IAEM Clinical Guideline

Management of Patients with Severe Pre-eclampsia and Eclampsia

Version 1.0

November 2023

Authors: Dr Andrew Ngaditono, Dr Suzanne Smyth, Dr Aoife O'Neill, Dr Aileen McCabe

Guideline lead: Dr Aileen McCabe, in collaboration with IAEM Clinical Guideline Committee and Tallaght Hospital

To reference this document please reference as:

Ngaditono A, Smyth S, O'Neill A, McCabe A. Management of Patients with Severe Pre-eclampsia and Eclampsia. IAEM Guidelines 2023. https://iaem.ie/professional/clinical-guidelines/ (accessed 17th July 2023)

Tallaght University Hospital | Ospidéal Ollscoile Thamhlachta

An Academic Partner of Trinity College Dublin

DISCLAIMER

IAEM recognises that patients, their situations, Emergency Departments and staff all vary. These guidelines cannot cover all clinical scenarios. The ultimate responsibility for the interpretation and application of these guidelines, the use of current information and a patient's overall care and wellbeing resides with the treating clinician.

Revision History

Date	Version	Section	Summary of changes	Author
November 2023	1.0	All	Final version	AN/SS/ AO'N/AMcC

CONTENTS

GLOSSARY OF TERMS **4**

INTRODUCTION **5**

PARAMETERS **6**

AIMS **6**

DIAGNOSTIC CRITERIA **7**

Pre-eclampsia **7**

Superimposed Pre-eclampsia **8**

Severe Pre-eclampsia **9**

MANAGEMENT OF SEVERE PRE-ECLAMPSIA **10**

Baseline Investigations **10**

Baseline Monitoring **10**

Fluid Management **11**

Severe Hypertension Management **11**

MEDICATION **12**

Labetalol **12**

Hydralazine **13**

Nifedipine **13**

Magnesium Sulphate **14**

Figure 1: Acute treatment algorithm for Pre-eclampsia 15

ECLAMPSIA **16**

Management of Eclampsia **16**

Delivery **17**

Transfer **17**

Figure 2: Management of Eclampsia 18

SPECIAL CONSIDERATION **19**

HELLP Syndrome (Haemolysis, Elevated Liver Enzymes, and Low Platelets) **19**

REFERENCES **20**

GLOSSARY OF TERMS

BP	Blood Pressure
CT	Computed Tomography
DIC	Disseminated Intravascular Coagulation
ED	Emergency Department
FBC	Full Blood Count
HELLP Syndrome	Haemolysis, Elevated Liver Enzymes, and Low Platelets
HIPE	Hospital In-Patient Enquiry
HSE	Health Service Executive
IMIS	Irish Maternity Indicator System
IV	Intravenous
LFT	Liver Function Test
MAP	Mean Arterial Pressure
MBRRACE	Maternal, Newborn and Infant Clinical Outcome Review Programme
MDE	Maternal Death Enquiry
OB/GYN	Obstetrics and Gynaecology
PCR	Protein/Creatinine Ratio
SLE	Systemic Lupus Erythematosus

Management of Patients with Severe Pre-eclampsia and Eclampsia

INTRODUCTION

Hypertensive disorders of pregnancy remain one of the leading causes of maternal and neonatal morbidity and mortality worldwide. Data extracted from the HIPE system in Ireland showed that out of 60,188 maternities reported in 2016, 5.9% of women had hypertensive disorder of pregnancy and 4.6% had pre-eclampsia. The most recent data published in 2022 by Maternal Death Enquiry Ireland in corporation with MBRRACE-UK reported 2 maternal deaths in Ireland caused by pre-eclampsia and eclampsia in 2009-2020 but noted no deaths occurring in 2018-2020.

Pre-eclampsia is defined as new-onset hypertension in a pregnant patient who is greater than 20 weeks' gestation accompanied by proteinuria, or other maternal organ or uteroplacental dysfunction. Early identification of patients with pre-eclampsia with severe features is necessary to initiate prompt intervention. This can prevent progression of disease to other severe sequelae including seizures, also known as eclampsia.

PARAMETERS

Target audience	This guideline has been developed for clinicians managing patients with severe pre-eclampsia and eclampsia in the ED.
Patient population	The target patient population is patients with severe pre-eclampsia and eclampsia in the ED.

AIMS

To provide an updated and evidence-based guideline in the diagnosis, evaluation, and timely management of severe pre-eclampsia and eclampsia.

