

ANTIHYPERTENSIVE AGENTS IN PREECLAMPSIA

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BACKGROUND

Early treatment of hypertension has consistently been found to reduce the incidence of hypertensive crisis, and data from multiple case studies revealed increased rates of heart failure, pulmonary edema, stroke and death when antihypertensive medications were not used in women with severe gestational hypertension or severe preeclampsia.¹ According to ACOG, a hypertensive emergency is an acute-onset, severe hypertension that is persistent for 15 minutes or more.²

Treatment should be initiated for blood pressures that are ≥ 160 mm Hg systolic or 105-110 mm Hg diastolic.³ It should be noted that others have suggested that treatment should be initiated at a lower threshold of 155/105 if the primary goal is to reduce maternal intracranial hemorrhage, which remains the leading cause of death from preeclampsia.⁴

The goal of blood pressure control is not to return it to “normal” but rather to lower it to a range of 140-160/90-100 mm Hg, a level at which the risk of intracranial hemorrhage is reduced. Lowering the blood pressure below this range may reduce placental perfusion and harm the fetus.^{4,5}

NOTE: Treatment of hypertension in the patient with chronic cocaine/amphetamine abuse may cause an exaggerated decrease in blood pressure. Hypotension may be difficult to treat due to altered vasopressor response and depleted endogenous catecholamine stores. Unexpected, severe hypotension may also occur after regional anesthesia or general anesthesia. (See Appendix T, pg.127.)

KEY LEARNING POINTS

1. Antihypertensive therapy is reserved for women with systolic blood pressure greater than 160 mm Hg or diastolic blood pressure greater than 105-110 mm Hg. Increasingly, risk of stroke is felt to be correlated with maximum systolic blood pressure.^{3,6,7}
2. Hydralazine and labetalol are the two “first line” agents used for hypertension in preeclampsia. Hydralazine is an arteriolar dilator that reduces blood pressure but may cause tachycardia. Possible side effects are headache, risk of delayed maternal hypotension, which can be associated with fetal bradycardia, and rarely, upper abdominal (e.g., “epigastric”) pain, which may be confused with worsening preeclampsia. Labetalol is a combined alpha and beta-blocking agent, which reduces

blood pressure by dilating arterioles and decreasing heart rate. Labetalol should be administered intravenously for acute hypertensive emergencies.² Asthma, cocaine and amphetamine use (including methamphetamine) is a contra-indication for labetalol use. (See Appendix T, pg. 127.)

3. Oral nifedipine (calcium channel blocker), IV esmolol (beta blocker) and IV nicardipine (calcium channel blocker) are second line drugs. Esmolol, is a very short-acting agent, and can cause the baseline fetal heart rate to decrease, but often resolves rapidly when esmolol is stopped.
4. First line therapy recommendations for acute treatment of critically elevated BP in pregnant women (160/105-110 mm Hg) are either with IV labetalol or hydralazine (see algorithms in Medication section, pg. 50)^{2,3} In the event that acute treatment is needed in a patient without IV access oral nifedipine may be used (10 mg) and may be repeated in 30 minutes.⁸ PO nifedipine appears equally as efficacious as IV labetalol in correcting severe BP elevations.⁹ Oral labetalol would be expected to be less effective in acutely lowering the BP due to the slower onset to peak and thus should be used only if nifedipine is not available in a patient without IV access.⁹

Hypertensive Medication Administration Oral versus IV	
IV Labetalol <ul style="list-style-type: none"> • Onset: 2-5 min • Peak: 5 min 	IV Hydralazine <ul style="list-style-type: none"> • Onset: 5-20 min • Peak: 15-30 min
PO Labetalol: <ul style="list-style-type: none"> • Onset: 20 min-2 hrs • Peak: 1-4 hrs 	PO Nifedipine <ul style="list-style-type: none"> • Onset: 5-20 min* • Peak: 30-60 min

*PO, not sublingual nifedipine onset of action is 15-30 minutes depending upon the source.^{8,10,11}

5. Sodium nitroprusside is a very potent vasodilator that acts immediately and is rarely used. It must be used by experienced providers accompanied by invasive (e.g., an arterial line) blood pressure monitoring.
6. Consideration for consultation with anesthesiologists who are accustomed to the titration of vasoactive medications should be considered early for patients with uncontrolled blood pressure.
7. Placement of an arterial line may be helpful in women whose blood pressure is particularly difficult to control. There may also be cases where repeated blood studies

will be necessary, e.g., magnesium levels, platelet counts, etc., and where repeated venipunctures may be difficult.

