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Review Article

Care of Neonates Under Phototherapy: A Narrative Review on the Impact of Phototherapy on Neonatal Genital Organs

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ABSTRACT

Background: Neonatal hyperbilirubinemia is one of the most common clinical conditions encountered during the neonatal period, affecting approximately 60% of term and 80% of preterm infants during the first week of life. Although physiological jaundice is usually self-limiting, severe unconjugated hyperbilirubinemia may progress to acute bilirubin encephalopathy and kernicterus, resulting in permanent neurological disability or death if left untreated. Phototherapy has become the standard treatment for neonatal jaundice because of its effectiveness, non-invasive nature, and excellent safety profile. Nevertheless, increasing experimental evidence has raised concerns regarding possible biological effects of prolonged blue-light exposure on neonatal tissues, particularly the genital organs of male infants.

Objective: To critically review current scientific evidence regarding the impact of neonatal phototherapy on genital organs and to discuss evidence-based nursing interventions for ensuring safe and effective phototherapy administration.

Methods: A narrative review of the literature was conducted using electronic databases including PubMed, Scopus, Google Scholar, ScienceDirect, MEDLINE, CINAHL, and the Cochrane Library. English-language articles published between 2000 and 2025 were considered. Search terms included neonate, phototherapy,hy perbilirubinemia, genital organs, testicular injury, oxidative stress, reproductive safety, and nursing care. Clinical studies, experimental animal studies, systematic reviews, meta-analyses, and international clinical guidelines were included.

Results: Available evidence demonstrates that phototherapy remains a highly effective and safe treatment for neonatal hyperbilirubinemia. Experimental animal studies have reported increased oxidative stress, transient histopathological alterations, and reduced antioxidant enzyme activity within testicular tissue following prolonged light exposure. However, human clinical studies have not demonstrated convincing evidence of permanent impairment of genital

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development, endocrine function, fertility, or reproductive health. International organizations, including the American Academy of Pediatrics (AAP), the World Health Organization (WHO), and the National Institute for Health and Care Excellence (NICE), continue to recommend phototherapy as the first-line treatment for neonatal hyperbilirubinemia. Appropriate nursing care—including eye protection, institutional genital shielding practices, thermoregulation, hydration, bilirubin monitoring, and parent education—remains essential to maximize therapeutic benefits while minimizing potential risks.

Conclusion: Current evidence supports the continued use of phototherapy as the safest and most effective treatment for neonatal jaundice. Although laboratory studies suggest theoretical concerns regarding oxidative injury to genital tissues, available human evidence does not indicate clinically significant long-term reproductive harm. Continued research involving long-term follow-up of exposed infants is warranted to further strengthen the evidence base. Neonatal nurses play a pivotal role in ensuring safe phototherapy administration through vigilant assessment, adherence to evidence-based guidelines, and family-centered care.

KEYWORDS

• Neonatal Jaundice • Phototherapy • Hyperbilirubinemia • Genital Organs • Testes • Oxidative Stress • Neonatal Nursing • Evidence-Based Practice

INTRODUCTION

Neonatal hyperbilirubinemia is one of the most common clinical conditions encountered during the neonatal period and remains a leading cause of hospital readmission during the first week of life. It is characterized by the yellow discoloration of the skin and sclera resulting from elevated levels of unconjugated bilirubin in the bloodstream. Approximately 60% of term newborns and 80% of preterm infants develop jaundice within the first week after birth. Although physiological jaundice is generally benign and self-limiting, severe hyperbilirubinemia can lead to bilirubin-induced neurological dysfunction (BIND), acute bilirubin encephalopathy, and kernicterus, which are associated with permanent neurodevelopmental impairment, hearing loss, cerebral palsy, and even death. Early recognition and timely treatment are therefore essential components of neonatal care.

The pathophysiology of neonatal jaundice is multifactorial. Increased destruction of fetal erythrocytes, immature hepatic glucuronidation pathways, reduced activity of uridine diphosphate-glucuronosyltransferase (UGT1A1), and increased enterohepatic circulation collectively contribute to elevated serum bilirubin concentrations. Additional risk factors include prematurity, breastfeeding difficulties, hemolytic disease due to ABO or Rh incompatibility, glucose-6-phosphate dehydrogenase deficiency, birth trauma, polycythemia, sepsis, and maternal diabetes.

