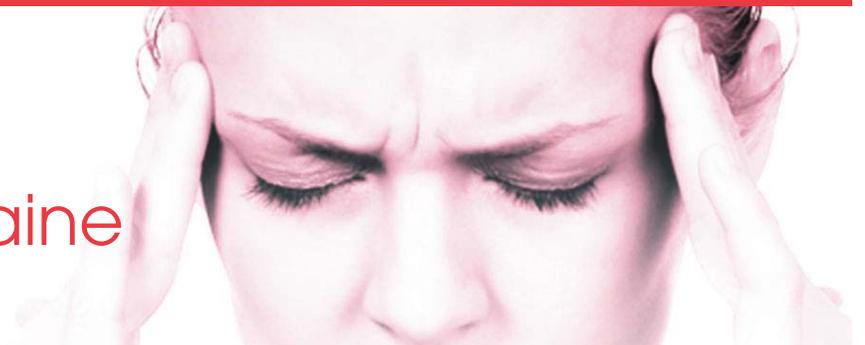


Headache Toolbox

Pregnancy and Lactation – Migraine Management



Along with the excitement of a possible pregnancy, migraineurs often experience a feeling of dread, wondering which headache medications need to be discontinued and how to manage expected migraines without their usual treatment regimen. This anxiety extends from the time when pregnancy is possible but not established, during the 9 months of actual pregnancy and beyond, when breastfeeding passes on mother's milk to the newborn infant.

The good news is that most women notice their migraines either go away or greatly improve in the 2nd and 3rd trimesters of pregnancy. At least 4-8% of women do not have this lucky break, and for them managing migraines can be particularly challenging. After delivery, most women quickly return to their pre-pregnancy migraine pattern. While nursing, many medications remain off the safe list because of potential problems passed through the mother's milk, but treatment options do improve.

Perhaps, the most difficult time is when a woman is planning pregnancy and it is unknown whether she is actually pregnant. Unfortunately, to avoid fetal exposure to potentially harmful medications, it is necessary to stop most migraine preventive medications and avoid the use of typical prescribed and over-the-counter as-needed medications previously used for headache. During normal menstrual periods, using these acute medications may be considered safe, as flow signals that a pregnancy has not actually taken place. At other times, it must be presumed a woman is pregnant if she is not using contraception.

Migraine preventive medications do not generally permit the luxury of stopping and starting abruptly, and need to be tapered when planning a pregnancy, or as soon as possible in the event of an unplanned pregnancy. Many medications are best removed by a gentle wean, although others can be stopped quickly, particularly in situations in which an unplanned pregnancy is confirmed. Any confirmed pregnancy while taking medications should result in a phone call to the headache treatment provider's office for immediate advice, followed by an office visit for migraine management counselling while pregnant.

Grouping medications into three broad categories, there are those known to cause fetal harm in humans or animals, those for which no harm has been found to date, and those that have been studied extensively through testing and/or patient and infant follow-up, with no increase in fetal or infant defects.

Before deciding if a medication is needed to help prevent or treat migraines in pregnancy, it may be best to consider the safest interventions, which are lifestyle changes likely to reduce the frequency and severity of migraine. These include eating regular, healthy meals, adequate sleep, and at least one half hour of exercise (walking is fine) per day. Behavioral treatment for stress reduction such as relaxation training, biofeedback, and yoga may be helpful.

Options are limited in prescription preventive medications, because of the need to avoid any medication that has shown some problem in animals or fetuses. Memantine (brand name Namenda, Actavis, New York, USA) is one of the few preventives not found to cause harm in developing fetuses. It is a drug typically used to treat dementia, but it has also been found to be helpful in some studies of migraine prevention. It works by blocking glutamate, a chemical associated with increased migraine pain and frequency.

Another preventive medication used in pregnancy is cyproheptadine, an antihistamine. It has been used for decades for migraine prevention, is considered safe in pregnancy, and is inexpensive. However, the major drawbacks include weight gain and fatigue, so this medication has limited appeal in those who are not pregnant. Taking cyproheptadine at night and at the lowest effective dosage can be helpful. It is not to be used in breastfeeding, though.

Magnesium is frequently cited as a safe migraine preventive medication in pregnancy. Unfortunately, there have been recent findings showing intravenous high-dose magnesium can be associated with bone abnormalities in the fetus. Since it is not known at what dosage these bone abnormalities may occur, or if they happen when magnesium is taken by mouth, magnesium is no longer recommended as a daily preventive medication in pregnancy.

Acupuncture is controversial with regards to effectiveness for migraine. Clear proof of effectiveness has not been found, and when used in pregnancy there can be an increased risk of miscarriage depending on the location of needle placement. Licensed massage can be helpful in the hands of a knowledgeable practitioner familiar with pregnancy precautions.

