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ORIGINAL ARTICLE

Evaluation of Phototherapy on Platelet Count in Neonates with Neonatal Hyperbilirubinemia

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ABSTRACT

Background: Phototherapy plays a significant role in the treatment of hyperbilirubinemia in neonates. However, this treatment may result in the development of some complications. There are limited studies with different results regarding the effect of phototherapy on platelet count. The aim of this research to detect the effect of phototherapy on platelet count in neonates with indirect hyperbilirubinemia.

Methods: Across sectional study was conducted during the period from January 2018 to June 2018 at Neonatal Intensive Care Unit of Benha children hospital. The study included 54 term neonates with symptoms, signs and laboratory findings of neonatal indirect hyperbilirubinemia treated with phototherapy. Apart from jaundice, their physical examination was normal. Platelet count of jaundiced neonates was measured on admission and at discontinuation of phototherapy.

Results: Total of 54 full term neonates were included in this study. The mean (+/-SD) platelet counts were 278.89 ± 60.63 before phototherapy and 319.67 ± 78.58 after phototherapy. There was an increase in the mean platelet count after phototherapy which was statistically significant (p=0.001). The study showed that mean platelet count increased with extended mean phototherapy time.

Conclusion: Phototherapy leads to rise in platelet count in term icteric neonates exposed to phototherapy for more than two days.

Key words: Phototherapy, Unconjugated Hyperbilirubinemia, Platelet count.

INTRODUCTION

Neonatal jaundice due to unconjugated hyperbilirubinemia is a common condition that affects about 60% of term and 80% of preterm neonates during first week of life **[1].**

Once unconjugated hyperbilirubinemia crosses the upper limits of physiological jaundice (unconjugated serum bilirubin level 5 – 6 mg/dl), it may be injurious for the brain. When bilirubin encephalopathy affect brain it will result in permanent developmental delay **[2].** Treatment options for unconjugated hyperbilirubinemia include phototherapy, exchange transfusion, IV immunoglobulins and metalloporphyrin. Out of these options, phototherapy is a non-invasive technique has been used for the treatment of neonatal hyperbilirubinemia**.**

Phototherapy is being considered worldwide as first line treatment for neonatal Jaundice **[3].**

Regarding the adverse effects of phototherapy, certain studies have documented various adverse effects including insensible water loss, inability to maintain body temperature, electrolyte imbalance, skin rash, increased incidence of allergies as allergic rhinitis, bronchial asthma and retinopathy of prematurity **[4].** Phototherapy may affect the hematological system. Certain past and recent studies have documented thrombocytopenia as a side effect of phototherapy as well **[5].** Although many studies have documented thrombocytopenia as a result of phototherapy, but few studies have proven the opposite effect of phototherapy on platelet count i.e., phototherapy exposure results in increased platelet count **[5].**

Phototherapy possibly causes an increase in platelet production rate possibly secondary to reduction in platelet life span and when bone marrow compensation is inadequate the platelet count may fall **[6].** So, the ultimate effect of phototherapy on platelet count still needs to be investigated further in various clinical settings. There is no national study reporting the effect of exposure to phototherapy over platelet count.

This study aimed to detect the effect of phototherapy on platelet count in neonates with indirect hyperbilirubinemia by measuring platelet

count on admission and at discontinuation of phototherapy.

METHODS

This study was cross sectional study which was conducted at neonatal intensive care unit at pediatric department, benha children hospital on 54 neonates during the period of sex month from January 2018 to june 2018. Inclusion criteria: Full term neonates aged between 1 to 28 days old and having clinical symptoms and signs of neonatal indirect hyperbilirubinemia with normal platelet count. Exclusion criteria: Neonates with comorbidities like septicemia, renal failure, birth asphyxia, apnea and respiratory distress. Also neonates with abnormal platelet count detected prephototherapy, neonates need exchange transfusion and preterm neonates were excluded. All neonates in the study were subjected to full history taking with special emphasis on age, onset of jaundice and family history of jaundice. A blood sample was taken at admission before exposure to phototherapy and at discontinuation of phototherapy measuring the bilirubin and platelet count. Platelet count was measured by a cell counter (swilab). Thrombocytopenia is defined as a platelet count <150,000/μL and thrombocytosis is defined as platelet count > 500,000/ μL . Bilirubin level was measured by cobas 6000 (Roch, Germany). The American Academy of Pediatrics guidelines were used for deciding when to initiate phototherapy **[7].** Phototherapy was emitted by LED Phototherapy equipment that emits light through an array of high powered light emitting diodes (LEDs). These LEDs emit a narrow wavelength of blue light (dominant wavelength 458nm). It was placed at a distance of 30-40 cm. Duration of phototherapy exposure was recorded.

