

Does conventional phototherapy have any effect on platelet count in full term neonates with indirect hyperbilirubinemia?

Alireza Monsef¹, Fatemeh Eghbalian^{2*}

¹Pathology Department, Hamadan University of Medical Sciences, Hamadan, Iran; *Corresponding Author: eghbalian_fa@ahoo.com

²Pediatric Department, Hamadan University of Medical Sciences, Hamadan, Iran

Received 2 August 2011; revised 12 October 2011; accepted 22 October 2011.

ABSTRACT

This study evaluates the platelet count changes in neonates with hyperbillirubinemia who received phototherapy. In this Prospective Descriptive-cross sectional study 144 full term newborns with indirect hyperbillirubinemia who received phototherapy in neonatal ward of Bessat hospital in Hamedan province of Iran were studied from September 2007 to February 2008 for evaluation the effect of phototherapy on platelet count. The platelet had counted by cell counter and it had controlled by slide platelet counting. The data were analyzed using spss version. 13 and compared with paired-samples T test. 58 neonates (40.3%) were boys and 86 (59.7%) were girls. The mean age of neonates was 7.04 +/- 5.49 days (2 - 29 days). The mean (\pm SD) platelet counts were 287833.3 + 92332.4 before and 299444.4 + 98565.2 after phototherapy. Analysis of data with paired T test showed significant difference in platelet count before and after phototherapy. Mean platelet count after phototherapy was higher than that before treatment. The study had propounded that mean platelet count increased with extended mean phototherapy time. This study had propounded this hypothesis that phototherapy in full term icteric newborns leads to increased platelet count. It may be due to accelerated platelet turnover in peripheral microvasculature with adequate platelet reserve.

Keywords: Newborn, Phototherapy, Platelet Coun

1. INTRODUCTION

Phototherapy is the most widely used therapeutic modality in infants with neonatal jaundice. In nearly all

infants, phototherapy reduces or blunts the rise of serum bilirubin concentration regardless of maturity, presence or absence of hemolysis or degree of skin pigmentation [1-3]. Generally, phototherapy is very safe and may have no serious long-term effects on neonates; however, the following adverse effects and complications have been noted: increase insensible water loss, loose stools, retinal damage, hypocalcemia, patent ductus arteriosus (PDA) and skin rash. The combination of hyperbilirubinemia and phototherapy can produce DNA-strand breakage and other effects on cellular genetic material. In vitro and animal data have not demonstrated any indication for treatment of human neonates [1-4]. Other adverse effects and complications of phototherapy which have been noted in vitro included: Copper retention, abnormal porphyrine metabolism, diminished head growth without effect on neurologic function, decrease erythrocyte-oxygen coupling capacity, mild increase IgM and reduction of IgG [4-6]. The effect of phototherapy on blood elements is unknown. There are limited studies with different results regarding the effect of conventional count [6-9]. Some animal and human studies suggest that hyperbilirubinemia and phototherapy may lead to thrombocytopenia [10,13]. Maurer *et al.* found that rabbits exposed to phototherapy phototherapy on platelet had decreased platelet count [9]. Sakha *et al.* study suggests that hyperbilirubinemia and phototherapy may lead to increase the platelet count [7]. In another study Karim showed there is not any correlation between phototherapy and platelet cont [6]. According to limited studies with controversial results, the aim of this research was evaluating the hypothesis that conventional phototherapy is able to change platelet count in neonates with indirect hyperbilirubinemia.

2. SUBJECTS AND METHODS

In this Prospective Descriptive-cross sectional study 144 newborns with indirect hyperbillirubinemia who

received phototherapy in neonatal ward of Bessat hospital in Hamedan province of Iran were studied from September 2007 to February 2008 to evaluate the effect of phototherapy on their platelet count. The including criteria were: age 2 to 29 days, full term newborn weight 2500 to 4000 gr, indirect hyperbilirubinemia, absence of hemolysis, ABO or Rh incompatibility, negative coomb's test, reticulocyte count less than 5%, negative CRP (C reactive protein). The excluding criteria were; laboratory results of hemolysis, ABO or Rh incompatibility, platelet less than 150,000/mm³, exchange transfusion, fever and mild dehydration (less than six diaper per day) and ill newborns.

