Abrupt discontinuation of psychotropic drugs during pregnancy: fear of teratogenic risk and impact of counselling

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Objective: To assess the consequences to mother and baby of abruptly discontinuing antidepressant or benzodiazepine medication during pregnancy and to assess the impact of our counselling. Participants: All women who consulted the Motherisk Program between November 1996 and December 1997 and who stopped taking antidepressant or benzodiazepine medication when pregnancy was confirmed agreed to participate in the study. Design and interventions: Subjects were interviewed, received counselling, and completed a questionnaire 1 month after their initial call and after the birth of their baby. Results: Of 36 women who completed the study, 34 discontinued their medication abruptly for fear of harming the fetus, 28 on the advice of their physician; 26 (70.3%) women reported physical and psychological adverse effects, 11 reported psychological effects only, and 11 reported suicidal ideation (4 were admitted to hospital). After counselling, 22 of 36 (61.1%) women resumed taking their medication, and 4 found that they no longer required it. One woman had a therapeutic abortion and 2 experienced spontaneous abortions; there were therefore 35 healthy babies (including 2 sets of twins) born to 33 women; 14 of 21 mothers breast-fed their babies while taking their psychotropic medication, with no adverse effects reported. Conclusions: When assessing the risks and benefits of taking psychotropic medication during pregnancy, women and their physicians should be aware that the abrupt discontinuation of psychotropic drugs can lead to serious adverse effects. Counselling is effective in reassuring women to adhere to therapy.

Objectif: Évaluer les répercussions sur la mère et le bébé d’une interruption soudaine de l’administration d’antidépresseurs ou de benzodiazépines pendant la grossesse et évaluer l’effet de nos conseils. Participants: Toutes les femmes qui ont consulté le programme Motherisk entre novembre 1996 et décembre 1997 et qui ont cessé de prendre des antidépresseurs ou des benzodiazépines lorsque la grossesse a été confirmée ont consenti à participer à l’étude. Conception et interventions: Les sujets ont été interviewés, ont reçu des conseils et ont rempli un questionnaire un mois après l’appel initial et après l’accouchement. Résultats: Sur 36 femmes qui ont participé à l’étude, 34 ont cessé soudainement...
Introduction

Depression and anxiety disorders are common among women of childbearing age, and they are often prescribed antidepressants and benzodiazepines. Although most recent studies have documented the relative safety of these medications during pregnancy, there remains a high level of anxiety among patients and physicians about their safety for women who are pregnant or breast-feeding. With a baseline risk of a major malformation of 1%–3%, chance alone would account for a substantial number of children being born with some birth defect to mothers took medication in early pregnancy. This concept is frequently misunderstood and, consequently, many birth defects have been attributed to the consumption of drugs. Moreover, the media often stress positive associations, while ignoring studies that find no effect or no adverse effects. Hence, it is not surprising that, either because of their own fears or on the advice of well-intentioned health care providers, some women abruptly discontinue their psychotropic medication when they discover they are pregnant.

The sudden discontinuation of antidepressants may cause either discontinuation symptoms or the re-emergence of the primary psychiatric disorder. The term “discontinuation” is preferred over “withdrawal” because the latter implies an addiction or dependence, and antidepressants, with an extremely low abuse liability, are not considered to be addictive.

Discontinuation symptoms may include general somatic, gastrointestinal, affective and sleep disturbances, which tend to occur abruptly within days to weeks of stopping or reducing the medication (Table 1); re-emergence of depression generally occurs gradually over weeks. Reinstatement of the antidepressant mitigates the symptoms of discontinuation within a day, whereas it takes several weeks for depression to respond.

