Examining Migraine Medications during Pregnancy Doesn't Have to be a Headache

Migraine headaches affect one billion people worldwide. Migraines are more common in people who could become pregnant, and during pregnancy their frequency can increase, decrease, or stay the same. Last year we talked to Caroline about treating her migraine headache at five months of pregnancy. Now she has reached out to us to discuss treatment options before she tries to get pregnant again. Back when she was pregnant with her first child, she was using acetaminophen and sumatriptan, but found that her migraines were much less responsive to these products over time. Today, Caroline is considering the newer drugs that have come onto the market since her last pregnancy. She has never used a preventive medication and was curious about the data on the new products. Caroline's healthcare provider has mentioned trying Emgality® (galcanezumab-gnlm) or Nurtec ODT® (rimegepant).

Since there are many new drugs marketed to treat and prevent migraines, let us start with an overview. These newer medications are called calcitonin gene-related peptide (CGRP) antagonists, CGRP receptor blockers and CGRP blockers, and are a new category of migraine treatments. Some treat migraine attacks, while some prevent migraines, and some do both (like those Caroline is interested in).

There are so many choices, so let's look at what the data says when these medications are studied during pregnancy.

Medications that *prevent* chronic migraines:

- Qulipta® (atogepant) – oral; CGRP receptor antagonist
- Ajovy® (fremanezumab-vfrm)-injection; CGRP blocker
- Vyepti® (eptinezumab-jjmr)- injection; CGRP receptor blocker
- Aimovig® (erenumab-aooe)- injection; CGRP receptor blocker
- Emgality® (galcanezumab-gnlm)- injection; CGRP blocker
- Nurtec ODT® (rimegepant)- tabs; CGRP receptor antagonist

Medications that *treat* the symptoms of acute migraines:

- Emgality®(galcanezumab-gnlm) – injection; CGRP blocker
- Nurtec ODT® (rimegepant)- tabs; CGRP receptor antagonist
- Ubrelvy® (ubrogepant)- oral; CGRP receptor antagonist

Medications that *prevent* and *treat* migraines:

- Emgality®(galcanezumab-gnlm) – injection; CGRP blocker
- Nurtec ODT® (rimegepant)- tabs; CGRP receptor antagonist

Unfortunately, there is very little information involving human data on Quilipta®, Nurtec ODT® or Ubrelvy® so we are left without the information we need for a full risk assessment of these medications. However, there are some data in humans on the medications on Ajovy®, Vyepti®, Aimovig® and Emgality®. These data are limited, meaning we don't have a lot of information.

Let's begin by breaking down the information that we have on Ajovy®, Vyepti®, Aimovig® and Emgality®. These four medications are all monoclonal antibodies, which in scientific terms means they are extremely large molecules. That means that they are unlikely to cross the placenta until around mid-pregnancy after the baby's structures and organs have developed. Therefore, these medications should not have a direct impact on the baby's development. It cannot be said that there is no increased chance of the baby being affected, but these medications may not be high risk exposures. These medications stay in the person's system for a very long time. So if Caroline would like to have any of these out of her system before she gets pregnant, it may take approximately 5 months to clear.

What are the specific reports that we have on Ajovy®, Vyepti®, Aimovig® and Emgality® that help us assess the risk of use in pregnancy?

There are 13 cases of exposure prior to pregnancy and 10 exposures during pregnancy in one report on Ajovy®

(fremanezumab-vfrm). In these cases, there was no increase in pregnancy loss, and one child was born with kidney and GI issues that cannot be proven to be caused by the medication treatment at this time.

There are two cases of Vyepti® (eptinezumab-jjmr) use during pregnancy. Outcome was reported on only one pregnancy which resulted in a miscarriage. However, based on what we know about monoclonal antibodies and the size of this molecule potentially being too large to pass through the placenta, it also would not be expected to have an increased risk of problems when used in the first trimester. More data and studies are needed to support this statement, though.

There are 116 cases of Aimovig® (erenumab-aooe) in one report. These studies include one prior to pregnancy, 108 during pregnancy, five during lactation and two at an unknown time. There was no increase in pregnancy loss or pattern of birth defects seen in the cases with known outcome. There were six cases of early birth in this group. One infant had growth issues but that mother was on multiple medications. There are at least five other cases in the medical literature that resulted in infants born without adverse pregnancy outcome or birth defects.

