

that it is not a “weight loss” drug. Metformin should therefore always be used as an adjunct to general lifestyle improvements and not as a replacement for increased exercise and improved diet. Figure 4 gives suggestions on how to induce ovulation in women with polycystic ovary syndrome.<sup>22–26</sup>

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## Hydralazine for treatment of severe hypertension in pregnancy: meta-analysis

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### Abstract

**Objective** To review outcomes in randomised controlled trials comparing hydralazine against other antihypertensives for severe hypertension in pregnancy.

**Study design** Meta-analysis of randomised controlled trials (published between 1966 and September 2002) of short acting antihypertensives for severe hypertension in pregnancy. Independent data abstraction by two reviewers. Data were entered into RevMan software for analysis (fixed effects model, relative risk and 95% confidence interval); in a secondary analysis, risk difference was also calculated.

**Results** Of 21 trials (893 women), eight compared hydralazine with nifedipine and five with labetalol. Hydralazine was associated with a trend towards less persistent severe hypertension than labetalol (relative risk 0.29 (95% confidence interval 0.08 to 1.04); two trials), but more severe hypertension than nifedipine or isradipine (1.41 (0.95 to 2.09); four trials); there was significant heterogeneity in outcome between trials and differences in methodological quality. Hydralazine was associated with more maternal hypotension (3.29 (1.50 to 7.13); 13 trials); more caesarean sections (1.30 (1.08 to 1.59); 14 trials); more placental abruption (4.17 (1.19 to 14.28); five trials); more maternal oliguria (4.00 (1.22 to 12.50); three trials); more adverse effects on fetal heart rate (2.04



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(1.32 to 3.16); 12 trials); and more low Apgar scores at one minute (2.70 (1.27 to 5.88); three trials). For all but Apgar scores, analysis by risk difference showed heterogeneity between trials. Hydralazine was associated with more maternal side effects (1.50 (1.16 to 1.94); 12 trials) and with less neonatal bradycardia than labetalol (risk difference  $-0.24$  ( $-0.42$  to  $-0.06$ ); three trials).

**Conclusions** The results are not robust enough to guide clinical practice, but they do not support use of hydralazine as first line for treatment of severe hypertension in pregnancy. Adequately powered clinical trials are needed, with a comparison of labetalol and nifedipine showing the most promise.

## Introduction

Reports into maternal mortality have consistently shown excess maternal mortality associated with hypertensive disorders of pregnancy, particularly the severe hypertension of pre-eclampsia. Three short acting antihypertensive agents—hydralazine, labetalol, and short acting (sublingual or orally administered) nifedipine—are commonly used to control acute, very high blood pressure in pregnancy.<sup>1</sup> All three agents have their proponents and detractors.

For many years, hydralazine has been the recommended antihypertensive of first choice for severe hypertension in pregnancy.<sup>1-3</sup> Its side effects (such as headache, nausea, and vomiting) are common and mimic symptoms of deteriorating pre-eclampsia. Although precipitous hypotension may occur with any antihypertensive agent used to treat pre-eclampsia,<sup>4-8</sup> a meta-analysis of clinical trials showed that maternal hypotension may be more common with parenteral hydralazine, which was also associated with an excess of caesarean sections, placental abruptions, and low Apgar scores ( $<7$ ) at five minutes.<sup>9</sup>

Short acting nifedipine has the clinical advantage of being able to be given by midwives in the absence of a doctor. However, uncertainty exists about how safe short acting calcium channel blockers are for the mother.<sup>10</sup> When used for treating hypertension in patients with coronary artery disease or diabetes, these agents have been associated with excess cardiovascular morbidity and mortality.<sup>11-12</sup> Two case reports of transient neuromuscular weakness in patients taking nifedipine and magnesium sulphate have caused concern about concomitant use of these agents.<sup>13-14</sup> Some markets have withdrawn short acting nifedipine.<sup>15</sup>

Labetalol has been used extensively in pregnancy and has a favourable side effect profile. However, concern has been raised about the risk of neonatal bradycardia with parenteral labetalol.<sup>16</sup>

This meta-analysis of randomised controlled trials for treatment of moderate to severe hypertension in pregnancy aimed to compare the effects of short acting antihypertensive agents (in comparison to parenteral hydralazine) on perinatal, maternal, and neonatal outcomes, particularly maternal hypotension.

