Phototherapy and the Risk of Photo-Oxidative Injury in Extremely Low Birth Weight Infants

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KEYWORDS

- Bilirubin • Reactive oxygen species • Photosensitivity
- Bilirubin-induced neurologic dysfunction

KEY POINTS

- The safety and efficacy of phototherapy have not been specifically tested as a drug in extremely low birth weight (ELBW) infants.
- The vulnerability of an ELBW infant to light-induced oxidative damage must be considered.
- An infant's hematocrit (Hct) may affect the efficacy of phototherapy, especially in ELBW infants; a lower Hct may allow for more penetration of light.

INTRODUCTION

Phototherapy has been used to treat newborns with jaundice for over half a century with the presumption that it is safe and effective for all infants. In fact, this presumption may not be true for all infants, especially the smallest and most immature. The safety and efficacy of phototherapy have never really been questioned or adequately tested in the latter, yet clinical applications of phototherapy have been further refined as its mechanisms of action have been better understood and alternative light sources have become available. This article addresses what is known about the possible risks of photo-oxidative injury in extremely low birth weight (ELBW) infants.

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PHOTOTHERAPY USE IN EXTREMELY LOW BIRTH WEIGHT INFANTS

Until recently, improvements in the efficacy of phototherapy have been mainly from the practice of increasing the radiant flux emitted by a phototherapy device to an infant's skin surface. This is accomplished by: (1) using a light source that can emit more energy (irradiance, $\mu W/cm^2/nm$) at the wavelengths shown to photodegrade bilirubin; (2) moving a particular light source closer to the baby; or (3) exposing more of an infant's body surface area to the light. Historically, wide-spectrum white light (most commonly emitted by fluorescent tubes) has been used, but unfortunately, infants were being exposed to extraneous light wavelengths, which were ineffective and possibly dangerous. Since the introduction of narrow-band light-emitting diode (LED) light sources, the wavelength applied during phototherapy is optimized to degrade the bilirubin molecule,[1–3] with minimal or no extraneous light. Most LED devices emit blue light in a narrow range ($\pm$10 nm) with a peak emission at approximately 450 nm. Actually, bilirubin has peak absorption around 478 nm and slightly more effective lights (in terms of wavelength emitted) are technically possible.[2] Another factor that can affect efficacy is how much light is available to interact with bilirubin. A molecule, such as hemoglobin, has an absorption spectrum that substantially overlaps with that of bilirubin, and hence can compete with bilirubin for light. Therefore, in infants with lower hematocrits (Hcts), more "light" (at least that which can be absorbed by bilirubin) is available to interact with bilirubin.[4,5]

VULNERABILITY OF EXTREMELY LOW BIRTH WEIGHT INFANTS

All of these preceding observations should be especially considered in the application of phototherapy to ELBW infants, who are immature with limited antioxidant defenses. Notably, the only large, randomized trial of phototherapy involving infants was conducted in the 1970s and reported in 1985 by Brown and colleagues.[6] They reported that phototherapy (at that time typically fluorescent white tubes were used) was shown to reduce the use of exchange transfusion, an important finding that changed clinical practice dramatically. However, the study was insufficiently powered to draw any conclusions about one vexing observation, that is, the risk of death relative to control subjects, especially for the lowest birth weight stratum: relative risk was 1.49 (95% confidence interval, 0.93–2.40) for infants with birth weight less than 1000 g.[6] This was observed even at a time when light sources emitted much lower irradiances and presumably with limited exposure to damaging wavelengths. Nonetheless, the trend toward a higher mortality in the light-exposed preterm infants less than 2500 g was still apparent (relative risk, 1.32; 95% confidence interval, 0.96–1.82).[7] Since then, the dose of phototherapy light has increased with improvements in light source technology, the placement of lights in closer proximity to the infant, or a deliberate effort to increase an infant's exposed body surface area. Also, what has changed over the years is that the infants being treated with phototherapy have become steadily smaller with thinner and more translucent skin. In fact, the overgeneralization of the efficacy and safety of phototherapy to its application in ELBW infants is a prime example of what Silverman had advised avoiding.[8] These smaller infants also have lower Hcts (thus less light-absorbing hemoglobin), allowing more of the light to interact not only with bilirubin, but also with molecules in many other tissues inside the body.[4,5] One of the most worrisome tissues in this regard is the brain, because an infant's head represents a large proportion of the total surface area compared with that of an adult. If one places a flashlight on an ELBW infant's head, the potential vulnerability of the infant is quickly revealed. The recent National Institute