Finally Emgality® (galcanezumab-gnlm) was suggested to Caroline. There are 125 cases with data to consider. Six cases were with use of the medication prior to pregnancy, 107 cases were with use during pregnancy, 5 were with use during lactation and 1 case was use of the medication by dad. Six cases had unknown timing of use. No increase chance for pregnancy loss or pattern of birth defects was reported in this group of cases.

Back to our call with Caroline, and how we advised her on the medications that she was interested in – remember these: Nurtec ODT® and Emgality®. Both of the choices offered to Caroline can treat ***and*** prevent migraines, so one doesn't have an advantage over the other in that area. We discussed with Caroline that at this time there are no human studies on Nurtec ODT®. However, the animal data looks promising and low risk at this time. Additionally, it is a drug that quickly clears from the body. So she would not have to be off of it for months to have it clear from her body prior to pregnancy. In that time, there may be new human data reported that we could share with her closer to when she would try to conceive. Otherwise, the current human data on Emgality® looks promising. Caroline stated she plans to discuss these reproductive data with her prescribing healthcare provider and come up with a plan of action. Caroline may decide to try either of these medications now see how they work for her before trying to get pregnant knowing there may be waiting periods to have the medications clear from her body.

At the end of the day, dealing with a migraine might be a pain, but examining up-to-date data doesn't have to be a headache. That's why MotherToBaby is here to help!

Questions? Call 866.626.6847 | Text 855.999.3525 | Email or Chat at MotherToBaby.org.

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Welcome, spring! Did someone say wildflowers? (***AHHH…) T***rees? ***(AHHH…) Gr***asses? ***(CHOO!) Ugh!*** While many people enjoy renewed energy brought on by the bursting forth of spring color, others feel only the misery of seasonal allergies due to pollen, mold, and other springtime triggers. Combine seasonal allergy symptoms with pregnancy, and you can end up short on sleep, long on fatigue, and with an increased chance of respiratory complications if you have asthma. None of these things are good for you or your baby, and keeping asthma symptoms under control is especially important during pregnancy.

Wash Your Cares Away

A simple over-the-counter (OTC) saline nose spray can rinse pollen, dust, and other allergy triggers from your nose. This option is not expected to result in an exposure for the pregnancy or to increase pregnancy risks.

Sleep, Magical Sleep

To help you sleep better, consider using OTC nasal strips to open your nasal passages at night. Use a pillow cover to reduce dust and other allergens. Also try sleeping with your head slightly elevated to help drain the sinuses and reduce inflammation.

Still Suffering?

It may be worth having a conversation with your healthcare provider about the pros and cons of various allergy medications. Before grabbing an over-the-counter medication to treat your symptoms, consider this:

- With any medication, take the time to read your labels. Some allergy medications marketed for cough and cold contain alcohol, which should be avoided during pregnancy. Also, multi-symptom formulas might contain additional medications that you don’t need. As with any medication in pregnancy, use allergy medications for the shortest amount of time needed, and follow dosing instructions carefully.
- **Antihistamines:** Older antihistamines like diphenhydramine (sold under the name Benadryl® and other brands) and chlorpheniramine can make you sleepy, so they aren’t ideal for daytime use. Newer antihistamines, such as cetirizine (Zyrtec®), fexofenadine (Allegra®), and loratadine (Claritin®), are less likely to make you drowsy and have not been shown to increase the chance of birth defects or other pregnancy complications when used as directed.
- **Eye drops:** Allergy eye drops may contain antihistamines, steroid medications, or other active ingredients. Eye drops result in lower exposure for the pregnancy than oral (swallowed) medications do. However, some eye drops have been better studied for use in pregnancy than others have. Check with your healthcare provider or

contact a MotherToBaby specialist for questions about your specific eye drop.