Ethical Declaration:

Written informed consent was obtained from all participants' parents, the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University. The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

STATISTICAL ANALYSIS

The collected data coded, entered and processed on computer using SPSS (Statistical package for social science) version 18. The results were represented in tabular and diagrammatic forms then interpreted. Data were statistically described in terms of mean, standard deviation, range and percentage when appropriate. The difference between two means was statistically analyzed using the Student t-test [Unpaired], paired t-test, Paired Wilicoxon test and Chi-square. Linear correlation coefficient (r) was calculated to test the association between two variables.

RESULT

This cross-sectional study included 54 newborn with indirect hyperbilirubinemia, of whom 28 (51.9%) were males and 26 (48.1%) were females . The newborns were full term neonates with post natal age between 1 and 8 days and mean±SD was 3.61 ± 1.96 days **(Table 1).** In This study the mean (± SD) platelet counts were 278.89 ± 60.63 before phototherapy and 319.67 ± 78.58 after phototherapy. Data analysis with paired T test showed significant difference between platelet count before and after phototherapy with platelet count after phototherapy more than before (P Value = 0.001) **(Table 2).** There were –ve significant correlation between percentage of change of platelets and age **(Table 3).** The study showed that mean platelet count significantly increased with extended mean phototherapy time **(Table 4).** In this study duration of phototherapy exposure range from 1 to 5 days with statistical significance difference between neonates had phototherapy for 1 to 2 days compared to neonates had phototherapy for 3 to 5 days in platelets count with marked increase in count among cases had 3 to 5 days phototherapy **(Table 5).**

Table (1): Demographic data of the studied cases

Variable	(n=54)	
Body weight: (gm) **Mean ± SD** **Range**	 2972.31 ± 256.97 2600 - 3800	
Gestational age: (week) **Mean ± SD** **Range**	 38.31 ± 0.58 38 - 40	
PNA: (D) **Mean ± SD** **Range**	 3.61 ± 1.96 1 – 8	
Variable	**N**	**%**

Variable	(n=54)	
Sex:		
Male	28	51.9
Female	26	48.1
Mode of delivery:		
NVD	19	35.2
CS	35	64.8
History:		
-ve	49	90.7
+ve	5	9.3
Consanguinity:		
-ve	50	92.6
+ve	4	7.4
Feeding:		
Breast feeding	41	75.9
Artificial feeding	13	24.1

SD: Standard deviation PNA: post natal age NVD: normal vaginal delivery
C/S: ceserian section N: number %: percentage

Table (2): Platelets count & bilirubin level pre and post phototherapy among the studied cases

Variable	*Pre (n=54)*	*Post (n=54)*	*Paired Test*	*P*	*Percentage of change*
Platelets: (x10^3/mm^3)			***t***		
Mean ± SD	*278.89 ± 60.63*	*319.67 ± 78.58*	***3.64***	***0.001***	*17.81%*
Range	*190 – 447*	*190 – 457*		**	
Total bilirubin: (mg/dl)			***t***		
Mean ± SD	*16.05 ± 2.46*	*10.21 ± 1.90*	***22.41***	***<0.001***	*-36.07%*
Range	*14 – 21*	*6 – 14*		**	
Direct bilirubin: (mg/dl)			***W***		
Mean ± SD	*0.65 ± 0.29*	*0.42 ± 0.14*	***5.78***	***<0.001***	*-25.76%*
Median (Range)	*0.60 (1 – 1.5)*	*0.4 (0.2 – 0.8)*		**	
Indirect bilirubin: (mg/dl)			***W***		
Mean ± SD	*15.40 ± 2.34*	*9.79 ± 1.86*	***22.12***	***<0.001***	*-36.10%*
Median (Range)	*13.7 – 20.20*	*5.5 – 13.4*		**	

