CLINICAL PRACTICE GUIDELINE

Hypertension in Pregnancy: Magnesium Anticonvulsant Therapy

This document should be read in conjunction with the **Disclaimer**

Magnesium sulphate therapy QRG

Err on the side of caution when a woman who has been treated with Nifedipine requires a MgSO4 bolus.

The Consultant Obstetrician **must** be consulted before prescribing and commencing MgSO₄ therapy.

Solution used at KEMH

The solution used at KEMH is **8g of MgSO**₄ in a **100mL** pre-packaged solution. This must be given via an infusion device. Infusion rates shall be checked and confirmed by 2 Registered Midwives when commencing and changing rates.

Loading dose regimen

Administer intravenous loading bolus dose of 4g of MgSO₄ over 20 minutes¹ via a controlled infusion device. The rate shall be checked and confirmed by 2 Registered Midwives.

This equates to an infusion rate of 150mL/hour for 20 minutes (i.e. the woman only receives 50 mL).

Maintenance dose regimen

The loading dose is followed by a maintenance infusion of 1g of MgSO₄ per hour.¹ When the rate is changed to the maintenance rate, the rate shall be checked and confirmed by 2 Registered Midwives.

This equates to an infusion rate of 12.5mL per hour. This is continued for at least 24 hours after the last seizure or after the birth of the neonate.

Treatment for recurrent seizures

If recurrent seizures occur a further 2 - 4g of MgSO₄ is given over 10 minutes. The rate shall be checked and confirmed by 2 Registered Midwives.

This equates to an infusion rate of 300 mL /hour for 5 minutes (i.e. the woman receives 25mL of MgSO₄).

Prior to the commencement of a magnesium sulphate infusion Ensure:

- Deep tendon reflexes (DTR) are present,^{2, 3} Respirations are more than 12 per minute,² and the urine output is >100ml during the previous 4 hours.³
- The correct order, medication, dose, and infusion rate are checked by 2 Registered Midwives; and
- A set of vital signs, DTR's, urine output, and conscious state are documented.⁴

Calcium gluconate

- <u>Calcium Gluconate</u> 1g in 10 mL (2.2mmol Calcium in 10mL) must be available at all times for treatment of MgSO₄ toxicity.⁴
- Dose administer ONE ampoule of Calcium gluconate 1g in 10mL (2.2mmol calcium in 10mL) intravenously (IV) slowly over 3 to 10 minutes into a large vein⁵
- Electrocardiogram (ECG) monitoring is recommended if Calcium gluconate is given.⁶

Maternal and fetal observations

Fetal observations

Apply continuous fetal monitoring.7,8

Maternal observations

Patella reflexes

- Perform every 15 minutes for the first 2 hours, then hourly thereafter.
- If deep tendon reflexes are absent:
 - ➤ Cease the infusion.^{3, 9}
 - Notify the Medical Officer.
 - Collect blood for serum magnesium levels (therapeutic magnesium concentration range is 1.7 - 3.5 mmol/L).

Respiratory rate and oxygen saturation monitoring

- Monitor respirations 15 minutely during the first 2 hours, then hourly thereafter.
- If respirations are less than 12 respirations/minute:
 - > Notify the Medical Officer.
 - > Cease the infusion until medical review.
 - Place the woman in the recovery position.
 - Maintain the airway and administer O₂ at 6-8L/minute.

- Administer IV (<u>Calcium Gluconate</u> 1g in 10mL (2.2mmol calcium in 10mL) slowly. Monitor heart rate with an ECG if available, or apply as soon as possible.
- Collect blood for serum magnesium levels.
- Apply continuous pulse oximetry. Record O₂ saturation levels hourly.
- If respiratory arrest occurs:
 - Stop infusion.^{3, 9}
 - Call a 'Code Blue Medical'.
 - Initiate respiratory support until the woman is intubated and ventilated.

Monitor urine output

- Measure and record urine output via a urometer bag hourly.⁸
- If urine output is <25mL/hour notify the medical staff.^{2, 8}

Blood pressure

 Monitor BP 15 minutely during the infusion for the first 2 hours, thereafter hourly.

