherapy involves changing the original compound bilirubin into other isomer compounds that can be broken down and consequently excreted by the body via the urine and feces. When these specific wavelengths penetrate the skin, they convert the bilirubin into these isomers, which can be removed from the body without or with the involvement of the liver.

Pereira and Shah [25] suggested that the liver also can excrete these isomers, and so the significant increase in the rate of biliary excretion of unconjugated, as well as the normally conjugated, forms of bilirubin and related bile pigments when either jaundiced rats or humans are irradiated with visible light of appropriate wavelength.

Kato et al. [26] found that the phototherapy is generally considered a safe method for the treatment of hyperbilirubinemia, the reported side effects are controversial debate and include rash, loose green stools, dehydration, Increased susceptibility to childhood asthma and allergic conditions, oxidative injury and ocular hazards.

Regarding eosinophilc count, in group (1), there was no significant difference in eosinophic count after 24 hours compared to its level at admission (p>0.05). In group (2), there was significant increase in eosinophils level after 24 hours compare to its level at admission (p>0.020).

Sangsari et al. [27] showed that the mean number of eosinophils before phototherapy was 377.96±181.24, which significantly increased in the first and second days after phototherapy. This increase in eosinophils in male neonates observed in the second day and females in the first and second days after phototherapy. Also, in the newborns less than a week old, this difference was significant.

Aydın et al. [28] and colleagues showed that eosinophilic count increased from 402.27 to 506.4 after phototherapy. They showed that high levels of bilirubin may result in decreased levels of eosinophils and treatment of jaundice can increase the number of eosinophils.

Aspberg et al. [29]*; Aspberg et al.* [30] there is a hypothesis that eosinophilia can occur in correlation to phototherapy which can stimulate allergic diseases. Bilirubin can be protective against allergic diseases. Some studies showed that infants who develop jaundice and receive phototherapy are 1.5 times prone to develop asthma and one study showed that neonatal jaundice or receiving phototherapy can induce asthma after 12 years of age. But these studies do not indicate that asthma is associated with bilirubinemia or phototherapy.

Beken et al. [31] studied the association of phototherapy on eosinophil and eosinophilic cationic protein levels with hyperbilirubinemia (> 20 mg/dL) in 30 neonates. They found that eosinophil levels were higher after photo therapy, but these high results were not significant, and there was no difference in these in respect of the levels of leukocyte, lymphocyte, neutrophil, and platelets.

Can and Hamilcikan [9] enrolled ninety-six term neonates with Hyperbilirubinemia and stated that fifty-two neonates (54.1%) were born by normal spontaneous delivery. After phototherapy, while total serum bilirubin, hemoglobin, hematocrit, leukocyte, and neutrophil levels were found to be

significantly decreased, eosinophil levels were significantly increased ($p>0.05$). No significant difference was found regarding lymphocyte and basophil levels after phototherapy. They thought that the non- severe hyperbilirubinemia, which was treated with phototherapy, may increase eosinophils in the early days of life. They showed a decrease in lymphocyte, monocyte, and basophil series and a significant increase in eosinophil levels in neonates with non-severe hyperbilirubinemia. These results can be explained by the inhibition of complement activation along the classical pathway giving rise to the prevention of leukocyte migration by hyperbilirubinemia.

Sangsari et al. [27] studied 163 neonates (52.1% male and 47.9% female) with a mean age of 5.49 ± 4.01 days. The prevalence of term neonates was 81% and 19% were preterm and indicated that there is a significant relationship between hyperbilirubinemia and phototherapy and increased level of peripheral blood eosinophilis, and this relationship is related to the age of the baby. This suggests that at an age of less than a week, the influence of exposure to phototherapy is higher than that of older ones, which can be due to the lack of maturity of the body's early immune system at the beginning of life.

Sangsari et al. [27] also reported that increased eosinophilic count in neonates with hemolytic jaundice was more marked than those with non-hemolytic type. Also, the increase in the number of eosinophils in preterm infants in the second day after phototherapy was significantly higher in comparison with term neonates, which means that preterm infants are more likely to develop allergies or asthma in the future. There was a significant negative correlation between the mean total bilirubin concentration of patients before phototherapy with mean eosinophilic count, that is, with the increase of bilirubin, the number of eosinophils was decreased; however, the mean eosinophilic count in the first and second

days after phototherapy was not significantly correlated with the severity of hyperbilirubinemia. *Can and Hamilcikan* [9] showed that non-severe hyperbilirubinemia may affect eosinophils and other blood cells.

