Guideline

Hypertension - Management of Acute

1. Purpose

Severe hypertensive disorders of pregnancy are associated with high rates of maternal and fetal morbidity and mortality.

It is imperative in this clinical situation that severe blood pressure in pregnancy is treated. This guideline provides information about the use and administration of oral Nifedipine, intravenous labetalol and when labetalol is contraindicated, the use and administration of intravenous hydralazine.

Also refer to Procedure: Observations – Birth Centre – Adult Escalation Criteria and Response Framework.

Where processes differ between campuses, those that refer to the Sandringham campus are differentiated by pink text or have the heading **Sandringham campus.**

2. Definitions

Hydralazine is a peripheral vasodilator that causes relaxation of arteriolar smooth muscle, which results in a lowering of blood pressure. The hypotensive effect occurs within 5-20 minutes. Maximum effect is 10-80 minutes and the duration is 2-6 hours. The onset of the drug's action is within 15 minutes, with a peak effect between 30 and 60 minutes. Duration lasts between 4 and 6 hours. Because of the slower onset, a loading dose is required.

Labetalol is a non-selective beta-adrenergic blocking agent, producing dose-related falls in blood pressure without reflex tachycardia and without significant reduction in heart rate. Onset of action of intravenous labetalol is at five minutes. Peak effect occurs at 10-15 minutes. Duration of action is 45 minutes to six hours. A fluid pre-load is advisable to counteract the potential for a sudden decrease in blood pressure.

Nifedipine is a calcium ion influx inhibitor (calcium channel blocker or calcium channel antagonist). After oral administration, the onset of action is 1.5 to 4.2 hours. The half-life of an immediate release dose form shows a mean of approximately 1.7 to 3.4 hours. Administration of the tablet results in a half-life of about 6 to 12 hours. The pharmacological action of nifedipine persists for up to 12 hours after administration of the tablet. Caution should be used in patients with impaired liver function.

3. Responsibilities

Obstetric medical staff are responsible for the medical management of women with acute hypertension. This includes prescription of antihypertensive medicines as appropriate to the woman, for advising midwifery staff of the target blood pressure and notification targets, for review of the woman and planning on-going care.

Midwifery staff are responsible for the midwifery care of the woman. This includes determining accurate blood pressure management and accurate fluid balance management and for escalating care to medical staff as directed.

Both clinical groups are responsible for being aware of the contraindications, precautions and side effects of nifedipine, labetalol and hydralazine and management of same.

See over the page for the guideline details.

4. Guideline

For all interhospital transfers W@S should contact PERS (ph 1300 137 650).

Clinical Practice Points

- Hydralazine remains the drug of choice for women with asthma or congestive heart failure.
- Blood pressure readings must be manually recorded during the titration phase.
- Blood Pressure recording:
  - The woman should be resting at an angle of greater than 45 degrees with her feet supported.
  - The blood pressure cuff should be of the appropriate size and should be placed at the level of the heart.
  - Standard cuff for arms <33cm circumference. Large cuff (15x 33cm bladder) for larger arms.
  - Inflate cuff to 20-30mmHg above palpated systolic pressure. Deflate slowly.
  - Read and record blood pressure to nearest 2mmHg.
  - Korotkoff phase 5 sound (sound disappearance) is the appropriate measurement of diastolic blood pressure.
  - Multiple levels should be taken to confirm the diagnosis of hypertension/ pre-eclampsia due to natural variation.
- **Automated blood pressure** readings may only be considered once the maintenance dose has been achieved and the blood pressure is stable.
- Abrupt and profound drops in blood pressure can occur when vasodilator therapy is not accompanied by **volume expansion** in severe pre-eclampsia. This can lead to fetal bradycardia and non-reassuring fetal status/ CTG patterns. Current literature suggests that there is no place for bolus fluid administration prior to initiating acute antihypertensive treatment.
- In case of a **severe hypotensive** episode while infusion in progress:
  - cease infusion.
  - place woman in the supine position, with her feet elevated and place a wedge under her right hip if undelivered (left tilt).
  - seek urgent medical review.
  - the infusion of plasma expanders may be required to reverse a non-responsive hypotensive episode.
- Continuous electronic fetal monitoring is required for all women undergoing IV antihypertensive management.
- **Target blood pressure**: Once the woman's BP has reached the target level then commence maintenance regimen aiming to maintain the systolic between 140-160 and the diastolic BP at 90-100mmHg.
- There is rarely a need to lower the BP further than this, and doing so may compromise the placental blood flow and fetus.