DIAGNOSTIC CRITERIA

There are subtypes of pre-eclampsia, each with their own diagnostic criteria:

1. Pre-eclampsia
2. Superimposed pre-eclampsia
3. Severe pre-eclampsia

Pre-eclampsia

Pre-eclampsia is a multisystem progressive disorder unique to human pregnancy occurring in the second half of pregnancy or postpartum, in a previously normotensive patient. Pre-eclampsia is caused by placental and maternal vascular dysfunction, and it resolves gradually after delivery. Rarely, pre-eclampsia presents before 20 weeks' gestation.

It is characterised by:

1. New onset of hypertension and proteinuria

   or

2. New onset hypertension and significant end-organ dysfunction with or without proteinuria.

Hypertension in pregnancy is defined as:

Systolic BP ≥140mmHg and/or diastolic BP ≥90mmHg.

Severe hypertension is defined as:

Systolic BP ≥160mmHg and/or diastolic BP ≥110mmHg.

As per NICE guidelines, **pre-eclampsia** can be diagnosed when hypertension occurs on at least 2 occasions at least 4 hours apart after 20 weeks' gestation in a previously normotensive patient, and is accompanied by one or more of the following signs of organ involvement:

- **Proteinuria**: spot urine protein/creatinine ratio (PCR) >30mg/mmol (0.3mg/mg) or >300mg/day or at least 1g/L ('2+') on dipstick testing.

OR, in the absence of proteinuria,

- **Other maternal organ dysfunction**:
    - **Renal insufficiency**: serum or plasma creatinine >90µmol/L
    - **Haematological involvement**: thrombocytopenia (<150,000/µL), haemolysis, or DIC
    - **Liver involvement**: raised serum transaminases, severe epigastric and/or right upper quadrant pain
    - **Neurological involvement**: eclampsia, hyperreflexia with sustained clonus, persistent new headache, persistent visual disturbances (photopsia, scotomata, cortical blindness, posterior reversible encephalopathy syndrome, retinal vasospasm), stroke
    - **Pulmonary oedema**
- **Uteroplacental dysfunction** (foetal growth restriction)

Gestational hypertension is diagnosed in patients with hypertension without proteinuria or other signs/symptoms of pre-eclampsia end organ dysfunction after 20 weeks of gestation. 10-25% of these patients may ultimately develop signs and symptoms of pre-eclampsia.

Superimposed Pre-eclampsia

Superimposed pre-eclampsia is diagnosed in a patient with pre-existing chronic hypertension or proteinuria who develops one or more systemic features of pre-eclampsia after 20 weeks' gestation. It is characterised by:

- worsening or resistant acute hypertension
- new onset or sudden increase in proteinuria, and/or
- significant new end-organ dysfunction after 20 weeks' gestation[2].

In such patients, raised suspicion of superimposed pre-eclampsia justifies closer surveillance.

Severe Pre-eclampsia

This is a subset of patients with pre-eclampsia who have severe hypertension and/or specific signs or symptoms of significant end-organ dysfunction that suggest a severe end of the pre-eclampsia spectrum. Criteria for managing these patients are subjective, but close assessment and monitoring are warranted with the following indicators:

- Eclampsia
- Severe hypertension (systolic BP ≥160mmHg and/or diastolic BP ≥110mmHg, taken as an average of 3 readings over 15 minutes) with at least 1+ proteinuria.
- Moderate hypertension with significant proteinuria (at least '2+' on urine dipstick, or PCR ≥30mg/mmol or 0.3g in 24 hours) and any of:
    - Severe headache with visual disturbance
    - Epigastric pain
    - Signs of clonus
    - Liver tenderness
    - Platelet count falling to below 150 x 10^9/L
    - Alanine amino transferase rising to above 50IU/L
    - Creatinine >100mmol/L.

MANAGEMENT OF SEVERE PRE-ECLAMPSIA

Patients with pre-eclampsia should ideally be managed in a hospital facility where an obstetrician & gynaecological service is readily available.

If pre-eclampsia is suspected, please involve OB/GYN on-call early.

Please refer to figure 1 for acute treatment algorithm of severe pre-eclampsia.

Baseline Investigations

- Bloods should be sent for:
    - Urea, creatinine, and serum electrolytes
    - Full blood count
    - Liver function tests
    - Clotting screen
    - Group and save serum.
- Urine dipstick to check for proteinuria.

Blood tests should be repeated every 12 hours; more frequent testing (every 4-8 hours) may be required if presence of abnormal or deteriorating haematological and/or biochemical markers.

