Medical Xpress

Outcomes of prolonged episodes of respiratory disorder among extremely preterm infants

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Among extremely preterm infants, prolonged episodes of hypoxemia (abnormally low levels of oxygen in the blood, which leads to shortness of breath) during the first 2 to 3 months after birth were associated with an increased risk of disability or death at 18 months, according to a study in the August 11 issue of *JAMA*.

Almost all extremely preterm infants (those born at neonatal intensive care unit. The relationship between neonatal hypoxemia or bradycardia and later neurodevelopment in this population of high-risk preterm infants is uncertain, according to background information in the article.

Christian F. Poets, M.D., of Tuebingen University Hospital, Tuebingen, Germany, and colleagues examined the association between intermittent hypoxemia or bradycardia and death or disability. The study included 1,019 infants with gestational ages of 23 weeks 0 days through 27 weeks 6 days who were born between December 2006 and August 2010 and survived to a postmenstrual age of 36 weeks. Follow-up assessments occurred between October 2008 and August 2012. The researchers used data from infants who were part of the Canadian Oxygen Trial (25 hospitals in Canada, the United States, Argentina, Finland, Germany, and Israel).

Average percentages of recorded time with hypoxemia for the least and most affected 10 percent of infants were 0.4 percent and 13.5 percent, respectively. Corresponding values for bradycardia were 0.1 percent and 0.3 percent. The primary outcome (a composite of death after 36 weeks' postmenstrual age, motor impairment, cognitive or language delay, severe hearing loss, or blindness at 18 months) was ascertained for 972 infants and present in 414 (43 percent). Hypoxemic episodes were associated with an estimated increased risk of late death or disability at 18 months of 56.5 percent in the highest decile (one of 10 groups) of hypoxemic exposure vs 37 percent in the lowest decile. This association was significant only for prolonged hypoxemic episodes lasting at least 1 minute.

Relative risks for all secondary outcomes (motor impairment, cognitive or language delay, and severe retinopathy of prematurity [a disorder of the retina]) were similarly increased after prolonged hypoxemia.

"If these observations are confirmed in future studies, further research on the prevention of such episodes will be needed," the authors write.

The researchers note that intermittent bradycardia did not significantly add to the risk of adverse outcomes, suggesting that bradycardia in the absence of concurrent hypoxemia may not be of prognostic importance. In addition, the severity of intermittent hypoxemia added little prognostic value to the simpler measure of the percentage of time spent with hypoxemia.

The authors add that should the observation be confirmed in future research that episodes of hypoxemia lasting less than 1 minute are not associated with adverse outcomes in extremely preterm infants, this would be important information for both clinicians and parents.

"If hypoxemia is proven to cause adverse neurodevelopment, any future interventions to reduce prolonged hypoxemic episodes, such as doxapram [a respiratory stimulant] or higher doses of caffeine, as suggested by Poets et al, must be evaluated in rigorous randomized clinical trials to minimize exposure to therapies that are useless or even harmful," writes Lex W. Doyle, M.D., of the University of Melbourne, Parkville, Victoria, Australia, in an accompanying editorial.

"Such trials should have long-term developmental outcome as the primary end point, rather than short-term end points, such as a reduction in the number or duration of hypoxemic episodes. Neonatal intensive care is littered with examples of treatments that were introduced based on observational data or even no data, only to be proven to be disastrous when tested properly in randomized clinical trials. In the meantime, other treatments known from randomized clinical trials to improve long-term neurodevelopmental outcome for extremely preterm infants, such as magnesium sulfate before birth, regular doses of caffeine, or developmental care interventions after discharge, should be maximized."

More information: *JAMA*, DOI: 10.1001/jama.2015.8841
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