Sd: Standard deviation Paired t: Paired t test Paired W: Paired Wilicoxon test p: p value
**:Highly significant (P<0.01) n: number mg: milligram dl: deciliter mm3: cubic millimeter

Table (3): Correlation between the percentage of change in platelets count and GA and PNA among the studied cases

Variable	% of Change in Platelets (*n*=54)	
	R	**P**
GA (week)	0.07	0.59 NS
PNA (D)	0.08	0.58 NS

r:Spearman correlation coefficient NS: Non significant (P>0.05)
PNA: post natal age GA: gestional age %: percentage

Table (4): Relation between change in platelets count and sex and duration of phototherapy among the studied cases

Variable	Decrease Platelet count (*n*=10)		No change in platelet count (n=5)		Increase in platelet count (n=39)		χ^2	P
	No	%	No	%	No	%		
Sex:								
Male	6	60	3	60	19	48.7	0.55	0.76
Female	4	40	2	40	20	51.3		NS
Duration of phototherapy:								
1 -2 day	10	100	4	80	4	10.3	**34.25**	**<0.001**
3 – 5 day	0	0	1	20	35	89.7		**

χ2:Chai square test NS: Non significant (P>0.05) **:Highly significant (P<0.01)

Table (5): Change in Platelets count pre and post phototherapy among the studied cases according to duration of phototherapy.

Variable	Duration of phototherapy		t	P
	1 – 2 days (*n*=18)	3 – 5 days (n=36)		
Platelets: (x10^3/mm^3) Pre				
Mean ± SD	303.22 ± 63.12	266.72 ± 56.35	2.06	0.06 NS
Range	200 – 447	190 – 370		
Platelets: (x10^3/mm^3) Post				
Mean ± SD	260.44 ± 58.48	349.28 ± 70.59	**4.60**	**<0.001**
Range	190 – 355	211 – 457		**
Paired t	**2.82**	**9.26**		
P	**0.01***	**<0.001****		

Sd: Standard deviation Paired t: Paired t test t: independent t test
NS: Non significant (P>0.05) *:Significant (P<0.05) **:Highly significant (P<0.01)

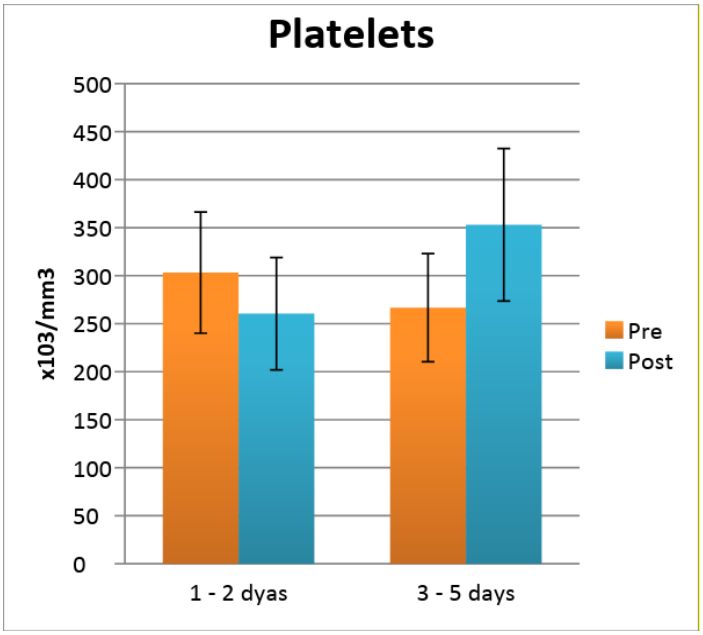

Figure (1): Platelets count among the studied cases pre and post phototherapy according to therapy duration.