8. Women with severe hypertension requiring antihypertensive medications need to be observed carefully for signs of pulmonary congestion such as agitation, low oxygen saturation, cough, or rales on lung exam suggesting pulmonary edema or heart failure. Careful monitoring should be implemented.
9. Proper lateral positioning should be employed for these patients, since aortocaval compression can exacerbate uteroplacental insufficiency due to preeclampsia itself.
10. One of the most common and severe complications is hypertensive encephalopathy or Posterior Reversible Encephalopathy Syndrome (PRES).

RECOMMENDATIONS FOR QUALITY IMPROVEMENT:

1. Timely initiation of medication for treating elevated blood pressure is critical. Initiation of therapy within 60 minutes is recommended. However, every attempt should be made to initiate therapy within 30 minutes after confirmation of severe range blood pressures if possible. Initial therapy should consist of labetalol 20 mg or hydralazine 5-10 mg IV over 2 minutes. Hydralazine begins to have an effect within 5-20 minutes with its maximum effect occurring at 15-30 minutes. Labetalol onset is within 2-5 minutes and has its maximum effect after 5 minutes. (See Appendix X, pg. 137).
2. Implementation of a “Preeclampsia Box” (see Appendix S, pg. 126) will assist in the initiation of rapid delivery of medication.
3. Maximum cumulative IV administered doses should not exceed the following: hydralazine 25 mg; labetalol 220 mg in 24 hours.³
4. The goal for blood pressure control is 140-160/90-100. Do not try to lower the blood pressure to “normal.”
5. The anesthesiologist should be seen as a resource for invasive blood pressure monitoring (if required) and medication titration.
6. An arterial line can be useful for acquiring multiple blood samples as well as for arterial pressure measurement.

SAMPLE PREECLAMPSIA/ECLAMPSIA MEDICATION BOX

Each institution should prepare its own medication box specific to its protocols.

L&D Severe Preeclampsia & Eclampsia Box – Content and Dose Guideline	
Magnesium 20 grams/500 ml bag	IV (Use Magnesium Sulfate Continuous Infusion under L&D protocol in Alaris Pump Library): <i>Initial (Loading Dose):</i> 4-6 g (100 ml – 150 ml) over 20 minutes <i>Maintenance Dose:</i> 1-2 g/hour (25 ml/hr – 50 ml/hr) continuous infusion
Labetalol 100 mg/20 ml vial	Initial: Draw 4 ml from the vial. 20 mg (4 ml) IV bolus followed by 40 mg (8 ml) if not effective within 10 minutes; then 80 mg (16 ml) every 10 minutes (maximum total dose of 300 mg/60 ml)
Hydralazine 20 mg/ml vial	Initial: Draw 0.25 ml from the vial. 5-10 mg (0.25-0.5 ml) doses IV every 15-20 minutes
Esmolol 100 mg/10 ml vial (By Anesthesiologists ONLY)	1-2 mg/kg (0.1-0.2 ml/kg) IV over 1 minute
Propofol 10 mg/ml, 20 ml vial (By Anesthesiologists ONLY)	30-40 mg (3-4 ml) IV bolus
Calcium gluconate 1000 mg/10 ml vial	1000 mg/10 ml IV over 2-5 minutes
Labetalol 200 mg tablets	200 mg PO and repeated in 30 minutes if needed
Nifedipine 10 mg PO	10 mg PO in 30 minutes if needed
Supply contents	3 ml, 10 ml, and 20 ml syringes, appropriate needles and appropriate tubing sets

EVIDENCE GRADING

Level of Evidence: III-C

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