Medical Xpress

Hydrocortisone effects on neurodevelopment for extremely low birthweight infants

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Hydrocortisone is one of the 15 most frequently prescribed medications in extremely low birth weight (?1000 g) infants in the newborn intensive care unit (NICU).

Despite widespread use, the effects on neurodevelopmental outcomes of stress doses of hydrocortisone or of dosing after 1 week of age have not been assessed in randomized trials. Additionally, the benefit of giving hydrocortisone in relation to infant risk of developing bronchopulmonary dysplasia (BPD) is not well documented.

"Despite advances in perinatal care, one of every two extremely low birth weight infants develops bronchopulmonary dysplasia and/or neurodevelopmental impairments," says Nehal Parikh, DO, principal investigator in the Center for Perinatal Research at The Research Institute at Nationwide Children's Hospital. "We've been using hydrocortisone in these patients without randomized, placebo-controlled studies."

BPD is characterized by systemic inflammation, pointing toward a potential link among BPD, abnormal brain development and neurodevelopment. The idea that an anti-inflammatory medication, such as hydrocortisone, could offer benefits in all of these areas has taken hold without necessarily having data to support it.

In a new study recently published in *PLoS ONE*, Dr. Parikh and colleagues assess the long- and short-term effects of stress doses of

hydrocortisone after 1 week of age via randomized, double-blind, placebo-controlled trial. Extremely low birth weight, ventilator-dependent infants between 10 and 21 days old were administered a seven-day taper of hydrocortisone or a saline placebo while being treated at Children's Memorial Hermann Hospital in Texas. The study period ended with neurodevelopmental checks in the 18 to 22 month corrected age period.

"Unlike dexamethasone, higher/stress dose hydrocortisone does not appear to be associated with brain injury or neurodevelopmental impairments," Dr. Parikh says.

The team found no evidence that the doses of hydrocortisone used in the study prevented BPD, but Parikh suggests even though lower doses of hydrocortisone do not appear to benefit the lungs, they may improve cognitive outcomes.

"Hydrocortisone as prescribed in our trial did not reduce the risk of BPD when compared to placebo, possibly because we used anti-inflammatory doses that were not sufficiently high and/or the enrolled population of extremely preterm infants was too sick," Dr. Parikh says.

As a result of this work, Dr. Parikh suggests neonatologists be more liberal with the use of stress dose hydrocortisone for relative adrenal insufficiency in extremely preterm infants (a common condition that can result in refractory hypotension) as the current data do not indicate adverse effects on neurodevelopment.

In follow-up work, Dr. Parikh and his team at Nationwide Children's are examining the relationship between hydrocortisone and risk of a common inflammatory brain abnormality - diffuse excessive high signal intensity (DEHSI) - which occurs in up to 75 percent of extremely preterm infants.

"Data from our pilot trial suggests a trend towards reduced cognitive deficits in hydrocortisone treated preterm infants," says Dr. Parikh. "Our initial study may have lacked sufficient power to show a significant difference. However, we have shown that increasing DEHSI volume is a significant predictor of lower cognitive score. Thus, examining a short term surrogate measure of cognitive outcomes, such as DEHSI, may reveal that stress dose hydrocortisone reduces risk of DEHSI and may indeed improve neurodevelopmental outcomes if tested in a larger trial."

More information: Parikh NA, Kennedy KA, Lasky RE, Tyson JE. Neurodevelopmental outcomes of extremely preterm infants randomized to stress dose hydrocortisone. *PLoS ONE*. 2015 Sep 16;10(9):e0137051

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