South Australian Perinatal Practice Guidelines

Seizures in pregnancy

Introduction

- This chapter refers to the acute management of a woman who presents with seizures in pregnancy
- For management in pregnancy of a woman with known epilepsy refer to Chapter 66
- The most common cause of seizures during pregnancy is pre-existing epilepsy
- New-onset seizures in the latter half of pregnancy or during the immediate postpartum period are most frequently caused by eclampsia
- Other causes of new onset seizures can be classified as either secondary to neurologic pathology or complications of critical illness[2]

Neurologic pathology

- Neurovascular
  - Stroke
  - Arteriovenous malformations
  - Cerebral vein thrombosis
  - Haemorrhage
- Tumour
  - Primary
  - Metastatic
- Infection
  - Cerebral abscess
  - Meningitis
  - Encephalitis
- Inflammatory disease
  - Vasculitis
  - Acute disseminated encephalomyelitis
- Traumatic brain injury
  - Contusion
  - Haemorrhage
- Primary central nervous system metabolic disturbance (inherited)

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Complications of critical illness

- Amniotic fluid embolism
- Hypoxia / ischaemia
- Drug / substance toxicity
    - Antibiotics
    - Antidepressants
    - Antipsychotics
    - Local anaesthetics
    - Immunosuppressives
    - Cocaine
    - Amphetamines
- Drug /substance withdrawal
    - Barbiturates
    - Benzodiazepines
    - Opioids
    - Alcohol
- Infection fever (febrile seizures)
- Metabolic abnormalities
    - Hypoglycaemia
    - Hyponatraemia
    - Renal dysfunction
    - Hepatic dysfunction e.g. due to acute fatty liver of pregnancy
    - Hypophosphataemia
- Surgical injury (craniotomy)

Non-eclamptic seizures

- New onset seizures with normal blood pressure should be investigated to exclude other causes (see above) as specific treatment directed to the cause may be necessary[2]
- The majority of focal or generalised seizures usually lasts for several seconds but may extend for up to 2 minutes
- The minimum duration of continuous seizure activity required for the diagnosis of **status epilepticus** is commonly agreed to be 30 minutes[3]. However, because most tonic-clonic seizures last only 1 to 2 minutes, it has been proposed that **treatment for status epilepticus should start after 5 minutes of continuous seizure activity** (see below)[3]
- It is an imperative to diagnose and effectively treat recurrent seizure activity[2] as status epilepticus is associated with high maternal and fetal mortality[4]
- Consider impending status epilepticus if three or more tonic, clonic seizures occur within a 24 hours period, especially if this represents an increase from the typical frequency

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Management of non-eclamptic seizures

Initial management

- The woman's condition takes priority over the fetal condition
- Remain with the woman, note time of commencement of seizure activity
- Call for medical (senior obstetric, anaesthetic) and midwifery assistance
- Consider calling code blue or equivalent
- Follow the ABCDEs of resuscitation
- Administer oxygen via non-rebreathing mask at 12 litres per minute
- Maintain a clear airway (after a seizure, the level of consciousness is commonly depressed for several minutes and continued airway support may be necessary)
- Assess breathing pattern, rate and colour and ventilate if required
- Turn the woman to the left lateral position to decrease the chance of aspiration and increase uterine blood flow
- Attach pulse oximeter, ECG and automatic BP monitors and monitor pulse oximetry, maternal pulse and blood pressure
- Obtain intravenous access
- Take blood for blood glucose, electrolytes and antiepileptic drug levels. Treat hypoglycaemia if present
- If the seizure persists, an intravenous benzodiazepine should be administered e.g.:
    - Diazepam 5 mg IV stat. A second dose of 5 mg can be administered if seizure activity continues
    - Management of any airway obstruction and respiratory depression is vital irrespective of whether it relates to seizure activity or drug treatment
- Maintain safety of the woman throughout the seizure e.g. padding to side rails during a vigorous seizure to prevent injury to an extremity
- Commence fluid balance chart and monitor urine output
- Assess and monitor fetal wellbeing (cardiotocography)
- Note type of seizure, duration and sequencing of seizure activity
- Perform a secondary survey including a neurological examination

Status epilepticus

- Immediate treatment of convulsive status epilepticus involves simultaneous protection of the airway, maintenance of oxygenation and termination of seizure activity using:
    - Clonazepam 1 mg IV, over 2 to 5 minutes, not exceeding 0.5 mg / minute. Repeat once 15 minutes later if status epilepticus continues

    OR

    - Diazepam 5 mg to 10 mg IV, over 2 to 5 minutes, not exceeding 5 mg / minute. Repeat once 15 minutes later if status epilepticus continues