4.1 Nifedipine

Initial management of acute hypertension can include the use of oral immediate release nifedipine- not slow release.

Presentation

- 10mg tablets.

Contraindictions

- Known hypersensitivity to nifedipine

- Within the first eight days after an acute episode of myocardial infarction
- Concomitant administration with rifampicin.

Precautions

- Nifedipine may be used in combination with beta-blocking drugs and other antihypertensive agents, but the possibility of potentiation of existing antihypertensive therapy should be noted
- Impaired hepatic function.

Adverse effects

- Palpitation, peripheral oedema, vasodilatation
- Nausea
- Dizziness.

Administration

- Administer 10mg nifedipine orally
- Monitor the blood pressure
- Commence continuous CTG monitoring.

A second dose may be administered 15-20 minutes later if there is inadequate response. Observations of mother and fetus should continue.

If there is inadequate response after the second oral dose, proceed to IV management with an alternative antihypertensive.

4.2 Labetalol

A stat dose of 200mg labetalol can be give orally. A second dose may be given orally if there is no response within 20 minutes. If blood pressure is still not controlled, IV maintenance therapy should be commenced.

Intravenous labetalol is considered to be the primary medicine of choice for the urgent control of severe hypertension in pregnancy. It is associated with a lower incidence of adverse side effects and supplants the use of hydralazine. Usage will depend on availability and the clinicians experience and familiarity with the medicine.

Please note: IV labetalol is a 'special access scheme (SAS)' drug. A form must be completed for each patient. These can be found in the drug room cupboard.

Presentation

Labetalol hydrochloride injection is a sterile clear solution containing 5mg/mL labetalol hydrochloride (Each 20mL vial contains 100mg labetalol hydrochloride).

Contraindications

Women with severe hypertension and the following conditions must not be administered labetalol (hydralazine is the alternative treatment):

- asthma and allergic disorders with a predisposition to bronchospasm.
- congestive heart failure.
- hypovolaemic shock.

Refer to the product information for labetalol - available at http://www.phebra.com.au/data/products/INJ148-pi.pdf for a full list of contraindications.

Precautions

The woman should always be nursed in and remain supine (with lateral tilt) during and up to three hours after IV administration due to the potential side effects of orthostatic hypotension.

Consider that recent administration of other antihypertensive drugs, such as nifedipine may potentiate the blood pressure lowering effect of labetalol.

Refer to the product information for labetalol - available at http://www.phebra.com.au/data/products/INJ148-

pi.pdf for a full list of precautions.

Compatibilities

IMPORTANT: Refer to the Australian injectable drugs handbook (4th edition) or contact pharmacy for drugs not appearing in the table below. Uncommon drugs have simply been omitted and may be incompatible.

	Compatible	Incompatible
Fluids	Sodium chloride 0.9% injection Compound sodium lactate (Hartmann's) Glucose/sodium solutions	Sodium bicarbonate 5% injection
Drugs	No information	Frusemide, ceftriaxone
Y-Site	Magnesium sulphate	

Adverse effects

Postural hypotension may occur if the initial dosage is too high or if the dose is increased too rapidly. Occasionally bradycardia and heart block have been reported.

Transient dizziness, headache, tiredness, depressed mood and lethargy may occur. There have been reports of a tingling sensation of the skin (especially of the scalp) associated with labetalol treatment, usually occurring early in treatment and is transient in nature.

Refer to the product information for a complete list of adverse effects – available at:

http://www.phebra.com.au/data/products/INJ148-pi.pdf

Administration

Labetalol hydrochloride injection is intended for IV use in hospitalised patients. Labetalol may be administered by IV infusion (refer to doses below).

Labetalol IV bolus

A medical officer must administer IV injection doses of labetalol:

- 20mg (4mL) administered by slow IV injection over two (2) minutes.
- One further bolus can be administered at 10 minutes if necessary.
- If 2 bolus doses are insufficient to control the blood pressure, IV therapy via infusion is required.

