The Heart of the Matter

Cardiology Associates, P.C.

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A Message from Cardiology Associates, LLC

Dear Colleagues,

Welcome to the June 2011 issue of our Cardiology Associates' Referring Physician Newsletter. The newsletter will focus on pregnancy-related cardiovascular disease, in particular hypertension (HTN) in pregnant and post-partum women. As women are waiting until later in life to have children, we are more often seeing patients with either chronic HTN, which needs to be managed throughout pregnancy, or are called on to help treat hypertension throughout and after pregnancy in women of advanced maternal age (greater than 35 years old at the time of conception). The risk of preeclampsia is typically higher in this age group. The case described below will outline some management issues related to HTN in pregnancy: definition of various hypertensive conditions, risks of hypertension in pregnancy, and review the pharmacologic treatment options that are safe in pregnancy and breastfeeding.

About the Author

Dr. Stephanie Jacobs is a CALLC cardiologist who has been board-certified in internal medicine and cardiovascular disease. Dr. Jacobs has a special interest in consultative cardiology, nuclear cardiology, and pregnancy-related cardiovascular disease. Dr. Jacobs graduated from the Georgetown University School of Medicine, and she is a member of the American Heart Association, the American College of Cardiology, the American Society of Echocardiography, and Alpha Omega Alpha.

Dr. Jacobs sees patients at our Annapolis and Bowie offices.

Cardiovascular Disease and Pregnancy

PRESENTATION OF CASE

• Patient is a 41-year-old Caucasian female who delivered a healthy baby boy on March 1, 2011.
• No cardiopulmonary issues or symptoms throughout pregnancy.
• Prior to the last week of pregnancy, the patient's blood pressure ran from 110/70 pre-partum to 90/68 - 120/70 up to 38 weeks.
• The patient's urine was negative for protein.
• At 39 weeks, the patient's blood pressure was noted to be 135/88, but her urine remained negative for protein.
• The patient delivered at 40 weeks and 1 day without complications. Nine days later, she presented to the Anne Arundel Medical Center ER with a severe headache and was found to have a blood pressure of 211/108.

DISCUSSION

There are 4 major hypertensive disorders that occur in pregnant woman.

- Preeclampsia-eclampsia
- Preexisting hypertension(chronic HTN)
- Preeclampsia superimposed upon preexisting hypertension
- Gestational hypertension (GH)

The diagnosis of a hypertensive disorder in a pregnant woman depends, in part, upon the gestational age at presentation. Preeclampsia refers to the syndrome of new onset of hypertension and proteinuria after 20 weeks of gestation in a previously normotensive woman or worsening hypertension with new onset proteinuria in a woman with preexisting hypertension (superimposed preeclampsia). Preexisting hypertension(chronic HTN) is defined as having a blood pressure reading higher than 140/90 mmHg that antedates pregnancy, is present before the 20th week of pregnancy, or persists longer than 12 weeks postpartum(1). Gestational hypertension refers to elevated blood pressure first detected after 20 weeks of gestation in the absence of proteinuria. Over time, some patients with gestational hypertension will develop proteinuria and be considered preeclamptic, while others will be diagnosed with chronic or preexsisting hypertension because of persistent blood pressure elevation lasting longer than 12 weeks post-partum.

Preeclampsia with proteinuria and blood pressure elevation higher than 140/90 is treated with blood pressure control medication for as long as necessary to gain fetal maturity and delivery. (Preeclampsia can result in maternal and fetal complications and was not present in our patient. It will not be discussed in further detail here.) Eclampsia is the additional manifestation of seizures and can be life-threatening to both mother and fetus. The treatment is emergent delivery.

The other two hypertensive states of pregnancy are not associated with proteinuria, and as such not all pregnant women with elevations in their blood pressure need to be given medication. Mild HTN in pregnancy without proteinuria, in general, has favorable maternal and fetal outcomes. The decision to start medication must balance the risks of drug therapy to the fetus versus the risk of no treatment to both mother and fetus. The major maternal indications for treatment of HTN in pregnant women are similar to those of non-pregnant women and include prevention of stroke and cardiovascular complications. Preexisting HTN increases the risk of adverse pregnancy outcomes. Superimposed preeclampsia is 2-4 times more likely in hypertensive women (10-20% risk) than in non-HTN women. Women with mild preexisting HTN have a .7-1.5% risk of abruption, 12-34% risk of preterm birth less than 37 weeks, and 8-16% risk of fetal growth restriction. For women with preexisting severe HTN, the risks were 2-to-5 fold higher. (2) Certainly too, a woman with symptoms of end-organ involvement such as chest pain, headache, or breathlessness should be considered for treatment.

