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Original Research Article

Effect of phototherapy on platelet count in neonates with unconjugated hyperbilirubinemia

Akash Y. Malekar*, Nitin S. Mehkarkar, Vaibhav J. Pustake, Ashwini B. Kundalwal

Department of Pediatrics, SMBT IMS and RC, Igatpuri, Nashik, Maharashtra, India

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***Correspondence:**
Dr. Akash Y. Malekar,
E-mail: akash.malekar47@gmail.com

ABSTRACT

Background: Hyperbilirubinemia in newborn is quite common. Phototherapy (PT) is one of the most common noninvasive methods for the treatment of this hyperbilirubinemia. There are limited studies available on effect of PT on platelet count with contrasting results. So, this study was conducted to determine the effect of phototherapy on platelet counts of hyperbilirubinemic neonates in tertiary care hospital.
Methods: This was a hospital based prospective study on 60 eligible neonates admitted in neonatal intensive care unit (NICU) for neonatal hyperbilirubinemia and phototherapy during January 2021 to June 2022. Platelet count was done before starting phototherapy, 24 hours after phototherapy and before discontinuing phototherapy. The results were analyzed statistically using Chi square test and t-test. P value <0.05 was considered as statistically significant.
Results: In this study, total of 60 neonates were included of which 33 were males and 27 were females. The mean (±SD) platelet counts were 201764.92±18 before phototherapy and 156578.33±38 after phototherapy. There was a significant decline in the mean platelet count 24 hours after phototherapy and before stopping phototherapy. ($p<0.05$).
Conclusions: In our study, the mean platelet count was decreased significantly after phototherapy. Hence, unnecessary use and prolongation of phototherapy should be avoided.

Keywords: Hyperbilirubinemia, Phototherapy, Thrombocytopenia

INTRODUCTION

Hyperbilirubinemia in new born is quite common which affect about 60% of term and 80% of preterm neonates within first week of life.[1,2] It is benign in nature in most of the cases. If it is not treated, severe unconjugated hyperbilirubinemia could prove potentially neurotoxic and conjugated hyperbilirubinemia can lead to underlying serious illness. And hence appropriate management of neonatal hyperbilirubinemia is of paramount importance.[3]

Hyperbilirubinemia can be treated by phototherapy, exchange transfusion and pharmacologic agents like phenobarbitone, tin metaloporphyrines, and clofibarate.[3] Phototherapy is the most common modality of treatment for jaundice in neonates.[4] Like any treatment has its side effects, phototherapy also have its adverse effects such as hyperthermia, feed intolerance, loose stools, skin rashes, retinal changes, dehydration, hypocalcemia, redistribution of blood flow and genotoxicity.[5] Hematological system may also be affected by phototherapy. Thrombocytopenia (meaning decrease in platelet count) has been reported as an adverse effect of phototherapy as well, as described briefly in some isolated case reports after the phototherapy came in vogue in 1958.[6-8] Some animal and human studies reported that phototherapy in hyperbilirubinemia can lead to thrombocytopenia.[3] A very few studies are available in literature depicting the effect of phototherapy on platelet count and those available are with controversial results. Hence, we conducted this study to determine the effect of phototherapy on platelet counts of hyperbilirubinemic neonates in tertiary care set up.

METHODS

This was a hospital based, prospective study conducted over a period of January 2021 to June 2022 after obtaining approval from institutional ethics committee. A predesigned proforma has aided the enrolment of new-borns into the study.

Inclusion criteria

Neonates born between 32 completed weeks to 42 completed weeks admitted in NICU for neonatal hyperbilirubinemia and phototherapy with platelet count more than 150,000/mm3 during January 2021 to June 2022.

Exclusion criteria

The neonates with history of birth asphyxia, sepsis, congenital anomalies, neonates with existing thrombocytopenia were excluded from the study.

Sample size was calculated using formula given with expected proportion of 0.25 at 5% level of significance.[5]

$$N = \frac{(Z_{1-\frac{\alpha}{2}})^2\, p\,(1-p)}{d^2}$$

Venous blood samples were collected from the neonates and sent for total bilirubin, direct bilirubin, platelet count and blood group. Total and direct bilirubin was measured by diazo method (diazotized sulphanilic test). Platelet count was measured by auto analyser. Blood group of newborn analysed by antisera method.

Thrombocytopenia was defined as platelet count <150,000/mm^3. Mild, moderate and severe thrombocytopenia were defined as platelet counts between 100,000-150,000/mm^3; 50,000-100,000/mm^3 and <50,000/mm^3, respectively.[9]

Platelet count was checked at 0 hours, 24 hours and at discontinuation of phototherapy. The first sample was considered as control. Comparative study was done to determine the changes in platelet counts. Chi square test was used to analyse the significance of difference between frequency distribution of the data. P value <0.05 was considered as statistically significant. Statistical package for the social sciences (SPSS)© for windows™ Vs 17, IBM™ Corp NY and Microsoft excel™ 2007, Microsoft® Inc USA was used perform the statistical analysis.