When a pregnant woman does get a migraine, there are as-needed medications that are considered likely to be safe. These include metoclopramide, diphenhydramine, caffeine, cyproheptadine, and acetaminophen. However, even acetaminophen, often felt to be the safest headache medication in pregnancy, has recently shown some possibility of risk. A large Danish study found an increased frequency of behavioral disorders such as hyperactivity in children whose mothers took acetaminophen while pregnant. Although this study is new and further investigation is needed, it serves as a caution against taking acetaminophen unless it is necessary, and not taking it too frequently in any case when pregnant.

Nerve block injections using lidocaine, which is similar to the medication used at the dentist's office for numbing the gums, represent another option for difficult-to-treat migraines in pregnancy. Lidocaine has not been found to cause birth defects or problems in pregnancy, and is injected using a needle to block nerve pain in the head and scalp. It is low risk, but as with any injection, there is the risk of side effects coming from spreading of the medication resulting in numbing of unintended areas, bleeding, and infection.

Table.—Commonly Used Migraine Medications Listed Under the Type of Risk Associated With Their Use in Pregnancy

Category A	Category B	Category C	Category D	Category X
None	Acetaminophen Caffeine Cyproheptadine Diphenhydramine Memantine Metoclopramide Ondansetron Lidocaine	Triptans (all) Promethazine Narcotics NSAIDs (1st and 2nd trimesters) Butalbital Prochlorperazine Aspirin (1st trimester) Methocarbamol Gabapentin Zonisamide Quetiapine Propranolol Nadolol Metoprolol SSRI and SNRI antidepressants (except paroxetine) Tizanidine Baclofen Amisulpride Onabotulinum toxinA	Magnesium Benzodiazepines Isometheptine NSAIDs (3rd trimester) Butorphanol Isometheptine Aspirin (2nd and 3rd trimesters) Valproic acid Topiramate Nortriptyline Imipramine Lithium Paroxetine	Dihydroergotamine (DHE)

Category A: Safety studies in pregnant women show no harm. *Category B:* There are no controlled studies in pregnant women, but in animal studies, no harm has been found. *Category C:* There are no controlled studies in pregnant women, but in animal studies harm has been found. *Category D:* Risk has been found to humans following use in pregnant women. *Category X:* absolutely contraindicated in pregnancy (Table).

Note that as of June 2015, the Food and Drug Administration (FDA) has determined that the use of letter categories will be abolished, and each drug will instead have a description of known and unknown risk findings. For purposes of facilitating an easier-to-read table, these category names are maintained here. Up-to-date changes in medication categories can be obtained online through FDA-connected websites.

The length of relief from nerve blocks varies, but overall they are considered a safe intervention if needed.

For nausea, ondansetron either in pill, dissolvable form, or given intravenously, is considered safe following extensive studies. Unfortunately, it has not been found to reduce the pain of migraine, although it is a very effective medication for the nausea.

In light of the difficulties in finding a safe medication for a pregnant woman, narcotics are sometimes used. Unfortunately, opioids can create a different set of problems, plunging a patient into a chronic migraine state without access to safe rescue medication options. Using narcotics as few as 2 days per week can lead to chronic migraine, and often once a migraine is treated with narcotics, other migraine options are less effective. Narcotics do cross the placenta and can affect a fetus by slowing the heart and breathing as well as increasing the incidence of birth defects.

Regular use can result in a withdrawal syndrome in the newborn. A woman who becomes pregnant while taking ongoing narcotics will need to consult with her provider as soon as possible for recommendations. Abrupt stopping of the narcotics after chronic use can result in miscarriage.

As noted, after pregnancy, migraines are likely to return to their previous pattern of frequency and severity. While nursing, any sedating medications will be transmitted through the mother's milk to her infant, and this includes benzodiazepine tranquilizers and narcotics. As noted before, antihistamines such as diphenhydramine and cyproheptadine are not recommended in a nursing mother. Sumatriptan has a registry of infants whose mothers used this

migraine medication, and no harm was found with its use acutely to treat migraine. The American Pediatric Association noted before, association cleared sumatriptan for use in nursing mothers without the need for "pump and dump." Other triptans have not been as well studied in this context, but so far there is no warning associated with their use other than the lack of controlled studies. In general, medications are passed on in a mother's milk to varying degrees, so weighing the potential risks versus the benefit of taking a given drug is necessary. An up-to-date LactMed database of medications and safety studies in nursing mothers is maintained at the web site <http://toxnet.nlm.nih.gov/newtoxnet/lactmed.htm>.

In summary, most women will experience migraine relief in the second and third trimesters of pregnancy. At other times, and when planning a pregnancy, medications need to be minimized and used only after weighing the risks and benefit. Lifestyle changes, healthy sleep, exercise, and stress management techniques can be very helpful for migraine management and overall health in pregnancy. After pregnancy, most medications are passed on to the infant in breast milk in varying degrees. Some acute medications such as sumatriptan can be used while nursing. Discussion concerning the pros and cons of all migraine medications is recommended between providers and women who may become pregnant, are pregnant, or are nursing.

Deborah Tepper, MD
Cleveland Clinic Headache Center



To find more resources, please visit the American Migraine Foundation