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In Utero Exposure to Antihypertensive Medication During Pregnancy and Neonatal and Child Health Outcomes

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Background

Although pharmacotherapy is to be avoided wherever possible during pregnancy, aggressive pharmacotherapy is required for the treatment of pregnancy associated hypertension, which remains a leading cause of morbidity and mortality in the UK. While the teratogenic effects of angiotensin-converting enzyme inhibitors are well documented, the possible long term effects, on the child, following in utero exposure to other antihypertensive agents remains unknown.

Approach

The aim of this study was to systematically review all published literature relevant to possible adverse outcomes on the child associated with in utero exposure to antihypertensive medications. OVID (Medline, Embase), Scopus, EBSCO Collections (PsycINFO, CINAHL), The Cochrane Library and Web of Science databases were searched from January 1950 to January 2016 and a total of 688 papers were identified. Following review 43 primary studies and 4 Meta-analyses were eligible for inclusion. The Critical Appraisal Skills Programme (CASP) checklists were used to assess study quality.

Results

Three studies were of excellent quality the remainder were either mediocre or poor. Increased risk of low birth weight, low size for gestational age, preterm birth and congenital defects following in utero exposure to all antihypertensive agents were identified. The clinical importance of these reported risks is unclear, as many study findings were based on small case numbers. Four studies of mediocre quality reported on the relationship between in utero exposure and neurological adverse effects in offspring.

Two studies reported an increased risk of attention deficit hyperactivity disorder following exposure to labetalol, and an increased risk of sleep disorders following exposure to methyldopa and clonidine. The remaining two studies identified no such associations.

Conclusion

This systematic review demonstrates a lack of published high quality studies. Available published studies indicate an increased risk of adverse child health outcomes, although it is unclear whether these outcomes are clinically significant. This review is the first step in a larger project, which is exploring child health outcomes in Scotland following in utero exposure to antihypertensive and psychotropic medications. Dispensed drug data will be used to identify mothers who have been prescribed antihypertensive or psychotropic medication during pregnancy. National databases (PIS, SMR02, SMR01, etc.) will be used to cross-link mother and child data to identify in utero exposure to the drugs of interest, and the resulting child outcomes. All aspects of child health outcomes will be assessed to identify possible adverse effects from in utero exposure to medications.

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