

## PREGNANCY PLUS

# Migraine in pregnancy

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The authors explore whether migraine affects pregnancy, how pregnancy alters migraine, and how to treat and prevent migraine in pregnancy

Migraine is common, with a one year prevalence of 12-15% in the Western world.<sup>1</sup> The case described here (see the Scenario box) illustrates many of the problems that arise when a patient who has migraines becomes pregnant.

Migraine is defined by the International Headache Society as a disorder involving headache with particular features—notably, it is usually unilateral and often throbbing and is associated with nausea and sensitivity to light, sound, and head movement.<sup>1</sup> More broadly the disorder can be regarded as a substantially inherited disorder in which physiological changes (both external, such as weather change, or internal, such as changes in sleep pattern) often trigger stereotypical attacks, with the features of migraine as defined above.<sup>3</sup> Migraine is three times more common in females than in males, and in females the highest prevalence rates are during the childbearing years, peaking (at 27%) at the age of 41. Migraine has not been proved to affect fertility or the course of a pregnancy,<sup>4</sup> but pregnancy substantially alters migraine.

### Does migraine affect the outcome of pregnancy?

Migraine has long been mentioned as a possible predictor of complications in pregnancy,<sup>5</sup> although because migraine is so common in females systemically establishing a link to complications in pregnancy has been a challenge. Several associations have been proposed, including miscarriage, pre-eclampsia, congenital anomalies, and low birth weight, but these associations remain clouded by a lack of well controlled studies.

### How does pregnancy alter the pattern of migraine?

Pregnancy will usually reduce the frequency and severity of migraine attacks. This is especially true for women with migraine without aura. A minority of women have their first migraine attack during pregnancy or in the postpartum period.<sup>15</sup> Migraine attacks often increase in frequency in the first trimester but can be expected to decrease later in pregnancy. However, although attacks are usually less frequent in the second and third trimesters, new onset aura may appear at that time.<sup>16</sup>

A recent large prospective study using the International Headache Society's definition criteria showed

that by the third trimester of pregnancy 89% of women had either no attacks or fewer attacks.<sup>17</sup> A prospective study of 49 women with migraine reported an 11%, 53%, and 79% reduction in attacks in the first, second, and third trimesters respectively.<sup>18</sup> An older retrospective study of 1300 women reported a 67% cessation of migraine in pregnancy,<sup>19</sup> and a smaller study of 18 patients found a 41% reduction in the overall frequency of headache.<sup>20</sup> Taken together, these studies show that pregnancy is a time of substantial reduction in migraine attacks.

Importantly, pregnancy can alter migraine aura and may trigger attacks of aura without headache. This often leads to a search for intracranial disease—in particular, arteriovenous malformations and intracranial venous sinus thrombosis. Clinically, however, these attacks are typical of aura, with the slow emergence of symptoms, and although cerebral ischaemia is often considered, it is seldom the cause. This change in migraine pattern during late

### SCENARIO

A 32 year old woman with a history of episodic headache has recently become aware she is pregnant. She has had troublesome headaches from childhood. She has no other medical problems. Her sister and mother have migraines. She is a non-smoker. In the previous five years, her headaches have become more frequent, with five to seven attacks a month of disabling left or right sided, throbbing pain around the parietal and temporal region. The pain is aggravated by physical activity and any movement and associated with nausea and marked vomiting, prominent photophobia, and phonophobia. The attacks last two to three days. She had no aura symptoms. Neurological and general physical examinations were normal, and thus her diagnosis is migraine without aura.<sup>2</sup>

She has had minimal benefit from over the counter analgesics, including paracetamol (acetaminophen) with and without codeine; aspirin; metoclopramide; prochlorperazine; domperidone; and non-steroidal anti-inflammatory drugs (notably ibuprofen and naproxen). She was started on sumatriptan 20 mg nasal spray. This provided headache relief in about two hours, with some mild chest discomfort. She was also started on topiramate as a migraine preventive, which, at a dose of 50 mg twice daily, reduced her attack frequency to two a month. Breakthrough attacks were treated with sumatriptan. She had some mild paraesthesia with topiramate but no other side effects. This pregnancy, her first, was unplanned. She is currently at six weeks' gestation by her last menstrual period.

This is one of a series of occasional articles about how to manage a pre-existing medical condition during pregnancy.

pregnancy is well recognised and usually easy to manage, with excellent prognosis.<sup>15</sup>

Although the relative hormonal stability in pregnancy is generally considered to be the basis for the improvement in headache, the detailed physiological mechanisms are not understood.<sup>4</sup>

### How is the acute attack treated in pregnancy?

The two main areas of concern are treating an acute migraine and preventing attacks. When planning pregnancy, women should find it useful to discuss the treatment options that exist for the acute attack (table 1). It should be noted that ergotamine is specifically contraindicated in pregnancy. Paracetamol (acetaminophen) is a safe treatment for acute migraine in pregnancy, but it may provide no benefit.