RESULTS

A total of 60 neonates were included in our study. Incidence of thrombocytopenia was as depicted Figure 1. Severity of thrombocytopenia was as shown in Figure 2. Table 1 depicts demographic parameters, clinical characteristics and lab parameters in patients with and without thrombocytopenia. Table 2 shows platelet count before starting phototherapy, after 24 hours and after stopping phototherapy. Tables 3 and 4 depict association between platelet count and phototherapy.

There was no statistically significant association between the gender, birth weight, period of gestation, age of onset of jaundice, parity of mother, dose of phototherapy, Sr. bilirubin and thrombocytopenia. There was significant association between duration of phototherapy and thrombocytopenia.

Table 1: Demographics, clinical characteristics and lab parameters in patients with and without thrombocytopenia (N=60).

Parameter	Patients with thrombocytopenia (n=19)	Patients without thrombocytopenia (n=41)	Total (n=60)	P value
Sex				
Male	9	24	33	0.596
Female	10	17	27	
Birth weight (kg)				
<2.5	3	16	19	0.133
≥2.5	16	25	41	
Period of gestation (weeks)				
<37	3	13	16	0.325
≥37	16	28	44	
Age of onset of jaundice (days)				
2-3 s	7	15	22	0.994
4-5	10	22	32	
>6	2	4	6	
Parity of mother				
Primipara	9	10	19	0.138
Mutipara	10	31	41	
Dose of phototherapy				0.99

Continued.

Parameter	Patients with thrombocytopenia (n=19)	Patients without thrombocytopenia (n=41)	Total (n=60)	P value
Dspt	10	20	30	
Sspt	9	21	30	
Duration of phototherapy (hours)				0.001**
<48	10	0	10	
>48	9	41	50	
Sr. bilirubin (mg/dl)				0.613
≤18	15	36	51	
>18	4	5	9	

*P value considered significant difference at 95% CI (P<0.05), **p value considered significant difference at 99% CI (p<0.01)

Table 2: Descriptive statistics of platelet counts (N=60).

Descriptive statistics	N	Minimum	Maximum	Mean	Standard deviation
Platelet count before starting phototherapy	60	158000	234000	201764.92	17792.031
Platelet count (24 hours)	60	50000	224000	167583.33	38119.034
Platelet count before stopping photo therapy	60	40000	192000	156578.33	37872.427

Table 3: Association of platelet counts with phototherapy (N=60).

One-sample test	T	df	Sig. (2-tailed)	Mean difference	95% confidence interval of the difference	
					Lower	Upper
Platelet count before starting phototherapy	87.841	59	0.000	201764.917	197168.75	206361.09
Platelet count (24 hours)	34.054	59	0.000	167583.333	157736.14	177430.52
Platelet count before stopping photo therapy	32.025	59	0.000	156578.333	146794.85	166361.82

Table 4: Association of platelet counts before and after phototherapy (N=60).

Paired samples statistics	Mean	N	Std. deviation	Std. error mean	T value	P value
Platelet count before starting phototherapy	201764.92	60	17792.031	2296.941	13.62	0.001**
Platelet count before stopping photo therapy	156578.33	60	37872.427	4889.309		

*P value considered significant difference at 95% CI (P<0.05), **p value considered significant difference at 99% CI (p<0.01)

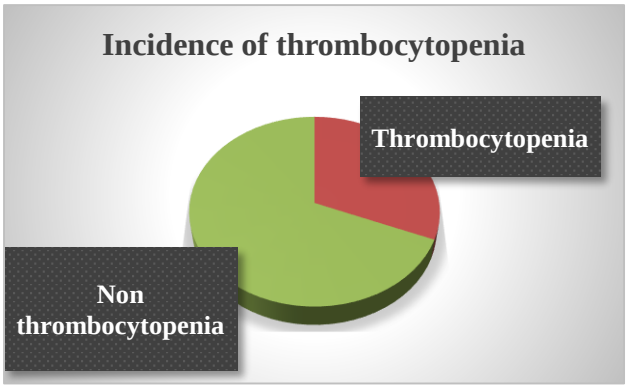

Figure 1: Incidence of thrombocytopenia.

