PERINATAL JOURNAL

Original Article

Perinatal Journal 2026; 34(2):640-649

https://doi.org/10.57239/prn.26.03420063

Phototherapy and neonatal ductal physiology: A reanalysis of a historical cohort with contemporary clinical implications

Ayhan Ceri, MD*

Department of Neonatology, Dr. Ali Kemal Belviranlı Maternity and Children's Hospital, Konya, Türkiye

Abstract

The systemic vascular effects of phototherapy remain incompletely understood, with conflicting evidence regarding its influence on Ductus Arteriosus (DA) closure. We aimed to evaluate the association between phototherapy and DA patency in term and preterm neonates using a reanalyzed historical cohort. In this retrospective cohort study, 229 neonates hospitalized between November 1994 and August 1995 were included. Infants were classified into phototherapy (n=111) and control (n=118) groups. Echocardiographic assessments were performed using blinded two-dimensional and color Doppler imaging. The primary outcome was persistent DA patency. DA patency was identified in 12 infants (5.2%). The incidence was higher in preterm compared to term neonates (8.1% vs. 3.9%). Phototherapy exposure was not significantly associated with increased DA patency (odds ratio [OR]: 0.75; 95% confidence interval [CI]: 0.23–2.43; p=0.628). The relatively small number of events and wide confidence intervals suggest limited statistical power to detect modest effects. The historical nature of the cohort, predating modern LED phototherapy and early pharmacologic ductal interventions, allowed evaluation in a relatively low-confounding physiological setting. Phototherapy was not associated with a statistically significant change in DA patency in this cohort. However, given the biological plausibility of light-induced vascular effects and the uncertainty reflected in wide confidence intervals, a clinically relevant effect cannot be excluded, particularly in preterm infants. These findings highlight the need for adequately powered prospective studies incorporating modern phototherapy technologies and biochemical markers.

Keywords: Phototherapy, Ductus arteriosus, Newborn, Premature Infant, Hemodynamics

1.Introduction

Neonatal jaundice remains the most common cause of readmission in term neonates, primarily due to the accumulation of unconjugated bilirubin [1,2]. More than 60% of term and 80% of preterm infants develop visible jaundice during the first week of life. Although usually benign, excessive bilirubin levels may lead to acute bilirubin encephalopathy or kernicterus if untreated. Phototherapy is the cornerstone of treatment and has significantly reduced the need for exchange transfusion and the long-term consequences of bilirubin-induced neurotoxicity [1,3].

Beyond its established neuroprotective role, phototherapy has been increasingly evaluated for potential systemic effects, particularly on neonatal cardiovascular physiology [4]. Light exposure may influence vascular tone through mechanisms involving nitric oxide signaling, oxidative stress, and prostanoid pathways [5–7]. These effects may be especially relevant in preterm infants, where immature vascular regulation may predispose to altered ductal tone and delayed closure of the Ductus Arteriosus (DA) [8,9].

The ductus arteriosus is a key fetal vascular structure that normally undergoes functional closure within the first 24-72 hours after birth, followed by anatomical obliteration. Disruption of this process, particularly in preterm infants, may result in Patent Ductus Arteriosus (PDA), which is associated with pulmonary overcirculation, respiratory morbidity, and increased mortality [10]. Given this clinical importance, potential external modulators of ductal closure, including phototherapy, warrant careful investigation.

Experimental and clinical studies have suggested a possible interaction between phototherapy and ductal physiology. Animal studies have demonstrated light-induced vasodilation of ductal tissue [11], while early clinical observations reported an increased incidence of PDA in phototherapy-exposed preterm infants and suggested that thoracic shielding might mitigate this effect [12]. However, subsequent studies have yielded conflicting results, and the relationship remains controversial, with potential confounding by gestational age, illness severity, and treatment duration [13].

Correspondence: Ayhan Ceri, Department of Neonatology, Dr. Ali Kemal Belviranlı Maternity and Children's Hospital, Konya, Türkiye **e-mail:** ceriayhan@hotmail.com, **Received:** March 16, 2026 **Accepted:** April 6, 2026

Despite decades of research, the optimal management of PDA, particularly in preterm neonates, remains debated, with increasing emphasis on individualized approaches. At the same time, the systemic vascular effects of phototherapy are not fully understood. Recent randomized trials and meta-analyses have reported inconsistent findings regarding the association between phototherapy and DA patency, and Cochrane reviews continue to highlight the lack of definitive evidence in this area, particularly with respect to optimal treatment parameters and systemic effects [8,14,15].

