Evidence of link between cancer and light therapy inconclusive but warrants consideration

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Infant undergoing phototherapy for newborn jaundice. Credit: Katherine C. Cohen, Boston Children's Hospital

Two new studies raise enough questions about a possible link between childhood cancer and light therapy for newborn jaundice that clinicians should exercise caution in prescribing the treatment for infants whose jaundice is likely to resolve on its own, a pediatric oncologist from Dana-Farber/Boston Children's Cancer and Blood Disorders Center argues in an editorial published today by the journal *Pediatrics*. The suggestion of a link, however, should not deter use of the treatment, also known as phototherapy, in babies who otherwise would be at risk of brain damage or hearing loss.

Despite the inconclusive findings, the editorial notes that the research represents an important and novel approach using "big data" to begin to discern whether environmental factors may be implicated in the development of pediatric cancer.

Two companion studies, also published today in *Pediatrics*, examined an association between phototherapy and pediatric cancers. The first study, the California Late Impact of Phototherapy Study (CLIPS), analyzed data from five million infants born in California hospitals between 1998 and 2007. The study used administrative data that linked the billing code for phototherapy and the diagnosis code of childhood cancer. The strongest association is a 1.6-fold increased risk of acute myeloid leukemia (AML). The risk of Wilms tumor, a kidney cancer of childhood, also rose to statistical significance. The second study—the Late Impact of Getting Hyperbilirubinemia of photoTherapy (LIGHT) study—analyzed data from 500,000 children born in the Kaiser

Permanente Northern California healthcare system between 1995 and 2011. The associations between phototherapy and childhood cancer were not statistically significant, but an association with AML was again observed.

The studies come at a time when the number of infants receiving phototherapy is increasing, in part, the researchers suggest, because of the availability of light therapy units that can be used in the home. In the Kaiser study, 16 percent of babies received phototherapy in 2011, up from 3 percent in 1995.

In both studies, the associations were stronger and statistically significant among children with Down syndrome. Children with Down syndrome are already known to be at an increased risk of leukemia.

Infant undergoing phototherapy for newborn jaundice. Credit: Katherine C. Cohen, Boston Children's Hospital

"Even though the results are inconclusive, they are worrisome enough that phototherapy should not be presented as risk-free. That being said, however, the brain damage and hearing loss from high bilirubin levels are real and well-documented, and the suggested risk of cancer from these new studies is both unclear and very small," says the editorial's lead author, Lindsay Frazier, MD, of Dana-Farber/Boston Children's. "What is concerning is the fact that, at least in the Kaiser Permanente Northern California healthcare system, the number of children receiving phototherapy has dramatically increased. The risks associated with such a prevalent exposure require close scrutiny."

Even in the CLIPS study, which found a statistically significant association between phototherapy and childhood cancer, the absolute numbers involved were very low. Of the 5 million infants studied, 58 who received phototherapy later developed cancer. The increased risk of AML, for instance, was based on 10 cases among the 178,000 children who received phototherapy, versus 103 cases in the 4.9 million children who did not.

"Studying why children get cancer is very difficult because it is such a rare disease," Frazier says. "The association between smoking and lung cancer was relatively easy to detect because the disease is well over 10 times more common than childhood cancer. There are about 225,000 new cases of lung cancer a year in the United States, versus 15,000 new cases of pediatric cancer. Thus, to study childhood cancer, a scientist needs to find a way to study large populations. The authors are to be commended for finding a way to do just that. But even in these studies

of huge populations, the number of children who actually develop cancer remains quite small."

Despite the small numbers, the editorial advises clinicians to weigh a possible link with cancer in determining which babies need phototherapy.

"In the end, acknowledging that the information is imperfect, general pediatricians and neonatologists must make a choice," the editorial concludes. "These data suggest that phototherapy may not be harmless, and that the risks as well as the benefits need to be weighed before flipping the switch."

Provided by Dana-Farber Cancer Institute