

ORIGINAL RESEARCH ARTICLE

EFFECT OF PHOTOTHERAPY ON HEMATOLOGICAL PROFILE OF NEWBORNS WITH UNCONJUGATED HYPERBILIRUBINEMIA

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Received: 20 Jan, 2021

Accepted: 20 May, 2021

Published: 19 Jun, 2021

Key words: Hyperbilirubinemia; Newborns; Phototherapy.

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Citation

Timilsina M, Gauchan E, BK G. Effect of phototherapy on hematological profile of newborns with unconjugated hyperbilirubinemia. Journal of Chitwan Medical College. 2021;11(36):15-8.



Peer Reviewed

ABSTRACT

Background: Phototherapy despite being very safe is found to be associated with various untoward effects. The objective of this article was to study the changes in various hematological parameters as a result of phototherapy in neonates treated for unconjugated hyperbilirubinemia.

Methods: A cross sectional study was conducted in 120 neonates with unconjugated hyperbilirubinemia to determine the changes in the blood cell counts. We compared the complete blood counts at the time of admission and after 48 hours of phototherapy. The data was analyzed in SPSS 25 using paired t test.

Results: We observed that there was an increase in the lymphocyte counts from 5,650 cells/mm³ before phototherapy to 6,360 cells/mm³ after phototherapy with a p-value 0.028. MCH increased from 32.22 pg before phototherapy to 33.34 pg after phototherapy with a p-value of 0.018. The mean monocyte counts decreased from 730 cells/mm³ before phototherapy to 530 cells/mm³ after phototherapy with a p-value of 0.016. The mean platelet count also decreased from 241×10³ cells/mm³ to 258×10³ cells/mm³ with a p-value of 0.041 which was significant. Rest of the blood cell counts seem to be unaltered by phototherapy.

Conclusions: Phototherapy was found to be associated with significant decrease in the absolute monocyte count and platelet counts and caused an increase in the lymphocyte count and MCH. However, it does not cause significant changes in the total count and hemoglobin levels.

INTRODUCTION

Neonatal hyperbilirubinemia is the most common cause of hospitalization in newborns,¹ but only 0.7% of normal term neonates have serum bilirubin level >20mg/dl² with bilirubin encephalopathy and kernicterus as dreaded complications in a fraction of them.³

Phototherapy is the most commonly used therapeutic intervention currently available for treatment of neonatal hyperbilirubinemia. Hematological side effects of phototherapy include decrease in the leukocyte counts, anemia and thrombocytopenia.⁴

Phototherapy has negative impact on numerous parts of oxidant/antioxidant defense system in newborns and has been considered as an oxidative stress that causes damage to cellular DNA. Phototherapy also causes disturbances in the pro-oxidant/antioxidant balance (PAB) causing many symptoms and side effects.⁵ These lead to changes in the peripheral blood counts.

Phototherapy can affect the synthesis and release of cytokines, interleukins and TNF immune mediators from the immune

system of the skin.⁶ These changes in regulation of immune responses may alter the leukocyte count in neonates receiving phototherapy.

Phototherapy in the presence of hyperbilirubinemia increases the osmotic fragility of normal erythrocytes leading to varying degree of alteration in the hemoglobin and various RBC parameters.⁷ To the author's best knowledge, there is no local study in Nepal reporting the effects of phototherapy on blood counts. More studies regarding this issue would help clinicians better understand the side effects of phototherapy and guide them to use phototherapy more cautiously. The aim of this study was to investigate if phototherapy as a therapeutic measure in neonates with hyperbilirubinemia caused alteration in total and differential counts, hemoglobin, platelet count and erythrocyte counts.

METHODS

A cross sectional study was conducted in the NICU of Manipal Teaching Hospital, Pokhara from December 2019 to November 2020. Approval for the study was taken from the Ethics and Research Committee of Manipal Teaching Hospital, Pokhara.

Term neonates aged 2-7 days and preterm neonates aged 2-14 days with unconjugated hyperbilirubinemia admitted to the NICU were included in the study. Neonates beyond this age group were excluded. Also, those neonates with congenital malformations, sepsis, HIE, respiratory distress, hemolytic diseases, those requiring exchange transfusion and those delivered to mothers with systemic illness, diabetes, preeclampsia or on steroids or antiplatelet agents were excluded. Those who failed to give consent were also excluded from the study.