Onset of action of intravenous labetalol is at five minutes. Peak effect occurs at 10-15 minutes. Duration of action is 45 minutes to six hours.:

- Measure a blood pressure immediately before, and at 5 and 10 minutes after administration of each dose to evaluate the response.
- Commence an infusion of sodium chloride 0.9% or Hartmans solution as a precaution measure to manage significant hypotension.
- Commence continuous electronic fetal monitoring.

Labetalol IV Infusion

Women receiving IV infusion of labetalol must be cared for in an environment where one-to-one midwifery/nursing care can be facilitated (Birth Centre/ Complex Care).

Prior to commencement the medical staff should explain to the woman the reason for administration of the medicine, the continuous observation required and potential adverse effects.

Dosage must be individualised depending upon the severity of hypertension and the response of the woman during dosing:

- Start the infusion at 20mg/hour.

- Titrate the infusion to stabilize the blood pressure by adjusting the infusion by 5mg (2.5mL of the labetalol infusion with a concentration of 2mg/mL).
- Note that the maximum dose for 24 hours is 300mg.

Measure a blood pressure immediately before, and at 5 and 10 minutes after administration of each dose to evaluate the response.

Use a labetalol solution of 2mg/mL:

- To make this solution: Use a 50mL syringe: draw up 20mL (100mg of labetalol solution).
- Further dilute this with 30mL sodium chloride 0.9% (using 3 ampoules of 10mL) to make 50mL.
- The resultant solution contains 100mg labetalol (2mg/mL).

This solution gives a final concentration of 2mg/mL (=100mg/ 50mL)

Use 2 Additive Labels to clearly identify the additive. To ensure visibility, place one label at eye-level and the other at the port into the multiflow adaptor.

Management of a woman receiving labetalol

Unless otherwise contraindicated, the woman should receive 300mL of Sodium Chloride 0.9% as a fluid preload over 15 minutes.

Note: this preload can be safely administered to those women who are fluid restricted.

Administer through a syringe infusion pump. Ensure all previous history is deleted from that pump.

See Appendix 'How to set up the Pump'.

Administration and Titration

Administer dose between 20-160mg/h.

The rate of infusion is to be titrated by 20mg/h (10mL/h) every 15 minutes (this equates to titrating by 5mg (2.5mL) every 15 minutes of the labetalol infusion with a concentration of 2mg/mL) until the blood pressure is stable. See Table 1 : Labetalol dose titration via infusion pump for guidance.

Continue with this titration process until the maximum dosage of 160 mg/hr is reached OR the woman's blood pressure is maintained at 140-160/ 90-100mmHg for two hours.

The infusion MUST be **weaned down.** This can be achieved by reducing the dose by 20mg (2.5mL) every 15 minutes provided the blood pressure remains stable. The maximum dose of labetalol to be infused is 300mg.

Table 1. Labetalol dose titration via infusion pump for guidance

Labetalol dose titration via infusion pump: concentration=2mg/mL				
Time Span	**Infusion rate titration**	**Dose to be infused over Time in mg (mL)**		**Total mg administered over time**
		Pump Volume	**Pump Duration set up**	
0 minutes	20mg/hr (10mL/hr)	5mg (2.5mL)	15 minutes	5mg
15 minutes	40 mg/hr (20mL/hr)	10mg (5 mL)	15 minutes	15mg
30 minutes	60 mg/hr (30mL/hr)	15mg (7.5 mL)	15 minutes	30mg
45 minutes	80 mg/hr (40mL/hr)	20mg (10 mL)	15 minutes	50mg
60 minutes	100mg/hr (50mL/hr)	25mg (12.5 mL)	15 minutes	75mg
75 minutes	120 mg/hr (60mL/hr)	30mg (15 mL)	15 minutes	105mg
90 minutes	140 mg/hr (70mL/hr)	35mg (17.5 mL)	15 minutes	140mg
105 minutes	160 mg/hr (80mL/hr)	40mg (20 mL)	15 minutes	180mg
120 minutes				

Note: at maximum dose the woman has already received more than half the 24 hour recommended dose of 300mg. The time to wean off the drug must also be considered. The woman's response to the titration must be reviewed at 1hour after commencement to determine the necessity to continue with this infusion or if a change in clinical management is required.

