

Thrombocytopenia after Phototherapy for Indirect Hyperbilirubinemia among Breastfed Term and Preterm Neonates

Jayendra R. Gohil¹, Chirag D. Gilitwala², Sonal V. Jindal³

¹Professor ^{2,3}Resident, Department of Pediatrics, Govt. Medical College, Sir T G Hospital, Bhavnagar, Gujarat 364002, India.

Abstract

Objective: To compare the incidence of thrombocytopenia in breastfed term and preterm neonates with unconjugated hyperbilirubinemia receiving phototherapy. **Material and Methods:** A prospective study was done over a period of 5 months in NICU of a tertiary care hospital; 64 breastfed term and preterm (≥ 34 - < 37 week) neonates with unconjugated hyperbilirubinemia requiring phototherapy were selected for the study after applying inclusion and exclusion criteria. Serum bilirubin and platelet count were sent on admission, after 24 hours and 48 hours of phototherapy. Phototherapy was administered according to AAP criteria, using LED phototherapy (10 bulbs) positioned within 15 - 20 cm of the patient's body. It was interrupted only for feeding and nursing for around 20 minutes every two to three hours. Platelet count and total serum bilirubin levels, before and after 24 and 48 hours of phototherapy were estimated. **Results:** After 24 to 48 hours of phototherapy, neonates showed statistically significant decrease in the platelet count; term (2.38 to $2.07 \times 10^9/L$, $p = 0.0245$) and preterm (2.27 to $1.96 \times 10^9/L$, $p=0.0177$), along with expected decrease of serum bilirubin levels. There was no association in the incidence of thrombocytopenia between the gestational age (term vs preterm, $6/32$ vs $9/32$ babies, $p= 0.4741$). **Conclusion:** Thrombocytopenia does occur following phototherapy in neonates. However it is clinically insignificant and asymptomatic. Gestational age of the neonate is not a factor associated with the incidence of thrombocytopenia after phototherapy in neonates with unconjugated hyperbilirubinemia.

Keywords: Thrombocytopenia; Indirect Hyperbilirubinemia; Phototherapy; Neonates; Platelet Count.

Introduction

Jaundice is a common problem in the first week of life of a newborn. Approximately 85% of all term newborns and most premature infants develop clinical jaundice [1]. In most cases, it is physiological and benign. However, in some neonates severe jaundice may lead to kernicterus with implications for future development. Treatment in the form of phototherapy and/or exchange transfusion is recommended. Human albumin or intravenous immunoglobulin [2] or fenofibrate [3] is also tried. Phototherapy has emerged as the most widely used form for the treatment of unconjugated hyperbilirubinemia.

Though phototherapy is relatively safe, Maurer [4] and Pishva [5] observed that neonates exposed

to phototherapy suffer from thrombocytopenia. There is no consensus till now according to AAP (American Academy of Pediatrics) and NNF (National Neonatology Forum of India) guidelines, whether thrombocytopenia should be considered as a definite side effect of phototherapy or not. In 1966, Zieve [6] 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 [7] observed similar kind of platelet abnormalities within 96 hours of

Corresponding Author: Sonal V. Jindal, Resident, Department of Pediatrics, Govt. Medical College, Sir T G hospital, Bhavnagar, Gujarat 364002, India.

E-mail: sonaljindal92@yahoo.in

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exposure in rabbits. It caused decrease in blood riboflavin levels and altered the excretory pattern of tryptophan metabolites, both of which are photosensitive. In the same study, phototherapy was also found to cause an increase in platelet production rate possibly secondary to reduction in platelet life span, and when bone marrow compensation was inadequate the platelet count fell [7].

Aims and Objectives

To compare the incidence of thrombocytopenia in breastfed term and pre term neonates after phototherapy.