Since its introduction in the late 1950s, phototherapy has revolutionized the management of neonatal hyperbilirubinemia. It has significantly reduced the incidence of kernicterus and the need for exchange transfusion. Phototherapy utilizes blue-green light with wavelengths between 460 and 490 nm to convert unconjugated bilirubin into water-soluble photoisomers and structural isomers that can be excreted without hepatic conjugation. The procedure is non-invasive, cost-effective, widely available, and recommended as the first-line treatment by the American Academy of Pediatrics (AAP), the World Health Organization (WHO), and the National Institute for Health and Care Excellence (NICE).

Although phototherapy is regarded as one of the safest interventions in neonatal medicine, it is not entirely free from adverse effects. Common complications include increased insensible water loss, dehydration, loose stools, skin rash, thermal instability, electrolyte imbalance, retinal injury in the absence of eye protection, and bronze baby syndrome in infants with conjugated hyperbilirubinemia. More recently, attention has shifted toward the biological effects of phototherapy-induced oxidative stress and its potential impact on rapidly developing neonatal tissues.

Among these tissues, the genital organs—particularly the testes in male neonates—have attracted scientific interest because of their superficial anatomical location and rapidly proliferating germ cells. Experimental animal studies have reported increased oxidative stress, lipid peroxidation, transient degeneration of seminiferous tubules, and reduced antioxidant enzyme activity following prolonged exposure to phototherapy. These findings have raised concerns regarding possible long-term effects on fertility and reproductive health.

However, translating these findings into human clinical practice requires caution. Human studies have not consistently demonstrated permanent damage to the testes, impaired endocrine function, delayed puberty, or infertility following neonatal phototherapy. Differences in light intensity, exposure duration, anatomy, physiology, and antioxidant defense mechanisms between animals and humans limit the direct applicability of experimental results. Furthermore, the overwhelming clinical benefits of phototherapy in preventing bilirubin neurotoxicity must be carefully balanced against these theoretical risks.

Nurses play a central role in the safe administration of phototherapy. Their responsibilities include assessing eligibility for treatment, ensuring correct phototherapy device placement, protecting the infant's eyes, applying genital shielding according to institutional protocols, monitoring body temperature and hydration, evaluating bilirubin response, preventing complications, and educating parents. Evidence-based nursing care is essential to maximize treatment efficacy while minimizing unnecessary exposure and potential adverse effects.

Given the widespread use of phototherapy and ongoing scientific debate regarding its effects on reproductive tissues, a comprehensive review of current evidence is warranted. This narrative review synthesizes experimental and clinical literature concerning the impact of phototherapy on neonatal genital organs and highlights implications for nursing practice, policy development, and future research.

Aim of the Review

The primary aim of this narrative review is to critically evaluate the available scientific evidence regarding the impact of phototherapy on neonatal genital organs and to discuss evidence-based nursing interventions that ensure safe and effective phototherapy administration.

OBJECTIVES OF THE REVIEW

The specific objectives of this review are to:

1. Review the epidemiology and pathophysiology of neonatal hyperbilirubinemia.
2. Describe the mechanism of action and therapeutic principles of phototherapy.
3. Evaluate experimental evidence regarding the effects of phototherapy on neonatal genital organs.
4. Critically examine human clinical studies investigating reproductive safety following neonatal phototherapy.
5. Summarize current recommendations from international organizations, including the AAP, WHO, and NICE.
6. Identify evidence-based nursing interventions that reduce potential risks and improve neonatal outcomes.
7. Highlight gaps in current knowledge and recommend priorities for future research.

METHODS

Study Design

This article was conducted as a narrative review to synthesize and critically appraise the available scientific evidence regarding the impact of phototherapy on neonatal genital organs. A narrative review design was selected because it allows integration of evidence from experimental animal studies, observational clinical studies, systematic reviews, clinical practice guidelines, and neonatal nursing literature to provide a comprehensive understanding of the topic.

Search Strategy

A systematic literature search was performed using the following electronic databases:

1. PubMed
2. MEDLINE
3. Scopus
4. Google Scholar
5. ScienceDirect

6. CINAHL
7. Cochrane Library

The search included studies published between **January 2000 and March 2025**.