Baseline Monitoring

Routine hourly monitoring of vital signs is required. Special attention should be given to the following parameters:

- BP and pulse should be monitored every 15 minutes until stabilised, and then every 30 minutes
- Close monitoring of fluid balance is required with an indwelling catheter inserted to measure hourly urine output.
- Foetal well-being should be assessed carefully with a cardiotocograph (typically done under supervision of obstetric team on an obstetric ward).

Arterial line insertion may be indicated if:

- Commencing on intravenous anti-hypertensive therapy
- Patient is unstable
- BP is very high
- Patient is obese, and non-invasive measurements are unreliable
- Presence of haemorrhage of >1000ml.

Fluid Management

Fluid loading is unnecessary, and should not be done prophylactically or routinely if the patient is euvolaemic. Avoid fluid overload with total input limited to 80ml/hour at the antenatal stage.

Severe Hypertension Management

Systolic BP ≥160mmHg requires prompt treatment. Target BP stabilisation:

- Reduction of BP to <135/85mmHg with mean arterial pressure* <100mmHg

*MAP = diastolic pressure + 1/3 (systolic pressure minus diastolic pressure)

Titrate treatment with close observation to avoid sudden drop in BP, and to ensure that BP is maintained at- or below target level.

MEDICATION

Labetalol

The first choice agent is labetalol.

Oral therapy	Intravenous therapy
-Initial dose 200mg • Should lead to reduction in BP in 30 minutes. • Second oral dose can be given after 30 minutes if needed. -Can be used if patient can tolerate oral therapy or intravenous access is unavailable.	-Bolus infusion: 50mg (10ml of labetalol 5mg/ml) given over at least 5 minutes. • Should have an effect by 10 minutes. • Repeated bolus infusion in 50mg doses, to a maximum dose of 200mg, at 10 minute intervals until target aim BP achieved. -Labetalol infusion should be commenced following a response to bolus doses. • Rate of 20mg per hour via a syringe pump: undiluted 5mg/ml solution at rate of 4ml/hour via syringe pump. • Infusion rate should be doubled every 30 minutes until target BP achieved, or a dosage of 160mg/hour (32ml/hr) is reached. o Occasionally, higher doses may be needed.
Contraindications: severe asthma. Use with caution in women with pre-existing cardiac disease.	

Second Choice Agents

If intravenous labetalol has not reduced BP target after 60-90 minutes despite maximal infusion dose, consider a second-line agent in addition to labetalol. Always consult a senior

Obstetrician before commencing a second line anti-hypertensive agent as it can cause precipitous drops in BP, particularly if magnesium sulphate is also being administered.

Hydralazine

This is an alternative agent if labetalol is contraindicated, or fails to control BP.

Intravenous therapy	**Infusion**
-Bolus: 2.5mg in 10ml of water over 5 minutes. -BP measured every 5 minutes. -Dose can be repeated every 20 minutes. -Maximum dose: 20mg.	-Following bolus dose, give infusion 40mg in 40ml NaCl 0.9%. -Rate: 1-5ml/hr (1-5mg/hr) -If labetalol is continued, hydralazine infusion may not be required if BP target aim achieved with bolus hydralazine doses.
Contraindications: Hypersensitivity to hydralazine, severe tachycardia, heart failure with high cardiac output, thyrotoxicosis, and idiopathic SLE and related diseases.	

Nifedipine

Oral nifedipine can be considered if labetalol +/- hydralazine has not adequately controlled BP. It should NOT be given sublingually to woman with hypertension. Give with caution as this can cause profound hypotension when administered with magnesium sulphate.

Oral therapy	• Start with 30mg once daily. • Once daily dose tablet preferable over twice daily dose. • Maximum dose 90mg once daily.

Magnesium Sulphate

Magnesium sulphate can be given as a prophylaxis in cases of severe pre-eclampsia to prevent progression to eclampsia. Magnesium sulphate is also the anti-epileptic medication of choice in eclampsia.

It is given as a loading dose followed by continuous infusion for 24 hours.