Conclusions

Phototherapy is an important the line of treatment in neonatal hyperbilirubinemia. Increase in the level of peripheral eosinophilis can occur in preterm neonates with neonatal hyperbilirubinemia treated by phototherapy. No significant difference in eosinophilic count after 24 hours compared to its level at admission in full-term neonatal patients with neonatal jaundice. Increased eosinophilic count may predispose to allergic disease.

Acknowledgements

The study group is grateful to the NICU team, Sohag teaching hospital for their support.

Author's contributions

All authors shared equally in this work. The authors have read and approved the manuscript.

Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper

Funding

The manuscript was funded by the authors

Author's details

[1]Department of Pediatrics, Faculty of Medicine, Al-Azhar University, Assiut, Egypt

[2]Department of Clinical Pathology, Faculty of Medicine, Al-Azhar University, Assiut, Egypt

Date received: 27th October 2023, accepted 29th January 2024

References

1- Davidson, M. R. Fast Facts for the Neonatal Nurse: Care Essentials for Normal and High-risk Neonates. Springer Publishing Company. 2020.

2- Mulquiney, T; and Dechert, S. Health Problems of the Newborn. Wong's Nursing Care of Infants and Children Australia and New Zealand Edition-E-Book: for Professionals. 2021, 168.

3- Khairy, M.A; Abuelhamd, W. A; Elhawary, I. M; and Nabayel, A. S. M. Early predictors of neonatal hyperbilirubinemia in full term newborn. Pediatrics & Neonatology 2019, 60(3): 285-290.

4- Abbey, P., Kandasamy, D. and Naranje, P. Neonatal jaundice. The Indian Journal of Pediatrics 2019, 86(9):830-841.

5- Hansen, T. W.R; Maisels, M.J; Ebbesen, F; Vreman, H. J; Stevenson, D. K; Wong, R. J; and Bhutani, V.K. Sixty years of phototherapy for neonatal jaundice-from serendipitous observation to standardized treatment and rescue for millions. Journal of Perinatology 2020, 40(2): ISO- 193.

6- Anand, P., Gopalakrishnan, S., Sachdeva, A., Sahoo, T., & Sivanandan, S. Screening, prevention, and management of neonatal hyperbilirubinemia. Journal of Neonatology 2020, 34(3): 153-169.

7- Rarokar, N., Gurav, S., Kokare, D.M., Kale, V. and Raut, N.A., Phototherapy: A critical review. Photophysics and Nanophysics in Therapeutics 2022:.3-14.

8- Young, K. M; and Layne, E.A. Eosinophils and their disorders. Schalm's veterinary hematology2022, 363-372.

9- Can, C; and Hamilcikan, S. Effect of Neonatal Phototherapy on Eosinophil Levels in Nonsevere Hyperbilirubinemia. American journal of perinatology 2020, 37(09): 929-932.

10- Keahey, P. A., Simeral, M. L., Schroder, K. J., et al. Point-of- care device to diagnose and monitor neonatal jaundice in low -resource settings. Proc Natl Acad Sci U S A 2017, 114, 965-971.

11- Coquery, S. S., Georges, A., Cortey, A., et al. Discharge of newborns with risk factors of severe hyperbilirubinemia: description of a hospital at home-based care monitoring and phototherapy. Eur J Pediatr 2022, 181: 3075-3084.

12- Dey, S. K., Jahan, S., Jahan, I., et al. Exchange Transfusion for Hyperbilirubinemia among Term and Near Term in NICU of a Tertiary Care Hospital of Bangladesh: Findings from a Prospective Study. Euroasian J Hepatogastroenterol 2021, 11: 21- 26.

13- Zhang, M., He, Y., Tang, J., et al. Intensive phototherapy vs. exchange transfusion for the treatment of neonatal hyperbilirubinemia: a multicenter retrospective cohort study. Chin Med J (Engl)2022, 135: 598-605.

14- Ondari, E., Calvino-Sanles, E., First, N. J., et al. Eosinophils and Bacteria, the Beginning of a Story. Int J Mol Sci 2021, 22: 25-9.