- Blood pressure should be monitored during IV administration.
- Titrate infusion and reduce blood pressure gradually to avoid adverse fetal side effects from a rapid decrease in uteroplacental perfusion.
- Maintain continuous fetal monitoring of the viable fetus while endeavouring to optimize blood pressure levels.

Monitoring/observations

Note: Onset of action of intravenous labetalol is at five minutes. Peak effect occurs at 10-15 minutes. Duration of action is 45 minutes to six hours.

- During titration monitor the blood pressure every 10 minutes, prior to each scheduled dose increase. The frequency of measurement is necessary to prevent sudden reduction in blood pressure that can affect placental perfusion.
- Continue until at least 2 stable consecutive readings are achieved.
- Once stable, blood pressure monitoring can be decreased to every half-hour.

Additional monitoring/observations (once blood pressure stable):

- ½ hourly blood pressure, pulse, respiratory rate while infusion in progress.
- 1 hourly urine output measurement.
- 2 hourly temperature.
- 4 hourly testing of urinary protein (full ward test).
- Continuous electronic fetal monitoring: The viable fetus MUST be continuously monitored before, during and after administration of labetalol.

Weaning the labetalol infusion:

- Labetalol must not be suddenly discontinued. It must be weaned over 2 hours.
- Decrease the infusion rate by 2.5mL/hr every 15 minutes.
- During weaning, blood pressure monitoring frequency must be increased to 15 minutely, prior to each reduction to ensure maintenance of blood pressure within target range.

4.3 Hydralazine

Hydralazine is used for the treatment of hypertensive crises - especially hypertension associated with pregnancy (pre-eclampsia or eclampsia).

Presentation

Hydralazine ampoules: 20mg dry powder for reconstitution (white crystalline powder).

Contraindications

- hypersensitivity to hydralazine.
- refer to full product information for extensive list.

Precautions

- cardiac dysfunction.
- renal or hepatic impairment.
- cerebrovascular disease.
- refer to full product information for extensive list.
- Consider that recent administration of other antihypertensive drugs, such as nifedipine may potentiate the

blood pressure lowering effect of labetalol.

Consider that recent administration of other antihypertensive drugs, such as nifedipine may potentiate the blood pressure lowering effect of Hydralazine.

Incompatibilities

Refer to the Australian injectable drugs handbook (4th edition) for a full list of incompatibilities or product information via MIMS online.

Adverse effects

The following symptoms are common at the start of treatment with hydralazine (especially if the dose is increased rapidly):

- tachycardia, palpitation, anginal symptoms, flushing, headache, dizziness, nasal congestion and gastrointestinal disturbances. Such reactions generally subside with further course of treatment.
- use of hydralazine can result in sodium and fluid retention producing oedema and reduced urinary volume.
- hydralazine is known to cross the placenta following intravenous administration and may be associated with fetal distress and fetal cardiac arrhythmia in the last trimester of pregnancy.

Refer to full product information for extensive list.

Note: Reactive tachycardia with hydralazine may necessitate the use of beta-blockers. Occasionally hypertension resistant to hydralazine requires administration of other medicines (e.g., nitroprusside, glyceryl trinitrate).

Women receiving IV infusion hydralazine must be cared fro in an environment where one-to-one midwifery/nursing care can be facilitated (Birth Centre/Complex Care).

Prior to commencement the medical staff should explain to the woman the reason for administration of the medicine, the continuous observation required and potential adverse effects.

Dose

Dosage must be individualized depending on the severity of hypertension and the response of the woman during dosing:

- Start the infusion at 1mg/min for 10 minutes.
- Titrate the infusion to stabilize the blood pressure by adjusting the infusion between 1-10mg/hr to maintain a diastolic BP of 90-100mmHg.

Administration

Hydralazine injection is intended for IV use in hospitalized patients. Hydralazine may be administered by IV infusion (refer to doses below).

Ensure an intravenous main line of sodium chloride 0.9% x 1000mL (at 80mL/hr) is insitu via a 'multiflow adaptor' prior to the administration of hydralazine.