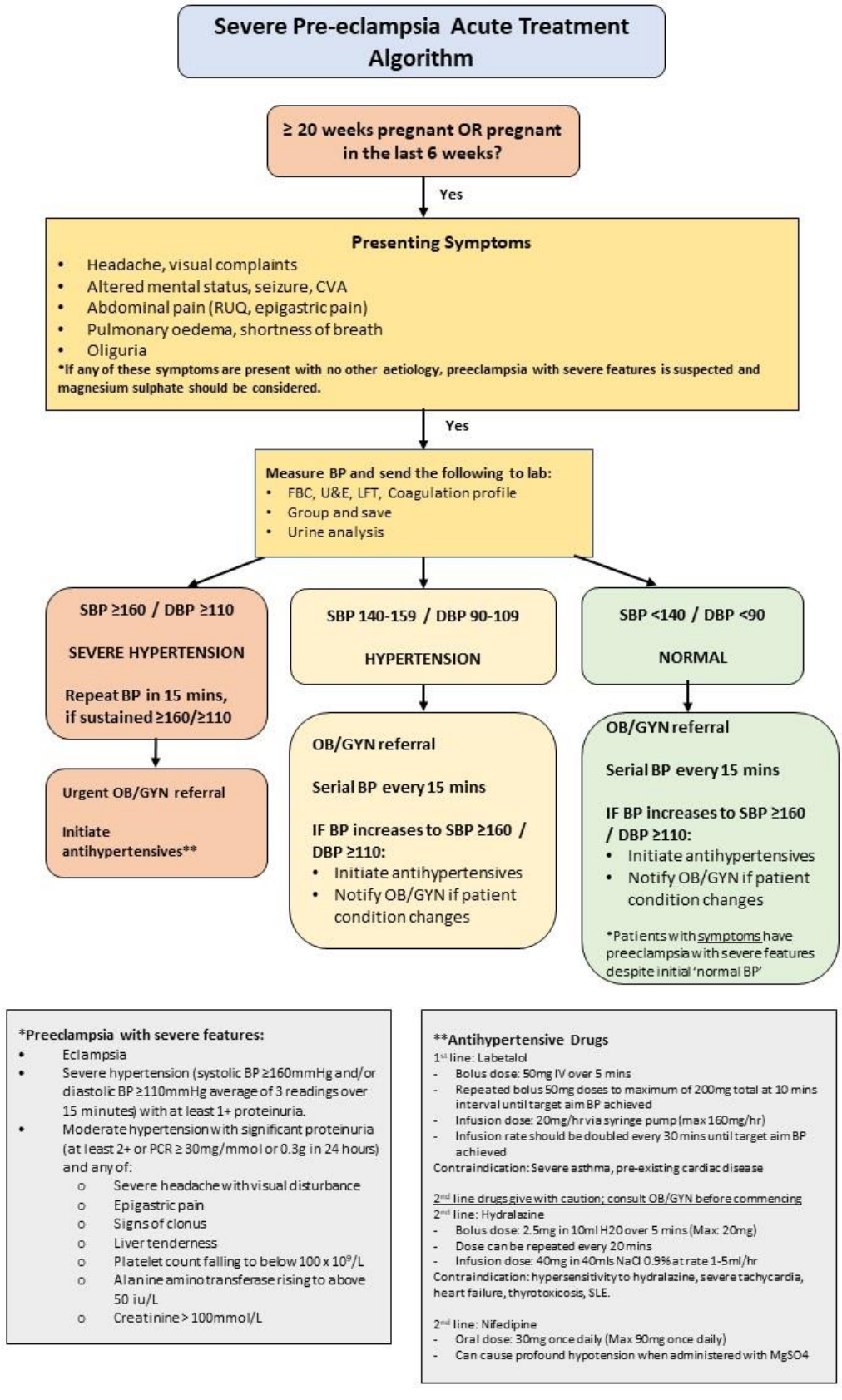
Loading dose: 4g over 5-10 minutes	**Maintenance dose: 1g/hr**

Maintain magnesium sulphate infusion until 24 hours after the last seizure or after delivery, whichever is later. If magnesium toxicity is suspected, cessation or reduction in infusion should be considered in the setting of:

- Absent deep tendon reflexes
- Motor paralysis
- Respiratory rate <12/min
- Cardiac arrhythmia
- Oliguria (urine output < 0.5ml/kg/hr).

The antidote for magnesium toxicity is 10ml 10% Calcium Gluconate given as a slow IV injection.

Figure 1: Acute treatment algorithm for Pre-eclampsia



ECLAMPSIA

Eclampsia is a clinical diagnosis based on the new onset of a generalised tonic-clonic seizure in a patient with pre-eclampsia, in the absence of other neurologic conditions that could account for the seizure. The HSE Irish Maternity Indicator System National Report in 2020 reported a total of 17 cases of eclampsia in 2019-2020. It is associated with increased morbidity and mortality for both mother and the foetus, and is an obstetric emergency.

