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"STUDY OF HAEMATOLOGICAL PARAMETERS IN NEONATES RECEIVING PHOTOTHERAPY FOR NEONATAL HYPERBILIRUBINEMIA IN A TERTIARY CARE HOSPITAL"

Gokul Krishnan.R[1]*, Vaishnavi Alam[2], Nirmala.P[3], Penchalaiah.A[4], Anusha.K[5]

1.Associate professor / Neonatologist, Department of Paediatrics, Narayana Medical College, Chinthareddypalem, Nellore, Andhra Pradesh, India
2.Consultant Neurologist, Medicover Hospital, Nellore, Andhra Pradesh, India
3.Assistant professor, Department of Obstetrics & Gynaecology, Narayana Medical College, Chinthareddypalem, Nellore, Andhra Pradesh, India
4.Associate professor, Department of Orthopaedics, Narayana Medical College, Chinthareddypalem, Nellore, Andhra Pradesh, India
5.Department of Paediatrics, Narayana Medical College, Chinthareddypalem, Nellore, Andhra Pradesh, India

Corresponding author:- Gokul Krishnan.R, Phone :- + 91 - 9444935896, drgokulkrishnan86@gmail.com

ABSTRACT

Background: Neonatal hyperbilirubinemia nearly affects 60% of term and 80% of preterm neonates during first week of life. Phototherapy plays a significant role in prevention and treatment of neonatal hyperbilirubinemia. There are only a very few studies that depicts the side effects of phototherapy on haematological parameters with controversial results. Hence, the present study was undertaken to find out any significant changes in haematological parameters in neonates receiving phototherapy.

Methods: This study is a prospective comparative study conducted at Narayana Medical college and hospital, Nellore. The study was conducted during the period from December 2018 to April 2020.

Results: In our study group, the mean Haemoglobin before phototherapy was 17.05 ± 0.14 gm% and 17.17 ± 0.07gm% in preterm and term babies respectively. The mean Haemoglobin after phototherapy was 16.68 ± 0.16 gm% and 16.76 ± 0.05gm% in Preterm and term babies respectively. The mean PCV in our study before phototherapy was 50.98 ± 0.44% and 50.6 ± 0.7 in preterm and term babies respectively. The mean PCV after phototherapy was 50.0 ± 0.49% and 49.5 ± 0.66% in preterm and term babies respectively. The decline in the mean PCV was noted in both the groups. The mean Retic count before phototherapy was 3.01 ± 0.26% and 3.08 ± 0.15% in preterm and term babies. The mean Retic count after phototherapy was 2.74 ± 0.23% and 2.79 ± 0.12% in preterm and term babies. The decline in the mean PCV was noted in both the groups. The p value obtained was statistically significant (≤ 0.001).

Conclusion: Significant change in mean values were seen in Haemoglobin, PCV and Retic count after phototherapy in preterm, term, LBW and normal birth weight neonates were as there was no significant effect of phototherapy on total count, neutrophils, lymphocytes and platelet count.

Keywords: Neonatal Hyperbilirubinemia, Phototherapy, Haematological parameters.

INTRODUCTION

Neonatal hyperbilirubinemia (NH) is commonest finding during the first week of life. Over two third of neonates develop clinical jaundice. The physical finding like yellowish discoloration of the skin and sclera in newborns is due to accumulation of unconjugated bilirubin. In most infants, unconjugated hyperbilirubinemia reflects a normal physiological phenomenon.[1]

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 01, 2024

Neonatal hyperbilirubinemia nearly affects 60% of term and 80% of preterm neonates during first week of life. If untreated, severe unconjugated hyperbilirubinemia is potentially neurotoxic and conjugated hyperbilirubinemia is a clue to underlying serious illness.[2] NH is a reflection of liver immature excretory pathway for bilirubin and is the most common reason for readmission of neonates in first week of life in current era.[3] Neonatal hyperbilirubinemia is a cause of concern for the parents.[4]
Premature babies have much higher incidence of neonatal jaundice requiring therapeutic intervention than term neonates. Hyperbilirubinemia was found to be the most common morbidity 65% among 137 extremely low birth weight neonates born over a period of 7 years in AIIMS[5]. Elevated levels of unconjugated bilirubin can lead to bilirubin encephalopathy and subsequently kernicterus, with devastating, permanent neurodevelopment handicaps.[6]

