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Prognostic evaluation of newborns with neonatal hyperbilirubinemia

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ABSTRACT

Aims: We aimed to investigate the effect of phototherapy treatment by showing that it increases systemic inflammation and changes in NLR (neutrophil count/lymphocyte count), PLO (platelet count/lymphocyte count), systemic Inflammation Index (platelet count × neutrophil count/lymphocyte count ratio) in peripheral blood.

Methods: It was conducted at Balıkesir University Health Practice and Research Hospital between April 2023 and August 2023. 60 babies with a gestational age of ≥36 weeks and a birth weight of ≥2500 g were included in the study.

Results: A statistically significant difference was detected between WBC, lymphocyte count, monocyte count, neutrophil count, lymphocyte/monocyte, systemic inflammatory index before and after phototherapy ($p<0.05$).

Conclusion: We concluded that phototherapy is associated with the inflammatory process and may increase cytokine release. To investigate these effects of phototherapy, studies on larger populations are needed.

Keywords: Neonatal jaundice, systemic inflammatory index, phototherapy

INTRODUCTION

Neonatal hyperbilirubinemia effects at least 2/3 of newborn. Most of them are benign and resolve spontaneously. However, some need phototherapy.[1] Blue light of 430-480 nm size is used in the treatment of hyperbilirubinemia.[2] Phototherapy treatment has been shown to stimulate the release of cytokines and growth factors by acting on cell surface receptors. Recent studies suggest that phototherapy increases the release of cytokines and causes an inflammatory process.[3] The effectiveness of phototherapy increases as the body cell surface increases.[4] Exposure of cells to this light may cause DNA chain breaks and chromatid fractures.[5]

In terms of phototherapy, serum crystalline level is evaluated and determined according to the Bhutani curves determined by the American Academy of Pediatrics (APA).[6,7] Nowadays, LED devices for phototherapy have begun to be widely used and fewer side effects have begun to be observed. In a study, the difference between conventional phototherapy and LED phototherapy devices was examined, and it was found that LED phototherapy devices had less effect on eosinophils, albumin and uric acid.[8]

Phototherapy application provides protection against acute bilirubin encephalopathy and kernicterus and saves blood exchange.[9-11]

In our study, we aimed to determine the place of phototherapy in the inflammation process by calculating the change in NLR (neutrophil count/lymphocyte count), PLO (platelet count/lymphocyte count), systemic inflammation index (platelet count x neutrophil count/lymphocyte count ratio) in peripheral blood before/after phototherapy.

METHODS

The study was carried out with the permission of the Balıkesir University Non-invasive Clinical Researches Ethics Committee (Date: 23/08/2023 Decision no: 2023/116). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

The study was conducted at Balıkesir University Health Practice and Research Hospital between April 2023 and August 2023. Newborns with a gestational age of ≥36 weeks and a birth weight of ≥2500 g were included in the study. 60 newborns younger than the 15th postnatal day were included in the study. Phototherapy treatment was given to 30 newborns, and 30 newborns were healthy controls who had blood tests done for any reason and did not receive phototherapy treatment. The charts of the newborns who received phototherapy with the diagnosis

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of indirect hyperbilirubinemia were retrospectively analyzed. Newborns who had complete blood counts one hour before phototherapy starts and twenty-four hours after phototherapy ends were included in the study. Newborns whose gestational age was less than 36 weeks, who were diagnosed with sepsis, and who had congenital anomalies were excluded from the study. NLR (neutrophil count/lymphocyte count), PLO (platelet count/lymphocyte count), systemic inflammation index (platelet count × neutrophil count/lymphocyte count ratio) were calculated from the blood taken before phototherapy, and from the peripheral blood taken for control 24 hours after phototherapy was given. The neonates' birth week, delivery method, birth weight, maternal age, maternal education level, and bilirubin level were recorded.

Statistical Analysis

SPSS 23.0 package program was used for statistical analysis of the study. Descriptive statistics of continuous variables are shown with mean, standard deviation, median, minimum and maximum values, and categorical variables are shown with frequency and percentage. Suitability of continuous variables to normal distribution Shapiro It was examined with the Wilk test. One-way analysis of variance (ANOVA) was used for comparisons of normally distributed continuous variables between 3 or more groups. Mann Whitney U test was used for comparisons of variables that did not show normal distribution between 2 groups, and Kruskal Wallis test was used for comparisons of 3 or more groups. Pearson chi-square, Yates corrected chi-square and Fisher exact chi-square tests were used for group comparisons of categorical variables. In all statistical comparisons in the study, comparisons with a p value below 0.05 are considered statistically significant.

RESULTS

60 newborns were included in the study. The control group consisted of 30 newborns and was the group in which venous blood was taken for any reason without phototherapy. Phototherapy treatment was applied to the patient group of 30 newborns. Criteria for inclusion in the study were postnatal age of less than 15 days, gestational age between 36 and 42 weeks, and birth weight of 2500 g and above. The median birth weight of all babies included in the study was 3120±408 g. Median bilirubin levels were determined as 16±1.9 g/dl. Maternal ages ranged from 18 to 42 years. The weight loss of the newborns at application was between 5-8%.