If seizure is witnessed, immediate issues to address include:

- Prevention of maternal hypoxia and trauma
- Treatment of severe hypertension
- Prevention of recurrent seizures
- Evaluation for prompt delivery

Management of Eclampsia (figure 2)

Call appropriate personnel – include OB/GYN on-call and senior Anaesthetists on-call for anticipated difficult maternal airway.

1. Airway, Breathing, Circulation.
    a. Position patient to their left lateral decubitus position
    b. Maintain airway patency and prevent aspiration
    c. Supplemental oxygen via non-rebreather face mask
2. Give loading dose of magnesium sulphate (4g over 5-10 minutes IV).
3. Start infusion of magnesium sulphate (see above).
4. Start antihypertensive therapy (see above).

5. Once stabilised, delivery should be planned.

6. If recurrent seizures:

    - Give further bolus dose of magnesium sulphate 2g.

        - Increase rate of infusion to 1.5g/hr.

    - Closely observe the patient, and consider intubation.

    - If unable to control seizures after 2 boluses, administer conventional anti-convulsants as per local hospital guidelines.

    - It is appropriate to organise CT brain to out rule other causes of seizures.

Delivery

Delivery should be well planned, done on the best day, performed in the best place, by the best route, and with the best support team.

If the mother is unstable, then delivery is inappropriate and increases risk.

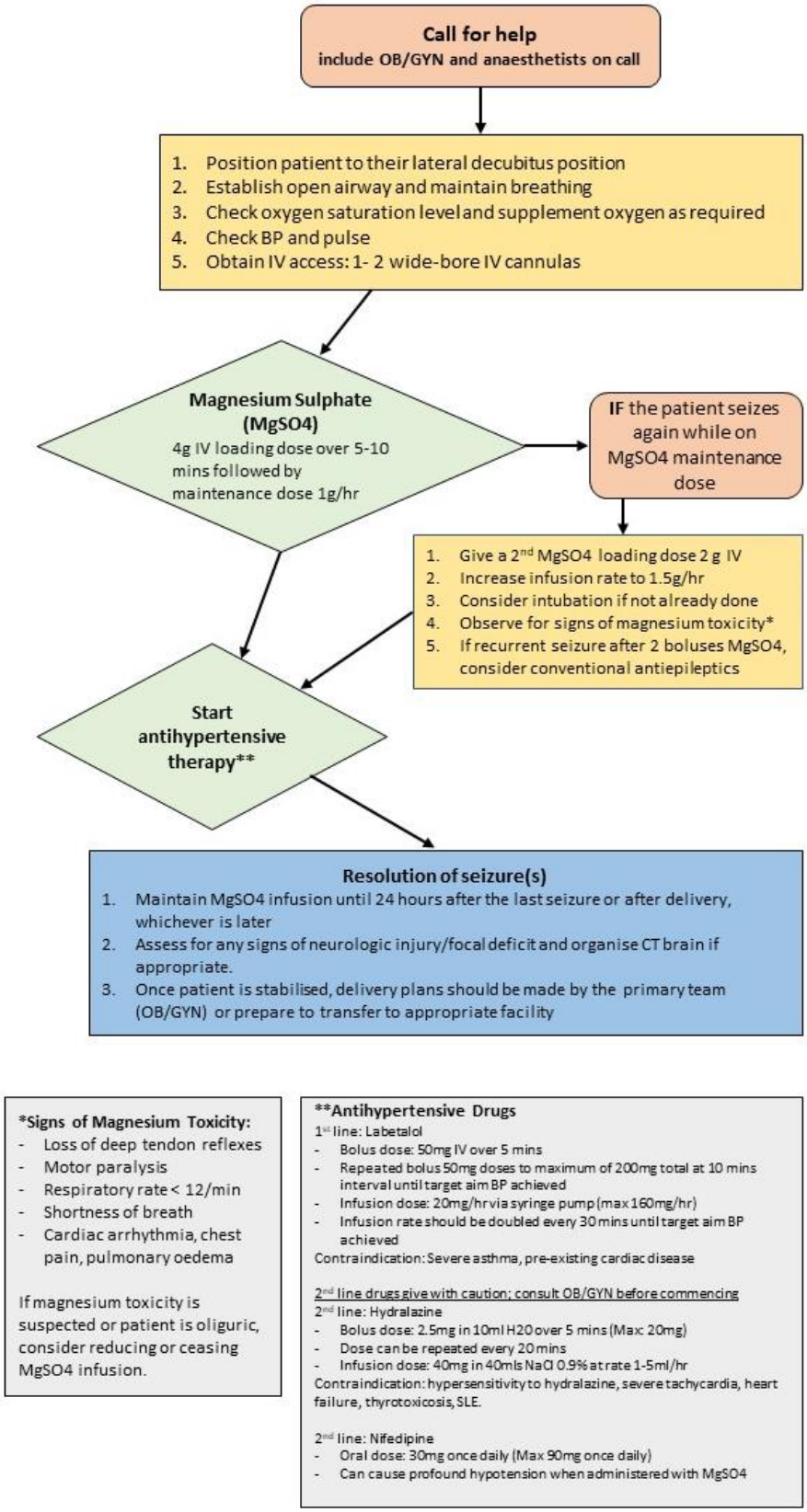
Decision to deliver should be made by the OB/GYN team once the patient is stabilised.

