



## Taking SSRI Antidepressants During Pregnancy: Considerations and Risks

For pregnant women or women contemplating pregnancy, reading literature about depression, pregnancy and medication often leaves them feeling only more confused. This fact sheet is intended to point out what is and is not known in the medical literature concerning the use of SSRI anti-depressants during pregnancy and, for women who decide ultimately that they do not want to start or continue using antidepressants, offers helpful information on how to come off them. It also offers some other options for dealing with depression and some resources for further reading.

### INTRODUCTION

#### **What are SSRIs?**

SSRIs (selective serotonin reuptake inhibitors) are a class of prescription drugs that are frequently prescribed for symptoms of depression.

Women are usually prescribed SSRI antidepressants because they have come to their doctor with concerns about their moods, their ability to function, an overall state of sadness or a sense of loss in their lives. There is conflicting information in the medical literature about how to diagnose clinical depression and what is the best solution for someone when it is diagnosed. Increasingly, regardless of degree of severity or whether this condition has been slow in progressing or happened suddenly, doctors are highly likely to prescribe SSRI antidepressants. In some cases women may be prescribed antidepressants before they become or while they are pregnant.

Many women who are pregnant or planning to become pregnant have questions about the effects of antidepressants on themselves and on their babies. They also want to know how effective SSRIs are for depression and the risks they face if they try to stop taking them. Women who are already taking SSRIs and who would like to stop taking them want information on how to do this safely.

Antidepressants are among the most frequently prescribed class of drugs for women of childbearing age in Canada. Data from BC's PharmaNet, which includes every prescription dispensed in the province, indicates that in 2003-2004, 11-14% of women between the ages of 25 and 39 received at least one prescription for an antidepressant.

Rates of prescribing have dramatically increased in the past two decades. In 2008, 80% of women in Canada who spoke about depression to their doctors were given a prescription, usually for an SSRI. This is despite the fact that medical research has not determined whether SSRIs work better than a sugar pill (placebo) for most people. In addition, SSRIs are often prescribed without offering other options that may help to get a woman through a difficult time.

Although fewer women use antidepressants during pregnancy, the rate of use in pregnancy has increased. In BC, by 1998, just over 2% of pregnant women used an antidepressant. By 2001—just 3 years later—the rate of use had grown to 5%.

## **TYPES OF ANTIDEPRESSANTS THAT MAY BE PRESCRIBED IN PREGNANCY**

There are many types of antidepressants being prescribed in Canada but the most common are SSRIs (selective serotonin reuptake inhibitors) and related drugs. Although the names of SSRI antidepressants are different, all of these drugs have similar chemical characteristics and act in similar ways on the brain and body:

- Citalopram (Celexa)
- Escitalopram (Cipralex, Lexapro)
- Fluoxetine (Prozac)
- Fluvoxamine (Luvox)
- Paroxetine (Paxil)
- Sertraline (Zoloft)

Venlafaxine (Effexor) and Duloxetine (Cymbalta) are antidepressants that are very similar in action to the SSRIs listed above. Their effects in pregnancy are likely to be similar.

Several other newer antidepressants have somewhat different characteristics and may have different effects in pregnancy than the antidepressants listed above. These include: Bupropion (Wellbutrin) and Mirtazapine (Remeron).

## **HOW DO SSRIS AFFECT THE BRAIN AND BODY?**

SSRI and related antidepressants act on neurotransmitters which are specialized chemical messengers released from nerve cells (“neurons”) in the brain that help send information from these to other cells in the body. Most SSRIs are designed to act on the neurotransmitter serotonin but others, such as Effexor, act on serotonin and noradrenalin. Wellbutrin also acts on dopamine.

Serotonin is very widely distributed in the body. It affects the central nervous, gastrointestinal, cardio-respiratory and hormonal systems, motor and sexual functions, sleep and appetite. These widespread effects help explain why SSRIs can have many different effects on the body and on psychological functioning.

Many people who have been taking SSRIs for at least two to four weeks will experience some degree of withdrawal effect if they try to increase, stop or reduce their dose levels. SSRIs lead to adaptations in the brain cells or increasing tolerance to the drug. When the drug dose is reduced or changed, the brain must readapt to doing without the drug.

