ANTIHYPERTENSIVE THERAPY FOR SEVERE PRE-ECLAMPSIA

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Background

Complications of severe uncontrolled hypertension are responsible for much of the morbidity and mortality associated with pre-eclampsia. To minimize the risk of such complications, international consensus statements recommend treatment of hypertension once blood pressure is persistently above 160/110 mm Hg. The three most commonly recommended and used first-line antihypertensive drugs for treatment of severe hypertension in pregnancy are hydralazine, labetalol, and nifedipine. Numerous randomised trials have compared one drug with another to evaluate the effectiveness and safety of each of these anti-hypertensive agents.

Methods

We identified randomised trials comparing hydralazine, labetalol, and nifedipine for treatment of severe hypertension in pregnancy using the Cochrane Pregnancy and Childbirth (PCG) group's trials register (up to March 2005). The PCG group's search strategy includes quarterly searches of CENTRAL, monthly searches of MEDLINE; hand searches of 30 journals and the proceedings of major conferences; and weekly current awareness search of a further 37 journals. Further searches were conducted on EMBASE (February 2005).

Findings

Five randomised trials (109 women) compared hydralazine with labetalol. Hydralazine was associated with an increased risk of maternal hypotension (RR 5.5, 95% CI 1.2 to 25.8) and maternal side effects (RR 2.9, 95% CI 1.6 to 5.1). There was no significant difference for any other outcome.

Ten trials (645 women) compared hydralazine with nifedipine. Hydralazine was associated with an increased risk of persistent hypertension (RR 2.5, 95% CI 1.4 to 4.3), adverse effects on fetal heart rate pattern (RR 6.4, 95% CI 1.7 to 24.7) and maternal tachycardia (RR 5.7, 95% CI 2.2 to 14.2), but reduced risk of facial flushing (RR 0.2, 95% CI 0.1 to 0.5) compared to nifedipine. There were no significant differences for any other outcome.

Conclusions

Although hydralazine appears to be associated with less favourable outcomes compared to labetalol and nifedipine, a number of factors may have influenced these results. Only two trials reported adequate allocation concealment, three were quasi-randomised trials, and the remaining ten trials were of uncertain quality with a potential for selection bias. All five trials involving labetalol were small, which increases the possibility of finding associations by chance.

Increased risk of maternal hypotension with hydralazine is based mainly on two trials that used relatively higher doses of hydralazine.
Increased risk of persistent hypertension is based on five trials, all of them using different definitions of persistent hypertension. At least one definition is not appropriate, given the pharmacokinetic properties of hydralazine. Adverse effect on fetal heart rate is based mainly on one trial of poor methodological quality. Although maternal side effects such as tachycardia were increased with hydralazine, side effects were not severe enough to discontinue treatment, therefore, their clinical significance may not be substantial.

Some have suggested that hydralazine should not be used as a first line anti-hypertensive despite a long history of safety and efficacy and familiarity with its use in acutely ill pregnant women. We believe that it is premature to preclude its use as a first line agent based on currently available evidence. However, as concerns have been raised, and there is a possibility that other agents may be safer and equally if not more efficacious, we suggest that a large randomised trial comparing hydralazine with the other first line anti-hypertensive drugs is the best way forward.