Materials and Method

A prospective study was done at an NICU of a tertiary care hospital during five months study period (March 2015 – Jul 2015); approved by IRB (Institutional Review Board)/ HEC (Human Ethics Committee). Unconjugated hyperbilirubinemia was defined as direct bilirubin less than 1.0 mg/

dl if total bilirubin is less than 5 mg/dl or less than 20% of the total bilirubin if the total bilirubin is greater than 5 mg/dl. Preterm birth was defined as delivery before 37 completed weeks of gestation and term birth after 37 completed weeks of gestation. Thrombocytopenia was defined as platelet count $<150 \times 10^9/L$. Mild, moderate and severe thrombocytopenia was defined as platelet counts between 100–150, 20–99 and $< 20 \times 10^9/L$, respectively [8]. 64 breastfed neonates; 32 term and 32 preterm, with unconjugated hyperbilirubinemia requiring phototherapy for at least 48 hours were included (Figure 1).

Neonates who had direct hyperbilirubinemia, inborn error of metabolism, neonatal septicemia, congenital anomalies, and anti-platelet drugs given to baby or mother were excluded. Also, neonates who developed features suggestive of sepsis during the course of phototherapy, severe hyperbilirubinemia requiring exchange transfusion or addition of any other modality of treatment besides phototherapy were excluded from the study.

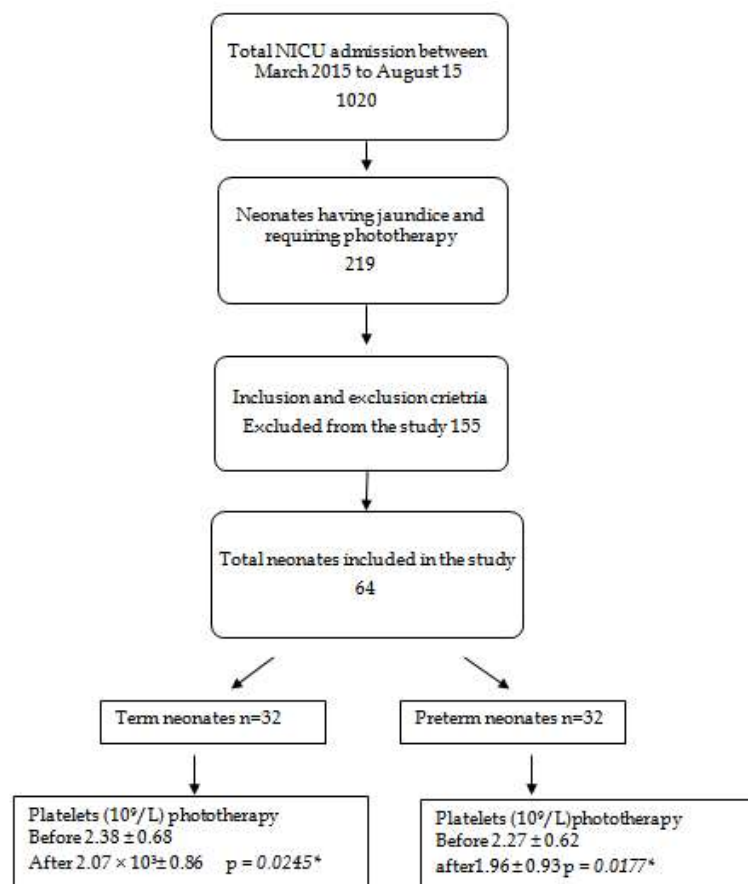


Fig. 1: Selection and outcome flow chart

*Chi square with Yates' correction

Informed written consent was obtained from parents or guardians. After history taking and clinical examination, baseline investigations like CBC, platelet count, serum bilirubin (total, direct, indirect), mother and baby blood grouping, direct and indirect Coomb’s test, C- reactive protein, G-6 PD and blood culture were sent on the day of admission. Serum bilirubin and platelet count were sent on admission, after 24 hours and 48 hours of phototherapy. Phototherapy was administered according to AAP criteria for treatment of neonatal hyperbilirubinemia [9]. All neonates received phototherapy using LED phototherapy (10 bulbs) positioned within 15 - 20 cm of the patient’s body. It was interrupted only for feeding and nursing for around 20 minutes every two to three hours.