Reconstitution/ set up:

- Requires three (3) ampoules of hydralazine 20mg powder.
- Reconstitute each 20mg ampoule powder with 1mL of sterile water for injection until dissolved.
- Prepare 2 syringes as follows. These can be prepared at the same time.

Administer through a syringe infusion pump. Ensure all previous history is deleted from that pump.

See Appendix 'How to set up the Pump'.

Syringe 1: loading dose (prescribed on 'ONCE ONLY' section of medicines chart:

- Draw up 0.5mL (10mg) concentrate into a 10mL syringe and make up to 10mL with sodium chloride 0.9%
- Label the syringe and connect to a minimum volume extension set
- Follow the instructions of the Alaris GH syringe driver for Hydralazine Loading Infusion.

Syringe 2: **maintenance dose:**

- Draw up 2.5mL (50mg) concentrate into a 50mL syringe.
- Make up to 50mL with sodium chloride 0.9%.
- Label the syringe and connect to the Alaris GH Syringe drive for Hydralazine Maintenance Infusion.

This solution gives a final concentration of 1mg/mL (= 50mg/50mL)

Use 2 Additive Labels to clearly identify the additive. To ensure visibility, place one label at eye-level and the other at the port into the multiflow adaptor.

Dose: IV infusion

Loading dose:

- Administer hydralazine at 1mg/min (i.e. 1mL/min of the prepared solution) for 10 minutes.
- Record blood pressure readings EVERY 5 MINUTES on the electronic partogram during administration of the intravenous loading infusion.
- If the blood pressure has reached the target range after 5 minutes administration of the loading dose (i.e. 5mg), the loading dose may be ceased.
- Commence the maintenance dose.

Maintenance infusion:

- Continue infusing hydralazine at 1-10mg/hr (1-10mL/hr) to maintain a diastolic BP of 90 - 100mmHg.
- Continue observation of BP every 15 minutes until stable and maintenance dose established.
- Maintain observation of BP **every 30 minutes** during administration of the infusion.

Monitoring/observations

Initial monitoring/observations:

- Record blood pressure readings EVERY 5 MINUTES on the electronic partogram during administration of IV /loading dose.
- Continue observation of BP every 15 minutes until the BP is maintained at 140-160/ 90-100mmHg for two hours.
- The frequency of blood pressure monitoring can then be reduced to every 30 minutes for the duration of the infusion.
- The fetal heart rate is recorded every 10 minutes during the loading infusion.

Other monitoring/observations:

- ½ hourly blood pressure, pulse, respiratory rate while infusion in progress.
- 1 hourly urine output measurement.
- 2 hourly temperature.
- 4 hourly testing of urinary protein (full ward test).
- Continuous electronic fetal monitoring: The viable fetus MUST be continuously monitored before, during and after administration of hydralazine.
- record on electronic partogram and fluid balance chart.

Discontinuation of the infusion

Hydralazine infusion does not require weaning down and can be ceased as directed.

The maximum dose of hydralazine should not exceed 30 mg. Alternative antihypertensive management, such as nifedipine must be considered be considered if the BP is not controlled once this dose is reached.

5. Evaluation, monitoring and reporting of compliance to this guideline

Compliance to this guideline will be monitored, evaluated and reported by review of clinical incidents reported

on VHIMS.

6. References

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4. MIMS Online Simple Search. https://www.mimsonline.com.au/Search/Search.aspx. Accessed 22 April 2010.
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7. Royal College of Obstetricians and Gynaecologists (RCOG), The Management of Severe Pre-Eclampsia/Eclampsia (Green-top 10A), March 2006. http://www.rcog.org.uk/womens-health/clinical-guidance/management-severe-pre-eclampsiaeclampsia-green-top-10a
8. Society of Hospital Pharmacists of Australia (AIDH). Australian Injectable Drugs Handbook. 4th Edition. 2008.
9. Southern Health (Monash Medical Centre). Preeclampsia and severe preeclampsia guideline. March 2010.

Royal Women's Hospital policies, guidelines and procedures:

- Pre-eclampsia: Management
- Magnesium Sulphate – Management of Hypertensive Disorders of Pregnancy
- Eclampsia Management

7. Legislation related to this guideline

Not applicable.

8. Appendices

1. How to set up the pump

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