Balancing Act: The Importance of Medication Dose in Pregnancy

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Shannon was newly pregnant and had been referred to MotherToBaby by her doctor. She was taking 50 mg of sertraline per day for general anxiety and her doctor thought that she may need to wean off the medication now that she was 5 weeks pregnant. Shannon had been taking the medication for 3 years and was feeling great on her current dose, so she had some concerns about this plan. On the MotherToBaby website's live chat service, Shannon was connected with me, a teratogen information specialist, where she asked "Do I really need to stop my anxiety medication, or could I just continue on a lower dose?"

I started by addressing the importance of weighing the risks vs. benefits of taking any mental health medication during pregnancy. Sertraline is very well studied and has not been associated with a risk for birth defects, but does have the potential to cause neonatal adaptation syndrome or withdrawal approximately 10-30% of the time and persistent pulmonary hypertension in less than 1% of exposed infants. On the other hand, we know that untreated anxiety can also cause problems for the pregnancy, including an increased risk for preterm delivery. For many patients, the benefits of staying on a medication like sertraline outweigh the potential risks, but each case is unique and ultimately the patient needs to decide what they are most comfortable with.

Getting to Shannon's next question about dose, I shared that although many pregnant women feel they need to decrease their dose once they get a positive pregnancy test, the opposite is in fact true. During pregnancy, there are many changes that occur including weight gain, increased blood volume and enlargement of the kidneys. On the outside, things won't look much different, but research shows these changes happen soon after conception. This means that medication doses that previously worked well to control a condition become "diluted," in a sense, and may not be as effective. In some cases, women need to actually increase their dose to continue to control the disease.

To learn more about how bodily changes during pregnancy impact medication dosing, we turn to Becky Spencer, PhD, APRN, PMHNP-BC, IBCLC, PMH-C, a psychiatric nurse practitioner who specializes in perinatal mental health at Texas Women's University with some more questions about this fascinating phenomenon.

Q. Can you tell us a little more about what is happening in the body during pregnancy and why medications become less effective?

Becky Spencer: You are correct, Kirstie, that pregnancy has a significant impact on drug absorption, which is how a drug is transported into the bloodstream, drug distribution, which is the disbursement of a drug as it moves through the blood and tissues of the body, and drug metabolism, which is the process by which the body breaks down and eliminates drugs or other substances. During pregnancy, especially later in pregnancy, drug absorption from the stomach into the bloodstream is decreased due to slower gastric emptying and slower movement of the bowel and colon, so it can take longer for a medication to be absorbed and get to work.

A pregnant woman's blood volume almost doubles during pregnancy which impacts drug distribution. With the dilution effect there is a lower concentration of medication in the blood plasma which results in less medication reaching the target tissues. Most drugs are metabolized in the liver or kidneys. During pregnancy, the increased blood flow to the kidneys results in an increased glomerular filtration rate (GFR), which means that medications are cleared from the

bloodstream quicker, meaning the drug stays in the body less time. Similarly, hormone levels increase during pregnancy which increases the activity of various metabolic enzymes in the liver that metabolize drugs. When the liver metabolizes a drug more quickly there is less drug that reaches the target tissues.

What these changes mean for pregnant women who take medication for mood and anxiety disorders is that the dose of medication that they were taking before pregnancy may have a decreased effect during pregnancy, because the biological changes effectively decrease the amount of medication reaching the target tissues, in this case, the brain. Pregnant women may have an increase in mood and anxiety symptoms that they interpret as a worsening condition when, in fact, the decrease in circulating medication is the cause for an increase in symptoms.

Q. In your practice, how often do you see women increasing their mood medication dose? Does the dose need to be increased substantially?

Becky Spencer: That is a great question. The answer is that it depends on the type of medication, the specific condition (depression, anxiety, obsessive compulsive disorder, bipolar, etc.), and the severity of symptoms. Psychiatric providers typically increase medication dosages in gradual amounts until the patient has symptom relief or desired therapeutic effect. If a patient is experiencing a partial response to a medication (some improvement in mood and anxiety symptoms) best practice is to increase the dose of that medication before considering adding an additional medication.