## Methods

We updated our previous literature review (1966-97)<sup>14</sup> by searching Medline (1997-September 2002), the

journal *Hypertension in Pregnancy*, conference proceedings, bibliographies, and textbooks. We looked for articles addressing the treatment of severe hypertension in pregnancy with short acting antihypertensive agents, comparing them with parenteral hydralazine (see [bmj.com](http://bmj.com) for search terms).

Criteria for inclusion were moderate to severe hypertension in pregnancy (regardless of type), randomised controlled trial, hydralazine compared with another short acting antihypertensive (generally via parenteral administration), and relevant clinical outcomes addressing maternal, perinatal, or paediatric benefit or risk. We contacted authors when necessary. Data were abstracted independently by two reviewers.

The severity of hypertension was defined according to mean diastolic blood pressure at enrolment: mild (90-99 mm Hg), moderate (100-109 mm Hg), or severe ( $\geq 110$  mm Hg).

Data from trials of single drugs were accepted for maternal haemodynamic outcomes and stillbirth, and for neonatal outcomes if the antihypertensive could be expected to be in the maternal-fetal bloodstream at delivery and could affect the health of the neonate.

We determined heterogeneity between trials by examining the forest plot (of relative risk for each trial, and with the  $\chi^2$  statistic, using  $P < 0.10$ ) to reflect statistically significant heterogeneity.<sup>17</sup> A  $P$  value  $< 0.10$  was considered significant given that  $\chi^2$  is known not to be sensitive to heterogeneity between trials.<sup>17-18</sup> When heterogeneity between trials was found, we examined differences in study design, characteristics of participants, intervention, and outcome definitions. The summary statistic was relative risk (and 95% confidence interval), a relative effect measure appropriate for use when summarising evidence.<sup>17</sup> In addition, we calculated risk difference, as recommended by the neonatal review group of the Cochrane Collaboration.<sup>19</sup> Risk difference is a measure of absolute effect and is sensitive to between trial differences in absolute event rates. In the calculation of risk difference, all trials (even those without reported events in either arm of the trial) contribute to the summary statistic. For outcomes with significant differences between groups, the median event rate and its range were also presented.

## Results

We identified 11 new trials in 16 publications (from 1991 to 2002) that met the inclusion criteria. Therefore, this study includes 21 trials (1085 women), including the 10 trials in the previous meta-analysis.<sup>14</sup> (See [bmj.com](http://bmj.com) for references to trials.)

About half (12/21 trials) enrolled mixed populations of women with pregnancy hypertension; hypertension was usually severe (16/21 trials). In two trials, single doses were given, and in three trials patients were switched to oral antihypertensives when blood pressure had been stabilised. Most commonly, hydralazine was compared with standard doses of other antihypertensives: nifedipine (eight trials); labetalol (five trials); ketanserin (four trials); urapidil (two trials); epoprostenol (one trial); or isradipine (one trial with three publications).

Most trials were small, with a median of 37 women enrolled (range 6-200). Half (11/21) described adequate methods of randomisation, but seven

publications did not describe the method at all. Assessment of outcome was blinded in four trials, and for some outcomes in one other trial. The quality of the methods had no discernible impact on outcome.

The table presents the maternal and perinatal outcomes in trials that compared hydralazine with other antihypertensives.