Review of magnesium sulphate infusion

- Report any side effects of MgSO₄ to the Medical Officer.
- Notify the obstetric staff of any signs of ongoing seizure activity despite MgSO₄.

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Magnesium Sulphate Anticonvulsant therapy

Aims

To prevent and treat eclamptic seizures

Background

Magnesium sulphate (MgSO₄) more than halves the risk for eclampsia, and probably reduces the risk of maternal death.¹⁻³ The Magpie Trial^{6, 7} indicated that the use of prophylactic MgSO₄ reduced the risk of eclampsia and caused no harmful effects to the mother or baby in the short term. A follow-up study also found that its use caused no associated mortality or morbidity to the woman after 2 years.⁸ Exposure of the fetus to MgSO₄ in utero is not associated with a clear difference in the risk of morbidity or disability for children at 18 months of age after use.⁹

The mode of action of MgS0₄ is unclear, but it is believed to have a neuromuscular blocking action¹⁰ which relaxes smooth muscles including the vasculature, thereby reducing cerebral ischaemia. The blocking of aspartate receptors in the brain reduces calcium influx which is responsible for causing cell injury in the neurones. MgS0₄ is mostly excreted in urine.¹⁰

Key points

- 1. MgS0₄ should be considered for women with pre-eclampsia for whom there is concern about the risk of eclampsia.^{4, 5} This is usually in the context of severe pre-eclampsia <u>once a delivery decision has been made</u> and in the immediate postpartum period.⁴ In women with less severe disease the decision is less clear and will depend on individual case assessment. Magnesium Sulphate should not be prescribed for the prevention of eclampsia without discussion with the Consultant Obstetrician on call¹¹, unless in an urgent situation of imminent eclampsia.
- 2. Err on the side of caution when a woman who has been treated with Nifedipine requires a MgSO4 bolus.
- **3.** MgS0₄ has been demonstrated to reduce the risk of eclamptic seizures and is also the medication of choice to control eclamptic seizures.^{1, 2, 7} See KEMH Clinical Guideline Magnesium Sulphate Infusion Loading Dose page 2.
- 4. When MgS0₄ is administered it should be continued for 24 hours following birth, or for 24 hours after the last seizure.^{5, 7, 11}
- 5. During use of MgS0₄, Calcium Gluconate 1g in 10 mL (2.2mmol Calcium in 10mL) should be available to give as an antidote for magnesium toxicity, ¹⁰ which can produce respiratory depression. ¹¹
- 6. Regular assessment of blood pressure, urine output, maternal deep tendon reflexes, respiratory rate and oxygen saturation may indicate the development of

- MgS0₄ toxicity. ^{5, 12}
- 7. Serum magnesium levels are not routinely measured unless renal function is compromised.⁵ Monitoring of plasma concentrations becomes important where tendon reflexes are absent or in the presence of renal dysfunction.¹³ However, if the woman has reduced renal function then plasma magnesium should be closely monitored⁵ 6 hourly (or more frequently if signs of oliguria).
- 8. If deep tendon reflexes are diminished or absent, the infusion must be stopped and a Magnesium level performed.¹⁴
- 9. All MgS0₄ solutions **must** be given via an infusion pump. 15
- 10. Do not use IV line to inject other drugs. 15 4

	PROCEDURE	ADDITIONAL INFORMATION
1	Prior to the commencement MgS0 ₄	
1.1	Obtain a medical history ¹⁰ and provide information to the woman about the use of MgSO ₄ . Obtain verbal consent, where appropriate. ¹⁶	If the typical features of severe pre- eclampsia are not present, consider further investigation of other medical problems. ⁵
1.2	 Two Registered Midwives must: Check the medication, dose and infusion rate. Set up the infusion line and pump. 	See Clinical Guideline: Pharmacy: Medication Administration (available to WA Health employees through Healthpoint) for details on checking and the administration of intravenous medication by medical and nursing / midwifery staff.
1.3	 Before commencement check and document that: The deep tendon reflex is present^{6, 7} The respiratory rate is > 12 respirations per minute⁷ Urine output >100mL during previous 4 hours⁶ Document a baseline set of vital signs, deep tendon reflexes, urine output and conscious state.¹⁰ 	To detect deviations from normal. Urine output should be >25mL/hr. ⁶
1.4	Commence the infusion.	

