Antipsychotic drugs in pregnancy and breastfeeding

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Summary

There are limited data on the safety of antipsychotic drugs in pregnancy and breastfeeding. Reports of congenital abnormalities in the babies of women taking typical antipsychotics are uncommon, although chlorpromazine may cause symptoms in the neonate. No increased risk with atypical antipsychotics has yet emerged. If women can be managed with a low dose of a single antipsychotic drug the benefits of breastfeeding are likely to outweigh the risk of harmful effects.

Key words: chlorpromazine, olanzapine.

(Aust Prescr 2007;30:162–3)

Introduction

The lifetime prevalence of schizophrenia is 0.5–1%. The peak incidence in women is during their childbearing years, but treatment can reduce fertility. The older antipsychotic drugs increase prolactin, resulting in significantly lower fertility rates than with the atypical antipsychotic drugs. The newer antipsychotics are also being used increasingly to treat other psychiatric disorders such as major depression and bipolar disorder. Many women with well-controlled psychiatric disease are therefore now able to contemplate pregnancy, but they have concerns about the effect of treatment on their offspring. Addressing these concerns is difficult because of a lack of data.

Typical antipsychotic drugs

Studies examining the use of the older antipsychotic drugs in pregnancy have not shown a significantly increased risk of birth defects above the baseline rate of 3% in the general population.[1] There have been reports of two infants exposed to haloperidol with isolated limb defects, but they were also exposed to other drugs and thus there is no clear causal relationship with haloperidol. In contrast, there have been several larger studies which have not shown an increased risk of birth defects. Babies exposed to haloperidol and chlorpromazine *in utero* may show extrapyramidal abnormalities, similar to those seen in adults, for weeks after birth. Other suspected withdrawal symptoms following intrauterine exposure to chlorpromazine have included paralytic ileus, necrotising enterocolitis, fever, cyanotic spells and transient heart block.

Long-term follow-up studies of children have been reassuring. While these drugs probably still have their place in the treatment of acutely psychotic patients, they have largely been superseded by the atypical antipsychotics for long-term therapy.[2,3]

Flupenthixol and the depot preparation zuclopenthixol are thioxanthene major tranquillisers. There are minimal human data apart from some case reports of normal outcomes following use in pregnancy. Like the older antipsychotic drugs they have been shown to affect fertility via dopamine and prolactin pathways.

Lactation

Chlorpromazine and haloperidol are excreted in human milk in small amounts. In one report, three breastfed infants exposed to haloperidol and chlorpromazine showed developmental regression which was not seen in infants exposed to trifluoperazine alone, suggesting that use of a single antipsychotic drug poses less of a risk to a breastfed infant. No adverse effects were reported in four infants exposed to flupenthixol via breast milk.

Atypical antipsychotic drugs

One study followed up over 150 cases of exposure to atypical antipsychotic drugs (olanzapine, risperidone, quetiapine and clozapine) in the first trimester of pregnancy. There were no differences in any of the pregnancy outcomes of interest, apart from low birth weight, which could not be explained by the study's authors. The rate of malformations in the exposed group was no greater than in the control group.[4]

Animal studies have not shown an increased risk of malformations with clozapine. Although human pregnancy data are relatively limited, there does not appear to be a significant increase in the incidence of birth defects or other adverse outcomes. There is one case report of a child with possible delayed speech acquisition following clozapine use during pregnancy and lactation.[5] No other long-term neurodevelopmental follow-up data are available.

Concerns have been raised that olanzapine in particular tends to be associated with significant weight gain. During pregnancy this could be associated with an increased incidence

of outcomes, including increased rates for birth defects such as neural tube defects and an increased risk of obstetric complications. Theoretical concerns about a relative folate deficiency have prompted some experts to suggest that women planning pregnancy while taking olanzapine should take 5 mg folate rather than the usual 0.5 mg to try and reduce the risk of neurodevelopmental disabilities.[6]

Lactation

Limited information shows that maternal doses of olanzapine up to 20 mg/day produce low levels in milk and undetectable levels in breastfed infants. Generally, short-term adverse effects have not occurred, and sedation has not been reported. Limited long-term follow-up of infants exposed to olanzapine has been reassuring, particularly with monotherapy.

Conclusion

The potentially harmful effects of taking an antipsychotic drug in pregnancy have to be balanced against the harm of untreated psychotic illness. Data are limited, particularly for the atypical antipsychotic drugs, but there are no clear associations with specific congenital abnormalities.

The benefits of breastfeeding are likely to outweigh the potential harm of medication. Women who wish to breastfeed should be managed with a single antipsychotic drug if possible. All antipsychotic drugs are sedating and have relatively long half-lives, so babies should be observed for lethargy, sedation and appropriate developmental milestones particularly if multiple antipsychotic drugs are used.

Note: A national register of antipsychotic medication in pregnancy has been developed. For information phone (03) 9076 6988 or email H.Gilbert@alfred.org.au

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Conflict of interest: none declared

New drugs

Some of the views expressed in the following notes on newly approved products should be regarded as tentative, as there may have been little experience in Australia of their safety or efficacy. However, the Editorial Executive Committee believes that comments made in good faith at an early stage may still be of value. As a result of fuller experience, initial comments may need to be modified. The Committee is prepared to do this. Before new drugs are prescribed, the Committee believes it is important that full information is obtained either from the manufacturer's approved product information, a drug information centre or some other appropriate source.

Abatacept

Orencia (Bristol-Myers Squibb)

vials containing 250 mg lyophilised powder

Approved indication: rheumatoid arthritis

Australian Medicines Handbook section 15.2

The primary goal of treatment for rheumatoid arthritis is to preserve and restore physical function as well as modify the disease process and slow down the development of joint damage. In Australia, methotrexate is initially used to manage the disease. It is often given with other disease-modifying antirheumatic drugs (DMARDs) for moderate to severe disease (Aust Prescr 2003;26:36–40). If these drugs are not effective or not tolerated, biological agents such as tumour necrosis factor (TNF) inhibitors may be considered.

Abatacept, a genetically-engineered protein, is a biological drug for rheumatoid arthritis which is designed to suppress T cell-mediated inflammatory reactions. It is made up of the extracellular part of the human cytotoxic lymphocyte-associated antigen (CTLA-4) linked to a fragment of human immunoglobulin G. Abatacept works by binding to two signal molecules (CD80 and CD86) on antigen-presenting cells, thereby preventing them from activating T cells.