Despite decades of widespread phototherapy use in neonatal practice, its potential systemic hemodynamic effects, particularly on Ductus Arteriosus (DA) physiology, remain incompletely understood. This question has gained renewed relevance in the modern era of high-intensity LED-based phototherapy systems, which differ substantially from conventional fluorescent units in spectral characteristics, irradiance, and thermal profile. Although contemporary devices have improved treatment efficacy and safety, uncertainty persists regarding whether light exposure may modulate vascular tone and influence ductal closure, especially in preterm infants with immature cardiovascular regulation. In this context, carefully reanalyzed historical cohorts provide a uniquely valuable low-confounding physiological model, allowing more direct evaluation of the intrinsic vascular effects of phototherapy independent of modern NICU interventions such as early pharmacologic PDA closure and advanced hemodynamic support. Therefore, the present study aimed to reassess the association between phototherapy exposure and DA patency in term and preterm neonates using a well-characterized historical cohort.

3. Materials and Methods

3.1 Study design: This study was conducted as a retrospective observational cohort between November 1994 and August 1995 in a tertiary neonatal intensive care unit. The historical nature of the dataset allowed for uniform phototherapy protocols and limited confounding from modern NICU interventions such as LED-based systems or early pharmacologic ductus closure strategies. All infants were treated under standard phototherapy protocols in use at the time, which relied on conventional fluorescent blue-light units positioned at a fixed distance. Similar retrospective designs have previously been employed to evaluate ductal patency under phototherapy exposure conditions [16].

Given the historical nature of the cohort, formal ethics committee approval was not routinely required at the time for noninvasive observational studies. The present retrospective analysis was performed using anonymized archived clinical records in accordance with current ethical principles and institutional standards.

3.2 Participants: A total of 229 neonates were retrospectively included in this study, drawn consecutively from hospital records between November 1994 and August 1995. Participants were divided into two cohorts: 111 infants received phototherapy, while 118 did not and served as controls. All neonates were admitted within the first 72 hours of life and had complete clinical and echocardiographic data available for analysis before and after the observation or intervention period. Infants with major congenital anomalies were excluded.

Additional exclusion criteria were: clinical or documented birth asphyxia, congenital heart disease affecting ductal patency (e.g., transposition of the great arteries, hypoplastic left heart syndrome), sepsis, or prior administration of medications known to influence ductal dynamics (e.g., prostaglandins, indomethacin). For subgroup analyses, infants were stratified by gestational age into preterm (<37 weeks) and term (≥37 weeks) categories. Stratification by gestational maturity is a common analytical approach in PDA research [17].

3.3 Phototherapy protocol: Infants in the phototherapy group received treatment using Philips 20W/52 blue fluorescent lamps, positioned approximately 40 cm above the neonate. The average spectral irradiance at this distance was 6 $\mu W/cm^2/nm$, consistent with international treatment thresholds of the time [18].

To minimize potential complications, eye shields and skin covers were routinely applied during therapy. Infants were rotated every 3 to 4 hours to ensure

uniform exposure and reduce localized heating.

Phototherapy was administered continuously for an average duration of 12 to 24 hours, depending on bilirubin levels and clinical response. The decision to initiate or discontinue therapy was made by the attending neonatologist, based on established bilirubin nomograms available at the time [19].

3.4 Echocardiographic assessment

All enrolled neonates underwent transthoracic echocardiography using a *Hewlett-Packard Sonos 1000* system with a 5 MHz sector probe. Assessments were conducted immediately before phototherapy initiation (or at a comparable time point in control infants), and repeated within 12 hours following the end of therapy. The timing and technique of postnatal ductal assessment by Doppler echocardiography was based on prior normative studies in healthy newborns [20].

The echocardiographic protocol included two-dimensional imaging for anatomical evaluation and color Doppler to assess ductus arteriosus patency, including flow direction (left-to-right, right-to-left, or bidirectional) and degree of residual shunting. This dual-modality approach is well-established for evaluating ductal patency in neonates [21]. All examinations were interpreted in a blinded manner by a pediatric cardiologist unaware of group allocation, ensuring unbiased evaluation.