	PROCEDURE	ADDITIONAL INFORMATION
2	IV Magnesium Sulphate (MgSO ₄)	
2.1	Infuse 4g of MgSO ₄ over 20 minutes ⁵ The rate shall be checked and confirmed by 2 Registered Midwives. This equates to an infusion rate of 150mL per hour for 20 minutes (i.e. the woman receives only 50mL). A solution of 8g of MgSO ₄ in 100mL bag is used at KEMH.	 The loading dose is given for: prophylaxis to prevent seizures or treatment of an initial seizure where no prior Magnesium Sulphate has been administered. Note: All infusions must be given via an infusion pump. Ensure the MgSO₄ solution has no particulate matter or cloudy appearance.¹⁰
3	MgSO ₄ Maintenance regimen The dose for maintenance infusion is 1g of MgSO ₄ per hour. ⁵ ⁶ The rate shall be checked and confirmed by 2 Registered Midwives. This equates to an infusion rate of 12.5mL per hour where a solution of 8g of MgSO ₄ in 100mL bag is used at KEMH. Treatment for eclampsia/seizures which treatment	When changing from the loading dose to the maintenance dose, this must be checked and performed by two Registered Midwives and documented that the correct rate has been commenced on the patient observation chart.
	MgSO ₄ regime for recurrent seizures 2 - 4g of MgSO ₄ is given over 5 ⁴ -10 minutes ^{5,6} The rate shall be checked and confirmed by 2 Registered Midwives. This equates to an infusion rate of 300mL per hour for 5 minutes (i.e. the woman receives 25 mL) where a solution of 8g of MgSO ₄ in 100mL bag is used.	If recurrent seizures occur a further dose of MgSO ₄ may be prescribed. ⁴

	PROCEDURE	ADDITIONAL INFORMATION
4	Monitoring during administration	
	As the woman is cared for in ASCU (Adult Special Care Unit) or Labour and Birth Suite - use an 'MR731 Adult Special Care Observation Summary' chart to record observations ¹⁷	
4.1	Deep Tendon Reflexes (DTR)	
	 Elicit, grade, and record every: 15 minutes during the first 2 hours of therapy, then hourly thereafter. 	Magnesium sulphate is a smooth muscle relaxant. ⁷ Reduction or loss of tendon reflexes precedes respiratory depression ⁷ , and should be immediately notified to the medical staff ⁷ . Cease the infusion immediately ¹⁸ .
	Deep Tendon Reflex Grading Scale: 4+ Hyperactive; very brisk, jerky - includes clonus if present; abnormal 3+ Brisker than average; may not be abnormal 2+ Average response, normal 1+ Diminished response; low normal 0 No response; abnormal	Deep tendon reflexes can be used to determine need for magnesium therapy, evaluate efficacy of magnesium therapy, and detect developing toxicity from magnesium therapy ¹⁹ .
4.2	Respiratory rate	
	 Take and record: every 15 minutes during the first 2 hours of therapy, then hourly thereafter If respiratory rate is less than 12 respirations/minute notify the medical staff, and cease the infusion until medical review^{7, 15}. The Medical Officer may administer Calcium Gluconate 1g in 10mL (2.2mmol Calcium in 10mL) if there is concern for respiratory function.¹¹ 	Magnesium sulphate is a smooth muscle relaxant and can cause respiratory depression; a decreasing respiratory rate may indicate Magnesium Sulphate toxicity ⁷ . If it is not recognised and managed immediately the woman is at risk for respiratory/cardiac arrest. If Calcium gluconate is administered apply ECG monitoring. ²⁰