Informed consent was taken from the parents or the caregivers of the patients. After detailed history and clinical examination, initial investigations including the complete blood count, serum bilirubin levels and blood grouping of the baby and the mother. In those neonates requiring phototherapy repeat complete blood count and serum bilirubin levels were sent after 48 hrs. The bilirubin level at which to provide phototherapy was decided as according to Bhutani nomogram. The first 120 neonates who were admitted to our NICU for phototherapy during the study period and met the inclusion criteria were included in the study.

The observed data was analyzed using paired t test on SPSS 25. P-value of <0.05 was considered to be significant.

RESULTS

The mean age of the neonates at the time of admission was 5.93 days and mean gestational age was 37.65 weeks. Of the total neonates 25 (21%) were preterm and rest 95 (79%) were term neonates. The mean birth weight of the neonates was 2.94 kg. Of the total neonates, 41 (34.1%) neonates were de-

livered by vaginal delivery and rest 79 (65.8%) were delivered by caesarean section. The other demographic parameters are listed in Table 1.

Table 1: Demographic profile of the study population

Parameter	Value
Age of Newborn (days)	5.93 (2-13)
No of Males	64
No of Females	56
Mother's Age (years)	25.12 (18-32)
Gestational Age (weeks)	37.65 (31-40)
Weight (kgs)	2.94 (1.5-4.5)
Length (cms)	48.70 (42-51)

The mean total leukocyte count was 16,580 cells/mm³ before phototherapy and 16,860 cells/mm³ after phototherapy with a p-value of 0.718. So, phototherapy is not associated with significant changes in the total leukocyte counts. The mean total lymphocyte count was 5,650 cells/mm³ before phototherapy and 6,360 cells/mm³ after phototherapy with a p-value of 0.028. So, phototherapy was found to significantly increase the lymphocyte counts. The mean monocyte counts also significantly decreased from a pre-phototherapy value of 730 cells/mm³ to 530 cells/mm³ after phototherapy with a p-value of 0.016. The mean platelet count was decreased from 241×10³ cells/mm³ to 258×10³ cells/mm³ with a p-value of 0.041 which was significant. Also, the MCH increased from 32.22 pg before phototherapy to 33.34 pg after phototherapy with a p-value of 0.018 which is significant. Rest of the hematological changes were not statistically significant.

Table 2: Hematological profile of the patients before and after phototherapy

Parameter	Value before phototherapy	Value after phototherapy	p-value
TLC (×10 ³ /mm ³)	16.58 (58-36.11)	16.86 (9.1-25)	0.718
Neutrophil (×10 ³ /mm ³)	9.61 (2.56-25.26)	9.6 (3.65-16.72)	0.989
Lymphocytes (×10 ³ /mm ³)	5.65 (1.39-11.26)	6.36 (2.28-16.11.83)	0.028
Monocytes (×10 ³ /mm ³)	0.73 (0-1.51)	0.53 (0-1.15)	0.016
Eosinophils (×10 ³ /mm ³)	00.52 (0-1.13)	0.46 (0-0.96)	0.263
PCV (%)	43.13 (31.3-61.2)	43.03 (32-59)	0.712
MCV (fl)	92.6 (79-111)	91.99 (81.5-102)	0.597
Hb (gm/dl)	14.77 (10-20.3)	14.5 (10.5-19)	0.113
Platelets (×10 ³ /mm ³)	258.69 (132-584)	241.97 (140-485)	0.041
MCH (pg)	32.22 (25.3-38)	33.34 (29-37)	0.018

DISCUSSION

We conducted this study to observe the changes in various hematological parameters after therapeutic phototherapy for neonatal hyperbilirubinemia.

In our study the mean lymphocyte count increased from 5,650 cells/mm³ before phototherapy to 6,360 cells/mm³ after phototherapy. This finding was similar to that observed by Mrkaić et al. in Serbia in 1994. They observed the effects of

phototherapy on infants without signs of infection, anoxia or birth injury and observed an increase in total WBC along with lymphocytes.⁸ They attributed this increase in lymphocytes to complication of existing subclinical infections. In another study done in Turkey by Karabayir et al., CD4+ lymphocytes were found to increase after eight hours of phototherapy.⁹

Phototherapy can significantly increase the levels of cytokines, including TNF-alpha, IL-1 beta, and IL-8, but decrease the level of IL-6 in newborn infants.¹⁰ These changes in the interleukins

and cytokines may be responsible for changes in lymphocytes.