Phototherapy plays a significant role in prevention and treatment of hyperbilirubinemia. The main demonstrated value of phototherapy is that it reduces the need for exchange transfusion. As any treatment has its side effects, phototherapy also have its adverse effects like hyperthermia, feed intolerance, loose stools, skin rashes, bronze baby syndrome, retinal changes, dehydration, hypocalcemia, redistribution of blood flow andgenotoxicity[4,5,7]
Unlike other side effects, a very few studies are currently available that depicts the side effects of phototherapy on haematological parameters with controversial results. Hence, the present study is undertaken to find out any significant changes in haematological parameters.

METHODS

Design of study

This study is a prospective comparative study conducted at Narayana Medical college and hospital, Nellore.

STUDY PERIOD
December 2018 to April 2020.

STUDY SETTING

The study was conducted in the Neonatal Intensive Care Unit, Department of paediatrics, Narayana Medical college and hospital, Nellore.

STUDY POPULATION

Neonates delivered at Narayana Medical College hospital satisfying the inclusion criteria.

INCLUSION CRITERIA
The Term and Preterm Neonates receiving phototherapy for unconjugated hyperbilirubinemia.

EXCLUSION CRITERIA
1)Neonates with Conjugated Hyperbilirubinemia.
2)Neonates with co-morbidities like Birth asphyxia, sepsis and renal failure.
3)Abnormal haematological parameters detected pre-phototherapy.

MATERIALS AND METHODS

Venous blood samples were collected from the neonates included in the study and sent for total bilirubin, direct bilirubin, Haematological parameters (Haemoglobin, Total count, differential count, Haemotocrit, Reticulocyte count, Platelet count) and blood group. Total and direct bilirubin is measured by Diazo method (Diazotized sulfanilic test). Principle - Bilirubin reacts with diazotized sulfanilic acid to produce azobilirubin which is quantified by spectrometry. Both direct and indirect bilirubin couple with diazo in the presence of cetremide. The terms direct and indirect are equivalent to conjugated and unconjugated fractions. Haematological parameters were measured by auto analyser (SisII). Blood group of newborn analyzed by antisera method.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 01, 2024

DATA ANALYSIS

Haematological parameters will be checked at 0 hours and at 48 hours of phototherapy or at discontinuation of phototherapy (second sample) whichever is earlier. The first sample will be considered as controls. Comparative study will be made between these groups to determine the changes in haematological parameters.

STATISTICAL METHODS

Proportions will be compared using chi-square test. All data of various groups will be tabulated and statistically analysed using suitable statistical tests (Student's t test). Both descriptive and inferential statistics were employed for data analysis. In the present study, descriptive statistics employed were frequencies & percentages. Inferential statistics employed were Chi-square test, Crosstabs (Cramer's V), Paired-Samples T Test

RESULTS

The study was conducted on 100 neonates admitted to NICU at Narayana Medical College and hospital for phototherapy. Performa was filled for each newborn. Data were analyzed using appropriate Statistical software like SAS 9.2 and SPSS 15.0.