15- Rossberg, S., Gerhold, K., Geske, T., et al. (2016): Elevated blood eosinophils in early infancy are predictive of atopic dermatitis in children with risk for atopy. Pediatr Allergy Immunol2016, 27: 702-708.

16- Nakagome, K. & Nagata, M. Involvement and Possible Role of Eosinophils in Asthma Exacerbation. Front Immunol 2018, 9: 22-9.

17- Khan, H. A., Akter, T., Rahman, S., et al. Comparative Study of Serum Bilirubin Level between Term and Preterm Babies in Mymensingh Medical College Hospital. Faridpur Med Coll J 2018, 12: 5-8.

18- Bebars, G. M., Kamel, B. A. & Allam, E. Comparison between preterm and full term neonatal cord selenium in correlation to maternal serum selenium levels. Gaz Egypt Paediatr Assoc 2018, 66, 96-99.

19- Mengesha, H. G., Lerebo, W. T., Kidanemariam, A., et al. Pre- term and post-term births: predictors and implications on neonatal mortality in Northern Ethiopia. BMC Nurs 2016, 15: 48-53.

20- Erduran, E., Arslan, M., Alperen, A., et al. In vitro investigation of the effect of ultraviolet-C light on lymphocytes. Turk Hematol Onkol Derg 1997, 7: 30-32.

21- Saber, M. A., Abd El Naby, S. A., Helwa, M. A., et al. (2014): The influence of phototherapy for neonatal hyperbilirubinemia on tumour necrosis factor-α. Menoufia Med J 2014, 27: 44-9.

22- Mrkaic, L., Kamenov, B., Najman, S., Dimitrijević, H., Mitrović, V., & Maglajlić, S. Neonatal immune system changes caused by phototherapy. Srpski arhiv za celokupno lekarstvo 1994, 122: 36-37.

23- Jahanshahifard, S., Ahmadpour-Kacho, M. & Pasha, Y. Z. Effects of phototherapy on cytokines' levels and white blood cells in term neonate with hyperbilirubinemia. J Clin Neonatol 2012, 1: 139-42.

24- Pereira, N. M. & Shah, I. Neonatal cholestasis mimicking biliary atresia: Could it be urinary tract infection? SAGE Open Med Case Rep 2017, 5: 2050313x17695998.

25- Kato, S., Iwata, O., Yamada, Y., et al. Standardization of phototherapy for neonatal hyperbilirubinemia using multiple-wavelength irradiance integration. Pediatr Neonatol 2020, 61: 100-105.

26- Sangsari, R., Saeedi, M., Kadivar, M., et al. Evaluation of Changes in the Number of Eosinophils Before and After Phototherapy in Neonatal Hyperbilirubinemia. Int J Pediatr 2020, 30: 972-9.

27- Aydın, B., Beken, S., Zenciroğlu, A., Dilli, D. and Okumuş, N., (2014): Blood eosinophil levels in newborns with severe indirect hyperbilirubinemia treated with phototherapy. Iranian Journal of Pediatrics 2014, 24(3):267.

28- Aspberg, S., Dahlquist, G., Kahan, T., et al. Is neonatal phototherapy associated with an increased risk for hospitalized childhood

bronchial asthma? Pediatr Allergy Immunol 2007, 18: 313-9.

29- Aspberg, S., Dahlquist, G., Kahan, T., et al. Confirmed association between neonatal phototherapy or neonatal icterus and risk of childhood asthma. Pediatr Allergy Immunol 2010, 21: 733-9.

30- Beken, S., Aydin, B., Zenciroğğlu, A., Dilli, D., Özkan, E., Dursun, A. et al., The effects of phototherapy on eosinophil and eosinophilic cationic protein in newborns with hyperbilirubinemia. Fetal and Pediatric Pathology 2014, 33(3): 51-156

Citation: Bayomy, A. E., Abd El-kareem Ahmed, H., El-sayed Ahmed, A. E., Abdallah Ismail, A. The Effect of Phototherapy on The Number of Blood Eosinophils in Neonates. A Prospective Case Control Study. *Annals of Neonatology*, 2024; 6(1): -. doi: 10.21608/anj.2024.261357.1080