Therapeutic drug dependence is a *physical* process and is not the *fault* of the person taking them. It is not an indicator of an addictive personality, nor does it mean a person has a brain that “needs” medication. Unfortunately, many women and their doctors often think that symptoms that are *caused* by antidepressants (adverse drug reactions) are signs that a woman is suffering more mental health problems. Instead of considering the effects of the drugs, physicians may recommend increasing the dose or adding other drugs. Prescribing additional drugs to treat the adverse reactions caused by other drugs is called the “prescription cascade.” *All women who are taking antidepressants and find that their symptoms are worsening or that they are feeling less well should first consider that the drug they are taking might be the cause.*

All people who are prescribed SSRIs should be warned about antidepressant-induced suicidality and become informed about the tolerance, addiction and adverse reactions *before* they go on the drugs or *if they plan to taper off*. Warnings about these types of risks have been posted by Health Canada and the US Food and Drug Administration.

## **DO SSRIS CURE IMBALANCES IN BRAIN CHEMISTRY CAUSING DEPRESSION?**

Many women who are depressed are told by the doctors that their depression has been caused by a chemical imbalance in their brains and that SSRIs can correct this imbalance. The idea that a chemical imbalance causes depression and that depression is therefore a *biological* disease has been widely promoted by pharmaceutical companies, many health care providers and by the media and yet *there is no scientific evidence to support the theory that depression is caused by a chemical imbalance in the brain*. Brain chemistry is part of a very complex feedback system involving many different parts of the body, as well as a person’s moods and emotions. There are at least 100 different chemical neurotransmitters in the body. We know very little about how they interact.

We *do* know that SSRIs work by generally stimulating the serotonin system. In some people this can lead to a lightening or improvement of mood. In others, the extra stimulation can lead to agitation, suicidal thoughts, anxiety and even depression-like symptoms.

## **ARE THERE NON-DRUG WAYS WOMEN CAN USE TO DEAL WITH DEPRESSION?**

Cognitive, talk or “listening” therapy, group or peer support, regular exercise and nutritional support have all been shown to reduce emotional distress and improve mood among women who are depressed. Providing information about the changes, doubts and concerns that many pregnant women experience before and after birth can help decrease fear, stress and worry. Community groups such as mother-baby, immigrant/settlement mother/child and prenatal and

breastfeeding support groups can also help women feel that what they are experiencing has been experienced by other women and that they are not alone. Direct information, provided to husbands and partners, on what women may experience during and after pregnancy, can also provide support.

Although the socio-economic problems that some pregnant women may be experiencing are difficult to resolve on a personal level, assistance to acquire income support, housing or to find other supports can be helpful in terms of reducing hopelessness, isolation and despair.

## **ARE SSRIS EFFECTIVE IN TREATING DEPRESSION?**

Recent studies of *all* of the studies examining the effectiveness of SSRIs show that the effectiveness of the SSRIs in treating depression appear to have been exaggerated.

Around half of the studies that have been submitted to the FDA *did not* find a significant benefit for use of SSRI antidepressants as compared with a placebo or “sugar pill.” Many of these studies were not published or were published in a misleading manner, as though they had shown a benefit. In clinical trials, around 4 of 10 people on a placebo get better and around 5 of 10 on an antidepressant.

No clinical trials have established that SSRI antidepressants are effective in pregnancy. This is because companies are reluctant to carry out clinical trials involving pregnant women. Some studies have followed up women who chose to use antidepressants in pregnancy but none have used standard methods to test effectiveness. These methods should include two key components: random assignment of study participants to the group getting a drug or placebo or other interventions, and “double-blind” methods, in which neither the pregnant woman nor clinicians evaluating her symptoms knows who is taking a drug or a similar-looking placebo. These methods allow researchers to separate out a drug’s effects from other factors that might affect judgments of effectiveness.

## **WHAT FACTORS CAN CONTRIBUTE TO DEPRESSION DURING PREGNANCY?**

There *is* substantial evidence that social, historical, economic or other factors can lead or contribute to depression in women. Women who are poor or economically insecure, isolated, lack support, have chronic health problems, or have been victims of violence are known to experience increased levels of worry, stress, sadness and depression.

