Review: treatment induced blood pressure reductions in pregnancy may be associated with decreased fetal growth


QUESTION: In pregnant women with mild to moderate hypertension, is treatment with oral antihypertensive medication associated with impaired fetoplacental growth?

Data sources
Randomised controlled trials were identified by searching Medline (1966–97) with the terms antihypertensive agents; bed rest; hospitalization; plasma volume expansion; plasma substitutes; maternal mortality; pregnancy; pregnancy complications; perinatology; neonatology; infant, newborn diseases; infant; and infant mortality. 1 journal was handsearched, and bibliographies of relevant studies were scanned.

Study selection
English and French language studies were selected if they included pregnant women with mild to moderate hypertension, oral antihypertensive medications were compared with each other or placebo, and outcomes of blood pressure changes and fetal growth were reported.

Data extraction
Data were extracted in duplicate on study quality; antihypertensive medications studied, including duration and dose; maternal hypertension (chronic or late onset during pregnancy); change in blood pressure, defined as change in mean arterial pressure (MAP), which was calculated by adding diastolic blood pressure to one third of the pulse pressure; gestational age at delivery; and fetoplacental growth (small for gestational age infants, birth weight, and placental weight).

Main results
45 randomised controlled trials in 41 publications met the inclusion criteria. 7 studies evaluated chronic hypertension, and 38 evaluated late onset hypertension. 3773 women were allocated to oral antihypertensive medication: methyldopa, 13 β-blockers, and 5 calcium channel blockers. Median duration of treatment was 8 weeks (range 2 to 28 wks), and all women were treated in their third trimester. A decrease in MAP was associated with an increase in the percentage of small for gestational age infants (p = 0.006), and a decrease in birth weight (p = 0.049) after elimination of 1 trial was seen as a statistical outlier. A 10 mm Hg fall in MAP was associated with a decrease in birth weight of 145 g (95% CI 5 to 285 g). No association was seen between the mean difference in duration of treatment and the incidence of small for gestational age infants or a minor decrease in birth weight. Furthermore, no relation was observed between the mean difference in duration of treatment and the incidence of small for gestational age births among women with late onset hypertension.

Conclusions
Treatment induced decreases in mean arterial blood pressure in pregnant women may be associated with an increased percentage of small for gestational age infants and a minor decrease in birth weight. Duration of treatment does not appear to have any effect on either variable.

COMMENTARY
This meta-regression analysis by von Dadelszen et al in concert with previously published data informs clinicians that the medical treatment of mild to moderate hypertension in pregnancy may provide some maternal advantage, but is unlikely to benefit the fetus. The studies included in this analysis contained abundant differences in the type of agents and patients studied and frequently did not mask treatment allocation. The latter concern is heightened by the fact that co-intervention with another agent, such as hydralazine, or assisted early delivery was permitted in many trials. Together, these limitations greatly increase the chances of prestatistical heterogeneity (the studies differ in content, format, and other aspects to such a degree that formal statistical testing for heterogeneity is not justified) and bias in the analysis.

In almost all studies included in this review, infants were born after 37 weeks of gestation regardless of treatment allocation and had a mean birth weight >2500 g. Because infant health is most dependent on gestational age at birth, parents would be comforted by knowing that treatment does not appear to increase the rate of preterm birth. Moreover, the observation of a 145 g lower birth weight for every additional 10 mm Hg fall in MAP with active treatment is of questionable clinical importance and, as pointed out by de Swiet, could be as little as 5 g or at most 285 g.

Although the risk for small for gestational age births was slightly higher among treated women with late onset hypertension (ie, gestational hypertension), this was not the case for treated women with chronic hypertension, in whom duration of treatment would probably have been longer. Furthermore, no relation was observed between the mean difference in duration of treatment and the incidence of small for gestational age births among women with late onset hypertension.

Experienced clinicians need to routinely monitor both mother and fetus in the presence of chronic or gestational hypertension. The point at which treatment should be initiated remains controversial.

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