### Maternal outcomes

Persistent severe hypertension was variably defined as diastolic blood pressure  $\geq 90$  mm Hg,  $\geq 95$  mm Hg,  $\geq 100$  mm Hg, or  $\geq 110$  mm Hg; mean arterial blood pressure  $\geq 120$  mm Hg; and failure to achieve a drop in systolic/diastolic blood pressure of 30/15 mm Hg. Hydralazine did not differ from other antihypertensives in impact on persistent severe hypertension or on use of additional antihypertensives (table). However, the results differed by more than could be expected by chance alone, with the heterogeneity explained largely by the type of the other antihypertensive. Hydralazine was associated with a trend towards lower rates of persistent severe hypertension (median event rate 0% (range 0-20%) *v* labetalol (5% (0-60%)); relative risk 0.29 (0.08 to 1.04); two trials;  $\chi^2=0.08$ ,  $P=0.78$ ; risk difference  $-0.11$  ( $-0.21$  to  $-0.02$ ); four trials;  $\chi^2=6.91$ ,  $P=0.08$ ; figure) and was not associated with use of additional antihypertensives (5% (0-10)% for hydralazine *v* 5% (0-10)% for labetalol; relative risk 1.00 (0.07 to 13.87); one trial;  $\chi^2=0$ ; risk difference 0 ( $-0.12$  to 0.12); two trials;  $\chi^2=0$ ,  $P=1.00$ ). Hydralazine was associated with a trend towards more persistent severe hypertension (29% (0-32%) compared with nifedipine or isradipine (5% (0-40%)); relative risk 1.41 (0.95 to 2.09); four trials;  $\chi^2=11.69$ ,  $P=0.009$ ; risk difference 0.08 ( $-0.01$  to 0.16); five trials;  $\chi^2=12.36$ ,  $P=0.02$ ; figure) and with use of additional antihypertensives (13% (0-32%) for hydralazine *v* 5% (0-24%)) nifedipine only; relative risk 2.13 (1.20 to 3.85); four trials;  $\chi^2=5.24$ ,  $P=0.15$ ; risk difference 0.08 (0.02 to 0.14); five trials;  $\chi^2=12.32$ ,  $P=0.02$ ), but there was still significant heterogeneity between trials within this subgroup. In the three trials with nifedipine or isradipine in which hydralazine was associated with more severe hypertension, the methods of allocation concealment were either clearly inadequate or unstated, but other characteristics of the trials did not differ.

In comparison with ketanserin, hydralazine was not associated with a consistent effect on maternal blood pressure (figure); this effect was partially explained by the doses of hydralazine used. A low dose hydralazine infusion was associated with a trend towards more persistent severe hypertension than ketanserin. Higher dose bolus hydralazine was associated with less persistent severe hypertension than ketanserin.

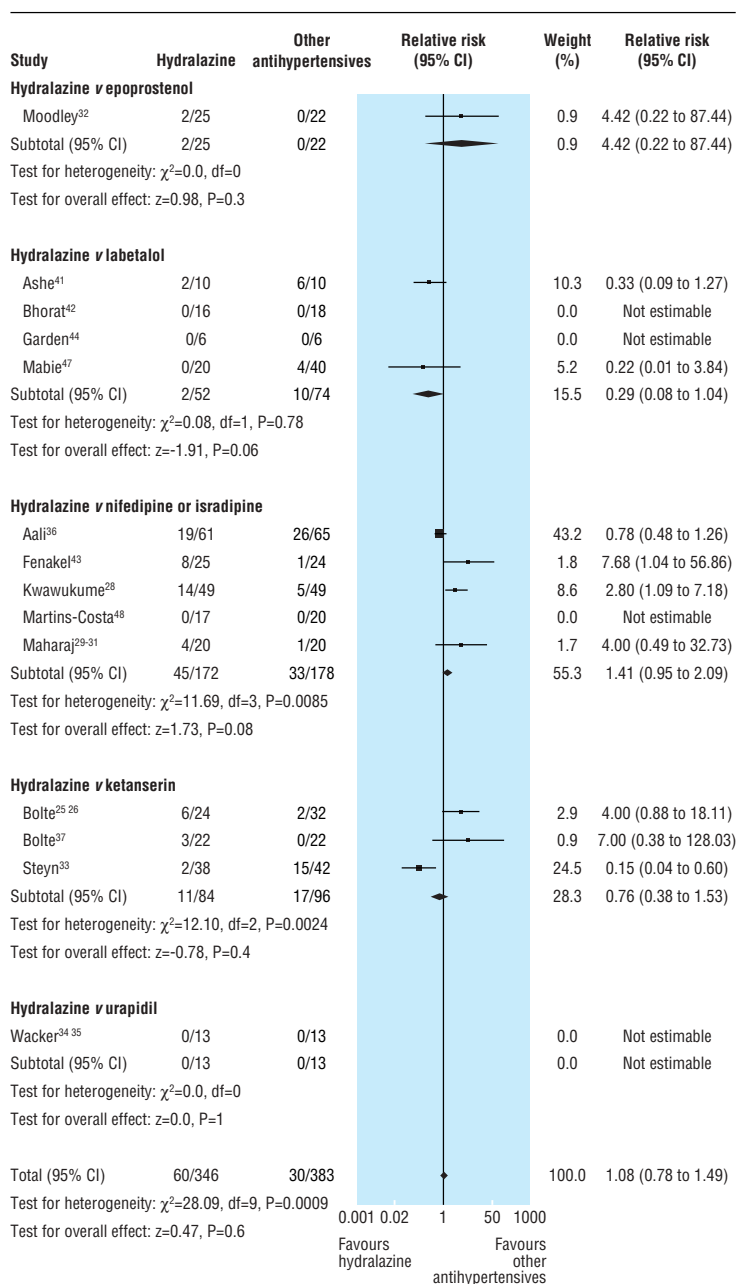
Hydralazine was associated with more maternal hypotension than other antihypertensives (0% (0-67%) *v* 0% (0-17%); table). Calculations of risk difference showed significant heterogeneity between trials, which was largely absent when subgroups of other antihypertensive agents were examined: hydralazine *v* labetalol (risk difference 0.10 (0 to 0.20); four trials;  $\chi^2=6.46$ ,  $P=0.09$ ); hydralazine *v* nifedipine or isradipine (0.01 ( $-0.01$  to 0.04); six trials;  $\chi^2=6.58$ ,  $P=0.25$ ); hydralazine *v* urapidil (0.16 ( $-0.11$  to 0.42); one trial); and hydralazine *v* ketanserin (0.18 ( $-0.04$  to 0.39); two trials;  $\chi^2=0.51$ ,  $P=0.47$ ). In the hydralazine *v* labetalol

