Neurological disease in pregnancy

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Abstract

Neurological disease presents a particular challenge to those providing obstetric care, to minimise maternal, foetal and neonatal morbidity. Women with pre-existing neurological disease should ideally be given a preconceptual assessment in order to optimise medical management. Headache is an extremely common problem both during and outside of pregnancy and requires a structured approach. Some conditions, such as eclampsia, are unique to pregnancy, whereas others, such as carpal tunnel syndrome, are seen much more frequently but not exclusively in pregnancy. The drug management of epilepsy in pregnancy represents a particular challenge, balancing the desire to limit foetal exposure on the one hand, with the need to maintain therapeutic benefit to the mother on the other. Assessment of all neurological conditions requires a sound knowledge of neuroanatomy and the physiology of pregnancy, with appropriate use of neuroimaging and neurophysiological testing. Management should involve a multidisciplinary team with specialist neurological input.

Keywords anticonvulsant drugs; cerebral thrombosis; cerebrovascular disease; epilepsy; headache; neurological disease; neuropathies; pregnancy

Headache

Headache is a very common experience in pregnancy. Only a small proportion of cases warrant detailed assessment and management, although a careful history and appropriate physical examination are always necessary. The association of headache with pre-eclampsia is not as strong as many suppose, but the condition must always be considered in the differential diagnosis when a woman presents with headache in advanced pregnancy.

Migraine

Migraine is a common problem in pregnancy. Women with migraine are equally likely to experience worsening, improvement or no change in pregnancy. Pre-existing migraine is associated with an increased incidence of early onset pre-eclampsia. Migraine is usually unilateral, throbbing and severe and may be preceeded by aura, most commonly visual. Other symptoms of aura may include numbness or paresthesiae most commonly on the face and hands. Less commonly motor weakness, symptoms of brainstem dysfunction or altered level of consciousness may occur, indicating particular subtypes of migraine.

Migraine is often accompanied by more general symptoms e.g. nausea (80%), vomiting and sensitivity to light or noise. More prolonged focal neurological symptoms, such as sensory or speech disturbance, may be present. New onset migraine is uncommon in pregnancy and often occurs in women with a family history of migraine. These women still require appropriate clinical assessment, but it is very rare to discover underlying structural pathology and investigation may be deferred until after delivery in most cases. The differential diagnosis of new onset headache in pregnancy and the puerperium includes all causes of secondary headache, as well as conditions unique or more common in pregnancy such as pre-eclampsia, idiopathic (previously called benign) intracranial hypertension and cerebral venous and sinus thrombosis.

Management of headache in pregnancy

There are three aspects to the management of migraine:

- avoidance of triggers
- treatment of the acute attack
- prophylaxis against recurrent migraine.

If migraine occurs infrequently, acute therapy and avoidance of triggers (such as cheese, chocolate, wine, oranges, bright sunlight, overwork) may be all that is required. Simple analgesics, for example, paracetamol (sometimes with codeine) may be adequate, with or without an antiemetic (e.g. metoclopramide). Non-steroidal anti-inflammatory drugs (e.g. naproxen or ibuprofen) are often useful analgesics in this condition but in the third trimester they should be avoided, as they may cause premature closure of the ductus arteriosus and oligohydramnios. Ergot agents may vasoconstrict the placental bed vessels and are, therefore, contraindicated during pregnancy. If they are used inadvertently, the woman should be reassured as there is no evidence of adverse effects. 5-Hydroxytryptamine receptor antagonists (e.g. sumatriptan, naritriptan and zolmitriptan) are highly effective for treating acute migraine. They are also vasoconstrictors, however, the limited data available about their use in pregnancy does not suggest any increase in adverse events.

In general, parenteral opiates should not be the first choice for treatment of migraine, and are subject to abuse and dependency considerations. Prophylactic treatment may be necessary if migraine is frequent or uncontrolled. During pregnancy, the most appropriate agents for this purpose are low dose aspirin (75–100 mg/day), propranolol (20–80 mg nocte), cyproheptadine (2–4 mg nocte), amitryptyline (10–25 mg nocte) or verapamil (40–80 mg nocte).

Pre-eclampsia

Most women with pre-eclampsia do not have headache. There are no specific features of headache in pre-eclampsia although there may be associated neurological symptoms of visual scintillations, visual loss or jitteriness. Headache in this condition is thought to be secondary to vasoconstriction, cerebral oedema and/or side-effects of anti-hypertensive medications, particularly the vasodilators hydralazine and nifedipine. Rarely, focal

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neurological signs – such as cortical blindness, altered mental state or transient lateralising features – may be present. A peculiar and easily demonstrable hyperreflexia of unknown genesis often accompanies severe pre-eclampsia and may lead to concern at the likelihood of eclamptic seizures. It has not been demonstrated as a risk factor for eclampsia. Severe headache in a woman with pre-eclampsia should lead to consideration of the possibility of intracerebral haemorrhage, a feared but rare complication of severe pre-eclampsia.