For many women pregnancy involves changing roles, increased responsibilities, a potential lessening of autonomy, reduced economic security, and a loss of social support, all of which can contribute to increased worry, stress and depression. These stressors may be exacerbated by the normal physical and hormonal changes taking place during pregnancy and additional health problems that may affect women during this time.

Challenging socio-economic factors may continue to exist *even if* a woman is taking antidepressants during pregnancy. For this reason, if a woman is taking an SSRI antidepressant she should also seek out supportive counselling or therapy.

Some women may not be affected by social isolation, economic factors, worry, have histories of violence or have chronic health problems and may *still* feel depressed for reasons that seem unexplainable. This points to how complex the human mind can be in relation to moods, emotions and daily functioning, and how the hope that one pill may be the only or the best answer needs re-examining.

## **THE SPECIAL CONCERNS ABOUT PRESCRIBING DRUGS TO WOMEN WHO ARE PREGNANT**

Extra caution is usually taken before prescribing any kinds of drug to pregnant women because of potential risks to their babies. These risks became clear when the outcomes of prescribing DES and thalidomide to pregnant women became evident. These events demonstrated that the effects of drugs on babies in utero may not become apparent until the babies have grown into adults.

DES (diethylstilbestrol) was prescribed between 1941 and 1971 to prevent miscarriage. Women who were exposed to DES before they were born are at increased risk of developing rare types of cancers of the cervix and vagina in their twenties and thirties, reproductive tract irregularities, pregnancy complications and infertility. Boys who were exposed to DES before birth also have increased risks for conditions such as non-cancerous cysts on the testicles.

Another drug, thalidomide, was prescribed to prevent morning sickness in pregnant women between 1957 and 1961. The drug was found to result in severe birth defects, including limb and internal system abnormalities. The thalidomide tragedy, which resulted in thousands of deformed babies, led to changes in the drug testing and approval process in the US and Canada, and an increased understanding that *any* drug has the potential of leading to serious and unanticipated harm.

At the time that DES and thalidomide were developed there was a lack of understanding that drugs taken by the mother pass through the placenta to their babies. Even today few clinical trials of drugs include pregnant women because we now understand that drugs taken by pregnant women do pass to babies.

With most drugs, risks are particularly of concern in the first trimester of pregnancy when the organ development of babies occurs. This may be a problem because many women may not know they are pregnant until well into their first trimester. As will be described below, there are also some specific concerns about using SSRI antidepressants in the third trimester of pregnancy.

## RISKS OF SSRIS ON BABIES IN UTERO

Despite the lack of random clinical testing of SSRIs on pregnant women, research has established linkages between SSRI use and the development of certain types of health problems in some babies born to mother taking SSRIs.

These are:

- For women who take SSRIs during the 3<sup>rd</sup> trimester of pregnancy, there is an increased likelihood their babies will experience complications at birth. These range from mild symptoms to more serious problems requiring prolonged hospitalization, breathing support and feeding problems (sometimes requiring tube feeding). Reported symptoms include: “feeding and/or breathing difficulties, seizures, muscle rigidity, jitteriness and constant crying.” These symptoms may be a result of the antidepressant or of the effect of withdrawal of the drug from the baby’s body after birth (neonatal withdrawal syndrome) (See Health Canada Advisory August 9, 2004).
- Lower scores on Apgar tests (the standard overall measure of newborn health), and more frequent admission to neonatal intensive care units.
- An increased risk of heart defects (holes and malformations in the chambers of the heart and cardiovascular anomalies) from exposure in the first trimester. Current estimates are around 1 additional baby per 200 exposed.
- An increased risk of Persistent Pulmonary Hypertension of the newborn (PPHN). This is an uncommon but very serious lung condition that can be life threatening or lead to ongoing neurological problems. The increased risk has been found following exposure to SSRIs in late pregnancy.

It is important to note that the level of risk of these problems varies, and that some babies born of women taking SSRIs appear to have no immediate problems. It is also important to note that some SSRIs appear to be more associated with certain risks than others although this has not been completely studied. There is some evidence that some effects are dose-related and are higher in women taking more than one antidepressant or an antidepressant combined with an anti-anxiety medication or sleeping pill. *Research into the possible effects of SSRIs on babies in utero is ongoing.*

## WHAT ARE THE RISKS OF DISCONTINUING SSRIS DURING PREGNANCY?

Some researchers have stated that untreated depression in a pregnant woman may be harmful to the mother and to her unborn baby. In these cases it is suggested that any potential risks of SSRIs are outweighed by the dangers to the mother and also to her baby if she stops taking the drug.

