

# Migraine management in pregnancy

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## Summary

In spite of the fact that migraines are one of the major problems seen by primary care providers, almost half of people with migraines do not obtain appropriate diagnosis or treatment. Migraine occurs in about 18% of women, and is often aggravated by hormonal shifts occurring around women's menses, during pregnancy, and during perimenopause. Quality of life with migraines is often greatly diminished, and many women miss work days with migraines. In women, the hormonal fluctuations seen during pregnancy and lactation can affect migraine frequency and magnitude. Understanding the evaluation of headache in pregnancy is important, especially given the increased risk of secondary headache conditions. Pregnancy and lactation can complicate treatment options for women with migraine because of the risk of certain medications to the fetus. This review includes details of the workup and then provides treatment options for migraine during pregnancy and lactation.

**Key words:** Migraine, pregnancy, headache, treatment.

## Introduction

Most epidemiological studies have demonstrated that the majority of women suffering from migraine note remarkable and increasing improvement of their attacks during pregnancy, from the first to the third trimester. Women suffering from migraine are also at higher risk of developing gestational hypertension, preeclampsia, or vascular complications related to pregnancy including ischemic stroke and other vascular events in the peripartum period. Primary headaches are most common in women during their reproductive years and are affected by the hormonal fluctuations during pregnancy. Pregnancy creates alterations in maternal physiology which predispose to unique neurologic disorders. Pre-eclampsia, eclampsia, certain types of ischemic and hemorrhagic stroke, reversible cerebral vasoconstriction syndrome, posterior reversible encephalopathy syndrome, and headache all appear to share a common origin from vascular endothelial dysfunction, with overlapping clinical presentations. Among primary headaches, migraine is the form more sensitive to the ovarian hormonal milieu. Migraine without aura benefits from the hyperestrogenic state of pregnancy and the lack of hormonal fluctuations, while migraine with aura presents distinctive features. Indeed, a very strong improvement of migraine without aura has been documented across gestation, and only a minority of pregnant women still suffers during the third trimester. On the other hand, fewer women with migraine with aura report improvement or remission, and new onset of aura may be observed during pregnancy. After delivery, breast-

feeding exerts a protective action on migraine recurrence. The persistence of migraine during gestation seems to affect neonatal outcomes, and several studies indicate a link between migraine and an increased risk of developing gestational hypertension, preeclampsia and other vascular complications. This article reviews the epidemiology, prognosis, and management of primary headaches during pregnancy and lactation, and considers secondary headaches that are important to exclude.

## Prevalence

Migraine is one of the most common neurological disorders among women, with a female/male proportion of 3-4:11. Women, compared with men, have a 1-year migraine prevalence nearly three fold higher and lifetime incidence more than twofold higher. Its prevalence among women varies from 4% before puberty to 25% during the reproductive life, decreasing later in perimenopause and postmenopause. Moreover, menarche, menstruation, pregnancy, and menopause as use of oral contraceptives and of hormone replacement treatment may influence migraine occurrence. Until puberty, migraine affects both sexes equally. After the menarche there is an increasing prevalence of migraine in women. Changes in migraine frequency can also occur during pregnancy, lactation and contraceptive use. During pregnancy, the frequency of migraine decreases in most women, with an increase in its remission from the first to the third trimester. One of the

explanations for these findings is the increased levels of estrogen in the first trimester and a tendency to stability during the second and third trimesters of pregnancy. The higher-than-expected incidence of vascular disease reported in migraineurs suggests that migraine may, in some cases, be a dangerous condition rather than just a troublesome, but innocent, disorder. [1-5].

### Headache types and risk factors

The International Classification of Headache Disorders categorizes primary and secondary headaches [6]. The most frequently reported triggers for tension-type headache and migraine are stress, irregular or inappropriate meals, high intake or withdrawal of coffee and other caffeine-containing drinks, dehydration, sleep disorders, too much or too little sleep, and reduced or excessive physical exercise [7, 8].