The following Medical Subject Heading (MeSH) terms and keywords were used individually and in combination using Boolean operators (AND, OR):

- Neonate
- Neonatal jaundice
- Hyperbilirubinemia
- Phototherapy
- Blue light therapy
- Genital organs
- Testicular injury
- Testes
- Male reproductive system
- Oxidative stress
- Reactive oxygen species
- Neonatal nursing
- Phototherapy complications
- Reproductive safety

Inclusion Criteria

Studies were included if they met the following criteria:

- Published in English
- Human neonatal studies
- Experimental animal studies
- Randomized controlled trials
- Cohort studies
- Case-control studies
- Cross-sectional studies
- Systematic reviews
- Meta-analyses
- International clinical guidelines
- Articles addressing phototherapy, oxidative stress, genital organs, or reproductive safety

Exclusion Criteria

The following studies were excluded:

- Conference abstracts without full text
- Editorials and expert opinions lacking original data
- Duplicate publications
- Studies unrelated to neonatal phototherapy
- Articles involving adult phototherapy

Data Extraction

Information extracted from each study included:

- Author and year
- Country
- Study design
- Sample size
- Population characteristics
- Type of phototherapy
- Exposure duration
- Outcome measures
- Major findings
- Conclusions

Data Synthesis

The findings were synthesized into the following thematic categories:

- Neonatal hyperbilirubinemia
- Mechanism of phototherapy
- Oxidative stress
- Experimental evidence
- Human clinical evidence
- Reproductive safety
- International recommendations
- Nursing implications

RESULTS

Neonatal Hyperbilirubinemia

Neonatal hyperbilirubinemia is characterized by elevated serum bilirubin concentrations during the neonatal period. It affects nearly **60% of term** infants and **80% of preterm** infants within the first week after birth. Physiological jaundice generally appears after the first 24 hours of life, reaches its peak between the third and fifth day, and resolves spontaneously.

Hyperbilirubinemia results from an imbalance between bilirubin production and elimination. Newborn infants have increased bilirubin production due to rapid breakdown of fatal erythrocytes and reduced hepatic conjugation because of immature glucuronic transferase enzyme activity.

Major risk factors include:

- Prematurity
- Hemolytic disease
- Rh incompatibility
- ABO incompatibility
- G6PD deficiency
- Birth trauma
- Polycythaemia
- Sepsis
- Delayed breastfeeding
- Dehydration

If untreated, excessive bilirubin crosses the immature blood-brain barrier and deposits within the basal ganglia, causing acute bilirubin encephalopathy and kernicterus.

Mechanism of Phototherapy

Phototherapy reduces bilirubin concentration through photochemical reactions occurring within the skin.

Blue-green light (460–490 nm) penetrates the epidermis and converts bilirubin into water-soluble compounds.

Three principal mechanisms are involved:

1. Structural Isomerization

Bilirubin converts into **lumirubin**, which is rapidly excreted through urine and bile.

This is considered the most effective pathway.

2. Configurational Isomerization

Natural bilirubin changes into more soluble photoisomers.

These compounds can be excreted without hepatic conjugation.

3. Photo-oxidation

A smaller fraction of bilirubin undergoes oxidation into colorless metabolites eliminated via the kidneys.

Although less significant therapeutically, photo-oxidation contributes to bilirubin reduction.

Phototherapy effectiveness depends upon:

- Wavelength
- Irradiance
- Distance from light source
- Exposed body surface area
- Duration of treatment

Modern LED phototherapy units provide greater irradiance with reduced heat production and improved energy efficiency compared with fluorescent lamps.

Effects of Phototherapy on Oxidative Stress

Although phototherapy is considered safe, blue light exposure may increase production of reactive oxygen species (ROS).

These include:

- Superoxide radicals
- Hydroxyl radicals
- Hydrogen peroxide

Premature infants are particularly vulnerable because of:

- Immature antioxidant defence systems
- Low vitamin E stores
- Reduced glutathione activity
- Rapid cellular proliferation

Several investigators have measured oxidative stress biomarkers before and after phototherapy.

Reported findings include increased:

- Malondialdehyde (MDA)
- Total oxidant status
- Lipid peroxidation
- and decreased:
- Superoxide dismutase
- Catalase
- Glutathione peroxidase

Fortunately, most biochemical alterations appear temporary and return toward normal after completion of phototherapy.

Experimental Evidence on Genital Organs

Interest regarding genital safety originated from experimental animal studies.

Histopathological Findings

Studies conducted using neonatal rats demonstrated:

- Degeneration of seminiferous tubules
- Mild interstitial edema
- Temporary reduction in germ cell numbers

- Increased apoptosis
- Increased oxidative DNA damage

Some investigators also observed decreased spermatogonia and Sertoli cell alterations following prolonged phototherapy exposure.

