A Review - Labetalol First-line Drug for Pregnancy-induced Hypertension

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Abstract: To study labetalol as a first-line drug for hypertension in pregnancy and endorse its superiority over alpha-methyldopa. Patients with diastolic blood pressure recorded 100 mmHg have been admitted and administered labetalol 100 mg twice-daily orally, the dose escalating to 1.2 g/day. The control of pressures and side effects have been noted. Labetalol is instrumental in causing a sustained and smooth fall in blood pressure and is free of the side effects of alpha-methyldopa. Thus, labetalol supercedes alpha-methyldopa as a first-line drug for hypertension in pregnancy.

Keywords: Labetalol, alpha-methyldopa, pre-eclampsia, fetal surveillance

Introduction:
Hypertensive disorders are the most common medical disorders in pregnancy contributing significantly to maternal and perinatal mortality and morbidity worldwide. The incidence is around 3-10% of all pregnancies. According to the National High Blood Pressure Working Group,1 hypertensive disorders in pregnancy are classified as:

- Pre-eclampsia superimposed on chronic hypertension
- Chronic hypertension
- The commonly used antihypertensive drugs in pregnancy with proven safety are:
  - Alpha-methyldopa
  - Nifedipine (calcium channel blocker)
  - Labetalol

Labetalol is an a-blocker with nonselective b-blocking properties. It is available in oral as well as injectable forms. Its safety in the first trimester of pregnancy has been documented. The aim of antihypertensives is to reduce and stabilize the blood pressure, in an attempt to minimize the risks such as placental abruption, maternal cardiac failure, cerebral hemorrhage; at the same time they should not have any adverse effects on the uteroplacental circulation and the fetus.

WHY NOT ALPHA-METHYLDOPA?

Upon introduction, alpha-methyldopa takes 24 hours for complete action, and upon starting with a 250 mg dose, it needs to be taken three times daily. Patients commonly suffer from postural hypotension due to a-receptor blockade. The common side effects are constipation, galactorrhea, postpartum depression and altered sleep pattern. Although minor, they could be distressing to some. It also causes headache, which can be confused with impending eclampsia.

The hematological manifestations include hemolysis and thrombocytopenia on blood smear, and false positive Coomb’s test in 10% cases. As regards antepartum fetal surveillance, it causes falsely nonassuring fetal heart patterns on electronic fetal monitoring. Alpha-methyldopa accumulates in renal failure, which can sometimes complicate pre-eclampsia.

WHY LABETA LOL?

Labetalol can boast of some characteristic merits over alpha-methyldopa. It is free of the above mentioned side effects. It results in good and sustained control of BP. There is no tachycardia and BP is stabilized. Labetalol has no effect on uteroplacental blood flow. Also, an injectable form is available for hypertensive crisis.

The National Guideline Clearinghouse,2 regarding treatment of hypertensive disorders of pregnancy has recommended that the initial antihypertensive therapy should be started with labetalol (IA evidence) or nifedipine, to bring down the target BP to 160 systolic and 110 diastolic. For women with preexisting hypertension, pre-conceptional counseling is recommended. Angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARB) are to be discontinued, and replaced with safer drugs - labetalol, nifedipine and alpha-methyldopa. In a Kuwaiti trial involving 104 primigravidas with mild-moderate PIH, the investigators compared alpha-dopa with labetalol for antihypertensive management, and concluded that labetalol is quicker, more efficient and better tolerated. Although it crosses placenta, there is no evidence of intrauterine growth retardation (IUGR), perinatal death and neonatal hypoglycemia. It may ripen the cervix, and reduce the latency of labor in term patients. A double-blinded controlled trial3 involving 152 patients of moderate hypertension involving labetalol versus placebo reported that labetalol reduced the incidences of preterm delivery, neonatal jaundice and RDS. Thus, there are possible advantages with no apparent disadvantages.
for the fetus. Thus, we foresee labetalol being considered over the traditionally used alpha-dopa as a first-line drug for hypertensive disorders in pregnancy, irrespective of gestational age.

AIM
The purpose of the trial was to study the role of labetalol (oral) as a first-line drug for hypertensive disorders in pregnancy in an open prospective trial, the primary efficacy parameter being control of blood pressure (BP) and secondarily studying tolerability and effects on labor and fetus.

METHODS
Labetalol was introduced in pregnant women with recorded diastolic blood pressures above 100 mmHg. The drug was started as 100 mg twice-daily with escalating doses at weekly intervals if uncontrolled, reaching a maximum of 1.2 g in 24 hours. Also, an injectable form is available for hypertensive crisis. The National Guideline Clearinghouse, regarding treatment of hypertensive disorders of pregnancy has recommended that the initial antihypertensive therapy should be started with labetalol (IA evidence) or nifedipine, to bring down the target BP to 160 systolic and 110 diastolic. For women with preexisting hypertension, pre-conceptional counseling is recommended. Angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARB) are to be discontinued, and replaced with safer drugs - labetalol, nifedipine and alpha-methyldopa. In a Kuwaiti trial involving 104 primigravidas with mild-moderate PIH, the investigators compared alpha-dopa with labetalol for antihypertensive management, and concluded that labetalol is quicker, more efficient and better tolerated. Although it crosses placenta, there is no evidence of intrauterine growth retardation (IUGR), perinatal death and neonatal hypoglycemia. It may ripen the cervix, and reduce the latency of labor in term patients. A double-blinded controlled trial involving 152 patients of moderate hypertension involving labetalol versus placebo reported that labetalol reduced the incidences of preterm delivery, neonatal jaundice and RDS. Thus, there are possible advantages with no apparent disadvantages for the fetus. Thus, we foresee labetalol being considered over the traditionally used alpha-dopa as a first-line drug for hypertensive disorders in pregnancy, irrespective of gestational age.

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