Steroid treatment offers no benefit in preemies, study suggests

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Results of a multicenter study led by Johns Hopkins Children's Center challenge the longstanding practice of treating premature babies with hydrocortisone, a steroid believed to fight inflammation and prevent lung disease. The researchers found that such treatment offers little or no benefit and that low cortisol levels are not even necessarily harmful. High cortisol levels, on the other hand, appeared to increase the risk of dangerous bleeding in the brain and require that babies be monitored aggressively to ward off life-threatening complications, according to the study published in the October issue of *Pediatrics*.

Premature babies and adults with a condition known as relative adrenal insufficiency have abnormally low levels of the stress hormone cortisol. The standard treatment for this condition in newborns has been hydrocortisone therapy. These findings, however, shed new light on the clinical meaning of low cortisol levels in preemies, showing that contrary to common belief, low blood concentrations of this hormone do not put extremely low-birth-weight babies (those born weighing less than 2.2 pounds) at higher risk for retinopathy of prematurity — a potentially blinding eye condition — inflammation and lung disease.

Researchers also found no difference in health outcomes between babies with low cortisol levels who were treated with hydrocortisone and those given a placebo. While hydrocortisone had no adverse effects on a baby's health, it also did nothing to prevent or reduce respiratory diseases, infections, hemorrhages or retinopathy.

"We were intrigued and somewhat surprised, but contrary to what we expected, low cortisol levels do not appear to be dangerous and may actually be the norm in premature babies," said study lead investigator Susan Aucott, M.D., a neonatologist at Hopkins Children's. "What this means is we should really think twice before rushing to treatment with hydrocortisone in our effort to 'correct' these low levels."

While surprising, the findings are not entirely counterintuitive, investigators say, because in utero babies have naturally low cortisol levels. "This may mean that, in a way, low cortisol levels are normal, and premature babies maintain them low, as they would have been in the womb," Aucott said.

Comparing the cortisol levels of 311 extremely low-birth-weight preemies immediately after birth and one week after birth, researchers found low cortisol levels did not increase the risk for adverse short-term outcomes or death. For example, bronchopulmonary dysplasia occurred in 58 percent of infants with low cortisol levels, in 58 percent of infants with midrange cortisol levels and in 62 percent of those with moderately elevated cortisol levels. Brain hemorrhages occurred in 24 percent of infants with low cortisol levels, in 36 percent of those with midrange cortisol levels and in 49 percent of those with mildly elevated cortisol levels.

Babies with moderately to severely elevated cortisol levels at birth and shortly after birth had a higher risk for life-threatening brain bleeds, dangerous gastrointestinal perforations and severe retinopathy, researchers found. Researchers have yet to pinpoint the exact mechanism leading to these dangerous spikes in cortisol, but past studies have suggested that severe pain may drive up production of this stress hormone. Regardless of the trigger, investigators say, neonatologists should aggressively monitor infants with elevated cortisol levels because of their vulnerability to hemorrhages and other life-threatening complications.

Elevated cortisol concentrations, especially values higher than 31 micrograms per deciliter of blood at 12 to 48 hours after birth, and more than 18 micrograms per deciliter at five to seven days after birth, appeared to make babies more prone to serious bleeding in the brain, although researchers

caution a cause-effect relationship could not be established from this study because elevated cortisol concentration could be a consequence of the hemorrhage but not necessarily a trigger of it. Very high cortisol levels, above 62 micrograms per deciliter, appeared to heighten a baby's risk for severe brain hemorrhages, gastrointestinal perforation and death. For example, death occurred in 12 percent of infants who had low cortisol levels 48 hours after birth and in 13 percent of infants with midrange levels of cortisol, but in nearly 30 percent of infants with severely elevated cortisol levels at 48 hours of birth. Gastrointestinal bleeds occurred in 3 percent of infants with low cortisol levels at 48 hours of birth, in 9 percent of infants with cortisol levels in the mid-range, but in 24 percent of those with significantly elevated cortisol levels.

Source: Johns Hopkins Medical Institutions