3.5 Statistical analysis: Data were analyzed using SPSS version 5.0 (1995, SPSS Inc., Chicago, IL). Continuous variables were expressed as mean ± Standard Deviation (SD), and comparisons between groups were performed using the Student's t-test. Categorical variables were analyzed with the Chi-square test (χ^2).

A p-value of <0.05 was considered statistically significant. Subgroup analyses were conducted to assess differences between term and preterm neonates and to evaluate potential confounding factors.

4. Results

4.1 Basic Demographic Characteristics: A total of 229 neonates were included in the study, comprising 86 preterm and 143 term infants. Of these, 111 received phototherapy, while 118 did not and served as the control group.

The gender distribution between groups was comparable, with no statistically significant difference ($p > 0.05$). In the phototherapy group, 60 (54.1%) were male and 51 (45.9%) female, whereas the control group included 63 males (53.4%) and 55 females (46.6%). These data are summarized in Table 1.

Table 1. Gender distribution of neonates according to treatment group

Group	Male, n (%)	Female, n (%)	Total, n
Phototherapy	60 (54.1)	51 (45.9)	111
Control	63 (53.4)	55 (46.6)	118

The mean duration of phototherapy ranged between 12 and 24 hours, with most infants receiving continuous exposure in accordance with established clinical protocols. No adverse effects related to phototherapy were observed during the study period. This duration and treatment approach are consistent with previously reported protocols and safety profiles of conventional blue light phototherapy [17,18].

4.2 Ductus arteriosus patency:

Among the 229 neonates, 12 infants (5.2%) were found to have persistent patent ductus arteriosus (PDA) on echocardiographic assessment. Subgroup analysis revealed a higher incidence in preterm infants (7/86, 8.1%) compared to term infants (5/143, 3.9%), consistent with the known immaturity of ductal closure mechanisms in premature neonates [10].

When analyzed according to phototherapy exposure, PDA was observed in 5 of 111 infants (4.5%) in the phototherapy group and in 7 of 118 infants (5.9%) in the control group. No statistically significant association was identified between phototherapy and PDA (odds ratio [OR]: 0.75; 95% Confidence Interval [CI]: 0.23–2.43; p=0.628) (Fig. 1).

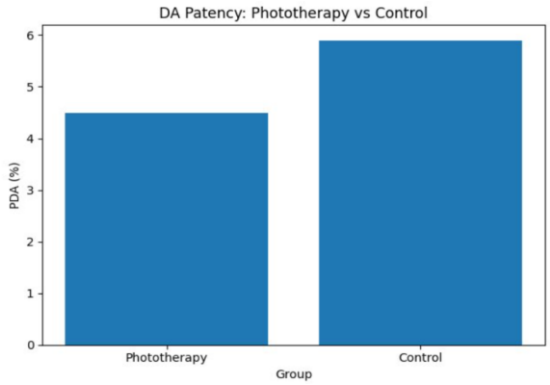

Figure 1. DA patency according to treatment group.

The difference in PDA incidence between preterm and term infants is further illustrated in Fig. 2, highlighting the higher vulnerability of premature neonates to delayed ductal closure.

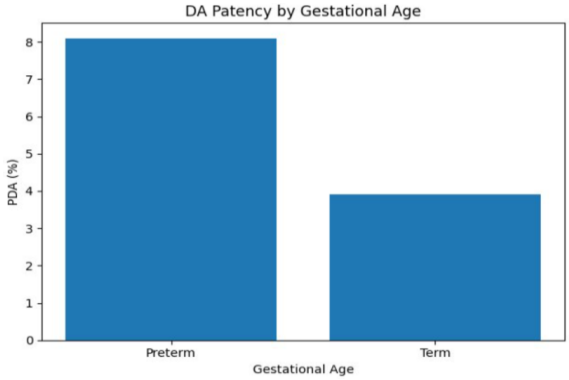

Figure 2. DA patency according to gestational age.

Although prior experimental and clinical studies have suggested that light exposure may influence vascular tone and ductal dynamics (7,15), such an effect was not demonstrated in this cohort. The relatively small number of PDA cases and wide confidence intervals indicate limited statistical power to detect modest associations.

A detailed comparison of PDA prevalence according to gestational age is presented in Table 2.