The sample size had calculated according to this formula and previous studies :

$$N = \left(Z_{1-\alpha} + Z_{1-\beta} \right)^2 \sigma^2 / (\mu_1 - \mu_2)^2 = 144$$

$$\alpha = 0.05 \quad \beta = 90\% \quad Z_{1-\alpha/2} = 1.96$$

$$p = 40\% \quad d = 0.085$$

Following case selection, the study was explained to patient's parents, and written parental consent was obtained according to ethical committee permission of Hamadan University of Medical Sciences. The platelet was counted by Sysmex K x-21 cell counter and controlled by platelet counting on peripheral blood smear slid. Phototherapy was performed by 5 newly changed white light lamp of Tusan company (Tehran-Iran), 30 centimeter away from the patients whose eyes and genitalia had been covered for protection. Before phototherapy and 24, 48 and 72 hr after it, blood collected and platelet had counted. Data such as birth weight, sex, the duration of phototherapy, and bilirubin level was included in the questionnaire list. The data were analyzed using SPSS (version 13) and compared with paired-samples T test. *P value* less than 0.05 was considered significant.

3. RESULTS

144 newborn infants with indirect hyperbilirubinemia were entered the study, from them 86 (59.7%) and 58 (40.3%) were females and males respectively. Mean age of studied newborns was 7.09 + 5.49 days, (range: 2 - 29 days, SD = 3.65). Mean Duration of hospitalization (day) was 2.63 + 1 - (1 - 7 day). Mean Duration of photother-

rapy was 2.58 + 1.08 - (1 - 7 day). The mean (\pm SD) platelet counts were 287833.3 + 92332.4 before and 299444.4 + 98565.2 after phototherapy. Data analysis with paired T test showed significant difference between platelet count before and after phototherapy. Mean platelet count after phototherapy was more than before (*P Value* = 0.015) (**Table 1**). The study showed that mean platelet count significantly increased with extended mean phototherapy time. As its *P value* after 2 - 3 days phototherapy was 0.001 and after 3 days of phototherapy was 0.002 (**Table 2**).

4. DISCUSSION

144 neonates were admitted in this study. Results had propounded this hypothesis that concomitant effect of phototherapy and hyperbilirubinemia increase the platelet count and it has direct correlation with duration of phototherapy. Mild dehydration and relative hemoconcentration had ruled out because an excluding criteria in our study was less than six diaper per day. Our result is similar with Sakha *et al.* report [7]. An overview on previous study about effect of phototherapy on platelet count shows different results [6-14]. It is not clearly defined the effect of phototherapy on blood cells because of limitation of investigations and controversy about effect of lamp on platelet *in vivo* studies. Photochemical reactions in platelet of newborn had proved *in vitro*. Decrease in platelet count may be due to sequestration of damaged platelet in the spleen [4,9,10]. In 1966 prior to the introduction of phototherapy for treatment of neonatal hyperbilirubinemia Zieve *et al.* described the effect of white light on human platelet *in vitro*. Platelets, which had been exposed to high-intensity, white lights loss the ability to aggregate and released potassium, acid phosphatase, serotonin and adenosine triphosphate [11]. Some authors point to mild thrombocytopenia due to photo-

Table 1. Mean platelet count before and after phototherapy.

Platelet count	Before phototherapy	After phototherapy	<i>P Value</i> *
Means \pm SD	287833.3 \pm 92332.4	299444.4 \pm 98565.2	<i>p</i> = 0.015 t = 2.45 df = 143 Significant

*Paired T test.

Table 2. Mean platelet count and its variation according to phototherapy duration, before & after.

Duration of phototherapy	Mean plt before phototherapy	Mean plt after phototherapy	plt variation	<i>P Value</i> *
1 - 2 day (N = 84)	289071.4 \pm 92407.2	288428.6 \pm 94251.4	↓642.8	<i>P</i> = 0.34
2 - 3 day (N = 36)	295777.8 \pm 98386.1	318277.8 \pm 107617.7	↑22500.0	<i>P</i> = 0.001
>3 day (N = 24)	271583.3 \pm 84142.1	309750.0 \pm 98040.9	↑0 38166.7	<i>P</i> = 0.002

*Paired T test; ↑: platelet increase; ↓: platelet decrease; Plt = platelet.

therapy and hyperbilirubinemia [4,10,12]. The cause of thrombocytopenia had not clearly defined, probably destruction of platelet in cutaneous microvasculature exposed to phototherapy has a major role [12]. It is concomitant with Maurer *et al.* experience. They had exposed plasma rich platelet to blue fluorescent light for 110 minutes and by electron microscope. They observed decrease in glycogen granules, platelet swelling and deformity [9]. In another research they had reported increased platelet turn over during low birth weight (LBW) neonate's phototherapy for 96-hour period. Regarding to low platelet reserve in LBW neonates bone marrow, the increased turn over results to thrombocytopenia [13]. However Karim *et al.* in a study in 1981 showed that phototherapy did not have any effect on platelets [6]. Photodynamic damage on platelets had studied by Tozzicancar *et al.* via measuring LDH level [14]. They exposed platelets rich plasma to visible light and measured LDH level after 2 hours. They found 20% increase of LDH level and they explained that it is due to photodynamic side effect associated with hyperbilirubinemia on platelets [14]. In a study Sakha *et al.* at 2007, on 150 full terms, healthy neonates that hospitalized for treatment of hyperbilirubinemia, showed increase of platelets and white blood cells (WBC) during Phototherapy. According to their study increase of WBC correlate with patient age and increase platelet count related to phototherapy duration [7]. In another study on 101 newborn, Pishva *et al.* showed 49.5% thrombocytopenia in treated patients. They concluded increased platelet turnover and damage during phototherapy as the responsible mechanism [8]. In our study the newborns were full term with adequate platelet reserve. Increased platelet turnover and release of bone marrow seems to be responsible mechanism for platelet count rise. Although we find a meaningful difference ($P = 0.015$) in platelet count before and after phototherapy, but it was in the normal reference range and we did not have any bleeding tendency nor hyper-coagulability state in them. It was not accessible for us to measure thrombopoietin in this study, so we propose it to other researchers. The limitations of this study was lack of high technology cell counter based on flowcy-tometry evaluation.