Oxidative Damage

- Animal studies consistently demonstrated:
- Increased malondialdehyde concentration
- Decreased antioxidant enzyme activity
- Elevated nitric oxide levels
- Increased lipid peroxidation

These findings suggest oxidative stress as the primary mechanism of tissue injury.

Cellular Recovery

Importantly, many experimental studies reported partial or complete recovery after discontinuation of phototherapy.

This suggests that most microscopic changes may be reversible rather than permanent.

Human Clinical Evidence

Compared with experimental studies, evidence from human newborns remains reassuring.

- Most observational studies have reported
- No abnormalities in genital appearance
- Normal testicular growth
- Normal endocrine function
- No increased incidence of infertility
- No evidence of impaired puberty

Several follow-up studies have found no clinically important reproductive abnormalities during childhood or adolescence.

Current evidence therefore does not support permanent reproductive injury following routine neonatal phototherapy.

Nevertheless, additional long-term prospective studies remain necessary.

Reproductive Safety

Several mechanisms have been proposed to explain the apparent difference between animal and human findings.

These include:

- Lower exposure intensity in clinical practice
- Shorter treatment duration
- Better thermal regulation
- Improved antioxidant defenses
- Routine nursing care
- Modern LED phototherapy devices

The overwhelming majority of experts conclude that the **benefits of preventing kernicterus greatly outweigh theoretical reproductive risks.**

Key Findings

- Phototherapy effectively reduces serum bilirubin concentrations.
- Experimental studies suggest transient oxidative and microscopic changes in testicular tissue after prolonged exposure.
- Human clinical studies have not demonstrated permanent impairment of reproductive function.
- Current evidence supports continued use of phototherapy according to established clinical guidelines.
- Appropriate nursing care and adherence to treatment protocols remain essential to optimize outcomes and minimize theoretical risks.

DISCUSSION

American Academy of Pediatrics (AAP)

The American Academy of Pediatrics (AAP) published updated clinical practice guidelines in 2022 for the management of hyperbilirubinemia in infants born at ≥35 weeks' gestation. The guideline recommends phototherapy as the primary treatment for significant unconjugated hyperbilirubinemia and emphasizes individualized treatment based on gestational age, postnatal age, bilirubin levels, and risk factors for neurotoxicity. Intensive phototherapy with high irradiance and maximum skin exposure is recommended when bilirubin concentrations reach established treatment thresholds. Although the AAP recommends protecting the infant's eyes during treatment, it does not identify phototherapy as a proven cause of long-term reproductive dysfunction. Routine monitoring of hydration, temperature, feeding, urine output, and bilirubin levels is emphasized to ensure safe and effective treatment.

World Health Organization (WHO)

The World Health Organization recommends phototherapy as the first-line treatment for neonatal jaundice, particularly in low and middle-income countries where exchange transfusion may not be readily available. WHO guidelines stress the importance of early diagnosis, appropriate device maintenance, thermal regulation, breastfeeding support, and regular clinical monitoring. Phototherapy should be initiated promptly when treatment thresholds are reached to prevent bilirubin-induced neurological injury. WHO does not identify genital injury as a clinically significant complication of standard phototherapy but encourages adherence to safe neonatal care practices.

National Institute for Health and Care Excellence (NICE)

The NICE guideline on neonatal jaundice recommends intensive phototherapy using LED or fiber-optic devices, with close monitoring of serum bilirubin concentrations and treatment response. Infants should have maximum skin exposure while maintaining eye protection, thermoregulation, and adequate hydration. NICE highlights the importance of minimizing unnecessary interruptions during treatment to improve efficacy. Similar to AAP and WHO, NICE guidelines do not report convincing evidence that phototherapy causes permanent injury to neonatal genital organs or future reproductive dysfunction.

Implications for Nursing Practice

Neonatal nurses play a pivotal role in the safe and effective administration of phototherapy. Beyond operating phototherapy equipment, nurses are responsible for comprehensive assessment, continuous monitoring, prevention of complications, family education, and documentation. Evidence-based nursing interventions are essential to maximize the therapeutic benefits of phototherapy while minimizing potential adverse effects, including the theoretical risk of oxidative stress on sensitive tissues.