Of the newborn receiving phototherapy, 12 had newborns ABO group incompatibility, 2 newborns had Rh incompatibility. There was no subgroup incompatibility. No cause was found in the others. 33 of them were born by cesarean section. 20% of the newborns' mothers were uneducated and 15% were university/college graduates. 30% of the newborns included in the study were admitted on the 3rd postnatal day. There was no statistically significant difference in terms of maternal age, education level and phototherapy treatment (p>0.05). Additionally, when the groups that received phototherapy and those that did not receive phototherapy were compared, no statistically significant difference was found between week of birth, method of delivery and day of admission (p>0.05).

WBC, hemoglobin, lymphocyte, monocyte, neutrophil, and platelet values in the peripheral blood of the newborns taken before/after phototherapy were recorded. Lymphocyte/monocyte count ratio, neutrophil/platelet count ratio, systemic inflammatory index (neutrophil × platelet count/lymphocyte count) values were calculated. A statistically significant difference was detected between WBC, lymphocyte count, monocyte count, neutrophil count, lymphocyte/monocyte, and systemic inflammatory index before and after phototherapy (p<0.05) (Table).

Table. Change and statistical analysis of peripheral blood values before/after phototherapy (p<0.05*)

Values	Before phototherapy	After phototherapy	p
WBC (×10⁹/L)	15106±2744	16625±2198	0.01*
Hemoglobin (g/dl)	16.7±1.3	16.9±1.1	0.1
Lymphocyte (×10⁹/L)	4514±1977	10580±5640	0.01*
Monocyte (×10⁹/L)	1159±490	1653±795	0.02*
Neutrophil (×10⁹/L)	8846±2472	9943±2044	0.0**
Platelet (×10⁹/L)	361033±58597	368500±56475	0.34
Lymphocyte/monocyte	4.27±2.15	3.10±1.60	0.01*
Neutrophil/lymphocyte	2.25±0.9	2.27±0.7	0.07
Neutrophil*platelet/ lymphocyte	848550±413427	917219±323494	0.02*

There was no significant difference in WBC, hemoglobin, lymphocyte, monocyte, neutrophil and platelet values after phototherapy compared to the control group. (p>0.05) (Table).

DISCUSSION

In our study, when the values before/after phototherapy were compared, a difference was detected especially between WBC, lymphocyte and monocyte levels, and these results are like the study by Kurt et al.[3] In the study conducted by Kurt et al.[3] an increase in WBC, lymphocyte, and monocyte was observed after phototherapy, but no statistically significant difference was detected with wbc. It has been said that the increase in WBC can be explained by the stress of newborns in

the first days. In a similar study, it was reported that phototherapy did not increase cytokine release but caused an increase in peripheral blood cells.[12]

In the study conducted by Yılmaz et al.[13] the effects of phototherapy on peripheral blood cells were examined, 30 term and 30 preterm babies who received phototherapy were taken, a significant decrease was detected in WBC, RBC, Hgb, MCV, RDW values in term babies after phototherapy, and a significant increase was detected in the MCHC and monocyte rate. It has been said that the change here can be attributed to ABO and Rh incompatibility. In our study, the monocyte percentage increased significantly after phototherapy. In a study conducted on babies with neonatal sepsis, the neutrophil/lymphocyte ratio was found to be significantly high, and it was suggested that it could be used as a marker of infection.[14]

In the study conducted by Khera et al.[15] it was found that platelet values decreased significantly after phototherapy. In this study, neonates with direct hyperbilirubinemia, whose mothers used anti-platelet medication, and who had sepsis were excluded from the study. Platelet values of these babies were measured 24 hours after phototherapy. Low platelet count was observed in 74% of the patients included in the study. The occurrence of thrombocytopenia did not vary depending on gender and gestational age. Thrombocytopenia has been attributed to the acceleration of platelet turnover due to ultraviolet light damage. A similar result was found in another study.[16]

A significant difference was observed between the neutrophil*platelet/lymphocyte ratio, calculated as the systemic inflammation index, before and after phototherapy.[17] We think that this marker, which is mostly used as a prognostic indicator in inflammatory diseases, is due to the relationship of phototherapy with the inflammatory process. In a study conducted on patients with Ulcerative Colitis, a significant relationship was found between the systemic inflammation index and disease progression.[18] In the study conducted by Ercan et al.[19] it was shown that the systemic inflammation index is effective in determining mortality in dialysis patients. The neutrophil/lymphocyte ratio was used to predict the prognosis of acute cholecystitis patients and was found to be compatible with the severity of cholecystitis. Additionally, it may differ depending on the shock index and serum lactate level measured in multitrauma patients.[20,21]

When the immunomodulatory and immunotoxic effects of phototherapy were examined, it was shown that especially the number of CD4 lymphocytes increased after phototherapy.

CONCLUSION

We concluded that phototherapy, which is an effective treatment method that is frequently used today and prevents kernicterus from bilirubin toxicity, may be associated with the inflammatory process. More studies are needed on a larger population to investigate these effects of phototherapy. Shock index in future trauma patients.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of the Balıkesir University Non-invasive Clinical Researches Ethics Committee (Date: 23/08/2023 Decision no: 2023/116).

Informed Consent: Because the study was designed retrospectively, no written informed consent forms were obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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