#### *Primary headaches*

Primary headaches account for the majority of headaches during pregnancy. Of the primary headaches, tension-type headache and migraine generally improve during pregnancy. A common cause of daily headache in a patient with a history of primary headache is medication overuse headache. They do not change in frequency compared to the prepregnancy state. Migraine headaches can occur with or without aura. They are frequently unilateral and pulsatile. Fluctuations in the estrogen level rather than the absolute level may trigger a migraine. The effect of pregnancy on cluster headache is limited because of the rarity of the condition, and the data are conflicting. During pregnancy migraine without aura tend to improve due to the stable level of estrogen. Sances and colleagues found that migraine without aura significantly improved in over 87% of patients by the third trimester. Breast-feeding reduced migraine recurrence within the first month after childbirth to 50% of patients in comparison to 86% that bottle-fed. The benefit lasted for 6 months. One year after delivery, 80% of both populations had experienced recurrence of headache [9].

Recurrent episodic headaches that last between 4 and 72 hours and are associated with photophobia, nausea, and disability in an otherwise well person are typical features of migraine. Up to 60% to 70% of women with preexisting migraine report fewer migraine attacks during pregnancy [10].

#### *Secondary headaches*

This type of headaches are caused by other conditions distinct from primary headaches. Secondary causes of headache that are more likely to occur during pregnancy include cerebral venous thrombosis, posterior reversible encephalopathy syndrome resulting from eclampsia, postdural puncture headache, stroke, and pituitary apoplexy. While migraine and tension type headaches do not have a negative impact upon pregnancy directly, the following differential diagnostic con-

siderations should always be kept in mind. The clinician should inquire about the character of the headache (acute onset? severe?), lack of similar headaches in the past, change in headache pattern and progressively worsening or persistent headache. On examination the clinician should be vigilant for focal neurologic findings, decreased level of consciousness, emesis or syncope at the onset of headache, convulsion, fever and meningismus [11].

### Diagnosis

Migraine that occurs for the first time during pregnancy necessitates a detailed history, physical examination and radiographic or laboratory tests as appropriate to exclude secondary causes of headache which may resemble migraine. Migraine is also associated with an increased risk of hypertensive disorders of pregnancy. Specific questions can help to evaluate secondary causes of headache that may need urgent assessment. Because secondary headaches can occur in a patient with a long-standing history of primary headache, it is important to elicit new symptoms. This approach can separate those who need further investigation from those with benign secondary headaches or typical histories of primary headaches. The latter can be reassured, treated, and followed by the neurologist or primary care physician as appropriate. Examination should focus on assessment for signs of concerning diagnoses such as infection or hemorrhage; severe hypertension; and neurologic signs including papilledema or hemorrhages on funduscopy, neck stiffness, altered consciousness, or weakness.

### Treatment

Headache presenting in pregnancy is of significant concern to the affected woman. Quick and correct diagnosis leads to the optimal management, minimizing risks to the pregnancy. Migraine in pregnancy can cause considerable concern to both patient and doctor, particularly if migraine starts for the first time during pregnancy or if the woman has her first attack with aura. Most headaches follow a benign course during pregnancy, although migraine is associated with increased risk of hypertensive disorders of pregnancy and stroke. Several strategies have been developed to distinguish secondary headaches that need urgent assessment and management from benign primary and secondary headaches and to minimize the risk of misdiagnosis. Primary headaches are common and typically improve during pregnancy. Management of primary headaches during pregnancy is essentially similar to management in the non-pregnant state, with a few exceptions. Secondary causes of headache that are more likely to occur during pregnancy include cerebral venous thrombosis, posterior reversible encephalopathy syndrome resulting from eclampsia, postdural puncture headache, stroke, and pituitary apoplexy. There is often confusion regarding which medicines are

safe to use during pregnancy and breastfeeding, leaving many women unable to control their attacks effectively.

Pregnant women with tension-type headache or migraine should be encouraged to avoid skipping meals, to take regular exercise, to drink plenty of fluids, and to maintain a regular sleep pattern. Alcohol and smoking are potentially harmful to the fetus and should be avoided during pregnancy.