There is some evidence that the babies of severely depressed mothers do less well than other babies although this evidence is not conclusive. In many cases, studies of the risks of depression during pregnancy do not include a clear definition of depression or an accounting of other factors that may contribute to poorer outcomes among mothers and their babies. For example, women

with previous difficult pregnancies or a previous baby with a serious health problem may be more likely to experience depression in their next pregnancy. Poverty and lack of adequate food and shelter lead both to higher rates of depression and to poorer birth outcomes. Many of the studies that look at effects of untreated depression have not fully addressed the impacts of these situational causes of depression.

One factor that is frequently *not* considered is that symptoms such as agitation, anxiety, panic or even those associated with depression may occur among women taking SSRIs or whenever a dose is increased, reduced or skipped. Withdrawal-type reactions can occur within hours of missing one dose, especially with medications that are metabolized (cleared from the body) quickly.

Women who are prescribed SSRIs need to be told about the potential effects of SSRIs before they are prescribed or when they are taking the drug. They should be reassured that psychiatric symptoms associated with a change in dose levels are NOT a re-appearance or worsening of their original condition.

Considering withdrawal from SSRIs may present a dilemma for pregnant women who are concerned about developing and coping with withdrawal symptoms when they are pregnant. Those who *are* considering reducing or withdrawing from SSRIs need to become fully informed about how the drugs work, how withdrawal can be managed safely and how long the process might take.

Some women may discover they are pregnant and want to stop taking an antidepressant right away. It is never a good idea to withdraw from an SSRI suddenly if a woman has been taking it for more than a few days, even in early pregnancy. A gradual withdrawal is much safer both for the women and her baby. Although the baby may still be exposed in the first trimester, gradually lowering the dose may lower the risk of harmful effects.

## HANDLING SSRI WITHDRAWAL SAFELY

Withdrawal symptoms *can* be lessened through a careful, slow and informed withdrawal process. The following are factors to consider by women and their care providers if withdrawal is being considered:

- Whether pregnant or not, a woman should NEVER abruptly withdraw from any SSRI, no matter how small the dose, unless she has only been taking it for less than one or two weeks. Abrupt withdrawal can lead to serious symptoms and, in the case of higher doses, could be life threatening.
- A decision to withdraw should be made carefully with health care providers who are informed about withdrawal, have experience designing slow tapering plans (or who are willing to explore this option), and are willing to provide monitoring and support during the withdrawal process.
- Anyone who has been on an antidepressant for more than a few weeks can experience withdrawal reactions. This even applies in cases where SSRIs drugs have not worked or if the dose is very small.