Although benzodiazepines can be abused, the majority of patients do not abuse them. However, benzodiazepine dependence is well documented and is characterized by loss of control over the use of the drug, escalation of the dose and time spent in acquiring, using or recovering from their effects. Patients physically dependent on benzodiazepines, whether they meet the Diagnostic and Statistical Manual of Mental Disorders, 4th ed., (DSM IV) criteria for “abuse” or “dependence,” may experience withdrawal symptoms when they abruptly discontinue benzodiazepines. Symptoms may last for weeks or months and can occur even when therapeutic doses are stopped suddenly. Patients report excess anxiety, palpitations, insomnia, labile mood and restlessness and can suffer from perceptual disturbances, primarily of vision and hearing (Table 1). In addition, seizures, psychosis and delirium can occur.

Our objective was to follow a group of women who stopped taking their psychotropic medication when they became pregnant and to assess the effects of the discontinuation on their well being. In addition, we assessed the impact of the counselling these women received on the reinstatement of drug therapy.

<table>
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<tr>
<th>Physical symptoms</th>
<th>Psychological symptoms</th>
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<tr>
<td>Nausea and vomiting</td>
<td>Anxiety and panic attacks</td>
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<tr>
<td>Diarrhea, sweating</td>
<td>Low energy and fatigue</td>
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<tr>
<td>Hot or cold flashes</td>
<td>Mood swings</td>
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<tr>
<td>Tremors, excess lacrymation</td>
<td>Insomnia, depression</td>
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<tr>
<td>Yawning, fainting</td>
<td>Suicidal ideation</td>
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Methods

The Motherisk Program is a counselling service for pregnant women and their health care providers that offers evidence-based information and guidance concerning the potential risks to the developing fetus or infant, from exposure to drugs, chemicals, diseases, radiation and environmental agents. Of the approximate 35 000 calls each year, 12%–15% of the inquiries concern psychotropic drugs. We followed all women who called the Motherisk Program between November 1996 and December 1997 and who abruptly discontinued their antidepressant or benzodiazepine medication.

After a Motherisk counsellor handled the intake call and provided information according to a standard protocol, the caller was passed on to our study coordinator for consideration for inclusion in the study. The coordinator repeated the information given by the Motherisk counsellor, reassuring the patient that according to current research, the drug they were taking was considered safe to take during pregnancy. They were then asked if they would participate in our follow-up program, which would include an interview within a months’ time and another after the delivery of the baby.

A detailed questionnaire, documenting the reason(s) the psychotropic medication was discontinued, any adverse events, whether medication was restarted and present psychiatric condition, was completed during the first interview. After delivery, participants were contacted again about pregnancy outcome and breastfeeding and medication status. These procedures were approved by our hospital’s Research Ethics Board.

Our primary endpoints of interest were: reasons for abrupt discontinuation of medication, effects of sudden discontinuation on psychiatric condition and pregnancy, and effect of Motherisk counselling on restarting drug therapy.

Results

All 44 women who were asked to participate in the study agreed to do so; 4 women were lost to follow up when their telephone numbers changed, and 3 who were planning a pregnancy at the time of the initial call did not become pregnant during the study period. Therefore, 37 first follow-up interviews and 36 first and second follow-up interviews were completed.

All women had been taking either an antidepressant, a benzodiazepine or a combination of both (Table 2), and they all reported discontinuing the drug for fear of birth defects and harming their fetuses. Thirty-four women discontinued the drugs abruptly, and 3 used some form of tapering off. This tapering was unsatisfactory, however, because even these patients suffered from some adverse effects. Many of the women suffered both physiological and psychological adverse effects, and a small number who were on SSRIs alone experienced psychological effects only (Table 3). Almost one-third (29.7%) of the patients reported suicidal ideation because of “unbearable” symptoms; 4 were admitted to a hospital. One woman had a therapeutic abortion because she did not feel that she could go through the pregnancy feeling so awful, and another women, who had abruptly discontinued a high daily dose of a benzodiazepine, used alcohol to combat abrupt discontinuation symptoms.