Nondrug therapies such as;

- Relaxation,
- Biofeedback,
- Physical therapy
- Acupuncture
- Magnesium sulfate
- Vitamin B2, D
- Coenzyme Q10 are safe and may be effective in pregnancy.

Coenzyme Q10 daily is effective for migraine prophylaxis and, when taken during pregnancy, has been associated with a significant reduced risk of preeclampsia. Similarly, magnesium supplements, which can be used for migraine prophylaxis, can halve the risk of eclampsia [12-16].

## Medical treatment

### *Acetaminophen*

It is the analgesic of choice for the short-term relief of mild to moderate pain and pyrexia. Recommended dosage of acetaminophen is 4 g or less per day.

### *Aspirin*

While aspirin can be taken during the first and second trimesters of pregnancy, it is best avoided near term because of increased risk of prolonged labor, postpartum hemorrhage, and neonatal bleeding. It should not be taken regularly during breast-feeding because of the theoretical risk of Reye syndrome and impaired platelet function in infants.

### *NSAID*

Ibuprofen is the NSAID of choice during the first or second trimester. NSAIDs and aspirin should be avoided during the third trimester because chronic use or high doses after 30 weeks are associated with an increased risk of premature closure of the ductus arteriosus and oligohydramnios.

### *Opiates*

Although safe for treatment of moderate to severe pain in pregnancy, opiates are inappropriate for migraine because they aggravate nausea and reduce gastric motility

## Cluster headache treatment

Preferred treatments for cluster headache during preg-

nancy and lactation are verapamil or prednisolone. Acute treatment includes oxygen (100% at 7 L/min for 10 to 15 minutes at onset of attack) or subcutaneous or intranasal sumatriptan.

## Emergency treatment

During pregnancy and lactation, prochlorperazine 10 mg or chlorpromazine 25 mg to 50 mg by IM injection are effective for emergency headache relief. IV magnesium sulfate 1 g given intravenously over 15 minutes was well tolerated and effective in acute cases [17]. Corticosteroids successfully treat intractable nausea and vomiting in hyperemesis gravidarum. A 6-day reducing course of prednisolone [18].

## Harmful treatment

It should be noted that some medications used to treat migraine in the nonpregnant patient carry increased risk to the fetus. Valproate may produce neural tube defects due to inhibition of folic acid metabolism. Other medications to avoid include topiramate, lithium, phenobarbital, angiotensin receptor blockers and second-generation ACE inhibitors, atenolol, paroxetine, methysergide, certain nonsteroidal agents and ergot alkaloids in the first trimester [19].

## Breastfeeding in migraine

Breast-feeding is encouraged because it maintains the protective effect of pregnancy on migraine headache during the postpartum period. A breast-feeding woman with migraine may forego treatment or even stop breast-feeding due to her fears of exposing her infant to medication. It is important to balance the risk of medication exposure with the benefit of migraine treatment. While many medications are considered to be compatible with breast-feeding, studies on breast-feeding women and their infants are rarely done due to obvious ethical concerns. To some extent, most drugs transfer into breast milk. Exceptions include heparin and insulin as their size is too large to cross biological membranes. The transfer of drugs into breast milk is commonly described quantitatively using the milk to plasma concentration ratio. For drugs that appear in breast milk to any significant extent, it may be reasonable to reduce infant exposure by alternating breast and bottle-feeding, or by adjusting the timing of when the medication is taken relative to breast-feeding. This approach may be particularly useful for medications with a short half-life and acute migraine treatments.

## Postdural puncture headache

Postdural puncture headache is the most common major complication following neuraxial anesthesia; this adverse

event is particularly frequent in obstetrics. The headache is usually benign and self-limited but if left untreated can lead to more serious complications that may be life-threatening. After accidental dural puncture the most important effective treatment is to leave the catheter inside the dura; epidural morphine infusion may also help. Once symptoms begin, treatment is conservative for the first 24 hours. If this approach fails, the most effective intervention continues to be a blood patch, which should not be delayed beyond 48 hours. If more than two blood patches are required, other possible causes of headache should be ruled out.

