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Effect of Conventional Phototherapy on platelet count in full term and Preterm Neonates with Indirect Hyperbilirubinemia - A Prospective Cohort Study

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Abstract

Jaundice in newborn is quite common and in most of the cases benign in nature. Phototherapy (PT) is one of the most common noninvasive methods of treatment. There are few studies on effect of phototherapy on platelet count with contrsting results. So, this study was done to see the effects of conventional phototherapy on platelet counts. Study group consisted of 100 consecutive neonates with hyperbilirubiemia. Serum bilirubin and CBC with Platelet count was performed before starting PT, Twenty four hours (24Hrs) after PT and fourtyeight hours (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. All the data analyzed using SPSS software (version 21) and compared with paired samples T test. A Total of 100 neonates with indirect hyperbilirubinemia were enrolled in the study of which 58 (58 %) were males and 48 (48%) were females. For Preterm neonates mean Platelet Count was decreased 24 Hr after Phototherapy when compared with the Platelet Count before starting Phototherapy which was statistically significant (p = 0.018).When entire study population was studied as a whole, it was found that the Mean Platelet Count 24 Hr after Phototherapy was decreased as compared to the Mean Platelet Count before starting Phototherapy which was also statistically significant (p = 0.008).Our study proves that Phototherapy in newborns with Indirect Hyperbilirubinemia leads to decrease in platelet count .This fall in Platelet Count is more significant in Preterm neonates.

Keywords: *Phototherapy, Indirect Hyperbilirubinemia, Platelet Count.*

Introduction

Jaundice in newborn is quite common affecting nearly 60% of term and 80% of preterm neonates during first week of life.[1, 2] In most cases it is a benign in nature. Nevertheless untreated, severe unconjugated hyperbilirubinemia is potentially neurotoxic and conjugated hyperbilirubinemia is a harbinger of underlying serious illness. Increased

levels of unconjugated bilirubin can lead to bilirubin encephalopathy and subsequently kernicterus, with permanent neurodevelopment disability.

Although most newborns with jaundice are otherwise healthy, every baby who is jaundiced necessitates attention at the earliest to look for features of pathological jaundice because unconjugated bilirubin is potentially toxic to the central nervous system. And hence appropriate management of neonatal hyperbilirubinemia is of paramount importance.

Hyperbilirubinemia can be treated by PT or by Exchange transfusion or by Pharmacologic agents like Phenobarbitone, Tin Metaloporphyrines, Clofibarate, etc. PT has emerged as the most widely used form of treatment and is the current treatment of choice to reduce severity of neonatal unconjugated hyperbilirubinemia, regardless of its etiology. PT is simple and easily available therapeutic intervention for effective management of hyperbilirubinemia. With timely intervention in both term and preterm, severe complications of hyperbilirubinemia are prevented. Generally, phototherapy is safe however; the following adverse effects and complications have been noted: Increased insensible water loss, loose stools, retinal damage, hypocalcaemia, Patent Ductus Arteriosus (PDA) and skin rash. Some animal and human studies suggest that hyperbilirubinemia and phototherapy may lead to thrombocytopenia. Though Thrombocytopenia as a side effect of phototherapy has not been described in the standard textbooks many authors did try to look into this particular side effect with controversial outcome.

Due to limited studies with controversial results, our study aim is to find out effect of conventional phototherapy on platelet count in neonates with indirect hyperbilirubinemia.

Materials and Methods

This was a prospective descriptive longitudinal study done in Inborn section of NICU in a tertiary care Municipal General Hospital of Mumbai, Maharashtra. The study group consisted of 100 consecutive neonates with hyperbilirubinemia, both preterm and full term included, born in the same Hospital from June 2013 to May 2014 i.e. Total 12 months duration. Neonates with base line platelet count less than 1,50, 000 were not included in the study. Similarly neonates who readmitted for Hyperbilirubinemia were not included in the study. The inclusion criteria to enroll the patients for the study were apparently healthy neonates in the age group of 2days -28 days with Negative DCT (Direct Coomb's test) & CRP (C-Reactive Protein). Neonates with co-morbidities like ABO or Rh incompatibility, Direct hyperbilirubinemia, sepsis, Birth asphyxia, antiplatelet drugs given to baby or mother, congenital anomaly were excluded from study.

