Behavioral disorders more common in children exposed to maternal antenatal corticosteroids

May 20 2020

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Maternal antenatal corticosteroid treatment is standard care when there is a risk for preterm delivery. The treatment improves the prognosis of

babies born preterm. However, a new study conducted by experts from the University of Helsinki, University of Oulu and THL Finnish Institute for Health and Welfare shows that children exposed to maternal antenatal corticosteroid treatment have higher rates of emotional, behavioral and psychological development disorders than nonexposed children.

The difference in the rates of these disorders was most evident in children born at term after maternal antenatal corticosteroid treatment exposure, as reported in the study published in *JAMA*. Of the term-born children who were exposed to this maternal treatment, 8.9% had been diagnosed with an emotional, behavioral or psychological development disorder. Of the nonexposed term-born children, the rate was 6.3%.

In high-income countries, antenatal corticosteroid treatment has been in routine use for over 30 years. Recommendations and clinical care guidelines for maternal antenatal corticosteroid treatment differ between continents and countries. In Finland the treatment is currently recommended when the risk for preterm delivery is at 34 gestational weeks or less. In select cases, the treatment is recommended even later in gestation. Corticosteroids accelerate fetal maturation, especially in the lungs, and increase the child's resilience to the stress that results from being born preterm.

The population-based register study used records from the Finnish Medical Birth Register and the Care Register for Health Care. The registers are kept at the THL Finnish Institute for Health and Welfare, which is the statutory statistical authority for social and healthcare data in Finland. The researchers followed up with over 670 000 singleton children born between 2006 and 2017. Of the pregnant mothers, 2.2% were treated with corticosteroids when preterm birth was imminent.

Maternal corticosteroid treatment is an effective

treatment—but the long-term benefits and harms should still be weighed

The researchers emphasize that maternal corticosteroid treatment is an effective treatment and can be life-saving for babies who are born extremely or very preterm. However, in recent years, there has been considerable debate on whether to expand the treatment indications beyond 34 gestational weeks. In Finland, this treatment is recommended, for instance, in the case of elective caesarean section, until 36 gestational weeks. Gestational week 36 refers to a pregnancy that has lasted for 36 weeks and six days.

"This is an observational study, and the results do not prove that antenatal corticosteroids are the cause of the increased risks found in the study. However, we conclude that it is important to weigh the balance between the long-term benefits and harms, in particular when considering whether to expand the treatment indications to later gestational weeks. The prognosis of babies who are born preterm at later gestational weeks is very good in high-income countries," says Professor Eero Kajantie from the University of Oulu and THL Finnish Institute for Health and Welfare.

"Of the mothers who were treated with antenatal corticosteroids, 45% went on to deliver a term baby. This means that prediction of preterm birth is often very difficult," he adds.

Finding not explained by genes, smoking or other factors

The study took into account a number of factors that increase the risk of preterm birth, including maternal pregnancy disorders and smoking during pregnancy. The study also compared term-born maternal sibling

pairs, of which one sibling was exposed to maternal antenatal corticosteroid treatment and the other sibling was not.

Also in these sibling comparisons, the treatment-exposed children had higher rates of emotional, behavioral and psychological development disorders, suggesting that shared genetic or familial factors do not explain these associations.

In term-born children, the findings could not be attributed to a single, specific disorder. However, in preterm children whose mothers had received corticosteroid treatment, the rate of mild intellectual disability was lower than in preterm children whose mothers had not received the treatment. This finding is in line with those showing that maternal antenatal corticosteroid treatment improves the prognosis of the children born preterm.

"Even though experimental studies in animals have shown that antenatal corticosteroid treatment has harmful effects on the neurodevelopment of the offspring, population-based cohort studies, like ours, cannot verify if any of the harmful effects on child disorders are accounted for by maternal corticosteroid treatment or if some other factor explains these associations. We tested for several candidates, but none of these factors explained the associations," says Professor Katri Raikkonen from the University of Helsinki.

More information: Katri Räikkönen et al. Associations Between Maternal Antenatal Corticosteroid Treatment and Mental and Behavioral Disorders in Children, *JAMA* (2020). DOI: 10.1001/jama.2020.3937

Provided by University of Helsinki