subgroup in which there was still heterogeneity, the incidence of maternal hypotension with hydralazine ranged from 0% (in 10 patients) to 67% (in 4 of 6 patients).

Several maternal outcomes occurred more often with hydralazine than with other antihypertensives: caesarean section (67% (8-100%) *v* 59% (5-100%) for other antihypertensives); placental abruption (18% (3-20%) *v* 0% (0-2%)); and maternal oliguria (17% (4-41%) *v* 0% (0-9%)) (table); however, the risk difference analysis showed heterogeneity between trials. Groups did not differ in other measures of maternal morbidity.

### Maternal side effects

Hydralazine was associated with more maternal side effects (of any sort) and headache than other



Persistent severe maternal hypertension in trials that compared hydralazine with other antihypertensives

Maternal and perinatal outcomes in trials comparing hydralazine with other antihypertensives for severe hypertension of pregnancy

Outcome	No of trials	No of women	Relative risk (95% CI)	Heterogeneity			Risk difference (95% CI)	Heterogeneity		
				$\chi^2$	df	P value		$\chi^2$	df	P value
<b>Maternal outcomes</b>										
Persistent severe hypertension	14	729	1.08 (0.78 to 1.49)	28.09	9	0.0009*	0.01 (-0.04 to 0.06)	44.36	13	<0.0001*
Additional drugs for blood pressure	10	564	1.32 (0.83 to 2.13)	14.06	6	0.029*	0.03 (-0.02,0.08)	22.92	9	0.006*
Maternal hypotension	13	687	3.29 (1.50 to 7.23)*	3.22	6	0.78	0.04 (0.01 to 0.08)*	40.66	12	0.0001*
Eclampsia	8	311	0.75 (0.20 to 2.86)	1.40	3	0.70	-0.01 (-0.05 to 0.04)	2.03	7	0.96
HELLP syndrome	2	142	2.33 (0.83 to 6.67)	3.70	1	0.05*	0.08 (0.00 to 0.17)	18.87	1	<0.0001*
Placental abruption	5	203	4.17 (1.19 to 14.28)*	1.29	4	0.86	0.08 (0.01 to 0.15)*	7.9	4	0.095*
Caesarean section	14	650	1.30 (1.08 to 1.59)*	12.19	11	0.35	0.08 (0.02 to 0.13)*	25.67	13	0.02*
Intracerebral haemorrhage	1	44	3.03 (0.13 to 100)	0	0	NA	0.05 (-0.08 to 0.17)	0	0	NA
Pulmonary oedema	3	161	4.00 (0.65 to 25.00)	1.09	1	0.30	0.05 (-0.01 to 0.12)	7.05	2	0.03*
Oliguria	3	105	4.00 (1.22 to 12.50)*	0.10	2	0.95	0.17 (0.05 to 0.29)*	7.44	2	0.02*
Disseminated intravascular coagulation	1	44	0.33 (0.01 to 7.69)	0	0	NA	-0.05 (-0.17 to 0.08)	0	0	NA
Maternal death	9	471	3.33 (0.52 to 20.00)	0	2	1.00	0.01 (-0.02 to 0.04)	2.11	8	0.98
<b>Maternal side effects</b>										
Any	12	494	1.50 (1.16 to 1.94)*	27.51	11	0.004*	0.12 (0.05 to 0.19)*	51.38	11	<0.0001*
Headache	11	528	1.61 (1.06 to 2.38)*	14.34	10	0.16	0.07 (0.01 to 0.13)*	29.15	10	0.001*