The study was approved by the Hospital Ethical Committee and the Scientific Committee. Written informed consent was obtained. Questionnaire method, Mother's ANC file and Newborn examination were used for obtaining the required data. Maternal variables like age, parity, ANC registration status, past medical and obstetrical history were obtained by history. The information on Gestational age, Maternal HIV, hbsag, VDRL status, blood group, ANC complications, ANC medications were collected from mother's ANC file.

As Transcutaneous Bilirubin estimation was not possible only neonates appearing icteric on clinical examination were investigated. After detailed history, clinical examination all icteric newborns were subjected to baseline investigations like Complete Blood Count (CBC) using automated cell counter with Peripheral smear, Serum Bilirubin, both Total and Indirect, CRP DCT, Baby's Blood Group.

After these baseline investigations, PT was started based on Total Serum Bilirubin level. Indications of PT were as per guidelines of National Neonatology Forum 2010.

Serum Bilirubin was repeated every 6 Hr till the Serum Bilirubin level falls to acceptable level

below Exchange Transfusion range. Feeding was continued throughout the period of Phototherapy.

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 were 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

A total of 100 neonates with indirect hyperbilirubinemia were enrolled in the study, of which 58 (58%) were male and 42 (42%) were female. 62 (62%) were Full term 38 (38%) were preterm. Among full term neonates 38(61.29%) were male and 24(38.71%) were female. In preterm 20 (52.63%) were male and 18(47.37%) were female.

Mean Pre PT Platelet Count among study population was 241700/mm^3 (SD ± 67903.601). Pre PT Platelet Count for Full Term and Pre Term neonates was 252935.48 / mm^3 (SD ±75640.407) & 223368.42 / mm^3 (SD± 48455.285) respectively. Lowest Platelet Count for Full Term neonates was 154000 / mm^3 and for Preterm neonates was 160000 / mm^3 (Table1).

Twenty-four Hour after PT mean Platelet count came 223800/mm^3 (SD± 95363.4197).Similar values for Full Term neonates 241096.77 (SD ± 100363.717) and Preterm were 195578.95 (SD ± 80044.795) .Lowest Platelet Count recorded after 24 hours of PT for Full Term was 95000 / mm^3 & for Preterm was 32000 / mm^3 without any complications. After forty eight Hours of PT the mean Platelet Count of entire study population was 233220 / mm^3 (SD± 98534.8813).The same values for Full term neonates were 245774.19 (SD ± 101682.634) and for Preterm were 212736.84 (SD± 90760.655) . Lowest Platelet Count for Preterm and Full Term were 56000 / mm^3 and 53000 / mm^3 respectively. All the neonates were clinically stable and none of the patients developed any hematologic complications. (Table 2)

Among study population 23 (23%) patients had Thrombocytopenia twenty four hours after Phototherapy and 21(21%) had after 48 Hr of Phototherapy. Total of 12(19.35%) Full Term & 11 (28.95%) Preterm developed thrombocytopenia after 24 Hr of Phototherapy i.e. Platelet Count <150000 / mm^3. 8 (21.05%) Preterm and 13 (20.97%) Full Term neonates had Thrombocytopenia 48 Hr after Phototherapy. Of these majority of the neonates had Platelet Count between 100000 and 150000.All were clinically stable. (Table3)

To evaluate the hypothesis that Phototherapy causes decrease in Platelet Count in neonates with indirect Hyperbilirubinemia, all the data was collected and tabulated. For statistical analysis SPSS software version 21 was used and following results were obtained by using paired t test. P value <0.05 was considered as significant. Preterm and Full Term neonates were evaluated separately. Three pairs were considered for analysis. In Pair1, Pre PT Platelet Count and Platelet Count 24 Hr after PT. In Pair 2, Pre PT Platelet Count and Platelet Count 48 Hr after PT or on stopping PT whichever is earlier. In Pair 3 Platelet Count 24 Hr after PT and Platelet Count 48 Hr after PT or on stopping PT whichever is earlier.

Preterm neonates showed that mean Platelet Count was decreased 24 Hr after Phototherapy when compared with the Platelet Count before starting Phototherapy. This decrease in Platelet Count was statistically significant also as indicated by p value (p = 0.018) .(Table 4) The mean Platelet Count 48 Hr after Phototherapy also decreased as compared to pre Phototherapy levels but this decrease was statistically not significant. When Platelet Count 48 Hr after Phototherapy was compared with that after 24 Hr of

Phototherapy, the Count was actually raised but again it was statistically insignificant.