TABLE 1: GENDER DISTRIBUTION OF NEONATES

Gender	NUMBER OF NEONATES (n)	PERCENTAGE (%)
MALE	55	55 %
FEMALE	45	45 %
TOTAL	100	100 %

In our study group, the incidence of males and females were 55% (55) and 45% (45) respectively. Male: Female ratio was 1.22:1

TABLE 2: WEIGHT DISTRIBUTION OF NEONATES

WEIGHT (Kg)	GENDER		TOTAL n (%)
	MALE	FEMALE	
Low Birth weight (<2.5 kg)	12(21.8%)	16(35.6%)	28(28%)
Normal	43(78.2%)	29(64.4%)	72(72%)
Total	55(100%)	45(100%)	100(100%)

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 01, 2024

Incidence of low birth weight babies was 28%. Mean birth weight was 2.83±0.3kg.

TABLE 3: GESTATIONAL AGE DISTRIBUTION OF NEONATES

GESTATIONAL AGE	GENDER		PERCENTAGE (%)
	MALE	FEMALE	
PRETERM (<37 weeks)	8(14.5%)	9(20%)	17(17%)
TERM (37 – 42 weeks)	47(85.5%)	36(80%)	83(83%)
TOTAL	55(100%)	45(100%)	100(100%)

In our study group, the incidence of preterm babies was 17% (17) compared to 83% (83) Term babies(37wks-42wks). The incidence of preterm male babies was 14.5% (8) vs preterm female 20% (9) in our study group. Mean gestational age in the study group was 38.49 ± 1.5 weeks.

TABLE 4: COMPARISON OF MEAN TOTAL BILIRUBIN AND HEMATOLOGICAL PARAMETERS BEFORE AND AFTER PHOTOTHERAPY WITH GESTATIONAL AGE

Variables	Before Phototherapy	After Phototherapy	Difference	t value	P value
Preterm GA< 37 weeks(n=17)					
Total Bilirubin (mg/dl)	16.73± 0.3	11.1941± 0.27	5.54	25.847	<0.001**
Haemoglobin (gm %)	17.05± 0.14	16.68/- 0.16	0.37	4.052	0.001**
Total Count (cells/cu.mm)	15826.4± 446.1	15676.4± 392.9	150.00	0.95	0.354
Platelets (Lakhs/cu.mm)	1.89± 0.04	1.78± 0.06	0.10	2.21	0.42
PCV (%)	50.98± 0.44	50.00± 0.49	0.988	3.32	0.04*
Retic count (%)	3.01± 0.26	2.74± 0.23	0.270	5.68	<0.001**
Term GA 37-42 weeks(n=83)					

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 01, 2024

Total Bilirubin (mg/dl)	17.46± 0.09	11.78± 0.13	5.67	51.71	<0.001**
Haemoglobin (gm %)	17.17± 0.07	16.76± 0.05	0.402	10.11	<0.001**
Total count (cells/cu.mm)	15394.66± 188.3	15298± 178.4	96.66	2.34	0.22
Platelets (Lakhs/cu.mm)	2.34± 0.37	1.83 ± 0.01	0.50	1.36	0.178
PCV (%)	50.60± 0.69	49.57 ± 0.66	1.02	7.76	<0.001**
Retic count (%)	3.08± 0.15	2.79± 0.12	0.28	6.59	<0.001**

In our study group, the mean Haemoglobin before phototherapy was 17.05 ± 0.14 gm% and 17.17 ± 0.07 gm% in preterm and term babies respectively. The mean Haemoglobin after phototherapy was 16.68 ± 0.16gm% and 16.76 ± 0.05 gm% in Preterm and term babies respectively. The decline in the mean Haemoglobin was noted in both the groups. The p value obtained was ≤0.001.

The mean PCV in our study before phototherapy was 50.98 ± 0.44 % and 50.6 ± 0.7 in preterm and term babies respectively. The mean PCV after phototherapy was 50.0 ± 0.49 % and 49.5 ± 0.66 % in preterm and term babies respectively. The decline in the mean PCV was noted in both the groups. However, the decline was found to be more statistically significant in Term babies ($p<0.001$) than in preterm babies ($p=0.04$).