Table 2. Ductus Arteriosus (DA) patency according to gestational age

Gestational age	Total, n	DA patent, n (%)	DA closed, n (%)
Preterm	86	7 (8.1)	79 (91.9)
Term	143	5 (3.9)	138 (96.1)

5. Discussion

The principal finding of this study is that phototherapy exposure was not associated with a statistically significant increase in persistent ductus arteriosus patency in the overall cohort. However, this absence of statistical significance should be interpreted cautiously in light of the relatively small number of PDA events and the wide confidence intervals observed. Importantly, the higher incidence of persistent ductal patency among preterm infants compared with term neonates reinforces the established concept that gestational immaturity remains the dominant determinant of delayed ductal closure. These findings suggest that while phototherapy may not represent an independent major risk factor in the overall population, subtle hemodynamic effects cannot be excluded in biologically vulnerable subgroups, particularly preterm infants.

5.1 Interpretation of the main findings: Among the 229 neonates examined, 5.2% were found to have persistent ductal patency, with a higher incidence in preterm infants (8.1%) compared to term infants (3.9%), consistent with established knowledge regarding immature ductal physiology in premature neonates [10,19,22].

In the overall cohort, phototherapy exposure was not associated with a statistically significant increase in ductus arteriosus patency (Odds Ratio [OR]: 0.75; 95% confidence interval [CI]: 0.23–2.43; p=0.628). However, the wide confidence interval and low number of events suggest limited statistical power to detect modest effects.

Phototherapy, while primarily aimed at reducing serum bilirubin through photoisomerization and photooxidation, may still exert secondary effects on vascular tone and prostaglandin metabolism. Several plausible physiological mechanisms may underlie such effects. Light exposure has been shown to induce cutaneous vasodilation and potentially systemic hemodynamic changes [7]. Experimental studies have further indicated that phototherapy may influence vasoactive mediators such as Nitric Oxide (NO) and prostaglandin E_2 (PGE_2), both of which are central to maintaining ductal patency during fetal and early neonatal life [8].

Therefore, although no statistically significant association was identified in this cohort, the possibility of a clinically relevant effect cannot be excluded, particularly in preterm infants with immature cardiovascular regulation. The findings should be interpreted within the context of biological plausibility and limited statistical precision.

5.2 Comparison with the literature: Phototherapy-related effects on ductal physiology have been discussed in both experimental and clinical studies, although the evidence remains inconsistent. Early clinical observations by Rosenfeld et al. first suggested that phototherapy might delay ductal closure in preterm infants and that thoracic shielding could reduce this effect. Similar concerns were later supported by subsequent clinical reports describing a higher incidence of PDA among phototherapy-exposed premature neonates [12,14].

Experimental data have also provided biological support for this hypothesis. Clyman and colleagues demonstrated light-induced vasorelaxation of ductal tissue in animal models, suggesting a direct photobiological effect on ductal smooth muscle. Additional mechanistic studies have implicated Nitric Oxide (NO), prostaglandin E_2 (PGE_2), and oxidative stress pathways as potential mediators of phototherapy-related vascular modulation, particularly in preterm infants with immature cardiovascular regulation 7,11,23. Figure 3 illustrates the proposed interaction between phototherapy exposure and neonatal ductal physiology, including potential pathways involving nitric oxide signaling, prostaglandin modulation, oxidative stress, and direct smooth muscle vasorelaxation.

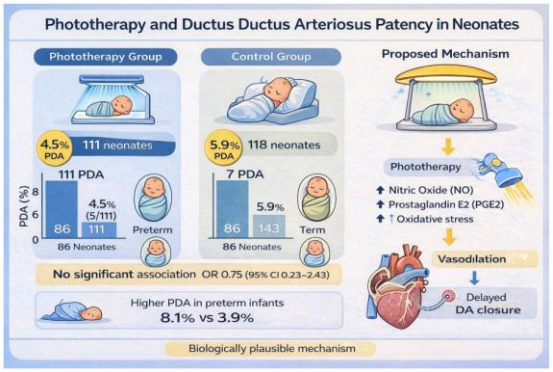

Figure 3. Proposed biological mechanism of phototherapy-related DA patency

More recent clinical studies have focused on systemic hemodynamic responses during phototherapy, including transient increases in cardiac output and reductions in vascular resistance. These findings support the concept that phototherapy may exert cardiovascular effects beyond bilirubin metabolism. However, reported associations with PDA have remained variable across studies, likely reflecting differences in gestational age distribution, phototherapy intensity, duration of exposure, and evolving NICU practices [8,16,24].