Visual symptoms	1	44	9.09 (0.51 to 100)	0	0	NA	0.18 (0.00 to 0.36)	0	0	N/A
Nausea or vomiting	6	210	2.22 (0.94 to 5.26)	4.17	4	0.38	0.08 (0.00 to 0.16)	12.61	5	0.03*
Epigastric pain	1	44	0.67 (0.12 to 3.57)	0	0	NA	-0.05 (-0.23 to 0.14)	0	0	N/A
Flushing	3	119	0.31 (0.12 to 0.79)*	8.08	2	0.02*	-0.20 (-0.32 to -0.08)*	30.42	2	<0.0001*
Palpitations	5	132	3.57 (1.72 to 7.69)*	3.11	4	0.54	0.28 (0.15 to 0.41)*	15.06	4	0.005*
Tachycardia >110 beats/min	5	305	5.56 (2.38 to 12.5)*	4.42	4	0.35	0.18 (0.11 to 0.25)*	11.96	4	0.02*
Dizziness	5	153	1.82 (0.53 to 6.25)	3.35	3	0.34	0.04 (-0.04 to 0.12)	5.72	4	0.22
Bronchospasm	1	12	0.33 (0.17 to 6.67)	0	0	NA	-0.17 (-0.59 to 0.25)	0	0	NA
Drugs changed because of side effects	7	328	2.44 (0.38 to 14.28)	0.03	1	0.86	0.01 (-0.02 to 0.05)	1.65	6	0.95
<b>Effects on fetus</b>										
Adverse effects on fetal heart rate	12	601	2.04 (1.32 to 3.16)*	13.60	8	0.09*	0.07 (0.03 to 0.12)*	45.97	12	<0.0001*
<b>Perinatal outcomes</b>										
Perinatal death	17	744	1.43 (0.77 to 2.63)	4.21	12	0.98	0.02 (-0.02 to 0.05)	7.25	16	0.97
Stillbirth	17	744	2.00 (0.85 to 4.76)	0.66	5	0.99	0.02 (-0.01 to 0.05)	4.61	16	1.00
Neonatal death	17	729	1.00 (0.43 to 2.38)	3.74	8	0.88	0.00 (-0.03 to 0.03)	5.47	16	0.99
1-minute Apgar <7	3	52	2.70 (1.27 to 5.88)*	4.03	2	0.13	0.36 (0.13 to 0.59)*	4.48	2	0.11
5-minute Apgar <7	6	271	1.23 (0.69 to 2.22)	3.74	5	0.59	0.03 (-0.05 to 0.11)	5.85	5	0.32
Admission to neonatal intensive care unit	1	98	1.18 (0.59 to 2.38)	0	0	NA	0.04 (-0.13 to 0.21)	0	0	NA
Neonatal bradycardia	3	50	0.16 (0.02 to 1.11)	0.01	1	0.91	-0.24 (-0.42 to -0.06)*	15.43	2	0.0004*
Neonatal hypotension	1	19	5.88 (0.28 to 100)	0	0	NA	0.17 (-0.20 to 0.53)	0	0	NA
Neonatal hypothermia	1	25	Not estimable				0.00 (-0.16 to 0.16)	0	0	NA
Neonatal hypoglycaemia	3	64	0.88 (0.14 to 5.26)	0.84	(1)	0.36	-0.01 (-0.13 to 0.10)	0.94	2	0.63
Respiratory distress syndrome	6	250	1.56 (0.78 to 3.13)	2.68	(5)	0.75	0.05 (-0.03 to 0.12)	3.72	5	0.59
Intraventricular haemorrhage	2	72	4.17 (0.47 to 33.33)	0.11	(1)	0.74	0.07 (-0.05 to 0.18)	0.75	1	0.39
Necrotising enterocolitis	1	53	2.86 (0.12 to 100.)	0	(0)	NA	0.04 (-0.06 to 0.14)	0	0	NA

NA=not applicable; HELLP=haemolysis to elevated liver enzymes to low platelets

\*Significant at the P<0.05 level, and discussed in the text.

antihypertensives (40% (10-82%) *v* 17% (0-75%) and 29% (0-67%) *v* 0% (0-20%), respectively; table). For any maternal side effects, the significant heterogeneity between trials was confined to the nifedipine subgroup.