Transfer

In cases where decision to transfer has been made, the recommended minimum requirements prior to transfer include:

- Patient's ventilatory requirements are stable, and oxygen saturations are being maintained.
- BP has been stabilised at <160/105mmHg.
- There are appropriate personnel to transfer; senior OB/GYN clinician, and Anaesthetist
- All basic investigations have been performed, and results are clearly recorded.

Figure 2: Management of Eclampsia



SPECIAL CONSIDERATION

HELLP Syndrome (Haemolysis, Elevated Liver Enzymes, and Low Platelets)

HELLP syndrome encompasses the predominant features in a subtype of severe pre-eclampsia. Most patients (82-88%) have hypertension and/or proteinuria (86-100%)[2]. Rare patients have neither of these signs. Other diagnoses associated with these abnormal laboratory serum markers should be excluded before HELLP syndrome can be diagnosed.

- Prophylactic transfusion of platelets is not recommended when platelet count is >50 $x10^9$/L and there is no excessive bleeding or platelet dysfunction.
- Consider blood products and platelets when platelet count <50 $x10^9$/L, platelet count is falling, and/or there are signs of coagulopathy.
- Platelet transfusion is recommended prior to caesarean section or vaginal delivery when platelet count is <20 $x10^9$/L.

REFERENCES

1. Corrigan L, O'Farrell A, Moran P, Daly D (2021). Hypertension in pregnancy: Prevalence, risk factors and outcomes for women birthing in Ireland. *Pregnancy hypertension, 24,* 1-6. https://doi.org/10.1016/j.preghy.2021.02.005

2. O'Hare MF, Manning E, Corcoran P, Greene RA on behalf of MDE Ireland. Confidential Maternal Enquiry in Ireland, Data Brief No 6. Cork: MDE Ireland, November 2022. Available at: https://www.ucc.ie/en/media/research/nationalperinatalepidemiologycentre/databriefs/MDEDataBriefNo6_.pdf

3. Institute of Obstetricians and Gynaecologists (2016) "The Diagnosis and Management of Severe Pre-Eclampsia and Eclampsia". Clinical Practice Guideline no. 3. Royal College of Physicians of Ireland and Clinical Strategy and Programmes Directorate, Health Service Executive. Available: https://www.hse.ie/eng/services/publications/clinical-strategy-and-programmes/diagnosis-and-management-of-pre-eclampsia-and-eclampsia.pdf

4. The National Institute of Health and Clinical Excellence (NICE) Clinical Guideline on Hypertension in Pregnancy: Diagnosis and Management. June 2019. Available at: https://www.nice.org.uk/guidance/ng133/resources/hypertension-in-pregnancy-diagnosis-and-management-pdf-66141717671365

5. Norwitz, E.R. (2022). "Eclampsia". *UptoDate*. Retrieved December 01, 2022 from https://www.uptodate.com/contents/eclampsia

6. Anthony J, Schoeman L.K.. "Fluid management in pre-eclampsia". Obstet Med. 2013 Sep; 6(3):100-104.

7. National Women and Infants Health Programme (2021) "Irish Maternity Indicator System: National Report 2020", Health Service Executive. Available at:

https://www.hse.ie/eng/about/who/acute-hospitals-division/woman-infants/national-reports-on-womens-health/irish-maternity-indicator-system-national-report-2020.pdf

8. CMQCC (2021). “Acute Treatment Algorithm”. California Maternal Quality Care Collaborative: Hypertensive Disorders of Pregnancy. Available at: https://www.cmqcc.org/sites/default/files/HDP_FINAL_Appendix_E_2022.pdf