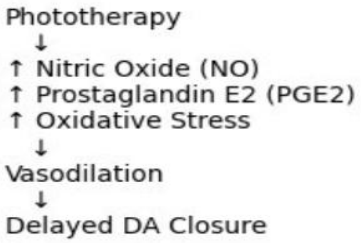

Fig 4. Phototherapy and DNA patency

In contrast to several earlier reports suggesting an increased PDA risk, our findings did not demonstrate a statistically significant association between phototherapy exposure and persistent ductal patency. This discrepancy may be explained by differences in study design, sample size, patient selection, and improvements in neonatal care over time. Importantly, recent randomized trials and meta-analyses have likewise reported inconsistent results, underscoring the persistent uncertainty in this field (26).

Nevertheless, the biological plausibility of light-induced vascular modulation remains clinically relevant, particularly in vulnerable preterm populations. Although our data do not support a definitive association, subtle hemodynamic effects cannot be excluded, especially in the setting of immature ductal smooth muscle responsiveness. These considerations may remain physiologically relevant in contemporary neonatal practice, where modern high-intensity LED systems provide greater irradiance and prolonged exposure compared with historical fluorescent units [27,28].

Taken together, the available literature and our findings suggest that the relationship between phototherapy and ductal patency remains unresolved. Rather than establishing causality, the current evidence supports continued investigation in adequately powered prospective studies, particularly in extremely preterm infants.

5.3 Relevance of historical cohorts: One of the key strengths of this study lies in the historical nature of the dataset, which allows evaluation of phototherapy-related vascular effects in a relatively low-confounding clinical environment. In contrast to modern Neonatal Intensive Care Units (NICUs), where multiple simultaneous interventions may influence ductal physiology, earlier cohorts provide a more controlled setting for physiological interpretation.

Contemporary NICU practice is characterized by the widespread use of high-intensity LED phototherapy systems, early pharmacologic ductal closure strategies (e.g., indomethacin or ibuprofen), and advanced hemodynamic support. While these advances have improved neonat al outcomes, they also introduce significant heterogeneity and potential confounding when assessing the isolated effects of phototherapy on vascular tone and ductal dynamics.

In contrast, the present cohort reflects a period with more standardized care conditions, absence of LED-based phototherapy, and limited early pharmacologic intervention for PDA. This creates a "cleaner" physiological model in which the direct vascular effects of light exposure can be more readily observed. Such conditions are difficult to replicate in modern clinical trials, where ethical and clinical constraints necessitate early interventions.

Importantly, even recent randomized controlled trials and meta-analyses, including a double-blind randomized trial by Mannan and Amin [25] and a contemporary systematic review by Simon et al. [26], have reported inconsistent and inconclusive findings regarding the relationship between phototherapy and PDA, underscoring the persistent uncertainty in this field [8,25]. This heterogeneity further supports the value of revisiting historical datasets, which may help isolate fundamental physiological mechanisms that are otherwise obscured in contemporary settings.

Therefore, rather than representing a limitation, the historical design of this study provides a unique opportunity to examine the intrinsic interaction between phototherapy and ductal physiology. These insights remain relevant in modern neonatal care, particularly in understanding the biological plausibility of light-induced vascular modulation.

5.4 Strengths and limitations: This study has several methodological strengths. The inclusion of 229 neonates allowed meaningful comparisons between term and preterm infants, and blinded echocardiographic assessments reduced the risk of diagnostic bias. In addition, the availability of echocardiographic evaluations before and after phototherapy exposure enabled temporal assessment of ductal patency in relation to treatment [19,20].

However, several limitations should be acknowledged. First, the retrospective design inherently limits control over potential confounding variables, including illness severity, hydration status, and endogenous prostaglandin activity, all of which may influence ductal closure. Second, the relatively small number of PDA events reduced statistical power and resulted in wide confidence intervals, limiting the ability to exclude modest but clinically relevant associations [29].

In addition, direct measurement of irradiance and biochemical markers such as nitric oxide, prostaglandin E_2, and oxidative stress indices was not available, restricting mechanistic interpretation and precluding causal inference. The phototherapy protocol also reflects clinical standards of the 1990s and primarily involved conventional fluorescent light systems, which differ substantially from current high-intensity LED devices in spectral characteristics and irradiance profile [27,30,31].

Despite these limitations, the historical nature of the cohort provides an important methodological advantage by allowing assessment in a relatively low-confounding physiological setting, with limited influence from modern interventions such as early pharmacologic PDA closure and advanced hemodynamic support. This may enhance the interpretability of the observed association between phototherapy exposure and ductal patency.