A small number of the patients decided on their own, without consulting a health professional, to discontinue their medication. However, the majority discontinued on the advice of a physician (both psychiatrists and family physicians); a small percentage noted

<table>
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<th>Table 2: Antidepressants and benzodiazepines women in the study were taking when they became pregnant</th>
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<tr>
<td>Medication women were taking, no. of women</td>
</tr>
<tr>
<td>Antidepressant</td>
</tr>
<tr>
<td>n = 25</td>
</tr>
<tr>
<td>Paroxetine 12</td>
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<tr>
<td>Fluoxetine 6</td>
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<tr>
<td>Sertraline 2</td>
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<td>Amitriptyline 3</td>
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<td>Fluvoxamine 1</td>
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<td>Venlafaxine 1</td>
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a combination of their own fears and their physicians’ advice led to their decision.

After being counselled by Motherisk, 22 of 36 (61.1%) women restarted their medication within a few days, and 4 patients didn’t think they required the medication any longer. The remaining women were still not convinced of the safety of taking medication during pregnancy and did not restart.

Two women in the study experienced spontaneous abortions and 1 had a therapeutic abortion. There were 35 live births (including 2 sets of twins); all babies were reported to be normal and healthy, with no reports of any major or minor malformations. Two babies had neonatal symptoms consistent with mild withdrawal (1 mother was taking paroxetine, and 1 was taking amitriptyline), but neither required medical intervention.

Of the 36 women, 21 (58.3%) breast-fed their babies, with 14 of those continuing to take their medication (Table 4). There were no reports of adverse effects from breast-feeding while mothers were taking medication. Women who breast-fed but did not take their medication (n = 7), reported doing so for fear of adverse effects on the baby. Most of the women who were taking their medication but did not breast-feed (n = 7) did so primarily for personal reasons not related to their medication.

**Discussion**

This study, the first of its kind to date, documents the consequences of pregnant women discontinuing antidepressants and benzodiazepines abruptly, including a high rate of suicidal ideation and admission to hospital. The symptoms of these women support the findings of previous studies and confirm that pregnant women and their physicians sometimes adopt the commonly held popular notion — that pregnant women should not take any medication. The physicians must have been aware that these medications should be tapered off, but because a pregnancy had been diagnosed, in their haste to ensure a “drug-free pregnancy” they may not have considered the consequences of their actions. Some physicians were either not aware of the concerns associated with abrupt discontinuation of medication or they were aware but failed to inform their patients. Even if the patient reports were inaccurate, it was clear that if patients were, in fact, informed by their physicians, they did not seem to appreciate the risks of abrupt discontinuation.

The number of reports of suicidal ideation (11 of 37) is very disturbing. Fortunately, none of the women followed through, but 4 had to be admitted to hospital. Because of the fear of teratogenicity, combined with the effects of abrupt discontinuation, 1 woman terminated an otherwise wanted pregnancy and another considered it, but did not follow through; this confirms a disturbing trend that we have documented in other studies.

It has been documented that paroxetine is associated with more serious abrupt discontinuation effects than other SSRIs. This was confirmed in our cohort of women who were taking paroxetine (13 of 36), who reported more severe side effects. Also, 6 of the 11 women who reported suicidal ideation were taking paroxetine.

Two-thirds (14 of 21 [66.7%]) of the women in the study breast-fed while they were taking medication. These particular drugs are excreted in the breast milk in minimal amounts and are considered safe to take when breast-feeding. Unfortunately, many physicians are unaware of this and instruct their patients not to take medication while breast-feeding “to be on the safe side.” This advice can be quite upsetting to a women who are anxious about breast-feeding. The case of the woman who substituted alcohol for her benzodiazepine is very disturbing because the adverse effects of alcohol on a developing fetus are well documented.
Our study documents, for the first time, the harmful effects of abrupt discontinuation syndrome in pregnancy that can be caused by misinformation about fetal safety. It also reveals the effectiveness of counselling — reassuring advice from Motherisk counsellors led many women to restart pharmacotherapy and continue their needed drug therapy while breast-feeding.

Physicians should ensure that pregnant women with psychiatric disorders receive evidence-based information that balances the benefits of treatment against unproven adverse effects on the fetus.

**References**