The mean Retic count before phototherapy was 3.01 ± 0.26% and 3.08 ± 0.15% in preterm and term babies respectively. The mean Retic count after phototherapy was 2.74 ± 0.23 % and 2.79 ± 0.12% in preterm and term babies respectively. The decline in the mean PCV was noted in both the groups. The p value obtained was statistically significant (≤ 0.001).

The mean value changes in Total count and Platelet count was found to be non- significant ($p > 0.05$).

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 01, 2024

TABLE 5: COMPARISON OF MEAN SERUM TOTAL BILIRUBIN AND HEMATOLOGICAL PARAMETERS BEFORE AND AFTER PHOTOTHERAPY WITH BIRTH WEIGHT

Variables	Before Phototherapy	After Phototherapy	Difference	t value	P value
LBW(n=28)					
Total Bilirubin (mg/dl)	16.72± 0.18	11.12± 0.18	5.59	36.44	<0.001**
Haemoglobin (gm %)	17.15± 0.11	16.74± 0.11	0.40	6.55	<0.001**
Total Count (cells/cu.mm)	15766.0±357.4	15628.5±321.6	137.50	1.29	0.205
Platelets (Lakhs/cu.mm)	1.93± 0.03	1.79± 0.04	0.14	4.06	<0.001**
PCV (%)	51.3± 0.36	50.1± 0.33	1.12	4.96	<0.001**
Retic count (%)	2.96± 0.19	2.72± 0.17	0.23	6.60	<0.001**
Normal weight(n=72)					
Total Bilirubin (mg/dl)	17.59± 0.08	11.89± 0.13	5.70	49.3	<0.001**
Haemoglobin (gm %)	17.16± 0.07	16.77± 0.05	0.39	9.6	<0.001**
Total count (cells/cu.mm)	15345.83± 179.6	15260.0± 169.7	85.83	2.02	0.047
Platelets (Lakhs/cu.mm)	2.01± 0.38	1.9± 0.01	0.50	1.31	0.194
PCV (%)	50.55± 0.71	49.59± 0.69	0.96	7.49	<0.001**
Retic count (%)	3.12± 0.17	2.82± 0.13	0.29	6.25	<0.001**

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 01, 2024

In our study group, the mean serum Haemoglobin before phototherapy was 17.15 ± 0.11gm % and 17.16 ± 0.07gm % in low birth weight babies and normal weight respectively. The mean serum Haemoglobin after phototherapy was 16.74 ± 0.11 gm % and 16.77 ± 0.05 gm % in low birth weight babies and normal weight respectively. The decline in the mean serum Haemoglobin was noted in both the groups. By chi-square test, using test for paired sample means, the p value obtained was statistically significant (< 0.001).

The mean serum Platelet count before phototherapy was 1.93 ± 0.03 lakhs / cu mm and 2.01 ± 0.38 lakhs / cu mm in low birth weight babies and normal weight respectively. The mean serum Platelet count after phototherapy was1.79 ± 0.04 Lakhs / cu mm and 1.9 ± 0.01 lakhs / cu mm in low birth weight babies and normal weight respectively. The decline in mean platelet count was noted in both the groups. By chi- Square test using test for paired sample, the decline was found to be statistically significant in LBW babies (p<0.001) than in normal weight (p = 0.194) which was not statistically significant.

In our study group, the mean PCV before phototherapy was 51.3 ± 0.36 % and 50.5 ± 0.71 in low birth weight babies and normal weight respectively. The mean PCV after phototherapy was 50.1 ± 0.33 % and 49.5 ± 0.7 % in low birth weight babies and normal weight respectively. The decline in the mean PCV was noted in both the groups. By chi-square test, using test for paired sample means, the p value obtained was statistically significant (< 0.001).

The mean Retic count before phototherapy was 2.96 ± 0.19 % and 3.12 ± 0.17 % in low birth weight babies and normal weight respectively. The mean Retic count after phototherapy was 2.72 ± 0.17 % and 2.82 ± 0.13 % in low birth weight Babies and normal weight respectively. The decline in the mean Retic count was noted in both the groups. By chi-square test, using test for paired sample means, the p-value obtained was statistically significant (< 0.001).

