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

Duley L, Henderson-Smart DJ. **Drugs for treatment of very high blood pressure during pregnancy.** Cochrane Database Syst Rev. 2002;(4):CD001449 (latest version 23 Aug 2002).

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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Comparative effectiveness of antihypertensive drugs in very high blood pressure (BP) during pregnancy*

Outcomes	NRCTs	Comparison	Weighted event rates	RRI (95% CI)	NNH (CI)
Persistent high BP	3	Ketanserin vs hydralazine	38% vs 5.7%	574% (149 to 1728)	4 (3 to 5)
				RRR (CI)	NNT (CI)
Cesarean section†	1	Labetalol vs diazoxide	13% vs 31%	57% (–2 to 82)	6 (3 to 100)
Low BP requiring treatment†	1		0% vs 18%	94% (1 to 100)	6 (4 to 17)

*NRCTs = number of randomized controlled trials. Other abbreviations defined in Glossary; RRI, RRR, NNH, NNT, and CI calculated from data in article using a fixed-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 hypotension 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.

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Reference

1. **de Souza MR, Nagib A, Bertini AM.** Use of hydralazine and nifedipine in hypertensive emergency in pregnancy. Progressos de Obstetricia y Ginecologia. 1994;37:90-6.