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KEY NOTE LECTURE

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# Headaches in pregnancy

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**Abstract** Most women with migraine improve during pregnancy. Some women have their first attack. Migraine often recurs postpartum and can begin for the first time. Drugs are commonly used during pregnancy despite insufficient knowledge about their effects on the growing fetus. Most drugs are not teratogenic. Adverse effects, such as spontaneous abortion, developmental defects and various postnatal effects depend on the dose and route of administration and the timing of the exposure relative to the period of foetal development. While medication use should be limited, it is not absolutely contraindicated in pregnancy. Nonpharmacologic treatment is the ideal solution; however, analgesics such as acetaminophen and opioids can be used on a limited basis. Preventive therapy is a last resort.

**Key words** Migraine • Pregnancy • Acute • Preventive • Prophylaxis

## Drugs and pregnancy

Most drugs cross the placenta and have the potential to adversely affect the fetus, and, although studies have not absolutely established the safety of any medication during pregnancy, some are believed to be relatively safe [1]. Adverse drug effects depend on the dose and route of administration, concomitant exposures and the timing of the exposure relative to the period of development. Death to the conceptus, teratogenicity, foetal growth abnormalities, perinatal effects, postnatal developmental abnormalities, delayed oncogenesis, and functional and behavioural changes can result from drugs or other agents (Table 1) [2].

The FDA has five categories of labelling for drug use in pregnancy [3–5]. An alternate rating system is TERIS, an automated teratogen information resource wherein the rating for each drug or agent is based on a consensus of expert opinion and the literature [6]. The FDA categories have little, if any, correlation to the TERIS teratogenic risk. This discrepancy results in part from the fact that the FDA categories were designed to provide therapeutic guidance and the TERIS ratings are useful for estimating the teratogenic risks of a drug and not *vice versa* [7].

## Headache treatment

The major concerns in the management of the pregnant patient are the effects of both the medication and the disease on the fetus. Because of the possible risk of injury to the fetus, medication use should be limited; however, it is not contraindicated during pregnancy [4, 8]. Because migraine usually improves after the first trimester, many women can manage their headaches with this reassurance

**Table 1** Definitions and drug effects

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| Spontaneous abortion | Death of the conceptus. Most due to chromosomal abnormality |
| Embryotoxicity | The ability of drugs to kill the developing embryo |
| Congenital anomalies | Deviation from normal morphology or function |
| Teratogenicity | The ability of an exogenous agent to produce a permanent abnormality of structure or function in an organism exposed during embryogenesis or fetal life |
| Fetal effects | Growth retardation, abnormal histogenesis (also congenital abnormalities and fetal death) The main outcome of fetal drug toxicity during the second and third trimesters of pregnancy |
| Perinatal effects | Effects on uterine contraction, neonatal withdrawal or haemostasis |
| Postnatal effects | Drugs may have delayed long-term effects: delayed oncogenesis, and functional and behavioural abnormalities |

and nonpharmacologic means of coping, such as ice, massage and biofeedback [4, 9]. Some women, however, will continue to have severe, intractable headaches, sometimes associated with nausea, vomiting and possible dehydration. These conditions may pose a risk to the fetus that is greater than the potential risk of the medications used to treat the pregnant patient [8, 9].

Symptomatic treatment, designed to reduce the severity and duration of symptoms, is used to treat an acute headache attack. Individual attacks should be treated with rest, reassurance and ice packs. Symptomatic drugs are indicated for headaches that do not respond to nonpharmacologic treatment. The NSAIDs, acetaminophen (alone or with codeine), codeine alone or other opioids can be used during pregnancy [10]. Aspirin in low intermittent doses is not a significant teratogenic risk, although large doses, especially if taken near term, may be associated with maternal and fetal bleeding. Aspirin use should probably be reserved unless there is a definite therapeutic need for it (other than headache). In general, NSAIDs may be safely taken for pain during the first trimester of pregnancy. However, their use should be limited during later pregnancy, as some NSAIDs may constrict or close the fetal ductus arteriosus [10]. Barbiturate and benzodiazepine use should be limited. Ergotamine, dihydroergotamine (DHE) and triptans should be avoided [4, 9]. However, Reiff-Eldridge et al. [11] recently reviewed the Glaxo-Wellcome pregnancy registries and found that sumatriptan did not provide a risk estimate exceeding that expected in the disorder treated, and no pattern of defects has been observed.

The associated symptoms of migraine, such as nausea and vomiting, can be as disabling as the headache pain itself. In addition, some medications that are used to treat migraine can produce nausea. Metoclopramide, which decreases the gastric atony seen with migraine and enhances the absorption of coadministered medications, is extremely useful in migraine treatment [12]. Mild nausea can be treated with phosphorylated carbohydrate solution (emetrol) or doxylamine succinate and vitamin B6 (pyridoxine) [10, 12]. More severe nausea may require the use of injections or suppositories. Trimethobenzamide, chlorpromazine, prochlorperazine and promethazine are available orally, parenterally and as a suppository, and can all be used safely. We frequently use promethazine and prochlorperazine suppositories. Corticosteroids can be utilised occasionally. Some use prednisone in preference to dexamethasone (which crosses the placenta more readily). Domperidone is an antiemetic used outside the United States. In the United Kingdom [13] its use is not advised during pregnancy, because of variable embryotoxic effects in animal tests. Severe acute attacks of migraine should be treated aggressively. We start IV fluids for hydration and then use prochlorperazine 10 mg IV to control both nausea and head pain. IV opioids or IV corticosteroids can supplement this.

## Preventive treatment

Increased frequency and severity of migraine associated with nausea and vomiting may justify the use of daily prophylactic medication. This treatment option should be a last resort. Preventive therapy is designed to reduce the frequency and severity of headache attacks. Prophylaxis should be considered when patients experience at least three or four prolonged, severe attacks a month that are particularly incapacitating or unresponsive to symptomatic therapy and may result in dehydration and fetal distress [9, 14]. Beta-adrenergic blockers such as propranolol have been used under these circumstances, although adverse effects, including intrauterine growth retardation, have been reported [10, 12, 14]. If the patient has a coexistent illness that requires treatment, one drug that will treat both disorders should be chosen. For example, propranolol [10] can be used to treat hypertension and migraine while fluoxetine can be used to treat comorbid depression.

## Drug exposure

If a woman inadvertently takes a drug while she is pregnant or becomes pregnant while taking a drug, determine the dose, timing and duration of the exposure(s). Ascertain the patient's past and present state of health and the presence of mental retardation or chromosomal abnormalities in the family. Using a reliable source of information (such as TERIS), determine if the drug is a known teratogen (although for many drugs this is not possible) [3, 6].

If the drug is teratogenic or the risk is unknown, have the obstetrician confirm the gestational age by ultrasound. If the exposure occurred during embryogenesis, then high-resolution ultrasound can be performed to determine whether damage to specific organ systems or structures has occurred. If the high-resolution ultrasound is normal, it is reasonable to reassure the patient that the gross fetal structure is normal (within the 90% sensitivity of the study). However, fetal ultrasound cannot exclude minor anomalies or guarantee the birth of a normal child. Delays in achieving developmental milestones, including cognitive development, are potential risks that cannot be predicted or diagnosed prenatally.

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