On studying Full Term neonates we found that there was decrease in Platelet Count both after 24 Hr and after 48 Hr of Phototherapy when compared with the Pre Phototherapy Platelet Count. But this decrease was not found to be statistically significant. (Table 5)

Here also there was increase in Platelet Count noted when compared Platelet Count 48 Hr after Phototherapy with that after 24Hr of Phototherapy. But again it was also statistically not significant.

Finally when entire study population was studied as a whole, it was found that the Mean Platelet Count 24 Hr after Phototherapy was decreased by 17900 / mm^3 as compared to the Mean Platelet Count before starting Phototherapy. This decrease was statistically significant also as indicated by p value (p = 0.008) (Table 6).

Also there was decrease in Mean Platelet Count 48 Hr after Phototherapy than Pre Phototherapy Mean Platelet Count. But this decrease was not statistically significant (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.

Table1: Pre Phototherapy Platelet Count (value / mm^3):

	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 2: Platelet Count 24 Hr and 48Hr after Phototherapy (value / mm^3):

	Preterm	Full Term	Total
Platelet Count 24 Hr after Phototherapy			
N	38	62	100
Mean	195578.95	241096.77	223800.00
Std. Deviation	80044.795	100363.717	95363.4197
Std. Error of Mean	12984.980	12746.205	9536.3420
Minimum	32000	95000	32000
Maximum	422000	452000	452000
Platelet Count 48 Hr after Phototherapy			
	Preterm	Full Term	Total
N	38	62	100
Mean	212736.84	245774.19	233220.00
Std. Deviation	90760.655	101682.634	98534.8813
Std. Error of Mean	14723.322	12913.707	9853.4881
Minimum	56000	53000	53000
Maximum	503000	468000	503000

Table 3: Thrombocytopenia after Phototherapy (value / mm^3):

	Preterm	Full Term	Total
Platelet Count 24 Hr after Phototherapy			
< 50000	1	0	1
50001 – 100000	2	2	4
100001 – 150000	8	10	18
Total	11(28.95%)	12(19.35%)	23 (23%)
> 150000	27	50	77
Platelet Count 48 Hr after Phototherapy			
< 50000	0	0	0
50001 – 100000	2	2	4
100001 – 150000	6	11	17
Total	8 (21.05%)	13 (20.97%)	21(21%)
> 150000	30	49	79

Table 4: Paired Samples Test for Preterm Neonates:

	Paired Differences			T	Df	Significance
	Mean	Std. Deviation	Std. Error of Mean			
Pair 1 Pre PT Platelet Count - Platelet Count 24 Hr after PT	27789.474	69115.320	11211.985	2.479	37	0.018*
Pair 2 Pre PT Platelet Count - Platelet Count 48 Hr after PT	10631.579	89977.902	14596.343	0.728	37	0.471
Pair 3 Platelet Count 24 Hr after PT - Platelet Count 48 Hr after PT	-17157.895	72765.275	11804.086	-1.454	37	0.154

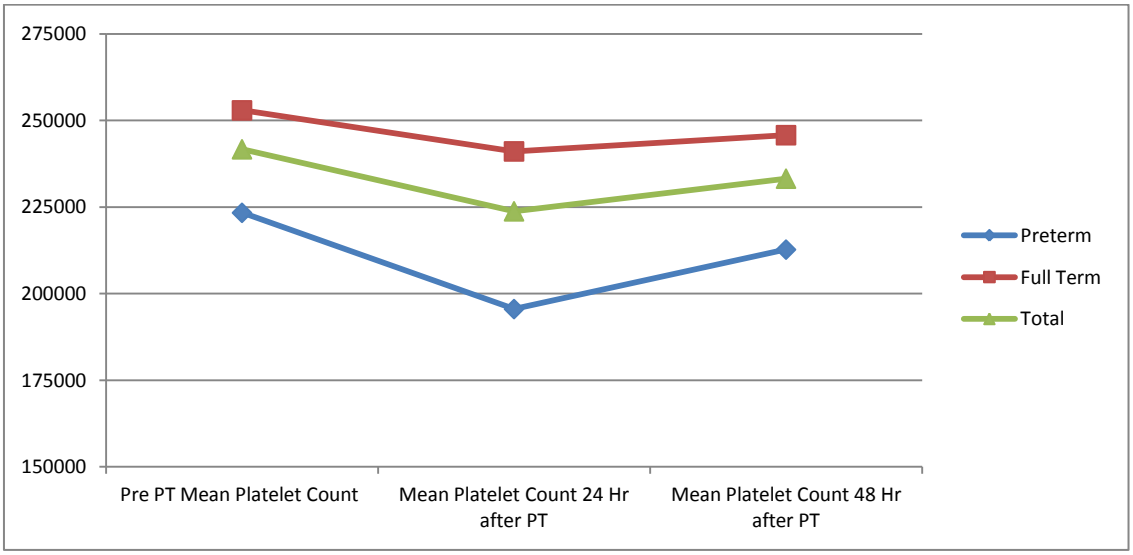
Table 5: Paired Samples Test for Full Term Neonates

