



RESEARCH ARTICLE

PHOTOTHERAPY INDUCED THROMBOCYTOPENIA IN NEONATES WITH UNCONJUGATED
HYPERBILIRUBINEMIA - A PROSPECTIVE COHORT STUDY

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ABSTRACT

Phototherapy (PT) is one of the most common non invasive methods of treatment of choice for unconjugated hyperbilirubinemia in neonate. There are very few studies which show the effect of phototherapy on platelet count. So, this study done to show the effect of phototherapy on platelet count. This is a prospective hospital based cohort study on 100 eligible neonates admitted in the inborn section of Neonatal Intensive Care Unit (NICU) receiving phototherapy at Municipal General Hospital Mumbai, Maharashtra from June 2013 to May 2014. Serum bilirubin and CBC with Platelet count were performed before starting PT, 24 Hours (24 Hrs) after PT and 48 hours (48 Hrs) after PT or at discontinuation of PT. The results were analyzed statistically. A total of 100 neonates were included in our study of which 58 (58 %) were males and 48 (48%) were females. It was found that the Mean Platelet Count 24Hrs after Phototherapy was decreased as compared to the Mean Platelet Count before starting Phototherapy which was statistically significant (p = 0.008). Our study proves that Phototherapy in newborns with Indirect Hyperbilirubinemia leads to decrease in platelet count.

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INTRODUCTION

Hyperbilirubinemia is one of the most common sign encountered in newborns. In most cases it is a benign problem. Nevertheless, if left untreated, severe unconjugated hyperbilirubinemia is potentially neurotoxic and leads to permanent damage (Maisels, 2005). Premature newborns have a higher risk of jaundice than term neonates (Amarjeet et al., 2012). Neonatal jaundice was found to be the most common morbidity 65% among 137 extremely low birth weight babies born over a period of 7 years in AIIMS (Narayana et al., 2003). Hyperbilirubinemia can be treated with PT or by Exchange Trasfusion or by Pharmacologic agents like Phenobarbitone etc. Phototherapy has emerged as one of the most widely used treatment choice to reduce severity of neonatal unconjugated hyperbilirubinemia. It is simple and easily available treatment modality for effective management of hyperbilirubinemia. Phototherapy is generally very safe and may have no serious long-term effects on neonates; however, the following adverse effects have been noted: Increase insensible water loss, loose stools, retinal damage, hypocalcaemia, Patent Ductus Arteriosus (PDA) and skin rash.

The combination of hyperbilirubinemia and phototherapy can produce DNA- strand breakage and other effects on cellular genetic material. The effect of phototherapy on blood components is unknown. Some animal and human studies suggest that hyperbilirubinemia and phototherapy may lead to decreased platelet counts. Though Thrombocytopenia as a side effect of phototherapy has not been described many authors did try to look into this particular side effect. Due to limited studies with controversial results, the aim of this research was to find conventional phototherapy causing platelet count in neonates with indirect hyperbilirubinemia.

MATERIALS AND METHODS

This prospective descriptive longitudinal study was conducted in the inborn section of NICU in a tertiary care Municipal General Hospital of Mumbai, Maharashtra. The study group consisted of 100 consecutive neonates, both preterm and full term were included, born in the same Hospital from June 2013 to May 2014 i.e. total 12 months duration. Neonates readmitted for Hyperbilirubinemia were not included in the study. Similarly newborns born to mothers with Rh negative Blood Group were also not included irrespective of the baby's Blood Group. Neonates with comorbidities were excluded from study similarly neonates with platelet count less than 1,50,00 /mm³ were excluded from study. The study was approved by the

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Hospital Ethical Committee and the Scientific Committee. Written informed consent was obtained from the parents of all the neonates enrolled in the study. Predesigned proforma used to enroll neonates for the study. After delivery all the neonates were examined at least twice daily or whenever required as per standard protocol. As a Transcutaneous Bilirubin estimation was not possible only neonates appearing icteric on clinical examination were investigated. After these baseline investigations, Phototherapy (PT) was started based on Total Serum Bilirubin level. Indications of PT were as per guidelines of National Neonatology Forum 2010. Serum bilirubin and CBC with Platelet count was performed before starting PT, 24 Hrs after PT and 48 hrs after PT or at discontinuation of PT whichever was earlier. The platelet count before starting PT was considered as the control value for respective neonate. Every child was monitored for development of any hematological complications following PT. All the data was tabulated and analyzed using SPSS software (version 21) and compared with paired samples T test. P value of <0.05 was considered as significant.