5.5 Clinical relevance: Clinically, these findings do not support a change in routine phototherapy practices in term neonates, where the risk of persistent Ductus Arteriosus (DA) appears minimal. However, in preterm infants, particularly those born before 34 weeks of gestation, a more cautious approach may be warranted due to their increased physiological vulnerability [18].

In this population, timely recognition and management of PDA remain critical, with pharmacologic closure using prostaglandin inhibitors such as indomethacin continuing to play a central role, especially in extremely preterm infants at highest risk [29].

Given the potential for light-induced vascular effects, clinicians may consider targeted strategies such as optimizing phototherapy duration, maintaining adequate hydration, and implementing focused echocardiographic monitoring in at-risk neonates [32]. These considerations are particularly relevant in extremely low birth weight infants, where even subtle alterations in vascular tone may lead to clinically significant hemodynamic changes.

Adjunctive approaches, including thoracic shielding or cyclical phototherapy, may offer a balance between effective bilirubin reduction and minimizing cardiovascular stress, as suggested by recent clinical studies [8].

Ultimately, individualized management, balancing bilirubin neurotoxicity risk against cardiovascular stability, remains essential, particularly in fragile preterm populations. In everyday neonatal practice, these findings may be particularly relevant when managing fragile preterm infants, where even subtle hemodynamic shifts can influence clinical decision-making.

5.6 Future research directions: To better understand the mechanisms underlying phototherapy-related ductal patency, future studies should prioritize prospective, randomized controlled trials with structured methodologies. These should incorporate serial biochemical measurements, including Nitric Oxide (NO), prostaglandin E_2 (PGE_2), and malondialdehyde (MDA), at critical time points such as pre-treatment, mid-treatment, and post-treatment phases [6,33].

Additionally, continuous hemodynamic monitoring using echocardiographic flow patterns and tissue perfusion metrics may yield deeper insights into the real-time cardiovascular effects of phototherapy [7,16]. Comparative clinical trials assessing systemic responses to traditional fluorescent versus high-irradiance LED phototherapy systems are warranted to identify technology-specific risks [27,34].

Emerging evidence suggests that phototherapy may induce oxidative stress and lipid peroxidation, particularly in preterm and low-birth-weight neonates, highlighting the need for further evaluation of its long-term safety profile [28,35].

Finally, longitudinal observational cohorts and multicenter studies are essential to confirm these findings in diverse clinical contexts, enabling evidence-based updates to current neonatal jaundice management protocols [2,17].

6. Conclusion

In this historical cohort, phototherapy was not associated with a statistically significant increase in ductus arteriosus patency. However, the limited number of PDA events and wide confidence intervals preclude exclusion of modest but clinically relevant effects, particularly in preterm infants.

These findings reinforce gestational immaturity as the primary determinant of delayed ductal closure while preserving the biological plausibility of light-related vascular modulation in vulnerable neonates

Given the increasing use of high-intensity LED phototherapy systems in contemporary NICU practice, the hemodynamic implications of phototherapy remain an important unresolved clinical question. Prospective adequately powered studies incorporating modern phototherapy technologies and mechanistic biomarkers are warranted to further clarify this association.

Data availability statement: The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Author contributions: The author contributed to study conception, data analysis, manuscript drafting, and final approval.

Conflict of interest: The author declares no conflicts of interest.

Funding: No funding was received for this study.

Ethics approval: The original data were collected during 1994-1995, when formal ethics committee approval was not routinely required for noninvasive observational studies. This retrospective reanalysis was conducted using anonymized historical data in accordance with current ethical standards.

Data availability: Available upon reasonable request.

Acknowledgments: This study is based, in part, on data originally collected as part of the author's specialty thesis, "Effect of Phototherapy on Ductal Closure in Healthy Newborns" (Selçuk University Faculty of Medicine, Department of Pediatrics, Konya, Türkiye, November 1994-August 1995). The author gratefully acknowledges Prof. Dr. Sevim Karaaslan, who supervised the original thesis as an Associate Professor at the time and performed the echocardiographic evaluations during the original study period.