Another question that I hear is whether or not dosages of medication should be based on achieving a specific blood plasma concentration level. The short answer is, for most medications, no. We don't routinely check blood plasma concentrations of most antidepressants because valid and reliable therapeutic plasma concentration ranges do not exist. Some mood stabilizing medications like valproate or lithium do require blood plasma monitoring both during pregnancy and outside of pregnancy. Euthymia, or stable mood, is the goal of medication dose adjustments for mood and anxiety disorders during pregnancy.

Q. What about after delivery? Does the dose need to be decreased right away?

Becky Spencer: It depends on the type of medication, and, to some extent, the symptoms that the patient is experiencing. The postpartum period is a vulnerable time for mood and anxiety disorders for several reasons including the significant hormonal shift that occurs after birth, lack of sleep, role adjustment to caring for a baby, and for some new parents, lack of necessary social and emotional support. Decreasing antidepressants too quickly after birth could exacerbate mood and anxiety symptoms during that very vulnerable time. The decision to decrease dosages of any medication prescribed for mood and anxiety disorders should be a collaborative decision between the patient and the provider. If decreasing mediation dose is desirable, it should occur gradually and any change in mood and anxiety symptoms should be reported to the provider. The one exception to this rule is for patients taking lithium. If lithium dosages were increased during pregnancy, they must be decreased to pre-pregnancy dosages after delivery.

Q. Shannon is asking about sertraline, an anti-anxiety medication, but are there other drugs that women need to also increase their dose of during pregnancy?

Becky Spencer: Any medications used to treat mood and anxiety disorders, including antidepressants, mood stabilizers, antipsychotics, and anti-anxiety medications, may need dose increases during pregnancy. The most important point is for pregnant women to monitor their mood and anxiety symptoms and report them to their provider. The decision to increase doses of medication should always be a collaborative decision between the patient and the healthcare prescriber.

Q. How should patients approach this conversation with their healthcare provider?

Becky Spencer: The decision to take any medication during pregnancy must be based on a discussion between healthcare providers and patients that takes into consideration the available research on the risks of specific medications AND the risks of untreated or undertreated mental conditions for both the pregnant woman and the baby. The risks of not treating mood and anxiety disorders during pregnancy are well documented and significant. Untreated or undertreated mood and anxiety disorders during pregnancy are associated with hypertension, preterm delivery, low birth weight, and long-term negative impacts on motor and cognitive development of the baby. Mental health conditions are the leading cause of maternal mortality in the United States. Effective treatment for mood and anxiety disorders in the perinatal period will literally save lives.

My top three tips for having a discussion with healthcare providers about medications for mood and anxiety disorders in the perinatal period include:

- Make an appointment with a psychiatric provider who specializes in perinatal mood and anxiety disorders or reproductive psychiatry. The provider directory on the Postpartum Support International website is a great place to find specialists in your state, and many provide telehealth services.

- If your obstetric provider is hesitant to treat your mood and anxiety symptoms, recommend that they make an appointment to speak with a psychiatric provider who specializes in treatment of perinatal mood and anxiety disorders during pregnancy at the Postpartum Support International Psychiatric Consult Line. This free service is staffed by perinatal psychiatrists who are available to share their skills and expertise and provide guidance to fellow medical professionals on prescribing medications during pregnancy and lactation.

- MotherToBaby Fact Sheets are an excellent resource and a great way to start a conversation with your provider about specific medications for mental health during pregnancy and lactation. I recommend that pregnant and lactating women who are taking medications for mood and anxiety disorders access and print out the MotherToBaby Fact Sheets for the medications that they are taking or are interested in learning more about, read them, jot down questions, and take them to their obstetric and/or psychiatric providers to start the conversation. Remember that you are your own best advocate for you and your baby's health.

Thanks so much for sharing your insight, Becky. It's always great to learn more about this topic.

Ultimately, Shannon decided to stick with her current dose for the first few weeks of pregnancy and make an appointment with her psychiatrist to discuss increasing her dose in a few weeks. In the meantime, she was planning to monitor her mood to make sure the anxiety remained well controlled.

If you have questions about mental health medications, dose, or any other exposures in pregnancy or lactation, please feel free to reach out to a MotherToBaby specialist via phone, chat, text, or email for more information. Additionally, you can visit our Mental Health Resource Hub to access fact sheets, blogs, and podcasts on mental health conditions and the medications used to treat them during pregnancy and breastfeeding.

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