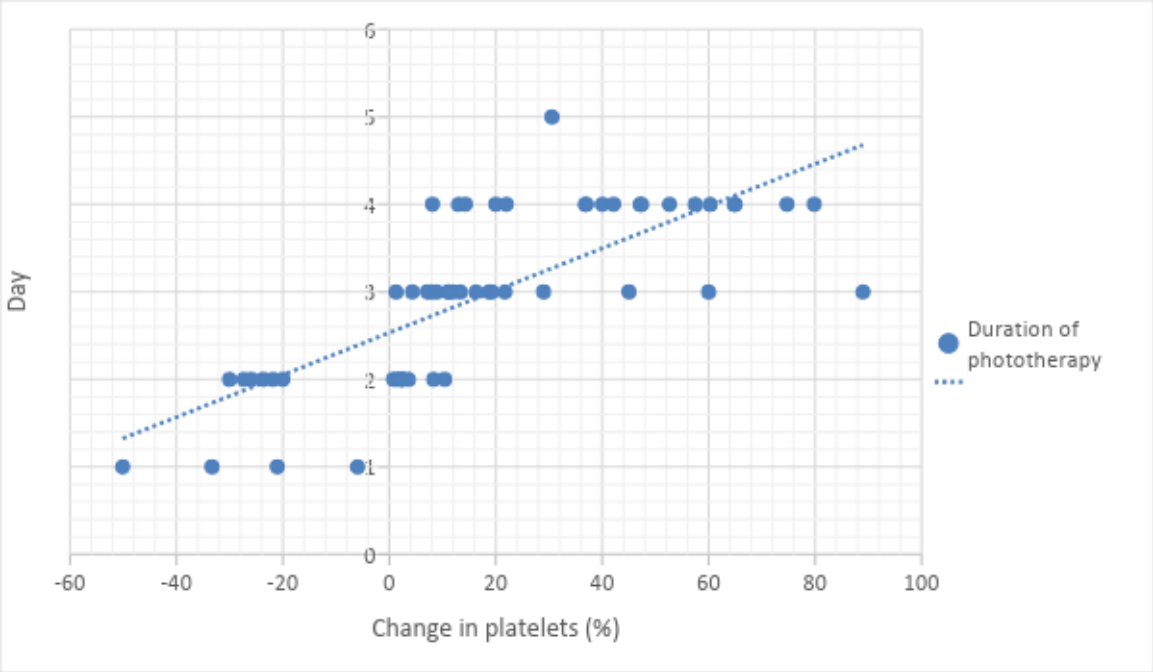

Figure (2): Correlation between the % of change in platelets count and duration of phototherapy among the studied cases.

DISCUSSION

Neonatal jaundice is a frequent cause of morbidity in newborns worldwide and the most frequent cause of hospitalization and readmission in the initial week of life **[8].**

For several years, phototherapy represented the most therapeutically efficient for clearance of bilirubin in icteric neonates. However, phototherapy may lead to complications including skin rash, diarrhea, rise in temperature, dehydration, trauma to eye. Although many studies have documented thrombocytopenia as a result of phototherapy, but few studies have proven the opposite effect of phototherapy on platelet count i.e., phototherapy exposure results in increased platelet count **[5].**

This work aimed to study the effect of phototherapy on platelet count in full term jaundiced neonates.

In this study, 54 full term jaundiced neonates received phototherapy from whom 51.9% were male and 48.1% were female.

The study showed a statistically significant decrease in Total & indirect serum bilirubin level after phototherapy (by 36.07% & 36.1% respectively). Also there were statistical significance increase in platelets count after phototherapy by (17.81%), (p value= 0.001). These data came in agreement with Monsef and Eghbalian who reported significant difference between platelet count before and after phototherapy. Mean platelet count after phototherapy was more than before (*P Value* = 0.015) **[9].**

In this study, the mean period of phototherapy among the studied cases was 2.96 days**.** In contrast to other studies mean period of phototherapy was 2.58 in Monsef and Eghbalian study. Regarding platelets count it increased in 72.2%, decreased in 18.5% and no change in 9.3% of the studied group after phototherapy exposure**.**

Monsef and Eghbalian reported that platelet count increased in 41.7 % and decreased in 58.3% of the studied group **[9].**

Ahmadpour et al in their study showed that there will be an increase in the platelet count after phototherapy which correlate with this study **[10].**

The study showed a difference in platelet count before and after phototherapy, but it was in the normal variety with no bleeding tendency nor hypercoagulability.

Similar to these findings, Monsef and Eghbalian found a meaningful difference in platelet count before and after phototherapy within the normal reference range and without any bleeding tendency nor hypercoagulability state in them **[9].**

In the contrary, Pishva et al stated that 49.5% thrombocytopenia in treated cases. They concluded increased platelet turnover and damage during phototherapy as the responsible mechanism **[11].**

Also, a study performed by Sanjeev et al reported that 35% of their study group had thrombocytopenia.