	PROCEDURE	ADDITIONAL INFORMATION		
4.3	Oxygen saturation			
	Apply continuous pulse oximetry. Measure and record the oxygen saturation hourly. 17	Cyanosis is an important sign of cardio- respiratory failure, and should be monitored visually and electronically. Cyanosis is an indication for the administration of oxygen. ¹⁷ Notify the Medical Officer if the oxygen saturation is less than 95%.		
4.4	Blood pressure ^{11, 21}			
	 Take and record: every 15 minutes during the first 2 hours of therapy, then hourly thereafter. 	Frequency of BP on maintenance therapy will depend on the maternal clinical condition and stability of BP.		
4.5	Fetal heart rate			
	The woman should have continuous CTG ^{17, 22} monitoring initially. On-going monitoring in the following 24 hours will depend on the maternal and fetal clinical condition. The decision regarding fetal surveillance should be made in liaison with the Consultant Obstetrician.	To monitor FHR for signs of placental abruption ²² or onset of labour- which may go unnoticed. ¹⁷ A sudden or rapid decrease in blood pressure may cause poor uteroplacental circulation, and therefore signs of fetal compromise ¹⁸ . Fetal surveillance		
4.6	Fluid balance management			
	 Maintain a strict fluid balance chart.¹⁰ Fluid restriction is advisable to reduce the risk of fluid overload in the intrapartum and postpartum periods. In usual circumstances, total fluids should be limited to 80 mL/hour or 1 mL/kg/hour¹¹. The regime of fluid restriction should be maintained until there is a postpartum diuresis, as oliguria is common with severe pre-eclampsia. If there is associated maternal haemorrhage, fluid balance is more difficult and fluid restriction is inappropriate. 	Increased peripheral resistance leads to generalised vasospasm and hypertension. The intravascular compartment is reduced, and endothelial damage leads to increased vascular permeability and oedema. Women with pre-eclampsia have leaky capillary membranes and a predisposition to low albumin levels: therefore if fluid administration is excessive or unmonitored, they are prone to developing pulmonary oedema. 18		

	PROCEDURE	ADDITIONAL INFORMATION	
4.7	Urinary output		
	 Record the urine output hourly via an IDC with a urometer measuring bag¹⁷ Report urine output to medical staff if below 25mL/hour and request review.^{7, 17} The MgSO₄ therapy may need to be reduced or ceased if there is <25mL of urine output in 1 hour^{7, 17} 	MgSO ₄ is eliminated via the renal system. ⁷ Toxicity can occur in the presence of oliguria. The infusion should be discontinued if signs of toxicity become evident. Calcium Gluconate (see point 5.2 below) may be required in addition, if toxicity is severe. ¹¹	
5	Magnesium sulphate toxicity		
	 Observe for signs of MgS0₄ toxicity: Nausea, hot flushes, weakness¹⁸ Slurred speech¹⁸ / Confusion / Blurred vision Loss of DTR¹⁰ / Absent patellar reflexes Hypotension¹⁰ / Pulse oximetry <95%¹⁸ Respiratory depression¹⁰ < 12 breaths /min Respiratory arrest¹⁰ Cardiac arrhythmia¹⁹ / ECG changes (e.g. widened QRS complex, increased PR interval, prolonged QT interval, heart block)¹⁰ Chest pains¹⁰ Oliguria¹⁰ / Urine output less than 25mL/hour⁷ 	If signs of magnesium toxicity develop, stop the magnesium sulphate infusion. ⁶ Because of the slow elimination, if signs of moderate toxicity are apparent, discontinuing the magnesium may not be sufficient. Intravenous Calcium gluconate (see 5.2 below), which quickly reverses the effects of magnesium toxicity, may be required when moderate to severe toxicity occur. ^{6, 23, 24}	
5.1	Absent / reduced patella reflexes		
	 Stop the infusion^{6, 18} Notify the Medical Officer Collect blood for serum levels¹⁸ Cease the infusion until reflexes return⁶ and the blood results are in the therapeutic range. 	Therapeutic magnesium concentration range is 1.7 - 3.5 mmol/L. ⁶	