Pre-phototherapy Assessment

Before initiating phototherapy, the nurse should conduct a thorough assessment to determine the infant's eligibility for treatment and establish baseline parameters. The following assessments are recommended:

- Confirm the physician's order and verify the indication for phototherapy based on gestational age, postnatal age, and serum bilirubin level.
- Record baseline vital signs, including temperature, heart rate, respiratory rate, and oxygen saturation.
- Assess skin color, extent of jaundice, hydration status, and neurological condition.
- Measure body weight to monitor fluid balance during treatment.
- Review laboratory investigations, including total serum bilirubin, direct bilirubin, blood group, Coombs test (if indicated), hemoglobin, and hematocrit.
- Explain the procedure, benefits, and expected outcomes to the parents to reduce anxiety and encourage cooperation.

Eye and Genital Protection

Protection of sensitive organs is a fundamental nursing responsibility during phototherapy.

- Apply appropriately sized eye shields before initiating treatment and remove them periodically during feeding and bonding to assess the eyes and prevent irritation.
- Follow institutional policy regarding genital shielding. Where practiced, ensure the shield is lightweight, dry, and does not obstruct the treatment area.
- Inspect the skin beneath protective coverings regularly for pressure marks, irritation, or moisture accumulation.
- Reposition the infant every 2–3 hours to maximize skin exposure while preventing pressure-related complications.

Temperature Regulation

Thermal instability is a recognized complication of phototherapy due to increased insensible water loss and environmental exposure.

Nursing interventions include:

- Monitor axillary temperature every 2–4 hours or according to unit protocol.
- Adjust the distance between the phototherapy unit and the infant as

recommended by the manufacturer.

- Avoid overheating by ensuring adequate ventilation around the phototherapy device.
- Use servo-controlled incubators for preterm or low-birth-weight infants when indicated.
- Observe for signs of hyperthermia or hypothermia and intervene promptly.
- Hydration and Feeding

Phototherapy increases insensible water loss, making adequate hydration essential.

Nurses should:

- Encourage frequent breastfeeding (8–12 feeds per day) or appropriate formula feeding.
- Monitor daily weight.
- Assess urine output and stool frequency.
- Observe for signs of dehydration, including dry mucous membranes, poor skin turgor, sunken fontanelle, and reduced urine output.
- Administer intravenous fluids when prescribed for infants unable to maintain adequate oral intake.

Bilirubin Monitoring

Continuous evaluation of treatment effectiveness is essential.

The nurse should:

- Obtain serum bilirubin samples as prescribed.
- Monitor trends rather than isolated values.
- Document the duration and intensity of phototherapy.
- Observe for rebound hyperbilirubinemia after discontinuation of treatment.
- Report inadequate response or rapidly rising bilirubin levels to the neonatologist promptly.

Parent Education

Parental involvement contributes significantly to successful neonatal care.

Education should include:

- Explanation of neonatal jaundice and its causes.
- Purpose and benefits of phototherapy.
- Importance of maintaining eye protection during treatment.
- Need for frequent feeding.
- Expected changes such as loose green stools and increased urine output.
- Signs that require immediate medical attention after discharge.
- Reassurance regarding the overall safety and effectiveness of phototherapy.

Documentation and Quality Improvement

Accurate documentation promotes continuity of care and supports quality assurance initiatives.

Essential documentation includes:

- Time phototherapy was initiated and discontinued.
- Type of phototherapy device used.
- Distance between light source and infant.
- Vital signs and temperature.
- Feeding pattern.
- Urine and stool output.
- Serum bilirubin results.
- Skin assessment findings.
- Parent education provided.
- Any adverse events or interventions.

CONCLUSION

Phototherapy has transformed the management of neonatal hyperbilirubinemia and remains the most effective non-invasive treatment for reducing serum bilirubin concentrations and preventing bilirubin-induced neurological injury. Although experimental animal studies have reported transient oxidative stress and histopathological changes in testicular tissue following prolonged light exposure, current human clinical evidence does not demonstrate permanent adverse effects on genital development, endocrine function, fertility, or long-term reproductive health.

The theoretical biological mechanisms identified in laboratory investigations warrant continued research; however, they should not overshadow the well-established clinical benefits of phototherapy. Modern

LED phototherapy devices, adherence to international guidelines, and comprehensive nursing care contribute significantly to the excellent safety profile of this therapy.

Neonatal nurses are central to ensuring safe phototherapy through careful assessment, eye and (where locally practiced) genital protection, temperature regulation, hydration management, bilirubin monitoring, parent education, and meticulous documentation. Continued professional education and adherence to evidence-based protocols will further enhance treatment outcomes and minimize potential complications.

Future multicentre prospective studies with long-term follow-up are required to clarify any subtle reproductive effects and strengthen the existing evidence base.

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