The mean value changes in Total count was found to be non-significant (p > 0.05) in both the groups.

TABLE 6: COMPARISON OF MEAN SERUM TOTAL BILIRUBIN AND HEMATOLOGICAL PARAMETERS BEFORE AND AFTER PHOTOTHERAPY WITH GENDER.

Variables	Before Phototherapy	After Phototherapy	Difference	t value	P value
Male(n=55)					
Total Bilirubin (mg/dl)	17.4± 0.11	11.72± 0.14	5.68	49.6	<0.01**
Haemoglobin (gm %)	17.2±0.09	16.8±0.07	0.4	7.8	<0.01**
Total Count (cells/cu.mm)	15180.9+/202.5	15144.0+/223.5	36.9	0.71	0.476
Platelets (Lakhs/cu.mm)	2.45±0.51	1.83±0.51	0.61	1.2	<0.01**
PCV (%)	50.4±0.90	49.5±0.93	0.96	5.8	<0.01**

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 01, 2024

Retic count (%)	3.1±0.19	2.8±0.15	0.30	5.3	<0.01**
Female(n=45)					
Total Bilirubin (mg/dl)	17.26±0.14	11.6±0.19	5.65	36.5	<0.01**
Haemoglobin (gm %)	17.07±0.08	16.68±0.07	0.38	9.3	<0.01**
Total count (cells/cu.mm)	15808.8±232.4	15631.11±225.3	177.7	2.5	0.013
Platelets (Lakhs/cu.mm)	1.96±0.02	1.81±0.03	0.15	6.58	0.232
PCV (%)	51.09±0.26	50.03±0.24	1.06	7.13	<0.01**
Retic count (%)	2.95±0.18	2.70±0.15	0.24	6.49	<0.01**

TABLE 7: CONCLUSIVE COMPARATIVE EVALUATION OF STUDY VARIABLES PRE AND POST PHOTOTHERAPY IN NEONATES

	Pre	Post	difference	t value	P value
Total Bilirubin	17.34±0.9	11.67±0.11	5.67	60.7	<0.001**
Haemoglobin	17.16±0.06	16.76±0.05	0.4	11.7	<0.001**
PCV	50.76±0.52	49.77±0.51	1.00	9.02	<0.001**
Retic count	3.07±0.13	2.79±0.10	0.28	7.85	<0.001**
Total count	15463.500±163.6	15363±151.83	100.3	2.37	0.20
Neutrophils	55.22±0.33	55.08±0.32	0.14	0.661	0.510

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 01, 2024

Lymphocytes	40.76±0.34	41.24±0.31	-0.48	-1.92	0.057
Platelet count	2.23±0.28	1.82±0.01	0.40	1.451	0.150

Overall, there was significant decline in Haemoglobin, PCV and Retic count along with total bilirubin following phototherapy.

DISCUSSION

Neonatal Hyperbilirubinemia (NH) is the commonest problem during the first week of life. Early discharge of healthy term newborns from the hospital after delivery has recently become a common practice for medical, social and economic reasons. However, it has been shown that neonates whose post- delivery hospital stay < 72 hours are at a significantly greater risk for readmissions than those whose stay is >72 hours. NH is the most commonly reported cause for readmission during the early neonatal period. There is concern regarding early discharge of healthy term newborns due to reports of bilirubin induced brain damage resulting in sequelae like kernicterus.

The need for early detection of hyperbilirubinemia in the early discharged newborns is therefore important. It is crucial to catalogue the babies who are at risk for significant jaundice before they are discharged from hospital to prevent the potential bilirubin neurotoxicity. So that, many of the significantly jaundiced neonates could see the light of the day from the nightmare of bilirubin encephalopathy. Phototherapy has emerged as the most widely used form of treatment and is the current therapy of choice to reduce severity of neonatal unconjugated hyperbilirubinemia.

