AETIOLOGY

Atypical antipsychotic use during the first trimester of pregnancy may not increase major malformations


Q Do antipsychotics negatively affect birth outcomes if taken during pregnancy?

METHODS

- Design: Prospective cohort study.
- Follow up period: Until birth.
- Setting: Three drug safety monitoring and advice services (Motherisk Program, Canada; Israeli Teratogen Information Service, Jerusalem, Israel; Drug Safety Research Unit, UK); time period not specified.
- People: 151 pregnant women who took atypical antipsychotics in their first trimester (olanzapine n = 60; risperidone n = 49; quetiapine n = 36; clozapine n = 6). 151 age and gestational stage matched pregnant women not exposed to antipsychotics (controls). Controls were recruited when they contacted the Canadian centre for advice on exposure to non-teratogenic agents.
- Risk factors: Taking atypical antipsychotics during the first trimester of pregnancy.
- Outcomes: Major malformations in babies; spontaneous or therapeutic abortion; birth weight; premature births (<37 weeks gestation).

MAIN RESULTS

More women exposed to antipsychotics elected to have abortions than unexposed women (9.9% exposed v 1.3% unexposed, p = 0.003). The rate of spontaneous abortion was higher in exposed women, but not significantly (14.5% exposed v 8.6% unexposed; p reported as not significant). There was no significant difference in numbers of premature births between groups (13% exposed v 8% unexposed), mean birth weight (3341 g exposed v 3411 g unexposed, p = 0.38), or major malformations (0.9% exposed v 1.3% unexposed, p = 1.0). More babies were low birth weight (not further defined) in the exposed group (10% exposed v 2% unexposed; p = 0.05).

CONCLUSIONS

Taking atypical antipsychotics in the first trimester of pregnancy does not seem to be associated with an increased likelihood of major malformations or premature birth, although there is some evidence to suggest that it may reduce birth weight. More studies are needed to confirm these findings.

NOTES

The duration and dosage of atypical antipsychotic usage was not reported. Women who had taken antipsychotics were significantly more likely to have had an unplanned pregnancy (p<0.001), to not have taken vitamins during pregnancy (p = 0.005), to have smoked during pregnancy (p<0.001), to have a higher pre-pregnancy body mass index (p<0.001), to have a lower level of education (p<0.001), and to be unemployed (p<0.001). Some women taking atypical antipsychotics also took a conventional antipsychotic (16%), an antidepressant (57%), a benzodiazepine (34%), lithium (6%), or an antiepileptic (17%). None of the babies exposed to antiepileptics, benzodiazepines, or lithium had major malformations. The study only had 80% power to detect a fourfold increase in major malformations.

Commentary

It is now recognised that the majority of women with psychotic disorders have children. Atypical drugs such as clozapine and olanzapine, which do not cause hyperprolactinaemia may increase fertility rates. GPs, obstetricians, and psychiatrists are therefore increasingly faced with difficult decisions as to whether to treat women with psychotic disorders with antipsychotic medication during pregnancy. If they do not, their patients may experience a relapse, leading to poorer interaction between mother and infant, but the impact of antipsychotic medication on a fetus is also unclear as no randomised controlled trials have evaluated the use of atypical antipsychotics or neuroleptics in pregnancy.

This study tries to address this important question by examining data from three different sources including a counselling service in Canada for pregnant women who are prescribed atypical antipsychotics. The study population is therefore not a representative sample of women with psychotic disorders and the controls are obtained from different populations than the cases leading to further selection bias. A lot of the data were obtained from GPs including obstetric data and prescriptions of atypical antipsychotics, although both come from secondary care, which means the data are not reliable. However, the major methodological flaw is the lack of power to detect differences in pregnancy outcome; although there were no significant differences between cases and controls, the sample size had only an 80% power to detect a fourfold increase in the rates of major malformation with an α of 0.05.

This study therefore cannot provide definitive data regarding the teratogenic potential of these drugs. More studies are needed, using a prospective methodology with larger sample sizes but without the selection bias of this study. Finally, although teratogenicity is important, longer term implications of these drugs are also relevant and studies are needed that investigate the neurobehavioural effects of these drugs on the exposed offspring.

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*Evid Based Mental Health* 2005 8: 115
doi: 10.1136/ebmh.8.4.115

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