



Do asthma medications cause birth defects?

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Asthma is a commonly encountered medical condition during pregnancy. First-line agents used during pregnancy include inhaled corticosteroids for patients with significant symptoms and β -agonists for those with acute exacerbations. Given the frequency with which these medications are used during pregnancy, population-based data supporting fetal safety are of significant value both to providers and patients. For some conditions, such as seizure disorders and autoimmune diseases, small but significant risks of teratogenesis from medical management must be weighed against the risks of worsening disease in the setting of suboptimal treatment. However, for medical conditions where treatment safety for the fetus is well established, optimal management often improves outcomes for both the mother and the pregnancy.

The results of the study by Garne et al. (DOI: 10.1111/1471-0528.14026) add significantly to the current literature on asthma medication use during pregnancy. Although the authors found a small adjusted increased risk for congenital

anomalies associated with medication use, their interpretation of these results is appropriately cautious. Whenever an association between a specific medication and congenital anomalies is discovered on a population basis, a number of possible causal relationships must be considered. Foremost is whether the underlying disease process or factors associated with it, and not the treatment, are responsible for the finding. For example, the best evidence supports that it is diabetes mellitus, and not treatment with insulin, that is responsible for the increased risk for congenital anomalies. With asthma, as the authors point out, there are many plausible environmental exposures that could increase both risk for the disease and the risk for birth defects. Alternatively, physiological changes associated with asthma could be directly responsible for the increased risk.

The study by Huybrechts et al. (*N Engl J Med* 2014;370:2397–407) evaluating antidepressant use during pregnancy and congenital cardiac defects is an excellent example of

how the relationship between drug exposure and congenital anomalies can be untangled. Although the authors found increased risk for cardiac anomalies with medication exposure, that risk was attenuated by controlling for depression, and, following a propensity-score analysis, no increased risk was found.

Despite the impressive analysis by Garne et al., the potential for residual confounding, as well as unmeasured confounding, remains. Although a propensity score methodology is helpful to address observed confounding, latent (or instrumental) variable analysis, and sensitivity analyses are powerful methods to address unmeasured confounding. A second issue for consideration is choosing an appropriate effect measure. Population-based cohort studies permit estimation of true risks, and by extension, relative risks (or risk/rate ratios), instead of an approximation—odds ratio (see Spiegelman and Hertzmark *Am J Epidemiol* 2005;162:199–200).

In summary, this analysis by Garne et al. adds important evidence to the research literature on the

safety of asthma treatment during pregnancy. The small increased risk that the authors found demonstrates the general safety of these medications, and represents an excellent starting point for further methodological analysis to determine the relationship between asthma,

asthma-related exposures, medication use and congenital anomalies.

Disclosure of interest

None declared. Completed disclosure of interests form available to view online as supporting information.

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