- **Steroid nasal sprays:** OTC options include budesonide, fluticasone, and triamcinolone (you can find the active ingredients listed on the label). Some older studies suggested that using oral steroid medications might increase the chance of cleft lip or palate and affect the baby's growth, but newer studies don't find this to be true. In addition, nasal sprays are not well absorbed into the bloodstream when used as recommended, so there is less exposure for the pregnancy. Compared to some other nasal spray ingredients, fluticasone might be absorbed in greater amounts, but these still would not reach the amounts seen with oral medications. No increased pregnancy risks have been seen specifically with OTC steroid nasal sprays.
- **Decongestants:** The overall research does not suggest that using decongestants for a short time would increase pregnancy risks. However, decongestants work by temporarily making the blood vessels narrower. There are concerns that this could limit the supply of oxygen to the placenta and the developing baby. Some healthcare providers recommend avoiding decongestants in the first trimester, and using them with caution any time in pregnancy. Short term use (3 days or less) of nasal spray decongestants results in less exposure for the pregnancy than oral decongestants do.
- **Allergy shots**: Most reactions to allergy shots (redness, swelling, itching) are not dangerous. If someone is already receiving allergy shots before they get pregnant, there is no general recommendation to stop during the pregnancy. However, there is a small chance that a person could have a life-threatening allergic reaction (anaphylaxis) if they are new to allergy shots or are building up their dose. For this reason, it is not recommended to start getting allergy shots for the first time or to increase the dose during pregnancy.

If you have questions about specific allergy medications during pregnancy, including those available by prescription, talk to your healthcare provider or contact us at MotherToBaby. Happy spring!

Select References:

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Katie recently reached out to us; she told us that she has lupus and has been taking hydroxychloroquine for years to successfully manage her lupus symptoms. Her concern? “I just found out I am pregnant and my rheumatologist was not sure if I can continue taking hydroxychloroquine during pregnancy. I am worried for my baby but I am also worried about stopping my lupus medication since it helps my symptoms so much. I haven’t had a flare in over a year! I can suffer through the flares if I have to, but I don’t want to harm my baby. I don’t know what to do.’

Katie’s concerns about how to balance the management of her chronic health condition against her baby’s health during pregnancy are not uncommon. Generally, the healthier a woman is during pregnancy, the better it is for both them and their baby. When taking medication during pregnancy, the risks and benefits of taking or not taking the medication should be carefully considered. More specifically, could the untreated condition cause more problems than taking the medication?

What is lupus and how could it affect a pregnancy?

Lupus, also known as systemic lupus erythematosus (SLE), is an autoimmune disease that affects many different parts of the body. The symptoms are variable; however, the kidneys, joints, and skin are commonly affected. It is very important for both the health of the pregnancy as well as the health of the woman who is pregnant to achieve optimal control of lupus and maintain that control without flares (relapses in symptoms) throughout the pregnancy. For those who are planning a pregnancy, it is generally advised that at least 6 months without flares reduces the chances of pregnancy-related problems.

Lupus, especially if not well controlled, can cause serious health complications for both the woman who is pregnant as well as the baby. These complications include nephritis (inflammation of the kidneys that causes difficulty filtering waste from the body) and blood conditions such as anemia (a condition in which you don’t have enough healthy red blood cells to carry adequate amounts of oxygen to your body’s tissues) and thrombocytopenia (a condition in which the blood does not clot as fast as it should, which can cause excess blood loss). Inflammation in the lungs, heart, or brain can also occur and cause serious health problems.

People who have lupus also have a higher chance to develop high blood pressure during pregnancy and preeclampsia (a pregnancy-related condition that has several symptoms including a dangerous rise in blood pressure). People with lupus, most often the ones who develop high blood pressure or other health problems, may also have a higher chance of having a baby with poor growth which can lead to late miscarriage and preterm delivery (delivery before week 37).

Rare complications for the baby may include being born with symptoms of lupus (called neonatal lupus erythematosus (NLE)). These may be temporary and often disappear by six months of age. NLE is mostly seen in children when the pregnant woman has anti-SSA and anti-SSB antibodies. The most serious complication of neonatal lupus is a heart rhythm problem called congenital heart block which can often be detected on ultrasound and may lead to health complications and death. If these antibodies are present, additional ultrasounds for the heart may be recommended.

Katie was surprised. 'I thought if I stopped my medications my flares would be painful and uncomfortable, but I never thought it could seriously affect my health or the health of my baby. Can you tell me more what is known about taking my lupus medication during pregnancy?'

