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

von Dadelszen P, Ornstein MP, Bull SB, et al. **Fall in mean arterial pressure and fetal growth restriction in pregnancy hypertension: a meta-analysis.** Lancet. 2000 Jan 8;355:87-92.

QUESTION

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

DATA SOURCES

Randomized controlled trials were identified by searching MEDLINE (1966 to 1997) 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 hand searched, 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, birthweight, and placental weight).

MAIN RESULTS

45 randomized 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 wk), 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 birthweight ($P = 0.049$) after elimination of 1 trial was seen as a statistical outlier. A 10-mm Hg fall in MAP was associated with a decrease in birthweight of 145 g (95% CI 5 to 285 g). No association was seen between duration of therapy and either mean birthweight or percentage of small-for-gestational-age infants. Changes in MAP were not associated with placental weight.

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 birthweight. Duration of treatment does not appear to have any effect on either variable.

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COMMENTARY

This meta-regression analysis by von Dadelszen and colleagues in concert with previously published data informs clinicians that the medical treatment of mild-to-moderate hypertension in pregnancy may provide some maternal advantage (1) 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 cointervention 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 birthweight > 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 birthweight for every additional 10-mm Hg fall in MAP with active therapy is of questionable clinical importance and, as pointed out by de Swiet (2), 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 (i.e., gestational hypertension), this was not the case for treated women with chronic hypertension, in whom duration of therapy would probably have been longer. Furthermore, no relation was observed between the mean difference in duration of therapy 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 therapy should be initiated remains controversial (3).

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References

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