On the other hand, Venaktamurthy et al Showed a decrease in mean platelet count after phototherapy but was not statistically significant (p=0.150). However the decrease in mean platelet count was statistically significant in LBW babies (p<0.001)

[12]. The cause of thrombocytopenia had not clearly defined, probably destruction of platelet in cutaneous microvasculature exposed to phototherapy has a major role **[13].** It is concomitant with Maurer et al. knowledge. They had exposed plasma rich platelet to blue fluorescent light for 110 minutes and by electron microscope. They observed decrease in glycogen granules, platelet swelling and deformity **[14].**

However Karim et al in a study in 1981 presented that phototherapy not have any result on platelets **[15].** In this study, there were +ve significant correlation between percentage (%) of increase of platelets and duration of phototherapy among studied cases**.** The study showed no statistical significance difference between the studied cases in platelets count pre phototherapy but there were statistical significance difference between cases had phototherapy for 1 to 2 days compared to cases had phototherapy for 3 to 5 days with marked increase in count among cases had phototherapy for 3 to 5 days**.**

Regarding comparing pre treatment and post treatment in each there were statistical significance decrease in platelets count among cases had phototherapy for 1 – 2 days post treatment and there were highly statistical significance increase in platelets count in cases had 3 to 5 days post treatment**.**

Similar to these findings, Monsef and Eghbalian documented that associated result of phototherapy and hyperbilirubinemia increase the number of platelet and it has direct association with period of phototherapy. Increased platelet turnover and release of bone marrow appears to be concomitant mechanism for increasing platelet number **[9].**

Also In a study Sakha and Soltani**,** on full terms, well newborns that hospitalized for treatment of jaundice, presented rise of platelets during Phototherapy. According to their study increase platelet count related to phototherapy duration**.** this result possibly due to increases the release of platelets from bone marrow in full term healthy neonates with sufficient platelet storage in response to phototherapy **[16].**

In this study, 39 babies out of 54 neonates developed increase platelet count with –ve significant correlation between percentage of change of platelets and age.

An overview on previous study about effect of phototherapy on platelet count shows different results. It is not clearly defined the outcome of phototherapy on blood cells due to limitation of investigations and controversy about effect of lamp on platelet in vivo studies. Photochemical reaction in platelet of newborn had showed in vitro. Reduction in number of platelet may be due to sequestration of destructed platelet in the spleen **[9].** In 1966 prior to the using phototherapy for dealing with neonatal jaundice, Zieve and Solomen showed the result of white light on platelet of human in vitro. Platelets, which had been exposed to high-intensity, white lights loss the capability to aggregate and released potassium, acid phosphatase, serotonin and adenosine triphosphate **[17].** Photodynamic destruction on platelets had studied by TizziCiancarelli et al. via measuring LDH level. They exposed plasma rich with platelets to light and measured level of LDH after 2 hours. They found 20% rise of level of LDH and they explained that it is due to photodynamic side effect associated with hyperbilirubinemia on platelets **[18].**

The phototherapy causes an increase in platelet production rate possibly secondary to reduction in platelet life span and when bone marrow compensation is inadequate the platelet count may fall **[6]** This study state the hypothesis that phototherapy in full term icteric newborns leads to rise in platelet count may be due to accelerated platelet turnover in peripheral microvasculature with adequate platelet reserve in marrow.

The main limitations of this research are as follows: first, small sample size include only fullterm neonates, other studies in preterm and fullterm neonates may be needed. Second, number of blood samples might be not enough, several blood samples needed, at admission, after 48 hours and after cessation of phototherapy to more detection of the effect of phototherapy on platelet count.

CONCLUSION

Phototherapy increases platelet count in full term icteric neonates exposed to phototherapy for more than two days without any noticed side effects.

RECOMMENDATIONS

Based on our results and controversial studies, more future multi centric and case-control studies in preterm and full term newborns should be done to evaluate the effect of phototherapy on platelet count.

Conflict of interest: The authors declare no conflict of interest.

Financial Disclosures: Nil

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