Headache in the postpartum period

Acute headache in the postpartum period is often a concerning symptom. The differential diagnosis includes primary headache but a number of specific causes need to be excluded. If the patient has received an epidural or spinal anaesthetic, a dural puncture is often blamed. It has been estimated that 39% of parturients report symptoms of headache unrelated to dural puncture following delivery. Post-dural puncture headache (PDPH) usually develops within 3 days. The symptoms are a fronto-occipital, throbbing or dull headache appearing within seconds of arising from the bed, relieved promptly by lying down. Dizziness, nausea and vomiting, visual disturbances, interscapular pain, neck stiffness, photophobia or auditory symptoms may accompany the headache.

This headache is related to loss of cerebrospinal fluid and lowering of the cerebrospinal fluid pressure. If PDPH is likely, a request for review by the anaesthetist is necessary as application of an epidural blood patch is promptly and remarkably effective at terminating the headache.

Cerebral vein and sinus thrombosis

Cerebral venous and sinus thrombosis (CVST) is a rare condition. Thrombophilias, pre-eclampsia, dehydration and puerperal infection may be significant risk factors. CVST can present at any stage of pregnancy, however, most present in the second to third week postpartum. Presentation is extremely varied, from isolated, slowly developing headache, focal neurological signs and symptoms, seizures, papilloedema, and behavioural changes to impaired consciousness, ranging from slight confusion to deep coma. The presence of severely altered state of consciousness and intracranial haemorrhage are strongly indicative of a poor prognosis.

Imaging is essential for the diagnosis. Plain computed tomography (CT) may be negative but should be performed to exclude haemorrhage or space occupying lesion. The gold standard for diagnosis is magnetic resonance imaging and angiography (MRI/MRA) or intra-arterial four-vessel angiography. Therapeutic anticoagulation, even in the presence of haemorrhage, is the mainstay of treatment, although rarely surgery or thrombolysis may be life saving. Antiepileptic drugs should be given as treatment or prophylaxis for seizures. Anticoagulation is usually continued for 3–6 months until MRI demonstrates sinus patency. Recanalisation occurs in most cases. The risk of recurrence is low, even in future pregnancies and most recurrence is within 1 year. A thrombophilic aetiology should always be sought in investigating CVST but such investigation is best deferred until the patient is no longer taking anticoagulants.

Epilepsy

The epilepsies comprise a group of disorders characterised by recurrent seizures and classified according to clinical or specific electroencephalographic (EEG) features. Most types of epilepsy are characterised by more than one type of seizure. Patients with focal or partial epilepsy syndromes may have simple partial, complex partial and secondarily generalised tonic-clonic seizures. Patients with generalised epilepsy may have one or more of the following seizure types: absence, myoclonic, tonic, clonic, tonic-clonic and atonic. Although epilepsy is the most commonly encountered neurological disease in pregnancy, it is still relatively rare with a prevalence of 0.6–1.0%. Medical therapy utilising anticonvulsant drugs (ACDs) is the most common form of treatment although surgery, or no treatment, may have a role in specific cases.

Preconception care

Ideally, all women with epilepsy should undergo counselling prior to pregnancy. The principles of drug review at this time are:

- withdraw any unnecessary medication where possible
- use monotherapy where possible
- use the smallest effective dose of medication
- withdraw drugs with foetal effects and replace with safer drugs if possible.

Preconception counselling may identify women who have been seizure-free for a number of years on minimal medication, particularly those with a normal EEG and normal cerebral imaging. In these cases, careful weaning of therapy over 6 months prior to pregnancy may be entirely appropriate, accepting a small risk of recurrence of seizures. However, tampering with stable and effective medication does carry hazards for the patient. Anticonvulsant therapy is usually chosen with great care, and often after the failure of other drugs. For these reasons, it is important to consult with the neurologist before making any substantive change.

All women with epilepsy taking ACDs should receive folate supplementation with higher doses (5 mg) reserved for those women taking valproate or carbamazepine. During pregnancy, antenatal screening for neural tube and cardiac defects with spine and nuchal translucency ultrasound should be performed at 12–13 weeks of amenorrhoea. Maternal alpha-fetoprotein testing at 16 weeks is less helpful. A careful 18–20 week morphology scan should be performed in a recognised centre. It is important to ensure that the sonographer is aware of the patient's additional risks for each of these scans. Most clinicians agree that for both the mother and her foetus, the benefits of controlling seizures outweigh the potential risks associated with the ACDs. Monotherapy is associated with significantly fewer adverse foetal effects than polytherapy. The genetics of epilepsy are complex and advice regarding heritability should be guarded.

Pregnancy

A minority of women with epilepsy experience an increase in seizure frequency during pregnancy, particularly those with poorly controlled epilepsy prior to pregnancy. This may be explained by changes in ACD pharmacokinetics, as well as vagaries of patient compliance. In practice, tiredness, nausea, vomiting, sleep disturbance and emotional stress may be important factors