	PROCEDURE	ADDITIONAL INFORMATION	
5.2	Respiratory depression		
	 Stop the infusion^{6, 18} Place the woman in the recovery position Maintain airway Administer 0₂ at 6-8L/min via a face mask Notify the Medical Officer urgently IV Calcium Gluconate must be administered by the Medical Officer diluted or undiluted (in a compatible fluid) slowly over 3 to 10 minutes into a large vein²⁵ 	Calcium gluconate opposes the action of magnesium. Note: Calcium gluconate 1g in 10ml (2.2mmol Calcium in 10mL) should be available at all times when Magnesium sulphate is in use. If Calcium gluconate is administered apply ECG monitoring. Rapid intravenous injection may cause vasodilatation, bradycardia, decreased BP, arrhythmias, syncope and cardiac arrest. Overdose can be rapidly fatal. Control of the action of th	
5.3	Respiratory arrest		
	 Stop the infusion^{6, 18} Summon emergency medical assistance by pressing the yellow assist bell, dial 55 stating 'Code Blue Medical', your identity & location. Initiate respiratory support until the woman is intubated and ventilated. 		
6	Ongoing management		
6.1	Women on Magnesium Sulphate therapy should be cared for in the Adult Special Care Unit (ASCU) until therapy has ceased, which is normally 24 hours following the last seizure ¹⁷ or after the birth. 11, 12 Parameters to monitor are, a return to normal blood pressure and an increase in urine output. 26	When the management above has resulted in birth of the neonate(s), continuous BP monitoring and hourly pulse, oxygen saturation, respiration, urine output and reflexes should continue in ASCU for 24-48 hours, or until the woman's condition improves, and she is transferred to the postnatal ward. 12 Often one to two days after the birth the woman's thrombocytopaenia and liver enzyme elevations worsen before improving. 5	

	PROCEDURE	ADDITIONAL INFORMATION
6.2	Consider anti-thrombotic agents and the use of anti-embolic (TED) stockings to reduce the risk associated with deep vein thrombosis (DVT). ⁵	Pre-eclampsia is a major risk factor for venous thrombotic embolism (VTE), and the reduced mobility (such as while on anticonvulsant therapy or hospitalised) contributes to an increased risk of DVT. ⁵
6.3	Anti-hypertensive therapy should be maintained and gradually reduced ²⁶ - to be followed up by GP.	Most antihypertensive drugs are compatible with breast feeding. ²⁶
		Encourage the woman to see her GP by 2 weeks (earlier as required) to continue the management of antihypertensive therapy.
6.4	In the presence of reduced renal function and/or oliguria (urine output <100 mL over 4 hours), regularly monitor the plasma magnesium concentration (e.g. 6 hourly). Reduce the dose if necessary (seek specialist advice). 6, 12	Therapeutic magnesium concentration is 1.7–3.5 mmol/L. ⁶
6.5	Report any side effects to the Medical Officer.	

Side effects of magnesium sulphate^{7, 27, 28}

Approximately 25% of women experience side effects from MgS0₄. These may include:

- Sensation of pain and warmth in arms
- Disruption to sensation, particularly in extremities
- Flushing⁶ of face, neck and hands
- Thirst, headache⁶, dizziness⁶, itching
- Nausea and vomiting⁶
- Loss of patellar reflexes- absent well before toxic serum levels are reached
- Muscle weakness, slurring of speech, drowsiness and visual disturbances
- Irritation at the injection site

Major side effects include:

Respiratory depression which may lead to respiratory/cardiac arrest

The use of MgS0₄ is contraindicated and should be avoided in women with:

• Heart block, 6 hypermagnesaemia, 6 or renal failure.

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Related WNHS policies, procedures and guidelines

KEMH Clinical Guidelines:

Obstetrics & Gynaecology:

- Hypertension in Pregnancy Medical Management
- Hypertension in Pregnancy Midwifery Care
- Hydralazine Infusion
- Severe Early Onset Pre-eclampsia post birth management
- Pre-conception counselling for women with a history of pre-eclampsia or significant risk factors

Pharmacy A-Z Medications: Calcium Gluconate; Magnesium Sulphate Infusion

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