Review: Antihypertensive drugs do not differ for comparative benefit or risk in severe hypertension during pregnancy


**Question**
In women with severe hypertension during pregnancy, which antihypertensive drugs have the greatest comparative benefit with the least risk for adverse outcomes?

**Data Sources**
Studies were identified by searching the Cochrane Pregnancy and Childbirth Group trials register (April 2002), the Cochrane Controlled Trials Register (Issue 2, 2002), and MEDLINE (up to April 2002).

**Study Selection**
Studies published in any language were selected if they were randomized controlled trials (RCTs) comparing 1 antihypertensive agent with another regardless of dose, route of administration, or duration of therapy and patients were women with severe hypertension (diastolic blood pressure ≥ 105 mm Hg) during pregnancy.

**Data Extraction**
Data were extracted independently by 2 reviewers on sample size, details of the intervention, study quality, and outcomes. Outcomes for women included blood pressure control, eclampsia, measures of serious maternal morbidity (e.g., kidney failure, cardiac failure, and stroke), cesarean section, use of health service resources, and side effects. Outcomes for the baby included fetal and neonatal death and measures of serious neonatal morbidity (e.g., low Apgar scores).

**Main Results**
20 RCTs (1637 women) met the selection criteria. 5 comparisons (each evaluating labetalol, calcium antagonists, prostacyclin, ketanserin, or urapidil) used hydralazine as the control. Other comparisons included labetalol vs methyldopa, labetalol vs diazoxide, nimodipine vs magnesium sulfate, nifedipine vs chlorpromazine, and nifedipine vs prazosin. Meta-analyses were done using random-effects models where significant heterogeneity was detected. More women in the ketanserin group than in the hydralazine group had persistent high blood pressure (3 RCTs, n = 144) (Table). 1 RCT (n = 90) reported that fewer women in the labetalol group than in the diazoxide group had low blood pressure requiring treatment or needed cesarean section (Table). For other comparisons, the groups did not differ for any of the outcomes.

**Conclusion**
In women with severe hypertension during pregnancy, evidence to discriminate among the choices of specific antihypertensive drugs is limited.

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<table>
<thead>
<tr>
<th>Outcomes</th>
<th>NRCTs</th>
<th>Comparison</th>
<th>Weighted event rates</th>
<th>RRI (95% CI)</th>
<th>NNH (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persistent high BP</td>
<td>3</td>
<td>Ketanserin vs hydralazine</td>
<td>38% vs 5.7%</td>
<td>574 (149 to 1728)</td>
<td>4 (3 to 5)</td>
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<tr>
<td>Cesarean section†</td>
<td>1</td>
<td>Labetalol vs diazoxide</td>
<td>13% vs 31%</td>
<td>57% (1.2 to 82)</td>
<td>6 (3 to 100)</td>
</tr>
<tr>
<td>Low BP requiring treatment†</td>
<td>1</td>
<td></td>
<td>0% vs 18%</td>
<td>94% (1 to 100)</td>
<td>6 (4 to 17)</td>
</tr>
</tbody>
</table>

*NRCTs = number of randomized controlled trials. Other abbreviations defined in Glossary, RRI, RRR, NNH, NNT, and CI calculated from data in article using a random effects model.
†Event rates not weighted.

**Commentary**
Severe hypertension during pregnancy is a relevant health problem, particularly in developing countries. The review by Duley and Henderson-Smart compared different antihypertensive drugs with the aim of identifying those with the greatest comparative benefit and least risk for adverse outcomes. Strengths of the review include a clear statement of the objective and a comprehensive literature search without language restrictions. A limitation is data heterogeneity. Contributing factors to the data heterogeneity include different criteria for severe hypertension, doses, diagnoses, and outcome definitions.

Hydralazine has been the first-line drug for decades and based on this systematic review, it will continue to be. Diazoxide causes a rapid decrease in blood pressure, and as expected, this systematic review shows some probable consequences, such as an increased number of maternal hypertension episodes and the need for cesarean section due to fetal distress.

Although the initial use of hydralazine has the greatest support from the evidence, the optimum dose is not mentioned. One RCT from Brazil included in the meta-analysis suggests that hydralazine, 5 mg, or nifedipine, 5 mg, is effective for reducing blood pressure in approximately 90% of the patients (1). Other effective medications used in the study include labetalol, nimodipine, prazosin, and methyldopa, often with concomitant use of magnesium sulfate. This systematic review provides important background information for a needed large collaborative clinical trial on hypertension in pregnancy.

**Reference**