    OR

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- Midazolam 5 mg to 10 mg IM or IV, over 2 to 5 minutes or midazolam 5 mg to 10 mg buccally or intranasally. Repeat once 15 minutes later if status epilepticus continues

Documentation and differential diagnosis

- Obtain history as soon as possible e.g. usual antiepileptic drug, time of last dose, compliance
- Document characteristics of seizure (see table 1), including presence or absence of aura, duration and sequencing of all phases of seizure activity, maternal fetal physiological responses, findings on physical examination and interventions
- Document findings of secondary survey and physical examination
- Establish if there is an underlying cause (see above) as specific treatment may be required
- Refer to the appropriate specialist for specific management of any underlying condition

Recurrent seizure activity

- It is imperative to diagnose and effectively treat recurrent seizure activity[2]
- Seek additional assistance and advice. Ensure a practitioner with airway skills is present, i.e. an anaesthetist or intensivist, as prompt airway protection and support of ventilation may be required
- Further doses of a benzodiazepine may be required (see status epilepticus above)
- If venous access is difficult, diazepam can be administered rectally
- Drug treatment for prolonged or recurrent seizure activity:
  - Commence a loading dose of phenytoin IV (15 to 20 mg / kg i.e. 1 to 2 g as ordered by medical officer) at a rate of no greater than 50 mg / minute if the woman is not already taking Phenytoin. (For further information, refer to PPG 'Phenytoin infusion regimen')
- Consider intubation, ventilation and sedation to prevent pulmonary aspiration, prevent cerebral oedema and decrease further seizure activity
- If cardiotocography indicates significant fetal compromise at a viable gestation, a decision to deliver should be made once the woman is stable and with appropriate senior personnel present

Management post seizure

- Check time of last dose of anti epileptic drugs. Administer dose if not taken
- Check laboratory findings, including electrolytes, anti epileptic drug levels, glucose, and toxicology screen
- Close maternal and fetal observations

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Eclampsia

- Eclampsia is the occurrence of convulsions or coma due to hypertensive disease in pregnancy
- From 1998 to 2007, eclampsia affected an average of 1 in 3,500 pregnancies in South Australia (Chan 2008; personal communication)
- The majority of initial seizures are self-limiting and seldom last more than 3 to 4 minutes
- Extreme hypertension is not a necessary predisposing factor of eclampsia. On average
    - 10 % of women have no prodomal signs or symptoms
    - 10 % have only proteinuria before the event
    - 20 % have only hypertension[8]
- A prospective study of the incidence of eclampsia in the United Kingdom[8] found that:
    - 38 % occurred antepartum
    - 18 % occurred intrapartum
    - 44 % occurred postpartum (especially at term and usually in the first 24 hours)
- Careful assessment of women with signs or symptoms indicative of pre-eclampsia is required
- The Collaborative Eclampsia trial showed that magnesium sulphate (MgSO4) is the drug of choice in preventing recurrent seizures[9]
- Magnesium sulphate reduces the risk of eclampsia by over 50 % and probably reduces the risk of death

Management of eclampsia

- Commence an intravenous infusion of magnesium sulphate and treat any coexisting severe hypertension with antihypertensives

Magnesium sulphate

- Magnesium sulphate is best administered intravenously
- In some countries a pre-diluted magnesium sulphate 20 % solution is available
- In Australia, each 5 mL ampoule of magnesium sulphate contains a 50 % solution (i.e. Either 2.5 g in each 5 mL or 5 g in each 10 mL)
- The product guidelines recommend that magnesium sulphate for intravenous use should be diluted with sodium chloride 0.9 % to a concentration of 20 % magnesium or less, which implies that further dilution is necessary
- Intravenous administration of magnesium sulphate may be via a syringe pump or an infusion pump
- For further information, refer to the PPG ‘Magnesium sulphate infusion regimen’

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Magnesium sulphate syringe driver infusion regimen

- The total adult daily dose should not exceed 30 g to 40 g of magnesium sulphate
- The undiluted syringe driver infusion may be connected into a mainline of sodium chloride 0.9 % or Hartmann's 1,000 mL; however, no other drugs may be administered into this line
- No more than 8 g of magnesium sulphate should be administered over 1 hour
- Continue for up to 24 hours after the last seizure activity and for 24 hours after birth

Magnesium sulphate undiluted 50 %

Loading dose set up

- Draw up 5 g (10 mL) magnesium sulphate
- Discard 2 mL magnesium sulphate to give 4 g in 8 mL
- Using medication added label write "magnesium sulphate 4 g in 8 mL" and attach label to syringe