Key points

- Phototherapy showed no significant PDA effect
- Preterm infants had higher DA patency
- Historical data minimized modern bias

7. References

1. Bhutani VK, Stark AR, Lazzeroni LC, et al. Predischarge screening for severe neonatal hyperbilirubinemia identifies infants who need phototherapy. *J Pediatr*. 2013;162(3):477-482. doi:10.1016/j.jpeds.2012.08.022
2. Maisels MJ. Managing the jaundiced newborn: a persistent challenge. *CMAJ*. 2015;187(5):335-343. doi:10.1503/cmaj.122117
3. American Academy of Pediatrics Subcommittee on Hyperbilirubinemia. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. *Pediatrics*. 2004;114(1):297-316. doi:10.1542/peds.114.1.297
4. Faulhaber FRS, Procianoy RS, Silveira RC. Side Effects of Phototherapy on Neonates. *Am J Perinatol*. 2019;36(03):252-257. doi:10.1055/s-0038-1667379
5. Does Phototherapy Affect Ductus Arteriosus Closure in Preterm Infants ≤32 Weeks of Gestation, and Can We Influence This Through Chest Shielding? Review of the Literature and a Meta-Analysis. *Biomedicines*. 2025;13(10):2567.
6. Ağırtaş G, Guzoglu N, Akbaş O, Kısa Ü, Aliefendioğlu D. THE EFFECT OF PHOTOTHERAPY TREATMENT ON OXIDATIVE STRESS AND INFLAMMATORY RESPONSE IN NEWBORNS. *J Kırıkkale Univ Fac Med*. 2023;25(1):16-22.
7. Javorka K, Maťašová K, Javorka M, Zibolen M. Mechanisms of Cardiovascular Changes of Phototherapy in Newborns with Hyperbilirubinemia. *Physiol Res*. 2023;72(S1):S1-S9.
8. Bozkaya D, Dizdar EA, Ertekin Ö, Derme T, Umaç HA. Effect of phototherapy on the ductus arteriosus diameter in extremely premature infants: A randomised controlled trial. *Early Hum Dev*. 2023; 183:105820.
9. Dani C, Remaschi G, Rossi F, et al. Splanchnic and cerebral oxygenation during cyclic phototherapy in preterm infants with hyperbilirubinemia. *Eur J Pediatr*. 2024;183(12):5313-5319.
10. Ambalavanan N, Aucott SW, Salavitabar A, Levy VY, Committee on Fetus and Newborn, Section on Cardiology and Cardiac Surgery. Patent Ductus Arteriosus in Preterm Infants. *Pediatrics*. 2025;155(5):e2025071425.
11. Clyman RI, Saugstad OD, Mauray F. Reactive oxygen metabolites relax the lamb ductus arteriosus by stimulating prostaglandin production. *Circ Res*. 1989;64(1):1-8. doi: 10.1161/01.RES.64.1.1
12. Rosenfeld W, Sadhev S, Brunot V, Jhaveri R, Zabaleta I, Evans HE. Phototherapy Effect on the Incidence of Patent Ductus Arteriosus in Premature Infants: Prevention with Chest Shielding. *Pediatrics*. 1986;78(1):10-14 PMID