So what do we know about lupus medications and pregnancy?

Many medications used to treat lupus are not thought to increase risks to a pregnancy over background chances that all pregnant individuals have. Medications work differently for different people. It is very important to talk with your healthcare providers before making any changes to how you take your medication. It is important to consider (with help of a rheumatologist) which medication works best to treat you. Regarding Katie's question, the Society of Maternal Fetal Medicine (SMFM) recommends continuing the use of hydroxychloroquine during pregnancy. This recommendation is based on studies which did NOT show an increased risk for pregnancy related problems when hydroxychloroquine is used. Additionally, the studies showed a lower chance of lupus related problems during pregnancy when hydroxychloroquine is used.

There are many other medications such as steroids and biologics that lower the body's immune system (immunosuppressants) that can also be considered for use during pregnancy. However, certain medications for lupus are not recommended for use during pregnancy because they can increase the chance for birth defects and other pregnancy-related problems. SMFM recommends that methotrexate should be stopped 1-3 months before pregnancy and mycophenolate mofetil/mycophenolic acid should be stopped at least 6 weeks before attempting pregnancy. NSAIDs (non-steroidal anti-inflammatory drugs), such as ibuprofen, high dose aspirin, etc. are not recommended for use during pregnancy.

For information on specific medications make sure you talk with your healthcare provider or contact MotherToBaby and see our medication fact sheets at https://mothertobaby.org/fact-sheets/ . It is very important to talk with your healthcare providers before making any changes to how you take your medication.

Katie summarized the information she was given very well, 'It seems like making sure my lupus is well controlled will set both me and my baby up for the highest chance of being healthy. I feel much more comfortable continuing my medication knowing that with my own health, I am helping my baby to be healthy as well. I will talk with my healthcare providers to plan for monitoring both me and the pregnancy. Is there anything else I should know?'

Other info to know about lupus and pregnancy

It's not uncommon for new medications to be developed for the treatment of lupus. If there is one thing that these new medications have in common, it's that they very rarely have adequate, real-world data that describes whether the medication is safe to take during pregnancy. Pregnancy registries are the types of studies that give us this information, which is what allows us to provide risk assessments to people like Katie. That's why we suggest to any pregnant woman with lupus that they consider joining the pregnancy registry for the medication(s) they are taking if one exists. The U.S. Food and Drug Administration (FDA) maintains a list of ongoing pregnancy registry studies on their website. If you're planning a pregnancy or are already pregnant, now is a great time to find out more about the benefits of joining a lupus pregnancy study.

Women who are pregnant and have lupus will require some additional monitoring during pregnancy. They should be followed by their rheumatologist to make sure their symptoms are well controlled. Additional monitoring during

pregnancy such as blood pressure checks, additional lab tests and additional ultrasounds may be recommended. Make sure you talk with your healthcare provider to discuss the management plan for your pregnancy.

Katie returned to MotherToBaby a few weeks later and told us she has been working together with her rheumatologist as well as her obstetric team including a high-risk pregnancy provider (also called Maternal Fetal Medicine (MFM) specialist) to make sure both her and her baby are as healthy as they possibly can be. 'I felt empowered by being informed, having all my healthcare providers in my corner and knowing that by taking care of myself, I am taking care of my baby too. Thank you, MotherToBaby!'.

For more information about lupus and pregnancy, including links to lupus-related MotherToBaby Fact Sheets, visit our lupus resources page at https://mothertobaby.org/pregnancy-breastfeeding-exposures/lupus/. You can also contact one of our information specialists for a no-cost risk assessment by visiting https://mothertobaby.org/contact/.

If you are pregnant and taking belimumab (Benlysta®) to treat SLE or lupus nephritis, please consider enrolling into our observational study. This study will give women with lupus better answers about how lupus and its management can affect a pregnancy and a developing baby. You will not be asked to take or change any medications, and you can participate from the comfort of your home.

LEARN MORE

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Last year I was pregnant with my first child. At the same time, I was going through the immigration process to apply for permanent residency in the United States. I wasn’t aware of the many things that you must do to get your health records cleared by immigration and how that process can be a great source of anxiety during pregnancy. If you are an immigrant, you may not have health insurance or cannot understand the language, which can be another challenge. In order to have sound and scientifically true advice during that critical period, I always consulted with my doctor and then MotherToBaby.