	Paired Differences			T	Df	Significance
	Mean	Std. Deviation	Std. Error of Mean			
Pair 1 Pre PT Platelet Count - Platelet Count 24 Hr after PT	11838.710	64482.097	8189.234	1.446	61	0.153
Pair 2 Pre PT Platelet Count - Platelet Count 48 Hr after PT	7161.290	66175.671	8404.319	0.852	61	0.397
Pair 3 Platelet Count 24 Hr after PT - Platelet Count 48 Hr after PT	4677.419	60111.310	7634.144	-0.613	61	0.542

Table 6: 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



Discussion:

In our study population the platelet counts before phototherapy was 252935.48 / mm^3 (SD ± 75640.407) and 223368.42 / mm^3 (SD ±48455.285) in the term and preterm neonates respectively. Term had higher platelet counts as compared to pre-term babies which was similar to findings of Tawab et al.[3] However, similar facts were not observed by Maurer et al [4] and Khera S et al [5]. Among study population 23 (23%) patients had Thrombocytopenia 24Hrs after the Phototherapy and 21(21%) had after 48Hrs of Phototherapy. Total of 12(19.35%) Full Term & 11 (28.95%) Preterm developed thrombocytopenia after 24Hrs Hours of Phototherapy. In a similar study by Maurer et al [4] in low birth weight infants, the effect of 96 hours of continuous daylight phototherapy on platelets showed that 38.7% of babies had thrombocytopenia and Pishwa et al observed similar findings in 49% neonates.[6] 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.[4] and Sanjeev K et al [5]

In our study The Lowest Platelet Count recorded for Full Term was 95000 / mm^3 & for the Preterm was 32000 / mm^3 without any complications. None of the neonates with thrombocytopenia, in ours as well as the other two studies, had manifestations of bleeding. The reason for the same could be the fact that thrombocytopenia was transient and rarely found to be severe in all the three studies.

Preterm babies has more severe drop in platelet Count complaired to Full term babies. Similar facts were also observed by Venaktamurthy et al.,[7] decrease in mean platelet count was statistically significant in LBW babies.

Maurer et al.[4] found thrombocytopenia was seen more with male sex, normal birth weight, term, higher age of onset of jaundice, multiparous mother, and DSPT given for more than 48 hours; however, these associations were not statistically significant. Similar observations were seen by Pishwa et al[7] in their study. We have not included control group in our study since the neonate with platelet count < 150,000/mm3 were excluded from the study.

Thrombocytopenia as a definite side effect of phototherapy has not been mentioned and only described briefly as isolated case reports after the phototherapy came since 1958. In 1966, Solomon et al [8] demonstrated effects of high intensity white light on human platelet in vitro. Platelets which had been briefly exposed to light following photosensitization by hematoporphyrin lost the ability to aggregate and release potassium, acid phosphatase, serotonin and adenosine triphosphate. Electron photomicrographs of these altered platelets showed depletion of cytoplasmic materials and smooth membrane contours as compared to controls. Maurer et al [4] observed similar kinds of platelet abnormalities within 96 hours of exposure in vivo. Ultraviolet light may increase platelet turnover and injury during a PT by an unknown mechanism. PT light is transmitted through living tissue to a degree which may lead to photochemical reactions to occur in the vascular bed.[9] It causes decrease in blood riboflavin level and alters the excretory pattern of tryptophan metabolites, both of which are photosensitive.[10] The PT 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.[4]The in vitro data suggest that photochemical reactions occur in the platelet membrane. Whether these reactions occur in vivo remains to be determined. Shortened platelet life span may be the result of sequestration of damaged platelets in the spleen; however, definite proof is lacking.