- Tapering from SSRIs requires a systemic reduction of dosage by cutting or dividing the pill or capsule and reducing the amount slowly every 1-2 weeks. A general guideline of reducing the dose level by 5% at intervals has been recommended *as long as symptoms are not overly severe*. Reductions should be made at regular intervals at the same time each day. It is dangerous to skip doses or to skip days. Although it may be tempting to try to skip doses during withdrawal, this may increase withdrawal symptoms.
- All types of antidepressants require a slow tapering process, even those that are extended or controlled release.
- Tapering can, in some cases, take weeks, and in cases of severe symptoms, four months or more. Withdrawal should *never be rushed* but should take into account the severity of symptoms. In some cases tapering needs to go more slowly as the amount of the drug being reduced becomes smaller.
- The pace of tapering is highly individual and no one can accurately predict how long withdrawal will take or how severe the symptoms will be. The size of the dose does not determine the severity of the withdrawal.
- Withdrawal symptoms can include both *psychiatric* (e.g. anxiety, agitation, crying spells, trouble concentrating, feelings of depression or “agitated depression,” irritation) or *physical* symptoms such as dizziness, insomnia, or headaches. Withdrawal symptoms can also mimic the flu or cause nausea, vomiting and diarrhea.
- Withdrawal symptoms can be mild, moderate or severe. Although mild symptoms will be noticeable, they are unlikely to be bothersome. Severe symptoms can be alarming and serious and include suicidal thoughts and behaviour, manic-like reactions, aggressiveness, paranoia and psychotic reactions.
- The presence of serious symptoms indicates that the tapering process needs to be slowed down dramatically.
- Women need to be assured that the symptoms they are experiencing during the most acute withdrawal phase are most likely the result of the drug rather than any pre-existing problems.
- Women who have had serious depression in the past should be provided with monitoring and additional support and counselling resources during the withdrawal process if they have chosen to try to withdraw.
- If slow reduction of the SSRI becomes problematic, the substitution of a longer-life SSRI may make it more possible to withdraw successfully. Substituting Prozac for another SSRI in the same class may be helpful because Prozac has a longer half-life. (See this site for this withdrawal protocol: <http://www.benzo.org.uk/healy.htm>)
- Some women who have been prescribed SSRIs are also on other prescribed psychiatric medications such as benzodiazepines and atypical antipsychotics. Women who are on multiple medications need to develop a longer-term plan that involves the slow tapering of each class of drug individually. For example, the tapering of a benzodiazepine such as Ativan should not be done at the same time as the tapering of an antidepressant.
- Women undergoing a tapering process should avoid alcohol or recreational drugs such as cannabis. Sometimes physicians may want to prescribe additional psychiatric drugs in an attempt to deal with withdrawal symptoms. It is important to remember that withdrawal is the process by which your brain and body are adjusting to a pre-drug state and that no drug can eliminate withdrawal symptoms. In addition, almost all psychiatric drugs, such as antipsychotics or tranquilizers can also cause tolerance and addiction and must be tapered off.



There are some helpful resources that provide advice on the SSRI withdrawal process. Dr. Joseph Glemullen's book, *The Antidepressant Solution: A Step-by Step Guide to Safely Overcoming Antidepressant Withdrawal, Dependence and 'Addiction,'* is a reputable resource that has been used by many people to withdraw safely from SSRIs.

Even after women have considered the information related to antidepressants, some women may decide to go on an SSRI when pregnant or continue a prescription that they are already on. In these cases, it is important that women report anything unusual to their physician, and that the baby, when born, receive a full pediatric examination.

### A FEW RESOURCES TO LEARN MORE

Anti-Depressants in Pregnancy: Is There Evidence of Benefit? Webinar (on-line seminar) with researcher Barbara Mintzes, recorded October 29, 2009. Available for viewing at: [www.cwhn.ca/en/frontpage\\_en?page=1](http://www.cwhn.ca/en/frontpage_en?page=1) (60 mins.)

Currie, Janet. (2005). *The Marketization of Depression: The Prescribing of SSRI Antidepressants to Women*. Toronto: Women and Health Protection. Available for download at: [www.whp-apsf.ca/pdf/SSRIs.pdf](http://www.whp-apsf.ca/pdf/SSRIs.pdf) (PDF 246 KB / 27 p.)

Glemullen, Joseph. (2005). *The Antidepressant Solution: A Step-by Step Guide to Safely Overcoming Antidepressant Withdrawal, Dependence and 'Addiction.'* New York: Free Press.

Saibil, Diane, for Women and Health Protection. (2005). *SSRI Antidepressants: Their Place in Women's Lives*. Toronto: Women and Health Protection. Available at: [www.whp-apsf.ca/en/documents/ssri.html](http://www.whp-apsf.ca/en/documents/ssri.html)

Shulman, Jane. (2009/10, Fall-Winter). Do pregnant women benefit from taking antidepressants? *Network*, 12(1): 11-13. Available at: [www.cwhn.ca/en/node/42065](http://www.cwhn.ca/en/node/42065)

Therapeutics Initiative. (2010, Jan.-Feb.). Are antidepressants safe in pregnancy? A focus on SSRIs. *Therapeutics Letter*, 76. Vancouver: Therapeutics Initiative. Available for download at: <http://ti.ubc.ca/letter76>

---

This fact sheet was prepared by Janet Currie for the Canadian Women's Health Network. April 2010. Available for download at: [www.cwhn.ca](http://www.cwhn.ca) Également disponible en français.