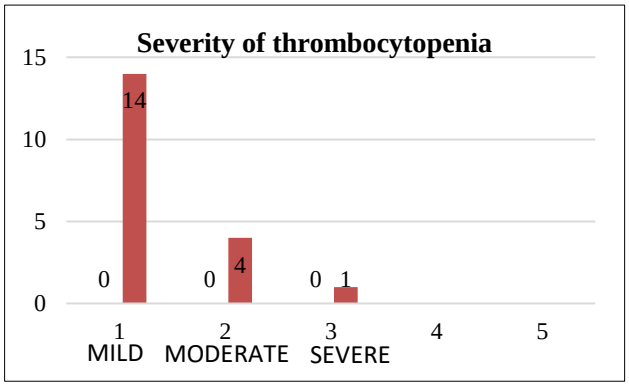

Figure 2: Severity of thrombocytopenia.

DISCUSSION

In our study, 60 neonates were included of which 33 were male and 27 were female. 19 (31%) neonates were with thrombocytopenia whereas 41 (69%) were without thrombocytopenia. 16 neonates were preterm and 44 were full term. The overall incidence of mild, moderate and severe thrombocytopenia was 14/19 (73.68%), 4/19 (21.05%), 1/19 (5.26%) patient respectively. Similarly, in a study by Shah et al, which also studied incidence of thrombocytopenia in neonates with uncomplicated indirect hyperbilirubinemia receiving phototherapy in a tertiary care hospital, it was reported that the overall incidence of post-phototherapy thrombocytopenia was 45.6% while mild, moderate and severe thrombocytopenia was present in 66%, 21.3% and 12.8% of babies respectively.[4] However, in a study by Venaktamurthy et al, incidence of thrombocytopenia was only 2% and was seen in 2 babies of which 1 was preterm and 1 was term.[5]

In this study, 30 patients were given double surface phototherapy (DSPT) and 30 patients were given single surface phototherapy (SSPT). 10 (33.33%) patients in DSPT group and 9 (30%) patients in SSPT group had thrombocytopenia. Khera et al and Pishva et al conducted similar studies and found a higher incidence of thrombocytopenia in babies who had received DSPT, but the results were not significant.[7,10] However, in a study by Shah et al, 30.7% patients in SSPT group had thrombocytopenia and 85.7% patients had thrombocytopenia in DSPT group which was far more than seen our study.

In our study, majority (52.63%) of cases showed thrombocytopenia within 48 hours of phototherapy and remaining cases (47.3%) cases after 48 hours of phototherapy. The incidence of phototherapy was more in neonates who received phototherapy within 5 days of life. Supporting our findings, according to Shah et al, the incidence of thrombocytopenia was significantly higher if the phototherapy was initiated within 72 hours of birth than beyond that.[4] This finding was in contrast to the studies; however, their results were not statistically significant.[8,11]

In the present study, thrombocytopenia was seen more with male sex, normal birth weight, term, higher age of onset of jaundice, multiparous mother, however, these associations were not statistically significant. This was in relation with findings by Khera et al and Pishva et al.[7,10]

In this study, the mean (±SD) platelet counts were 201764.92±18 before phototherapy and 156578.33±38 after phototherapy. In our study, there was statistically significant difference in platelet count before starting, 24 hours after and before stopping phototherapy. In consistency with our findings, Pishva et al in his study found that 49.5% babies had decreased levels of platelet count after phototherapy.[7] Harold et al who were first to study on the effect of phototherapy on platelet count in which they studied on low birth weight infants and found out that there is a fall in platelet count in 12 out of 31 babies receiving phototherapy.[12] Similarly, in a study by Sanjeev et al, it was found out that 35% of his study group had thrombocytopenia.[13] However, studies by Modanlou et al, Sakha K et al, Monsef et al, and Ahmadpour et al showed that there will be an increase in the platelet count after phototherapy which is in contrast to our study findings which showed a decline in the platelet count after phototherapy.[14-17]

The phototherapy causes increased platelet production probably secondary to reduction in platelet life span and when bone marrow compensation is inadequate the platelet count can fall. The in vitro data report that photochemical reactions occur in the platelet membrane. Whether these reactions occur in vivo is yet not determined. Short platelet life span may be due to the sequestration of damaged platelets in the spleen; however, definite proof is absent.[10]

The strengths of the study were that this was a prospective cohort study. The indication as well as the methodology of subjecting a neonate to phototherapy was as per the standard guidelines. Sample size was substantial with adequate power of study. Well-defined inclusion criteria, study of single outcome variable, i.e. thrombocytopenia which was again well-defined and doubly checked by automated counter. Single centre study, inability to quantify flux of phototherapy could be the weaknesses of the study.

CONCLUSION

This study reveals an association of phototherapy as a cause of thrombocytopenia in hyperbilirubinaemic neonates. Though the incidence of thrombocytopenia is substantial, it is clinically insignificant. In cases of thrombocytopenia in neonates, while using phototherapy, the practitioner should be vigilant about other causes of thrombocytopenia.

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