Maintenance dose set up

- **NB: To avoid mixing up the syringes, do not draw up the maintenance dose until after the loading dose has been commenced**
- Draw up 10 g (20 mL) magnesium sulphate
- Using medication added label write "magnesium sulphate 10 g in 20 mL" and attach label to syringe

Prevent eclampsia (prophylaxis)

- Use loading dose syringe
- Set syringe driver at 24 mL / hour to infuse 4 g (8 mL) over 20 minutes
- After 20 minutes, use maintenance dose syringe to commence maintenance at 1 g / hour (2 mL / hour)

For eclamptic seizures

- Use loading dose syringe
- Set syringe driver at 48 mL / hour to infuse 4 g (8 mL) over 10 minutes
- After 10 minutes, use maintenance dose syringe to commence maintenance at 1 g / hour (2 mL / hour)
- **ECG monitoring and anaesthetist on site**

Recurrence of seizure during maintenance treatment

- Set syringe driver at 24 mL / hour to infuse 2 g (4 mL) IV over 10 minutes
- Once the condition is stable, reset syringe driver to maintenance dose of 1 g / hour (2 mL / hour)
- Alternatively, increase the maintenance infusion rate to 2 g / hour (4 mL / hour)
- Check for hyporeflexia and reduced respiration rate

Ensure calcium gluconate is available

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Magnesium sulphate volumetric infusion pump regimen

- **A volumetric infusion pump should only be utilised for the administration of magnesium sulphate where there is no access to a syringe driver**
- The total adult daily dose should not exceed 30 g to 40 g of magnesium sulphate
- No more than 8 g of magnesium sulphate should be administered over 1 hour
- Continue for up to 24 hours after the last seizure activity and for 24 hours after birth

Magnesium sulphate diluted

Loading dose set up

- Draw up 5 g (10 mL) magnesium sulphate
- Discard 2 mL magnesium sulphate to give 4 g in 8 mL
- Withdraw 8 mL from a 100 mL bag of sodium chloride 0.9 % and discard
- Add the 8 mL magnesium sulphate (4 g) to the remaining 92 mL bag of sodium chloride 0.9 % to make 100 mL
- Using medication added label write “magnesium sulphate 4 g (8 mL) in sodium chloride 0.9 % to a total volume of 100 mL” and attach label to bag

Maintenance dose set up

- **NB: To avoid mixing up the infusion bags, do not draw up the maintenance dose until after the loading dose infusion has been commenced**
- Draw up 20 g (40 mL) magnesium sulphate
- Withdraw 40 mL from a 100 mL bag of sodium chloride 0.9 % and discard
- Add the 40 mL magnesium sulphate (20 g) to the remaining 60 mL bag of sodium chloride 0.9 % to make 100 mL
- Using medication added label write “magnesium sulphate 20 g (40 mL) in sodium chloride 0.9 % to a total volume of 100 mL” and attach label to bag

Prevent eclampsia (prophylaxis)

- Use loading dose bag
- 4 g (set at 300 mL / hour) over 20 minutes
- After 20 minutes, use maintenance dose infusion bag to commence maintenance at 1 g / hour (5 mL / hour)

For eclamptic seizures

- Use loading dose bag
- 4 g (set at 600 mL / hour) over 10 minutes
- After 10 minutes, use maintenance dose infusion bag to commence maintenance at 1 g / hour (5 mL / hour)
- **ECG monitoring and anaesthetist on site**

Recurrence of seizure during maintenance treatment

- 2 g (set at 60 mL / hour) IV over 10 minutes
- Once the condition is stable, reset volumetric infusion pump to maintenance dose of 1 g / hour (5 mL / hour)
- Alternatively, increase the maintenance infusion rate to 2 g / hour (i.e. 10 mL / hour)
- Check for hyporeflexia and reduced respiration rate

Ensure calcium gluconate is available

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- For refractory cases, consider intubation to protect the airway and maintain oxygenation. Transfer to an Intensive Care Unit is indicated in these circumstances

Antihypertensive Treatment

- Treat hypertension if systolic > 170 mm Hg or diastolic > 110 mm Hg with **either intravenous hydralazine or labetalol**
  - **Hydralazine** 5 mg to 10 mg IV slowly. Note that the onset of action of hydralazine is 10 to 20 minutes
  - Repeated doses of hydralazine 5 mg IV 20 minutes apart may be given if necessary as ordered (for further information, refer to PPG 'Hydralazine infusion regimen')
  - **Labetalol** 20 mg (4 mL) IV over 2 minutes. The maximal effect usually occurs within 5 minutes of each injection
  - If no change in blood pressure, repeat labetalol 20 mg (4 mL) every 10 minutes (titrated to blood pressure) to a maximum of 4 doses (80 mg = 16 mL) (for further information, refer to PPG 'Labetalol infusion regimen')

