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Victoria W Persky

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Acetaminophen and Asthma

Victoria W Persky

The article by Perzanowski et al in this issue of Thorax (see page 118) adds one more piece of evidence supporting a possible role for acetaminophen in the development of asthma in children. Five previous studies, including three prenatal prospective cohorts, have suggested that in utero ingestion of acetaminophen may increase the risk of asthma and respiratory symptoms in children. Increased risk of asthma from postnatal use of acetaminophen is also suggested by reports of children and adults that associations of prenatal acetaminophen use with asthma are present only in smaller cohorts with sufficient numbers of participants similar effects were not seen with the other analgesics, and a randomized trial in children with asthma found significantly lower risk of outpatient visits for asthma in those randomized to ibuprofen versus acetaminophen.

The lack of consistency among studies regarding timing of use in pregnancy has implications for biological plausibility. The current study found similar associations throughout pregnancy that were not significant in the first trimester. Two of the three previous prospective cohorts noted stronger effects towards the end of the pregnancy while the large Danish cohort noted stronger effects with use earlier in gestation. It has been suggested that the fetal liver is not able to metabolize acetaminophen early in pregnancy. Effects from use in the first trimester would therefore imply other mechanisms related to GSTP1 genotypes.

Loss to follow-up and the fact that the relationships reached significance only in year 5 in this study is of some concern. In other cohorts the effects were seen at younger ages. The follow-up of this cohort is 69% suggested—301 of the original 714—and there could be biases inherent in the drop-out rate. Reassuring is the fact that there were no differences in reported acetaminophen use in those who did and did not remain in the study. The authors indicate, however, that follow-up was greater among Hispanics—there could have been other factors related to acetaminophen use, follow-up and diagnosis of asthma, such as differential prenatal and postnatal care, that could have affected the results. Imprecise measures of dose and frequency could also account for some of the differences among studies. The study of Perzanowski et al found a significant dose response with days of use. Increased frequency had stronger associations in one, but not another, study in which frequency of use was available. Data on medication use in all these studies, however, were not obtained by diaries and do not allow careful quantification of use. The lack of precision, however, should bias towards the null hypothesis, and, while contributing to differences among studies, could not account for the general consistency in overall results.

As is often the case, this paper in the context of emerging literature raises as many questions as it answers. If the effects seen are related to modulation of antioxidant defences can they be reversed, as shown by Romieu’s group, with adequate nutrition? Are we comfortable changing our current recommendations of use of
anti-inflammatory medication? It was estimated that in 2004, 65% of women took acetaminophen in pregnancy, with 18% taking ibuprofen and 4% taking aspirin. A shift from acetaminophen to ibuprofen might have other associated risks. Can we justify a randomised controlled trial of acetaminophen versus other anti-inflammatory with and without antioxidant supplementation? Would a safer course perhaps be increased efforts at pollution control and continued recommendations to limit all medication in pregnancy? Finally, it is important to continue research in the area with animal models and more precise measures of the amount and timing of exposure, possible confounding associated symptoms, and benefit versus risk assessments of alternative approaches. Competing interests None. Provenance and peer review Commissioned; not externally peer reviewed.


REFERENCES