Although there is very little maternal risk to lowering blood pressure, there is some data to suggest that blood pressure lowering therapy may compromise fetal well-being as a result of reduced placental perfusion. (3) This conclusion was further supported by a meta-analysis that looked at maternal and fetal outcomes in randomized trials of treatment versus no treatment of pregnant women with mild to moderate hypertension (defined as blood pressure of 140 to 169/90 to 109 mm Hg). (2)

- Antihypertensive therapy of mild hypertension significantly decreased the incidence of severe hypertension by one-half to two-thirds and the need for additional antihypertensive drugs by almost two-thirds. (2)
- Antihypertensive therapy of mild hypertension did **not** decrease fetal risks associated with maternal HTN including: perinatal mortality rate or the frequency of prematurity, preeclampsia, delivery of a small for gestational age infant, or abruptio placentae

Another meta-analysis showed that fetal growth was impaired by a reduction in maternal blood pressure: a 10 mmHg decrease was associated with a 176 gram decrease in birth weight. This was unrelated to the type of medication used. (3)

The definition of HTN in pregnancy does not follow that of non-pregnant individuals (pre, stage 1,2,3) but rather is either normal, mild (140-159/90-109mmHg), or severe (>160/110 mmHg). Thus, the guidelines from an obstetrical standpoint (ACOG) state that "the only demonstrable benefit of antihypertensive therapy in women with mild hypertension is a reduction in risk of developing severe hypertension, which is considered insufficient to warrant exposing the fetus to the potential adverse effects on its growth." Most experts do agree, however, that severe hypertension should be treated to prevent maternal vascular complications. (1) One may initiate treatment in younger women with lower baseline blood pressure (<90/75) before the 150/100 mmHg mark. Our patient had clear indication for treatment.

The patient was started on IV labatelol, and HCT negative for bleed or CVA, and CXR and labs were normal. Her 12 lead EKG was normal. She was sent home on PO labetalol 400 mg TID. She returned to the ER three days later with continued blood pressure elevations of 170-180/90-110 and occasional controlled blood pressure readings of 120-135/80-95.

The choice of drug to treat anything other than mild HTN is based on general agreement, historical use/safety reporting, and limited trial data. All anti-HTN drugs cross the placenta and there are no large randomized trials upon which to recommend one drug over another. Drugs that have been found to be safe include: methyldopa or labatelol as first line agents, nifedipine as second or third line, and pindolol or metoprolol as acceptable alternatives. Verapamil and diltiazem have been reported as safe, although studies were conducted with small numbers of women. The dose ranges for the three most common drugs are:

Drug	Dose
Methyldopa	250 mg twice daily orally, maximum dose 3 g/day
Labetalol	100 mg two or three times daily orally, maximum dose 1200 mg/day
Nifedipine	30 to 90 mg once daily as a sustained release tablet, increase at 7 to 14 day intervals, maximum dose 120 mg/day

It is generally agreed that ACE-I/ARB and direct renin inhibiters NOT be administered during pregnancy, and some beta-blockers such as propranolol specifically have had reports of premature labor, neonatal apnea, bradycardia, and hypoglycemia. Amlodipine is not often used as there is sparse data to support it.

Initiation of treatment is for blood pressure higher than 150/100 mmHg, or signs of maternal end-organ damage and the goal of pharmacologic therapy is a blood pressure target of 140-150/90-100 mmHg. If the patient is breastfeeding or planning to, certain drugs are deemed safe by AAP: propranolol, metoprolol, labatelol, diltiazem, nifedipine, and verapamil. Drugs to be avoided in lactating women are acebutolol, atenolol and ACEI (due to higher rates of newborn hypotension, oliguria,seizures). (4,5)

Procardia XL 60 mg qd was added. The following day the patient's blood pressure was 99/67 and she was lightheaded, diaphoretic, and felt weak. She presented to Cardiology Associates, LLC, two days later. Her blood pressure was 120/78, pulse 62, physical exam normal, and EKG normal. She was taking Labatelol 400 mg PO tid and Procardia XL 60mg PO qd.

Gestational hypertension, which by definition is what our patient experienced, occurs in about 6% of pregnancies and is a temporary diagnosis for women who do not meet criteria for preeclampsia or chronic HTN (preexisting). The diagnosis is changed if proteniuria develops (preeclampsia), if blood pressure elevation persists beyond 12 weeks postpartum (chronic HTN) or is simply determined to be transient HTN given that blood pressure returns to normal by 12 weeks postpartum. Gestational HTN prior to delivery increases the risk of the development of preeclampsia and therefore patients should be screened for signs or symptoms of preeclampsia (severe H/A, n/v, RUQ pain or epigastric pain, dec urine output, visual changes). (6)

Over the next week in our office the patient's only complaint was fatigue and a feeling of "sluggishness with activity" with a resting heart rate of 50-60 bpm. An echocardiogram was performed (which showed nothing out of the ordinary), and the patient's blood pressure continued to steadily decline. Her labatelol was decreased to 200mg PO bid, and her procardia XL remained 60mg PO qd.

It is unclear if the patient will progress to chronic HTN at 5 weeks post partum. She has about a 15% risk of doing so. We will follow her out to 12 weeks, but if her blood pressure continues to decline, we will stop the labatelol and wean the procardia.

References:

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