As any treatment has its side effects, phototherapy also has. Unlike other side effects a very few studies are currently available that depicts the adverse effects of phototherapy on haematological parameters. A few studies in the recent past, have stressed on the incidence of thrombocytopenia or increased platelet count following phototherapy and very few studies till date regarding the effect of phototherapy on all Haematological parameters.

Hence, our study was designed to determine the haematological changes in neonates receiving phototherapy for neonatal jaundice.

Mean total serum bilirubin (TSB) in our study group was 17.3 ± 2.5mg/dl before phototherapy and 11.6 ± 3 mg/dl after phototherapy. Mean total serum bilirubin (TSB) were 16.7 ± 12.7mg/dl and 17.8 ± 2.1 mg/dl in preterms and term neonates respectively before phototherapy. Mean duration of phototherapy in our study was 30.17 ± 10 hour.

In our study there was a decrease in mean platelet count before and after phototherapy but was not statistically significant (p=0.150). However, the decrease in mean platelet count was statistically significant in LBW babies ($p < 0.001$) when compared to normal birth weight babies ($p = 0.194$) and also in males ($p < 0.001$) when compared to females ($p = 0.232$) before and after phototherapy. Harold M et al (1976) where the first to study on the effect of phototherapy on platelet count where 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 whereas fall in platelet count was seen in only 3 out of 26 babies who were not receiving phototherapy. This study was in correlation with our study where there was a significant difference in mean platelet value in LBW babies ($p < 0.001$).[8] Sanjeev et al (2011) found out that 35% of his study group had thrombocytopenia and majority of neonates had mild thrombocytopenia (74%). This study was in correlation with our study which showed that majority (80%) had mild thrombocytopenia.[9]

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 01, 2024

In our study there was a decrease in mean Total count after phototherapy but was not statistically significant (p = 0.20). However, there was a decrease in mean Total count in babies born to primi parous mothers when compared to babies born to multi parous mothers which was statistically significant (p=0.001) but which was of no importance.

Ahmadpour et al (2013) found that there was no significant difference in change in neutrophils (p=0.112) and lymphocytes(p=0.178) after phototherapy and concluded that phototherapy has no significant effect on WBC. This study was in relation to our study which showed no significant change in Total count including neutrophil (p = 0.510) and lymphocytes (p = 0.057)[10]

Our study showed that there was significant effect of phototherapy on Retic count. There was a decrease in mean retic count after phototherapy which was statistically significant(p<0.001).Ahmadpour et al [10] (2013) in his study found that there was no significant effect of phototherapy on Retic count which was in contrast to our study which showed that phototherapy has a significant effect on retic count.

To conclude, in our study there is significant effect of phototherapy on Haematological parameters but this has to be evaluated with larger sample studies to know the exact relation between phototherapy and Haematological parameters. With respect to platelet counts our study showed an insignificant effect of phototherapy on platelet counts except in LBW babies. So, we should keep other causes of Thrombocytopenia in mind while treating these babies.

CONCLUSIONS

1)Effect of phototherapy was seen on Haemoglobin, PCV and Retic count where there was a significant change in mean values after phototherapy and was seen in preterm, term, LBW and normal birth weight neonates.

2)There was a decline in mean platelet counts after phototherapy which was seen in all groups but the decline in LBW neonates was significant when compared to normal birth weight babies.

3)There was no significant effect of phototherapy on total count, neutrophils, lymphocytes and platelet count.

RECOMMENDATIONS

1)The effect of phototherapy on haematological parameters have to be studied in detail on large study groups.

2)In case of thrombocytopenia during phototherapy we should keep other causes of thrombocytopenia in mind.

3)Monitoring of haematological parameters during phototherapy can be recommended but further studies should be done on large study groups.

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ISSN: 0975-3583,0976-2833 VOL15, ISSUE 01, 2024

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