Opioids during pregnancy not linked to substantially increased risk of psychiatric disorders in children

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Opioid use during pregnancy is not associated with a substantial increase in the risk of neuropsychiatric disorders such as ADHD in children, finds a large study from South Korea published by The BMJ today.

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A slightly increased risk of neuropsychiatric disorders was found, but the researchers say this should not be considered clinically meaningful because it was limited to mothers exposed to more than one opioid prescription, high doses, and over longer time periods during pregnancy.

According to 2019 data from the Centers for Disease Control and Prevention, around 7% of women in the United States were prescribed opioids during pregnancy.

Previous studies have shown mixed findings on the association between opioid use in pregnancy and various health outcomes in offspring due to small sample sizes and short follow-up periods.

To address this knowledge gap, an international team of researchers set out to investigate the potential association between opioid exposure during pregnancy and risk of neuropsychiatric disorders in offspring. Their findings are based on data from the National Health Insurance Service (NHIS) of South Korea for 3,128,571 infants born between 2010 and 2017 and 2,299,664 mothers (average age 32).

Mothers were grouped according to dose, duration, and frequency of opioid prescriptions during pregnancy and infants were followed up for an average of six years.

Factors including mother's age at delivery, household income and pre-existing health conditions, and infant sex, birth weight and breastfeeding history were taken into account. A sibling comparison analysis was also carried out to account for genetics, lifestyle, and environmental influences.

Overall, 216,012 (7%) of the 3,128,571 infants were exposed to opioids during pregnancy (prenatal exposure).
A small increased risk of neuropsychiatric disorders was found among children exposed to prescription opioids during pregnancy compared with those not exposed, but the researchers interpret this as clinically insignificant. And no significant association was noted in the sibling comparison group.

However, exposure to prescription opioids during the first trimester of pregnancy, at higher doses, and for 60 days or more were associated with a slightly increased risk of mood disorders, ADHD, and intellectual disability.

This is an observational study so no firm conclusions can be drawn about cause and effect, and although the researchers adjusted for a range of factors, they can't rule out the possibility that others may have influenced their results, or that some misclassification of opioid use may have occurred.

Nevertheless, this was a large study based on high quality data and several statistical analyses were carried out to test the strength of the results, providing greater confidence in the conclusions.

As such, they conclude, "These results support cautious opioid prescribing for relief of pain during pregnancy, highlighting the importance of further research for more definitive guidelines."

In a linked editorial, researchers agree that while short term use of lower dose prescription opioids after the first trimester appears relatively safe, caution is warranted when prescribing opioids for longer durations or at higher dosages.

This study "provides additional evidence to inform clinical decision making for women requiring pain management during pregnancy," they write.
"Given the unique clinical value of opioids for managing severe pain, additional research is needed to fully characterize the degree of risk and thoroughly disentangle the association among pain, pain management, and various pregnancy outcomes," they conclude.


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