### Postpartum headache

The large majority of postpartum headaches are recurrences of preexisting primary headache disorders, which recur within a month after delivery in 55% of prior migraineurs. Prior headache history, dural puncture, increasing age, multiparity, and shorter length of second-stage pushing have been identified as potential risk factors for postpartum headache shortly after delivery. Tension-type headaches and migraine flare-ups are the most common headache complications after delivery, but the differential diagnosis of postpartum headache is broad. The clinician must distinguish common headache syndromes from dangerous causes of postpartum headache [21]. Nearly all women report the return of migraine attacks after delivery. Factors accelerating the return of migraine attacks in the postpartum include bottle-feeding and age of 30 years or less. Although preexisting headache often improves during pregnancy, approximately one-third of mothers experience postpartum headache within the first week after delivery making headache one of the three most common reasons for acute care visits during the puerperium.

### Menstrual migraine

Migraine is a biological disorder and providing an understanding of the role of estrogen in the frequency and severity of migraine can guide treatment choices. Genomic patterns in adolescent girls differentiate between menstrually related migraine and non-menstrually related migraine. According to some studies, menstrual migraine attacks are accompanied by nausea and vomiting more than non-menstrual attacks although this finding is not unanimously shared by all the studies. Correlations have been identified between premenstrual syndrome and menstrual migraine [22]. Menstrually-related migraine before pregnancy often predicted lack of headache improvement during pregnancy [23]. Management of hormonally influenced migraine involves a clear identification of the relationship between migraine and hormone change. A thorough history and detailed diary are critical in identifying this relationship and in predicting response or following response to hormonal therapies. Although limited, clinical evidence suggests that OCs

use in young women with episodic migraine may transform their pattern into chronic migraine. There is a well-documented association between COCs and migraine. They may induce a *de novo* migraine in women without a previous history of the disease, worsen a previous existing migraine, or change the pattern of a previous existing migraine. Thus, particular attention to changes in migraine patterns following either endogenous or exogenous hormonal changes is crucial. The age at initiation of estrogen replacement therapy appears to be significant with respect to stroke. No increase in stroke occurred in women on low-dose (50 µg or less) transdermal estrogen replacement compared to women not using estrogen replacement. Pharmacologic treatments include acute therapy, with short-term and standard prevention offered where appropriate. Hormonal therapies are not first-line therapies but may be important choices for a woman with migraine whose estrogen fluctuation is continually exacerbating migraine attacks. Overall wellness should also be emphasized; regular exercise, balanced diet, smoking cessation, weight control, and sleep hygiene are important in the management of migraine [24].

### Conclusion

Headache is a common symptom in pregnant women. Although most headaches seen in women are primary headache disorders (migraine, tension-type headache), complications or conditions associated with pregnancy can present with a secondary headache. Headaches are common symptoms in idiopathic intracranial hypertension, eclampsia, and reversible cerebral vascular syndrome. Migraines may begin or worsen during pregnancy, but pregnancy tends to reduce migraine frequency and severity. Although it is desirable to avoid medications for headaches during pregnancy, treatment should be considered when headaches are severe and cause significant disability. Being aware of possible treatments for migraine and headaches during pregnancy is essential. Finally, migraine does not adversely affect the outcome of pregnancy in otherwise healthy women. However migraine during pregnancy is associated with increased risk of arterial and venous thrombosis, preeclampsia, and gestational hypertension. Therefore pregnant women with migraine should be monitored for rising systolic or diastolic blood pressure should prompt a check for proteinuria. Breast-feeding is encouraged because it maintains the protective effect of pregnancy on migraine headache during the postpartum period.