The data are still accumulating, but current evidence suggests that sumatriptan does not carry a risk to either the fetus or the mother.<sup>12-14</sup> The best data for sumatriptan can be found on the sumatriptan and naratriptan pregnancy registry, where the most recent data have been reported in February 2008. The authors report 516 cases of exposure to sumatriptan and 46 cases of exposure to naratriptan in pregnancy, with a reported 4.4% (95% confidence interval 2.7% to 7.0%) rate of birth defects for exposure in the first trimester, which is in line with the prevalence of birth defects in women with migraine (3.4%; 2.1% to 4.6%).<sup>11</sup>

For many patients, the first trimester will be well advanced by the time the pregnancy is confirmed. The most important thing the pregnant woman who experiences migraine can do in the first trimester is to see her physician and establish a treatment plan. Preventive agents not recommended during pregnancy should be stopped, so a plan should be drawn up for treating any migraine attacks that occur. The nausea and vomiting that often accompany migraine may be

### METHODS

We searched the literature from PubMed using the terms "migraine" and "pregnancy" and reviewed our own database of references from meetings of the International Headache Society and the American Headache Society over the past 20 years.

exacerbated by pregnancy associated nausea, which places the woman at risk for dehydration. We believe that opioids and antiemetics are often the treatment of choice for acute migraine during pregnancy whereas that is not the case outside pregnancy. Prochlorperazine (both the oral and the suppository form) is safe and effective for both nausea and headache.

### How is migraine treated in the postpartum period?

No particular problems arise for women with migraine around the time of the birth. Postpartum headache is common, occurring in about 34% of women.<sup>18</sup> It is most common during days 3 to 6 postpartum and is associated with a personal history or family history of migraine. Postpartum headache, although usually less severe than patients' typical migraine, is usually bifrontal, prolonged, and associated with photophobia, nausea, and anorexia.<sup>21-22</sup>

No direct data exist to establish that any particular triggers are worse than others in the postpartum period. In the absence of a specific contraindication such as coronary or cerebrovascular disease, sumatriptan by injection is an ideal way to deal with disabling migraine in this period, even for breastfeeding women. Preventive agents can be reintroduced during breastfeeding. Table 2 lists the current options for prevention and the level of recommendation as classified by the US Food and Drug Administration and TERIS (the Teratogen Information System).

**Table 1 | Safety profiles in pregnancy and breast feeding for drugs commonly used for treating acute attacks of migraine<sup>23-24</sup>**

Drug	Fetal risk		Breast feeding
	FDA	TERIS	
Paracetamol (acetaminophen)	B	None	Caution
Dihydroergotamine	X	Minimal	Contraindicated
Ergotamine	X	Undetermined	Contraindicated
5-HT <sub>1</sub> agonists	C	Undetermined	Probably compatible
Aspirin	C*	Minimal	Compatible
Caffeine	B	None	Compatible
Ibuprofen	B*	Minimal	Compatible
Naproxen	B*	Undetermined	Compatible
Codeine	C**	Unlikely	Compatible
Pethidine (meperidine)	B**	Unlikely	Compatible
Morphine	B**	Unlikely	Compatible
Prednisolone	C*	None or minimal	Compatible
Prochlorperazine	C	None	Concern

FDA=US Food and Drug Administration.

TERIS= Teratogen Information System (a consensus of expert opinion and literature that assesses teratogenic risk from drug exposure).

FDA ratings: A=controlled studies show no risk; B=no evidence of risk in humans; C=risk cannot be ruled out—use if benefit justifies potential risk; D=positive evidence of risk—use if benefits outweigh risk; X=contraindicated in pregnancy—risk outweighs any possible benefit). \*Rating D if used in third trimester. \*\* = rating D if used when pregnancy is prolonged or at term.

The FDA categories provide therapeutic guidance.

**Table 2 | Safety profiles in pregnancy and breast feeding for drugs commonly used for preventing migraine<sup>23 24</sup>**

Drug	Fetal risk		Breast feeding
	FDA	TERIS	
<b>β blockers</b>			
Atenolol	D	Undetermined	Caution
Metoprolol	C**	Undetermined	Compatible
Nadolol	C**	Undetermined	Compatible
Propranolol	C**	Undetermined	Compatible
Timolol	C**	Undetermined	Compatible
<b>Neuromodulators</b>			
Gabapentin	C	Undetermined	Probably compatible
Topiramate	C	Undetermined	Caution
Semisodium valproate	D	Moderate	Compatible
<b>Serotonin antagonists</b>			
Pizotifen	NA	Safety not established	Caution
Methysergide	X	Safety not established	Contraindicated
<b>Calcium channel blockers</b>			
Flunarizine	NA	Safety not established	Contraindicated
<b>Tricyclics</b>			
Amitriptyline	C	Unlikely	Concern
Imipramine	C	Unlikely	Concern
Nortriptyline	C	Undetermined	Concern

FDA=US Food and Drug Administration.

NA= not applicable.

TERIS=Teratogen Information System (a consensus of expert opinion and literature that assesses teratogenic risk from drug exposure).

FDA ratings: A=controlled studies show no risk; B=no evidence of risk in humans; C=risk cannot be ruled out—use if benefit justifies potential risk; D=positive evidence of risk—use if benefits outweigh risk; X=contraindicated in pregnancy—risk outweighs any possible benefit. \*\* = rating D if used when pregnancy is prolonged or at term.

The FDA categories provide therapeutic guidance.

**How is a migraine attack prevented in pregnancy?**

Migraine prevention is more difficult when a patient is pregnant. Preventive agents are associated with the possibility of complications during pregnancy, so they should ideally be stopped in women planning to conceive (table 2). Propranolol is both effective and safe. Unfortunately, the neuromodulators, valproate (semisodium), topiramate, and gabapentin, are not established as safe; valproate is a known teratogen.<sup>23 24</sup>

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