First, I was told that I needed to get revaccinated for certain diseases, even though I may have had them or may have been previously vaccinated in the past. Those vaccinations included measles, mumps and rubella (MMR), varicella, polio, tetanus diphtheria pertussis (Tdap), hepatitis B, and COVID-19. As soon as I heard this long list, I went online and checked the MotherToBaby facts sheets about those vaccines one by one to see what was known about their use in pregnancy. It turns out the Hepatitis B and COVID-19 vaccines are not associated with risk during pregnancy. Even more, it is recommended to get a Tdap vaccine during pregnancy to provide protective antibodies to your baby against pertussis (whopping cough). Live vaccines like MMR and varicella (chickenpox) are not recommended during pregnancy. Thankfully I was able to get bloodwork done to check antibody levels (protective proteins) showing prior protection. If you can show full protection, you no longer need to get vaccinated for these diseases after pregnancy.

One other thing I had to find out was my tuberculosis (TB) status. This is done by blood work, but if the results don’t rule out the disease, you would need a lung x-ray. In general, X-rays are not recommended during pregnancy. However, if needed, studies show that a single chest x-ray is not associated with an increased risk for birth defects or pregnancy complications for the developing baby. It is important to know your tuberculosis status before pregnancy since active infection can be associated with preterm labor (early birth before 37 weeks), low birth weight of the baby, or even maternal death. Getting TB treated as soon as possible, even when you are pregnant, is so important. Tuberculosis is a slow-growing, pesky disease that is common in certain countries, including my home country, Turkey, but not common in the United States. That is why it is important to get it checked during the immigration process to prevent spread.

In addition to making sure I was getting my immigration to-do list sorted out, I also had to contend with new feelings brought on by pregnancy, both happy and stressful ones. This included all day nausea, aka the morning sickness, I had lots and lots of morning sickness. My first instinct was to call my mom and ask for help. She gave me a recipe for a concoction that included turmeric, sage, ginger, and mistletoe. I made it and drank it a couple of times without thinking whether that might be safe during pregnancy since it was all natural and herbal. A few days later, I was talking with one of my best friends, who was pregnant as well, complaining about morning sickness and asking for suggestions that have helped her. She said she would not drink any herbal tea without checking with her doctor. Ding ding, after talking with her, I was terrified to research the topic, and when I did, it confirmed my worst fears. The mistletoe in my nausea drink might cause miscarriage if consumed in large amounts. Many of the other herbs hadn’t been studied in pregnancy at all. I didn’t consume any more of the morning sickness drink and am fortunate that I had a healthy term baby. Lesson learned!

As immigrants, we bring our full heritage with us and try to combine the best of both worlds. Those herbal remedies and recipes are our culture; however, pregnancy is a special and very vulnerable time period. Everybody should be cautious about what we put into our bodies, especially herbal remedies since they are mostly not well studied during pregnancy to show whether they are associated with risks to the baby or not. Even if they are studied, the production and harvesting are not regulated or controlled by the Food and Drug Administration (FDA), or other governmental agencies, and contaminations might happen. Better safe than sorry, right?

Carrying my baby through the immigration process and following my dreams along the way was challenging, but I learned on that road that it is important to question my customs and traditional medications when pregnant. Not everything my mother or grandmother did is safe and effective. Also, I was glad that MotherToBaby was there for me when I was going through the immigration process while pregnant to ask my burning questions about vaccinations and x-rays.

Anyone with questions about herbals, vaccines, TB testing, or any other exposure in pregnancy should know that MotherToBaby is a great resource. Call or chat today to get your individual questions answered by a teratogen information specialist so you can rest assured that you and your baby can have a healthy and well-informed entry into America.