- 3725493.
13. Mahmoud AMA, Elagamy AEA. Association of Patent Ductus Arteriosus and Phototherapy in Infants Weighing Less Than 1500 Grams. *Egypt J Hosp Med*. 2022;87(1):2072-2074.
14. Mannan J, Amin SB. Effect of chest shielding during phototherapy for hyperbilirubinemia on symptomatic patent ductus arteriosus – a double-blind randomized placebo-controlled trial. *Pediatr Res*. 2024;96(7):1771-1776.
15. High- versus low-dose phototherapy for neonatal jaundice - Lai, NM - 2026 | Cochrane Library. Accessed March 28, 2026. https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD003308.pub3/full
16. El Amrousy D, Adel R, Ayoub D, Rowisha M. Effect of phototherapy on cardiac function in full term neonates with unconjugated hyperbilirubinemia. *Pediatr Res*. Published online May 8, 2025:1-6.
17. Hansen TWR, Maisels MJ, Ebbesen F, et al. Sixty years of phototherapy for neonatal jaundice – from serendipitous observation to standardized treatment and rescue for millions. *J Perinatol*. 2020;40(2):180-193. doi:10.1038/s41372-019-0439-1
18. Kapoor S, Mishra D, Chawla D, Jain S. Chest shielding in preterm neonates under phototherapy—a randomised control trial. *Eur J Pediatr*. 2021;180(3):767-773. doi:10.1007/s00431-020-03836-9
19. Gentile R, Stevenson G, Dooley T, Franklin D, Kawabori I, Pearlman A. Pulsed Doppler echocardiographic determination of time of ductal closure in normal newborn infants. *J Pediatr*. 1981;98(3):443-448. doi:10.1016/S0022-3476(81)80649-2
20. Knight DB, Yu VY. Contrast echocardiographic assessment of the neonatal ductus arteriosus. *Arch Child*. 1986;61(5):484-488. doi:10.1136/adc.61.5.484
21. Biały ŁH, Talar T, Gulczyńska E, Strzelecka I, Respondek-Liberska M. Prenatal Diagnosis of Ductal Constriction in Normal Heart Anatomy—Are There Any Neonatal Consequences? *J Clin Med*. 2025;14(10):3388. doi:10.3390/jcm14103388
22. Reller MD, Ziegler ML, Rice MJ, Solin RC, McDonald RW. Duration of ductal shunting in healthy preterm infants: an echocardiographic color flow Doppler study. *J Pediatr*. 1988;112(3):441-446. doi:10.1016/S0022-3476(88)80088-6
23. Ergenekon E, Gücüyener K, Dursun H, et al. Nitric Oxide Production in Newborns under Phototherapy. *Nitric Oxide*. 2002;6(1):69-72.
24. Taksande A, Vagha J, Dalal Y. Effect of Phototherapy on Cardiac Functions in Neonates with Hyperbilirubinemia. A Prospective Cross-Sectional Study. *Ann Neonatol*. 2021;3(2):88-107.
25. Mannan J, Amin SB. Meta-Analysis of the Effect of Chest Shielding on Preventing Patent Ductus Arteriosus in Premature Infants. *Am J Perinatol*. 2017;34(4):359-363.
26. Simon M, Gall Z, Rusneac M, et al. Does Phototherapy Affect Ductus Arteriosus Closure in Preterm Infants ≤32 Weeks of Gestation, and Can We Influence This Through Chest Shielding? Review of the Literature and a Meta-Analysis. *Biomedicines*. 2025;13(10). doi:10.3390/biomedicines13102567
27. Novoa RH, Huaman K, Caballero P. Light-Emitting Diode (LED) Phototherapy versus Non-LED Phototherapy Devices for Hyperbilirubinemia in Neonates: A Systematic Review and Meta-analysis. *Am J Perinatol*. 2023;40(15):1618-1628. doi:10.1055/a-1827-7607
28. Schoor LWE van der, Faassen MHJR van, Kema I, et al. Blue LED phototherapy in preterm infants: effects on an oxidative marker of DNA damage. *Arch Dis Child - Fetal Neonatal Ed*. 2020;105(6):628-633. doi:10.1136/archdischild-2019-317024
29. Hermes-DeSantis ER, Clyman RI. Patent ductus arteriosus: pathophysiology and management. *J Perinatol*. 2006;26 Suppl 1:S14-S18. doi:10.1038/sj.jp.7211468
30. Woodgate P, Jardine LA. Neonatal jaundice: phototherapy. *BMJ Clin Evid*. 2015;2015:0319 PMID - 26069642.
31. Awad KH, Elmorsy WA. Impact of Phototherapy on Oxidative Stress Indices in Preterm Neonates with Unconjugated Hyperbilirubinemia. *Egypt J Hosp Med*. 2020;81(4):1815-1821.
32. Shin T, Choi H, Lee EJ, Yoo YM. Effect of Phototherapy on Blood Pressure, Heart Rate,

and Body Temperature in Early Preterm Infants with Gestational Age <32 Weeks. *Perinatology*. 2025;36(1):15-25.
33. Gathwala G, Sharma S. Oxidative stress, phototherapy and the neonate. *Indian J Pediatr*. 2000;67(11):805-808. doi:10.1007/BF02723953
34. Conventional intensive versus LED intensive phototherapy oxidative stress burden in neonatal hyperbilirubinaemia of haemolytic origin: Paediatrics and International Child Health: Vol 40 , No 1 - Get Access. Accessed March 28, 2026. https://www.tandfonline.com/doi/full/10.1080/20469047.2019.1586185
35. Yurdakök M. Phototherapy in the newborn: what's new? *J Pediatr Neonatal Individ Med JPNIM*. 2015;4(2):e040255-e040255. doi:10.7363/040255