RESULTS

Of the total 100 neonates enrolled in the study 58 (58%) were males and 42 (42%) were females. 38 (38%) were born Preterm and rest 62 (62%) was born Full Term. Among Preterm, 20 (52.63 %) were males and 18 (47.37 %) were females. Among Full term 38 (61.29 %) were male and 24 (61.29%) were female. 72 (72%) neonates were having weight < 2.5 kg of which 38 (52.77%) were preterm and 34 (47%) were full term. The mean age at which Hyperbilirubinemia was first detected was 63.63 (SD \pm 28.221) Hr of life. In Preterm neonates Hyperbilirubinemia was first detected at mean age of 65.55 Hr (SD \pm 26.156) of life. The same value for Full Terms was 62.45 (SD \pm 26.156) Hr of life. Mean Serum Bilirubin before starting Phototherapy in Preterm was 11.939 mg/dl (SD \pm 2.915). For Full Terms Phototherapy was started at mean Serum Bilirubin of 15.268 (SD \pm 2.4906 mg/dl. Mean duration of Phototherapy required for the entire study population was 65.72 Hr with Preterm requiring 74.84 Hr and Full term 60.06 Hr. 11 (28.95%) Preterm and 12 (19.35%) Full term neonates developed Thrombocytopenia i.e. Platelet Count <150000 /mm³ after 24 hrs of PT. 8 (21.05%) Preterm and 13 (20.97%) Full Term neonates had Thrombocytopenia 48 Hr after Phototherapy. Overall 23 (23%) patients had Thrombocytopenia 24 Hr after Phototherapy and 21 (21%) had it after 48 Hr of Phototherapy. The study population mean Pre PT Platelet Count was 241700 (SD \pm 67903.601). The Mean Platelet Count 24 Hr after Phototherapy was decreased by 17900 / mm³ as compared to the Mean Platelet Count before starting Phototherapy which was significant p value (p = 0.008). Also there was decrease in Mean Platelet Count 48 Hr after Phototherapy than Pre Phototherapy Mean Platelet Count (p = 0.265).

DISCUSSION

Out of 100 enrolled neonates 58 (58%) were males and 42 (42%) were females. This indicates that neonatal Hyperbilirubinemia is more common in males compared to females, which is a well-known fact also noted by Venaktamurthy *et al.* (2016) and Khera *et al.* (2011) in their study. Neonates with Birth weight between 1501 gm and 2000 gm had maximum number of cases 34 (34%) in our study which makes it the most vulnerable group to develop neonatal

Hyperbilirubinemia Table 1. Though Venaktamurthy *et al.* (2016) in their study found only 25 (25%) of neonates were weighing <2.5Kg and similarly Khera *et al.* (2011) had 28 (28%) only cases those weighing less than 2.5 Kg.

Table 1. Birth weight distribution (gm)

Birth Weight (gm)	Preterm	Full Term	Total
1000 – 1500	19	0	19
1501 – 2000	17	17	34
2001 – 2500	2	17	19
2501 – 3000	0	21	21
> 3000	0	7	7

Table 2. Hyperbilirubinemia detected at Hr of Life

	Preterm	Full Term	Total
N	38	62	100
Mean	65.55	62.45	63.63
Std. Deviation	26.156	29.562	28.221
Std. Error of Mean	4.243	3.754	2.822
Minimum	30	27	27
Maximum	120	160	160

Table 3. Pre Phototherapy Platelet Count (value / mm³)

	Preterm	Full Term	Total
N	38	62	100
Mean	223368.42	252935.48	241700.00
Std. Deviation	48455.285	75640.407	67903.601
Std. Error of Mean	7860.485	9606.341	6790.360
Minimum	160000	154000	154000
Maximum	337000	410000	410000

Table 4. Platelet Count after Phototherapy (value / mm³)

	Preterm	Full Term	Total
Platelet Count 24 Hr after Phototherapy			
< 50000	1	0	1
50001 – 100000	2	2	4
100001 – 150000	8	10	18
> 150000	27	50	77
Platelet Count 48 Hr after Phototherapy			
< 50000	0	0	0
50001 – 100000	2	2	4
100001 – 150000	6	11	17
> 150000	30	49	79

Hyperbilirubinemia was detected in preterm babies at mean age of 65.55 Hr (SD \pm 26.156) of life compared to term 62.45 (SD \pm 26.156) Hr of life baby in a study population. This indicated that Preterm neonates had slight delayed onset of Physiologic Hyperbilirubinemia as compared to the Full Term neonates. Preterm, as expected, required more. Hours of Phototherapy than Full Term neonates. The thrombocytopenia was seen in maximum number of cases during the first 24 hours of phototherapy. Similar findings were noted in study by Maurer *et al.* (1976) and Khera *et al.* (2011) in their studies. These majority of the neonates had Platelet Count between 100000 and 150000 (Mild thrombocytopenia). The Mean Platelet Count 24 Hr after Phototherapy was decreased by 17900 / mm³ as compared to the Mean Platelet Count before starting Phototherapy which was significant p value (p = 0.008). Also there was decrease in Mean Platelet Count 48 Hr after Phototherapy than Pre Phototherapy Mean Platelet Count (p = 0.265). Though there was slight increase in Mean Platelet Count between 24 Hr and 48 Hr of Phototherapy, this difference was statistically insignificant. All the patients were clinically stable and none of them developed any complications due to decreased Platelet Count.