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by Sarah Obican, MD, MotherToBaby President

Though I wish I didn’t remember the day well, I do. I was a maternal fetal medicine fellow in NYC and I was sitting with my two beautiful co-fellows. When I say my co-fellows were beautiful, I mean that inside and out. We were an odd pairing of three musketeers. Young, bright, professional women, training to take care of women with high-risk pregnancies… and all three of us were pregnant. It was completely unplanned and highly unusual for all three of us to conceive, all within a few short weeks of each other. But there we were one day, sitting at our desks, talking about our individual research projects and occasionally interjecting in each other’s conversations with excitement about our future babies. I loved my two colleagues so much, and I was so excited to imagine that we would follow each other’s careers and see our children grow up, all similar in age.

In the middle of this conversation, something made me just get up and say to them “I’ll be right back!” I still don’t know what made me do it. I had a feeling hard to describe, but it made me walk over to our ultrasound unit and ask my sonographer colleague to please do an ultrasound.

I was on the examining table within minutes. But her silence after she put the probe down on my ultrasound gooped-up belly felt like an eternity. Another sonographer came into the room. I knew. That’s when the world went dark.

Now, I am physician and I cannot explain this. For a few moments, quite literally, the bright NYC day, the room, the people in the room, went completely dark. I couldn’t see. I didn’t lose consciousness, but I couldn’t see. In my career, I sadly had to care for countless women who went through a miscarriage and in that darkness, I wondered if they had experienced the same. A few moments later I was back in the ultrasound room, now with an overcoming wave of sadness which made me wish I was in the numbing darkness again.

The American College of Obstetricians and Gynecologists estimates that 26% of all pregnancies end in a miscarriage and a significant proportion of those are in already clinically recognized pregnancies (when the pregnant woman already knows she is pregnant).

Miscarriage vs. Abortion

The words miscarriage and abortion are often used interchangeably. For example, a missed abortion in the world of obstetrics means that pregnancy stopped naturally and that there is no heartbeat or if early enough in the pregnancy, that there is no continuation of fetal growth or development. These pregnancies can pass naturally with bleeding or can be aided by a physician by giving medication of performing a procedure. During this time, there is a lot in terms of discussion of possible contributing factors including abnormal genetics and counseling on recurrence for the next pregnancy. It’s a tough, sensitive time for patients. I know it from both sides.

Ectopic Pregnancy

Sometimes desired pregnancies present themselves as ectopic pregnancies. An ectopic pregnancy is when an already fertilized egg implants and begins to grow outside of the uterus in an area that cannot adequately support the pregnancy. Most of the ectopic pregnancies (>90%) occur in the fallopian tube, but no matter where the pregnancy implants, it can be life threatening for the pregnant woman. This is because the location in which the ectopic pregnancy has implanted cannot grow, expand and adequately support the pregnancy nutritionally and can result in the structure rupturing and causing internal bleeding. While all miscarriages can feel devastating, an ectopic pregnancy is an emergency that requires immediate treatment by a physician. Depending on the size and development of the ectopic pregnancy and the patient’s symptoms, the ectopic pregnancy can be treated with medication or by surgery. This too gives a great sense of loss for patients because often these pregnancies were highly desired.

It is important to note that being treated for a miscarriage or an ectopic pregnancy either by the use of medications or surgery is not considered a termination. As a high-risk obstetrician, I know that providing great medical care for a miscarriage, an ectopic pregnancy or providing access to desired abortion care is essential for the pregnant woman’s health and safety.

Shedding Light on the Darkness

With my personal journey of years of infertility and in vitro fertilizations, there are not many positives from that sunny day in NYC. However, that personal darkness shed light on all of what my patients in similar situations had to go through. I talk about my history openly, if asked. When appropriate, I share with my patients about my loss and about infertility. I am reminded by my patients that we have to speak more about these human experiences. To normalize them, to not feel alone. As for the experience of that day, I am thankful for that knowledge and when I have to be the first to tell my patient that she just had a pregnancy loss, I get close to her and I hope that my words, my actions and my demeanor show them what I am thinking inside…. I see you and I've got you.

References/Resources

https://www.acog.org/advocacy/abortion-is-essential

https://www.acog.org/advocacy/facts-are-important/understanding-ectopic-pregnancy

https://www.ncbi.nlm.nih.gov/books/NBK532992/#:~:text=The%20American%20College%20of%20Obstetricians%20and%20Gynecologists%20%28ACOG%29,early%20pregnancy%20loss%20occurs%20in%20the%20first%20trimester

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