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Association of Acetaminophen Use During Pregnancy With Behavioral Problems in Childhood

Evidence Against Confounding

ONLINE FIRST

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ABSTRACT

ABSTRACT | INTRODUCTION | METHODS | RESULTS | DISCUSSION | CONCLUSIONS | ARTICLE INFORMATION | REFERENCES

Importance

Acetaminophen (paracetamol) is used by a large proportion of pregnant women. Research suggests that acetaminophen use in pregnancy is associated with abnormal fetal neurodevelopment. However, it is possible that this association might be confounded by unmeasured behavioral factors linked to acetaminophen use.

Objective

To examine associations between offspring behavioral problems and (1) maternal prenatal acetaminophen use, (2) maternal postnatal acetaminophen use, and (3) partner's acetaminophen use.

Design, Setting, and Participants

From February 2015 to March 2016, we collected and analyzed data from the Avon Longitudinal Study of Parents and Children (ALSPAC), a prospective birth cohort. We studied 7796 mothers enrolled in ALSPAC between 1991 and 1992 along with their children and partners.

Exposures

Acetaminophen use was assessed by questionnaire completion at 18 and 32 weeks of pregnancy and when the child was 61 months old.


Main Outcomes and Measures


Maternal reports of behavioral problems using the Strengths and Difficulties Questionnaire (SDQ) when the children were 7 years old. We estimated risk ratios for behavioral problems in children after prenatal, postnatal, and partner's exposure to acetaminophen and mutually adjusted each association.


Results


Maternal prenatal acetaminophen use at 18 (n = 4415; 53%) and 32 weeks of pregnancy (n =


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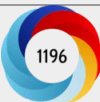
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3381; 42%) was associated with higher odds of having conduct problems (risk ratio [RR], 1.42; 95% CI, 1.25-1.62) and hyperactivity symptoms (RR, 1.31; 95% CI, 1.16-1.49), while maternal acetaminophen use at 32 weeks was also associated with higher odds of having emotional symptoms (RR, 1.29; 95% CI, 1.09-1.53) and total difficulties (RR, 1.46; 95% CI, 1.21-1.77). This was not the case for maternal postnatal (n = 6916; 89%) or partner's (n = 3454; 84%) acetaminophen use. We found the associations between maternal prenatal acetaminophen use and all the SDQ domains unchanged even after adjusting for maternal postnatal or partner's acetaminophen use.

**Conclusions and Relevance** Children exposed to acetaminophen prenatally are at increased risk of multiple behavioral difficulties, and the associations do not appear to be explained by unmeasured behavioral or social factors linked to acetaminophen use insofar as they are not observed for postnatal or partner's acetaminophen use. Although these results could have implications for public health advice, further studies are required to replicate the findings and to understand mechanisms.

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