Table 5. Paired Samples Test for All the Neonates enrolled in the study

	Paired Differences			T	Df	Significance
	Mean	Std. Deviation	Std. Error of Mean			
Pair 1 Pre PT Platelet Count - Platelet Count 24 Hr after PT	17900.00	66391.4775	6639.1477	2.696	99	0.008*
Pair 2 Pre PT Platelet Count - Platelet Count 48 Hr after PT	8480.00	75676.6753	7567.6675	1.121	99	0.265
Pair 3 Platelet Count 24 Hr after PT Platelet Count 48 Hr after PT	-9420.00	65133.3023	6513.3302	-1.446	99	0.151

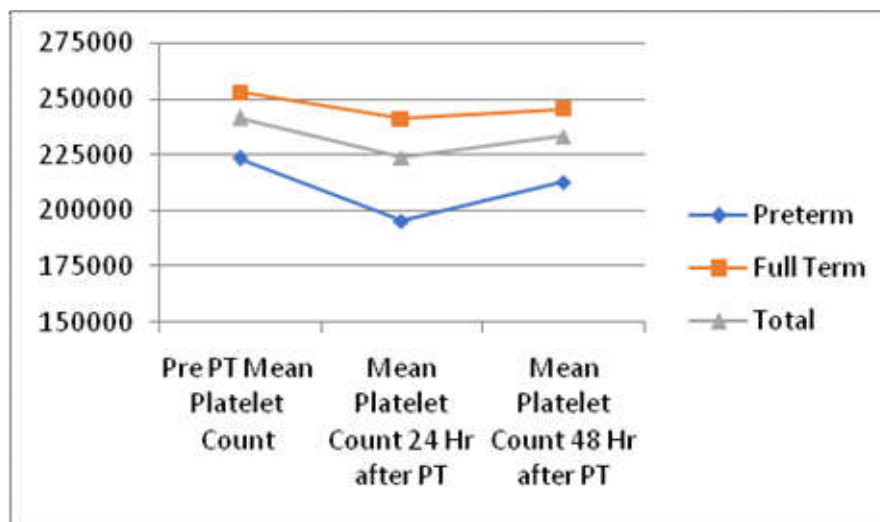


Figure 1. Comparison of Platelet Count during Phototherapy

Maurer *et al.* (1976) studied the effect of phototherapy on platelets in vitro. The results indicate that platelets are damaged in vitro when exposed to amounts of blue light used in phototherapy. But when Karim *et al.* (1981) studied the same using beta-thromboglobulin as the indicator of platelet damage. Their results suggest that the lower levels of irradiance used clinically are not harmful to platelets and that the results of studies done with three times as much irradiance have little clinical relevance. Photodynamic damage on platelets had studied by Tozzi-Ciancarelli *et al.* (1985) via measuring LDH level. They found 20% increase of LDH level and they explained that it is due to photodynamic side effect associated with hyperbilirubinemia on platelets. Khera *et al.* (2011) studied the effect of phototherapy on platelet counts and observed that 35% had thrombocytopenia and a majority of neonates had mild thrombocytopenia (74%). Thrombocytopenia was seen in 74% during the first 24 hours of phototherapy. This study was in correlation to our study. Pishva *et al.* (2000) in his study found that 49.5% babies had decreased levels of platelet count after phototherapy, where as in our study 23% babies had decreased platelet count post phototherapy. He also found out that in 19.8% babies the platelet count was below one lakh, but in our study there was only 4% babies with platelet count less than one lakh. Sakha K e t al, Modanlou *et al.*, Ahmadpour *et al.*, Alireza Monsef *et al* in their respective studies showed that there will be an increase in the platelet count after phototherapy which all were in contrast to our study which showed a decline in the platelet count after phototherapy (Sakha and Sultani, 2006; Modanlou *et al.*, 1997; Ahmadpour-kacho *et al.*, 2012; Monsef and Eghbalian, 2011).

The strengths of the study were that this was a consecutively enrolled prospective cohort study. The indication as well as the methodology was as per the standard guidelines. Well-defined exposure variable and inclusion criteria, adequate sample size, study of single outcome variable, i.e. thrombocytopenia, make this study a simple and powerful. Single centre study and inability to describe the causes of hyperbilirubinaemia in the neonates could be the weaknesses of the study.

Conclusion

Our study proves that Phototherapy in newborns with Indirect Hyperbilirubinemia leads to decrease in platelet count. Based on our results and controversial studies, platelet count measuring before and after phototherapy is suggested as a routine protocol.

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