5. CONCLUSIONS

Present study state the hypothesis that phototherapy in full term icteric newborns leads to rise in platelet count. This may be due to accelerated platelet turnover in peripheral microvasculature with adequate platelet reserve in marrow. Based on our results and controversial studies, platelet count measuring before and after phototherapy is suggested as a routine protocol. Also more future multi centric and case-control studies in preterm and full term newborns should be done to evaluate this hypothesis.

6. ACKNOWLEDGEMENTS

The authors would like to acknowledge the office of Vice chancellor for research of Hamadan University of Medical Sciences for financial support of this study. Also we would like to thank Dr M. Fallah for his assistance in statistical analysis, Dr S. Shabani and staff of neonatal ward for their contribution and collaboration.

REFERENCES

- [1] Kleigman, R. and Jaundice, N. (2007) In: Behrman, R.E., Kliegman, R.M. and Jenson, H.B., Eds., *Nelson Textbook of Pediatrics*, 17th Edition, Saunders, Philadelphia, 753-766.
- [2] Wong, R., Gillen, H. and Sibley, D. (2006) Therapy for unconjugated hyperbilirubinemia. *Fanaroff & Martin's Neonatal Prenatal Medicine*, 8th Edition, Saunders, Philadelphia, 1419-1427 and 1440-1445.
- [3] Eghbalian, F. (2003) Phototherapy and hyperbilirubinemia. In: Eghbalian, F., Ed., *Neonatal Jaundice*, 1st Edition, Hamadan University of Medical Sciences, Hamadan, 33-50.
- [4] Maisels, J. and Watchko, J. (2000) Phototherapy in neonatal jaundice. 11th Edition, Harwood Academic Publishers, New York, 177-199.
- [5] Johnson, L., Brown, A. and Bhutani, V. (2002) System-based approach to management of neonatal jaundice and prevention of kernicterus. *Journal of Pediatrics*, **140**, 386-397. doi:10.1067/mpd.2002.123098
- [6] Karim, M., Clelland, I. and Chapman, I. (1981) Beta-thromboglobulin levels in plasma of jaundiced neonates exposed to phototherapy. *Journal of Perinatal Medicine*, **9**, 141-144. doi:10.1515/jpme.1981.9.3.141
- [7] Sakha, K. and Soltani, A. (2007) Effect of phototherapy on platelet and leukocyte count in hyperbilirubinemic neonates. *Journal of Tabriz University of Medical Science*, **28**, 59-62.
- [8] Pishva, N. and Pishva, H. (2000) Incidence of thrombocytopenia in hyperbilirubinemic neonates during phototherapy. *Acta Medica Iranica*, **38**, 7-9.
- [9] Maurer, H., Haggins, J. and Still, W. (1976) Platelet injury during phototherapy. *American Journal of Hematology*, **1**, 89-96. doi:10.1002/ajh.2830010110
- [10] Nathan, D. and Oski, F. (1998) Hematology of infancy and childhood. 15th Edition, Saunders, Philadelphia, 125-127.
- [11] Zieve, P. and Solomen, M. (1966) The effect of hematorporphyrin and light on human platelets. *Journal of Cellular Physiology*, **67**, 281-284.
- [12] Christensen, R. (2000) Hematologic problems of the neonates. 1st Edition, Saunders, Philadelphia, 296-310.
- [13] Maurer, H., Fratkin, M., McWilliams, N., *et al.* (1976) Effects of phototherapy on platelet count in low birth weight infants and on platelet production and life span in rabbits. *Pediatrics*, **57**, 506-512.
- [14] Tzziciancarelli, M., Amicosante, G. and Menichelli, A. (1985) Photodynamic damage induced by bilirubin on human platelets: Possible relevance to newborn pathology. *Biology of the Neonate*, **48**, 336-340. doi:10.1159/000242190