Neonatal factors like sex, gestational age, birth weight, age at onset of jaundice and laboratory parameters like platelet count and level of serum bilirubin before starting phototherapy were compared between the two groups. Parameters like platelet count and incidence of thrombocytopenia after phototherapy were also recorded for both the groups.

Results

Thirty two (32) breastfed term neonates and 32 preterm neonates with unconjugated hyperbilirubinemia requiring phototherapy for at least 48 hours were selected for the study. There was no difference in sex and age at onset of jaundice in studied groups. The gestational age and birth weight were statistically different and comparable. There was significant difference in serum bilirubin level before starting phototherapy (Table 1).

Table 1: Neonatal parameters of study subjects at the start

	Term (32)	Preterm (32)	p value
Sex (M:F)	20:12	14:18	0.2104*
Gestational age (weeks)	38.2± 1	35.4± 1	<0.0001†
Birth weight (kg)	2.6±0.4	1.7±0.3	<0.0001†
Age at onset of jaundice	4.2±2.1	4.2±1.6	0.843†
Serum bilirubin (mg/dl)	19± 3.4	13.1±4.1	<0.0001*
Platelet count (x 109/L)	2.38± 0.68	2.26±0.62	0.468*

*Chi square with Yates’ correction, † Unpaired t test

After the phototherapy, both term and preterm neonates showed a statistically significant change in the platelet count as compared to pretreatment level (Table 2).

Table 2: Changes in platelet count before and after phototherapy

	Term (32) Platelets (x 109/L)	Preterm (32) Platelets (x 109/L)
Before phototherapy	2.38 ± 0.67	2.26 ±0.62
After phototherapy	2.07± 0.86	1.96±0.92
p value	0.025	0.018
Thrombocytopenia	6 (18.75%)*	3 (9.38%)*

*p= 0.474

There was no association between the gestational age (term/preterm) and the incidence of thrombocytopenia (p=0.4741, Fisher’s exact test).

Discussion

We studied 64 subjects, 32 breastfed term and 32 breastfed preterm neonates with unconjugated hyperbilirubinemia who were treated with phototherapy. Both the groups differed in gestational age and birth weight as per the study design. There was a significant difference in serum bilirubin level before starting phototherapy between the two groups as the cut-off value for starting phototherapy is lower in preterm babies. However, there was no significant difference in platelet counts before starting the treatment.

In our study, the incidence of thrombocytopenia after phototherapy was found to be 18.75% and 9.38% in term and preterm neonates respectively (Table 2), which is low as compared to previously reported incidence of 39.02% and 16.66% by Khera [10]. The term group had higher incidence of thrombocytopenia after phototherapy as compared to preterm neonates; however there was no statistical significance when compared for gestational age by Fisher’s exact test. Similar observations were seen by Khera [10] and Pishva [5] in their study. None of the neonates with thrombocytopenia, in our (9/64) as well as other studies had clinical manifestations of bleeding or other complications [5,10]. The reason for the same could be that thrombocytopenia was transient and rarely severe in all the three studies.

Limitations of our study were that, maternal parameters like pregnancy induced hypertension, and flux of phototherapy were not recorded.

Conclusion

After phototherapy, both term (p = 0.0245) and preterm (p=0.0177) neonates showed statistically significant decrease in the platelet count as compared to pretreatment levels. However, there was no association between the gestational age (term/

preterm) and the incidence of thrombocytopenia ($p=0.4741$). Although thrombocytopenia occurs following phototherapy in both term and preterm neonates, it is not life threatening, or causes any clinical signs or symptoms.

What is Already Known?

Transient thrombocytopenia can occur following phototherapy for unconjugated hyperbilirubinemia in breastfed term and preterm neonates and this decreased platelet count is not associated with bleeding manifestations.

What this Study Adds?

Gestational age of the neonate is not a factor associated with the incidence of thrombocytopenia following phototherapy.

Recommendation

When evaluating a healthy term or preterm neonate undergoing phototherapy, for thrombocytopenia (only); treatment modalities like antibiotics (considering sepsis), or platelet transfusion are not recommended- based on decreased platelet counts only; until and unless other indications are present.

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