### References

- [1] Lipton RB, Bigal ME, Diamond M, Freitag F, Reed ML, Stewart WF. Migraine prevalence, disease burden, and the need for preventive therapy. *Neurology*, 2007, 68, 343-349.
- [2] Migraine in women. 2012, 18, 835-52.
- [3] Zaccur HA. Hormonal changes throughout life in women. *Headache*, 2006, 46 (Suppl), 50-55.
- [4] Silberstein SD. Sex hormones and headache. *Rev Neurol.*, 2000,



- 156(Suppl 4), 30-41.
- [5] Sances G, Granella F, Nappi RE, Fignon A, Ghiotto N, Polatti F, Nappi G. Course of migraine during pregnancy and postpartum: a prospective study. *Cephalgia*, 2003, 23, 197-205.
  - [6] Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition (beta version). *Cephalgia*, 2013, 40, 629-808.
  - [7] Rasmussen BK. Migraine and tension-type headache in a general population: psychosocial factors. *Int J Epidemiol.*, 1992, 21, 1138-1143.
  - [8] Rasmussen BK. Migraine and tension-type headache in a general population: precipitating factors, female hormones, sleep pattern and relation to lifestyle. *Pain*, 1993, 53, 65-72.
  - [9] Hoshiyama E, Tatsumoto M, Iwanami H, Saisu A, Watanabe H, Inaba N, Hirata K. Postpartum migraines: a long-term prospective study. *Intern Med.*, 2012, 51, 3119-3123.
  - [10] Granella F, Sances G, Zanferrari C, Costa A, Martignoni E, Manzoni GC. Migraine without aura and reproductive life events: a clinical epidemiological study in 1300 women. *Headache*, 1993, 33, 385-389.
  - [11] Bateman BT, Olbrecht VA, Berman F, Minehart RD, Schwamm LH, Leffert LR. Peripartum subarachnoid hemorrhage. Nationwide data and institutional experience. *Anesthesiology*, 2012, 116, 324-333.
  - [12] Marcus DA, Scharff L, Turk DC. Nonpharmacological management of headaches during pregnancy. *Psychosom Med.*, 1995, 57, 527-535.
  - [13] Nestoriuc Y, Rief W, Martin A. Meta-analysis of biofeedback for tension-type headache: efficacy, specificity, and treatment moderators. *J Consult Clin Psychol.*, 2008, 76, 379-396.
  - [14] Linde K, Allais G, Brinkhaus B, Manheimer E, Vickers A, White AR. Acupuncture for tension-type headache. *Cochrane Database Syst Rev* 2009, 21;(1):CD007587
  - [15] EFNS guideline on the drug treatment of migraine-revised report of an EFNS task force. *Eur J Neurol.*, 2009, 16, 968-981.
  - [16] Mag Altman D, Carroli G, Duley L, Farrell B, Moodley J, Neilson J, Smith D; Magpie Trial Collaboration Group. Do women with pre-eclampsia, and their babies, benefit from magnesium sulphate? The Magpie Trial: a randomised placebo-controlled trial. *Lancet* 2002, 359(9321), 1877-1890.
  - [17] Demirkaya S, Vural O, Dora B, Topcuoglu MA. Efficacy of intravenous magnesium sulfate in the treatment of acute migraine attacks. *Headache* 2001, 41, 171-177.
  - [18] Jurgens TP, Schaefer C, May A. Treatment of cluster headache in pregnancy and lactation. *Cephalgia*, 2009;29,391-400.
  - [19] McGregor EA. Headache in pregnancy. *Neurol Clin.* 2012, 30, 835-866.
  - [20] López Correa T, Garzón Sánchez JC, Sánchez Montero FJ, Muriel Villoria C. Postdural puncture headache in obstetrics, 2011, 58, 563-73.
  - [21] Headache in pregnancy., 2014, 20:128-47.
  - [22] Facchinetti F, Neri I, Martignoni E, Fioroni L, Nappi G, Genazzani AR. The association of menstrual migraine with the premenstrual syndrome. *Cephalgia*. 1993, 13, 422-425
  - [23] Sances G, Granella F, Nappi RE, Fignon A, Ghiotto N, Polatti F, Nappi G. Course of migraine during pregnancy and postpartum: a prospective study. *Cephalgia*, 2003, 23, 197-205.
  - [24] Brandes JL. The influence of estrogen on migraine: a systematic review. *JAMA* 2006;295,1824-1830.

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