

## Migraine in Pregnancy

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## **Background**

Migraine is an extraordinarily common neurological disorder that disproportionately affects women of childbearing age. Important issues to consider when approaching pregnant women with migraine include:

1. The assessment of pregnant and postpartum women presenting with acute headache.
2. The prognosis of migraine during pregnancy and the postpartum period.
3. The appropriate therapies available to treat pregnant and lactating women with migraine.
4. The risks of adverse labor and delivery outcomes in pregnant women with migraine.

## **Acute headache in pregnant and postpartum women**

New headache in pregnancy may be a red flag prompting evaluation for secondary headache, even in women with a migraine history. The more specific red flags in pregnant women include the occurrence of new or acute headache with elevated blood pressure sustained over 2 readings, seizures, fever, and a lack of a headache history. In pregnant women with a history of migraine, a more prolonged attack duration may be a specific red flag. The most common secondary etiologies encountered include, but are not limited to, headache related to hypertensive disorders of pregnancy (especially preeclampsia), pituitary disease, systemic infection, and cerebral venous thrombosis.

Migraine often relapses in the postpartum state, though acute headache during the immediate postpartum headache can be attributed to a variety of secondary etiologies, often indicated by important clinical clues. These may include an orthostatic headache pattern (postdural puncture headache even with just epidural anesthesia), thunderclap headache (reversible cerebral

vasoconstriction syndrome [RCVS], aneurysmal subarachnoid hemorrhage, pneumocephalus related to obstetrical anesthesia), elevated blood pressure (preeclampsia, posterior reversible encephalopathy syndrome [PRES]), visual loss (preeclampsia, PRES, pituitary apoplexy), Horner's syndrome (cervical artery dissection), papilledema (cerebral venous thrombosis), and focal neurological symptoms or signs (ischemic or hemorrhagic arterial or venous stroke, PRES, RCVS).

### **Migraine prognosis in pregnancy and postpartum**

The prognosis of migraine during pregnancy is generally favorable. Most women who have migraine without aura do quite well, with the majority experiencing migraine improvement or even remission as the gestational weeks advance. Women who have migraine with aura have a more uncertain prognosis, and may not improve to the same extent; in addition, the presence of aura may be overrepresented in women who experience migraine for the first time during pregnancy. Unfortunately, little is known about the prognosis of chronic migraine during pregnancy. Over half of women who have a migraine history may experience a migraine attack within one month postpartum. Though the evidence is not strong, breast-feeding may be protective in minimizing the occurrence of postpartum migraine.

### **Migraine treatment in pregnancy and postpartum**

Fetal safety concerns in pregnant women prompt a shift in the usual hierarchy of migraine therapies utilized. No single therapy is without any potential fetal or maternal adverse effects, so the benefits and risks must be weighted against each other. For acute treatment, the preponderance of evidence suggests acetaminophen and antiemetics, particularly

metoclopramide, are safe and potentially effective in pregnant women with migraine. Other acute treatments that can be utilized include select corticosteroids such as methylprednisolone, particularly after the first trimester, as well as peripheral nerve blocks (PNBs) with lidocaine, which should have no systematic or direct teratogenic adverse effects. PNBs also have the advantage as working as a short-term preventive treatment strategy that can be repeated. Though research experience with the use of triptans during pregnancy is limited, the birth defect rate seems to be in line with the general population, and if the patient has a prior track record for success and other options are limited, their use could be considered. The use of nonsteroidal anti-inflammatory drugs is generally discouraged by obstetricians, but there may be a relatively safer period of time to use them in the second trimester if absolutely necessary. Intravenous magnesium was previously felt to be a safe therapy for pregnant women with migraine but repetitive exposure for the treatment of preterm labor was recently associated with fetal bone demineralization, creating uncertainty for single use for acute treatment and orally for preventive treatment in pregnant women with migraine.

Preventive therapies are often unnecessary for pregnant women with migraine as the natural history during pregnancy is generally favorable. However, some pregnant women may require prophylaxis, and many therapies are relatively safe, including select beta blockers and potentially memantine and cyproheptadine as well. Topiramate and valproic acid should be avoided as the teratogenic potential almost never justifies their use. Though botulinum toxin is a large molecule which should not cross the placenta and some evidence suggests no clear teratogenic signal, experience is very limited and most practitioners avoid its use in pregnancy, and stop administering it well in advance of attempted conception. Repeated PNBs may also be quite

safe, and though evidence is somewhat limited, can likely be employed safely for preventive purposes. Finally, it is reasonable to consider approved devices for migraine treatment in pregnant women as theoretically their use should be safe in pregnancy, including transcutaneous supraorbital neurostimulation and single pulse transcranial magnetic stimulation.

Most migraine therapies are relatively safe to use in breastfeeding women, but practitioners should be aware of drug milk:plasma ratios, which may shift choices. For example, eletriptan has the lowest milk:plasma ratio and may be the preferred triptan for lactating women. In addition, the use of any therapy with the potential to depress the central nervous system would ideally be avoided in mothers nursing premature infants. One strategy commonly employed is to discard the first pumped breast milk after use of a medication for migraine that may adversely impact a breastfeeding infant.

### **Risks of adverse pregnancy outcomes in women with migraine**

A migraine history elevates the relative risk of many medical and obstetrical complications during pregnancy and the puerperium, particularly preeclampsia and ischemic stroke. The mechanisms are not certain but could relate to endothelial dysfunction, hypercoagulability, and comorbidity. Less certain are associations with preterm delivery and low birthweight, as well as labor and delivery outcomes among those pregnant women whose migraine is more active during the same gestation.

### **References**

1. Robbins MS, Farmakidis C, Dayal AK, Lipton RB. Acute headache diagnosis in pregnant women: a hospital-based study. *Neurology*. 2015;85:1024-1030.
2. Wells RE, Turner DP, Lee M, Bishop L, Strauss L. Managing Migraine During Pregnancy and Lactation. *Curr Neurol Neurosci Rep*. 2016;16:40.
3. Hutchinson S, Marmura MJ, Calhoun A, Lucas S, Silberstein S, Peterlin BL. Use of common migraine treatments in breast-feeding women: a summary of recommendations. *Headache*. 2013;53:614-627.
4. Govindappagari S, Grossman TB, Dayal AK, Grosberg BM, Vollbracht S, Robbins MS. Peripheral nerve blocks in the treatment of migraine in pregnancy. *Obstet Gynecol*. 2014;124:1169-1174.
5. Wabnitz A, Bushnell C. Migraine, cardiovascular disease, and stroke during pregnancy: systematic review of the literature. *Cephalalgia*. 2015;35:132-139.