Differential diagnosis / documentation

- Note characteristics of seizure, document presence or absence of aura, duration and sequencing of all phases of seizure activity, associated symptoms, e.g. headache, visual disturbance, abdominal pain, maternal fetal physiological responses, interventions
- Document findings of clinical examination
- Establish cause of seizure (see introduction)

Management post seizure

- If still pregnant – stabilise the woman and then arrange for delivery
- Monitor the respiratory rate, pulse oximetry, blood pressure and level of consciousness
- Examine the lungs to exclude aspiration
- Uterine activity may start or increase with the seizures; monitor for signs of precipitous labour or placental abruption (if significantly elevated blood pressure)
- Monitor urine output hourly (insert urinary catheter) and maintain fluid balance chart
- Follow fluid management as per PPG 'Fluid management and monitoring in severe preeclampsia'

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Useful web site

International League against Epilepsy (ILEA). Available from URL: http://www.ilae.org/

Abbreviations

ABCDE	Airway, breathing, circulation, drugs / disability and examination
BP	Blood pressure
CTG	Cardiotocography
ECG	Electrocardiograph
e.g.	For example
et al.	And others
g	Gram(s)
i.e.	That is
IV	Intravenous
JOGNN	Journal of Obstetrics, Gynecology and Neonatal Nursing
kg	Kilogram(s)
mg	Millogram(s)
$MgSO_4$	Magnesium sulphate
mL	Millilitre(s)
mm Hg	Millimetres of mercury
%	Percentage
RCOG	Royal College of Obstetricians and Gynaecologists
URL	Uniform resource locator

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Table 1 - Classification of epileptic seizures according to clinical type

Partial (focal, local) seizures	
Simple partial seizures (SPS)	
Temporal lobe SPS are the most common type of SPS	Symptoms can include: > An 'epigastric rising sensation' > Dèjá vu (the feeling of 'having been here before') or jamais vu (where familiar things seem new) > A flashback of memory > A sudden, intense feeling of fear or joy > A funny taste or smell
Frontal lobe SPS can be harder to describe	Some people experience: > Strange movements > A feeling of a wave going through the head or body > Stiffness or jerking of part of the body that might start in one place, for example the face, and spread to other parts of the body
Parietal lobe SPS	Often include strange sensations such as: > Numbness or tingling > Burning sensations or a feeling of heat > A feeling that part of the body, an arm or leg, is bigger or smaller than they really are
Occipital lobe SPS	Involve visual sensations, such as: > Distortion or loss of vision > Seeing flashing lights or coloured shapes > Seeing people or objects that are not there (hallucinations)
Complex partial seizures (CPS)	
Temporal lobe CPS	Most common CPS > Automatisms such as lip-smacking or chewing movements, or rubbing, stroking or fiddling with their hands; > Or looking from one side to another in a confused way
Frontal lobe CPS	Often much shorter than temporal lobe CPS, usually lasting about 15-30 seconds: > Make strange postures with their arms or legs; or > Make juddering movements

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Generalised seizures (convulsive or non convulsive)	
Tonic-clonic seizures	Tonic–clonic seizures involve a tonic phase, in which the muscles suddenly contract, causing the person to fall and lie rigid. Up to a minute later, the seizure enters the clonic phase, when the muscles begin to alternate between relaxation and rigidity. The person may lose bowel or bladder control. The seizure usually lasts for 2–3 minutes, after which the person remains unconscious for a while. On waking, the person is likely to have a headache and to be confused and tired
Clonic seizures	A series of myoclonic contractions that regularly recur at a rate of 0.2 – 5 per second
Atonic seizures	Cause a loss of postural tone. The result is loss of posture (head drops, falls) and are often preceded by a short myoclonic seizure
Myoclonic seizures	Short muscle contractions, usually lasting < 400 milliseconds
Absence seizures	Impairment of consciousness alone or with: mild clonic, atonic or tonic components, automatisms and/or autoimmune symptoms or signs
Secondarily generalized seizures	
Partial seizures evolving to **secondary generalized seizures** (may be generalized tonic-clonic, tonic or clonic)	SPS evolving to generalized seizures
	CPS evolving to generalized seizures
	SPS evolving to CPS and then evolving to generalized seizures
Unclassified seizures	

Adapted from: International League against Epilepsy (ILEA) classification.
Available from URL: http://www.ilae.org/ and Luders H, Acharya J, Baumgartner C, Benbadis S, Bleasel A, Burgess R *et al*. Semiological seizure classification. *Epilepsia* 1998; **39:**1006-13.

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