In our study, MCH increased from 32.22 pg before phototherapy to 33.34 pg after phototherapy. Standard and intensive phototherapy have been found to cause hemolysis and increase the mean corpuscular hemoglobin levels.¹¹ This is because with hemolysis, the lysed RBCs will not be counted to hematocrit but spectrophotometrically measured hemoglobin concentration will be unchanged. As a result, MCH will be increased.

The monocyte counts decreased from a pre-phototherapy value of 730 cells/mm³ to 530 cells/mm³ after phototherapy. Similar to our observation, Trend et al. found significant short-term increase in the frequency of monocytes in patients undergoing narrow band UVB phototherapy.¹²

We observed that the mean platelet count decreased from 241×10³ cells/mm³ before phototherapy to 258×10³ cells/mm³ after phototherapy. Similar to our finding Maj Sanjeev Khera et al. in 2011 found that 35% of the 100 neonates studied had thrombocytopenia after phototherapy.¹³ Similarly, Pishva N et al. observed that in 101 newborns, 50 (49.5%) had decreased levels of platelets and 20(19.8%) of them had a platelet count of below 1,00,000 and also the decreased platelet count was maximum during first 24 hours of phototherapy.¹⁴ In another study Sajid et al. found that Phototherapy caused thrombocytopenia in 8.1% cases after 24 hours, 18.4% cases after 48 hours and 33.3% cases after 72 hours.¹⁵

This decrease in the monocytes and platelets might be due to induction of apoptotic cell death and/or induction of immunosuppression¹⁶ or because of transient decrease in overall DNA, RNA and protein synthesis.¹⁷ Also bilirubin is an antioxidant and its reduced level with phototherapy may also have an effect on cellular level by shifting the oxidant-antioxidant balance towards oxidant damage.¹⁰

A study similar to ours done by Abdelhakeem et al. in Egypt found a significant rise in total WBC count at 36 hours and 72 hours after phototherapy was initiated, platelet count also decreased significantly at 36 and 72 hours while hemoglobin and RBC levels were not altered.¹⁸

Although we observed increase in the lymphocyte and MCH and decrease in the platelets and monocytes, none of the neonates required interruption of the phototherapy or any medical intervention to correct the change. So, the observed changes were not clinically significant.

Many other studies have found changes in the blood parameters

that are different from our findings.

While platelet count decreased and total leukocyte count was unchanged in our study, an increase in platelet and WBC count was observed by Sakha et al. in a 2006 study that included 150 healthy, full term icteric neonates admitted in Tabriz Children's Medical center, Tabriz, East Azarbaijan Province, Iran.¹⁹ Similarly Monsef et al. found mean platelet counts to be higher after phototherapy than that before in a study on 144 patients in Bessat hospital in Iran between September 2007 to February 2008.²⁰

While our study reported no changes in eosinophils and basophils, Altuntas et al. found that phototherapy was associated with a significant increase in eosinophils and basophils, significant decrease in leucocytes and neutrophil counts but no changes in monocyte and lymphocyte counts.²¹

This study has its own limitations. First limitation is a relatively small sample size. The other limitation is that we did not include a control group of healthy newborns who did not undergo phototherapy. Had it been done, we could have an idea about possible normal physiological changes in the various blood cell counts. Term and preterm neonates were not studied separately. Due to limited resources, further hematological parameters could not be included in the study limiting the scope of this study to only peripheral blood cell counts.

CONCLUSION

Our study shows that phototherapy causes significant changes in the hematological parameters. We found that there was a significant decline in the monocyte and platelet counts. The lymphocyte counts and mean corpuscular hemoglobin value was found to increase after phototherapy. At the same time there was no changes in the total leukocyte counts and hemoglobin level as a result of phototherapy. Despite these changes being observed, no therapeutic intervention was required to counter those effects and they were found to have no clinical significance. But further prospective clinical researches are required before concluding the findings of this study.

ACKNOWLEDGEMENT

We would like to thank Dr Aslam Ansari, NICU staffs and all patients for their cooperation during this study.

CONFLICT OF INTEREST: None

FINANCIAL DISCLOSURE: None

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