Mondanlou et al, Ahmadapour et al, Monsef et al , Sakha K 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 platelet count after phototherapy.[11-14]

The strengths of our study were that this was a consecutively enrolled 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 also substantial and caters for adequate power of study. Well-defined exposure variable and inclusion criteria, study of single outcome variable, i.e. Thrombocytopenia which was again well-defined and doubly checked by automated counter, and experienced pathologists make this study a simple but effective one. Single centre study, inability to quantify flux of phototherapy, and inability to delineate the cause of hyperbilirubinaemia in the neonates studied could be the weaknesses of the study.

Conclusions

Phototherapy in newborns with Indirect Hyperbilirubinemia leads to decrease in platelet count both in term and preterm baby. Fall in Platelet Count after Phototherapy is transient. This fall in Platelet Count is more significant in Preterm neonates and after 24 Hrs of PT.

Conflict of Interest: None
Sources of support: None

Bibliography

1. Meharban Singh. Neonatal Jaundice. In: Care of the Newborn. 7th ed. New Delhi: Sagar Publications; 2010.p.254-74.
2. Namasivayam A, Carlo WA. Jaundice and Hyperbilirubinemia in the Newborn. In: Kliegman RM, Behrman RE, Stanton BF, Schor N, Geme JS, editors. Nelson text book of Pediatrics. 19 th ed. New Delhi: Saunders Elsevier; 2012.p 603–08.
3. Tawab CN, Saldanha PR, Mithun HK. Phototherapy induced thrombocytopenia-a comparative study among breastfed term and preterm neonates with hyperbilirubinemia. International Journal of Medical and Health Sciences. 2014;3(4):256-60.
4. Maurer HM, Fratkin M, mcwilliams NB, Kirkpatrick B, Draper D, Haggins JC, Hunter CR. Effects of phototherapy on platelet counts in low-birthweight infants and on platelet production and life span in rabbits. Pediatrics. 1976 Apr 1;57(4):506-12.
5. Khera S, Gupta R. Incidence of thrombocytopenia following phototherapy in hyperbilirubinemic neonates. Medical Journal Armed Forces India. 2011 Oct 1;67(4):329-32.
6. Pishva N, Pishva H. Incidence of thrombocytopenia in hyperbilirubinemic neonates during phototherapy. Acta Medica Iranica. 2000;38(1):7–9.
7. Venaktamurthy M, Balaji MD, Reddy K. A study on effect of phototherapy on platelet count in neonates with neonatal hyperbilirubinemia in a tertiary care rural hospital. International Journal of Contemporary Pediatrics. 2016 Dec 31;3(1):253-5.
8. Solomon HM, Zieve PD, Krevans JR. The effect of hematoporphyrin and light on human platelets. II. Uptake of hematoporphyrin. Journal of cellular physiology. 1966 Apr 1;67(2):281-4.
9. Sisson TR, Wickler M. Transmission of light through living tissue. Inpediatric Research 1973 Jan 1 (Vol. 7, No. 4, pp. 316-316). 351 WEST CAMDEN ST, BALTIMORE, MD 21201-2436: WILLIAMS & WILKINS.
10. Rubaltelli FF, Allegri G, Costa C, De Antoni A. Urinary excretion of tryptophan metabolites during phototherapy. The Journal of pediatrics. 1974 Dec 1;85(6):865-7.
11. Modanlou HD, Ortiz O, Wu PK. Lack of thrombocytopenia in newborn infants treated with phototherapy. Pediatric Research. 1977 Apr 1;11(4):538.
12. Ahmadpour-kacho M, Zahedpasha Y, Taghavi M, Bijani A. Effect of phototherapy on platelet, reticulocyte and white blood cells in full term neonates

with hyperbilirubinemia. Medical journal of mashhad university of medical sciences. 2012;55(4):211-7.

13. Monsef A, Eghbalian F. Does conventional phototherapy have any effect on platelet count in full term neonates with indirect hyperbilirubinemia?. Health. 2011 Dec 8;3(12):709.
14. Sakha K, Sultani H. Effect of phototherapy on platelet and white blood cell count in term infants. Med J of Tabriz University of Medical Sciences. 2006;28(3):14-8.
15. Sarin M, Dutta S, Narang A. Randomized controlled trial of compact fluorescent lamp versus standard phototherapy for the treatment of neonatal hyperbilirubinemia. Indian pediatrics. 2006 Jul 1;43(7):583.