Hydralazine was associated with more palpitations than other antihypertensives (18% (11-81%) *v* 0% (0-17%)). Three of the five trials compared hydralazine with labetalol, and within this subgroup the effect was significant (relative risk 5.26 (2.00 to 14.28); three trials;  $\chi^2 = 0.29$ ,  $P = 0.87$ ; risk difference 0.48 (0.30 to 0.67); three trials;  $\chi^2 = 4.79$ ,  $P = 0.09$ ).

Hydralazine was also associated with more maternal tachycardia than other antihypertensives (24% (10-67%) *v* 0% (0-6%)). Three of the five trials

were comparisons of hydralazine against nifedipine, and within this subgroup the results were significant (relative risk 5.56 (2.17 to 14.29); three trials;  $\chi^2 = 4.10$ ,  $P = 0.13$ ; risk difference 0.18 (0.11 to 0.25); three trials;  $\chi^2 = 11.96$ ,  $P = 0.02$ ).

Hydralazine was associated with less flushing than nifedipine (0-12.5% *v* 0-58%; only comparisons with nifedipine reported flushing); however, there was heterogeneity between trials. Groups did not differ in other measures of maternal side effects.

Despite the high prevalence of side effects (in 85 of 227 patients given hydralazine and 61 of 257 patients given other antihypertensives), few women changed drugs because they experienced side effects (3 of 161

changing from hydralazine, 1 of 167 changing from other antihypertensives); the proportion did not differ between groups.

#### Adverse effects on fetal heart rate

Hydralazine was associated with more adverse effects on fetal heart rate than other antihypertensives (11% (0-56%) *v* 0% (0-50%)), with the significant heterogeneity isolated to the hydralazine *v* labetalol subgroup. However the doses of hydralazine and labetalol differed in the two trials comparing these two drugs; otherwise, the differences remained unexplained, although both trials were small and the 95% confidence intervals overlapped substantially.

#### Perinatal outcomes

Hydralazine was associated with more low Apgar scores at one minute than other antihypertensives (67% (38-83%) *v* 15% (14-67%); table), but the incidence of low Apgar scores at five minutes did not differ between groups. Hydralazine was associated with less neonatal bradycardia than labetalol (0% (0-0%) *v* 21% (0-100%)), but the results differed more than could be expected by chance alone, as we reported earlier.<sup>9</sup> Few trials reported other perinatal outcomes, and these outcomes did not differ between groups. However, there was a statistical trend towards more stillbirths with hydralazine than with other antihypertensives (11/357; 0% (0% to 31%) *v* 5/387; 0% (0% to 22%)).

## Discussion

This meta-analysis of randomised controlled trials for the treatment of severe hypertension in pregnancy shows that hydralazine was associated with some poorer maternal and perinatal outcomes than other antihypertensives, particularly labetalol and nifedipine. Hydralazine was found to be a less effective antihypertensive than nifedipine or isradipine, and did not clearly differ from labetalol.

Hydralazine was more poorly tolerated than other antihypertensives. More maternal side effects were seen than with labetalol or ketanserin. More headaches (raising the issue of imminent eclampsia), palpitations, and maternal tachycardia were seen than with other antihypertensives, with the exception of nifedipine; in trials that showed these side effects, outcomes differed more than could be expected by chance alone, possibly because of differences in design of the trials.

#### Use of summary statistics

We used relative risk as the primary summary statistic for this meta-analysis and used risk difference in a secondary analysis. All outcomes for which relative risk was significantly increased, without heterogeneity, showed significant heterogeneity in the analysis that used risk difference, with the exception of low Apgar scores at one minute. Risk difference is sensitive to heterogeneity between trials, and the results of the risk difference analyses highlight the great variability in event rate between trials, due in part to the small sample sizes. The variability in event rates precludes us from extrapolating the results to a specific patient population.

#### Alternatives to hydralazine

These results are biologically plausible. Rapid or excessive falls in maternal blood pressure may decrease placental perfusion (reflected by abnormal fetal heart rate patterns) and lead to placental abruption, caesarean section, and low Apgar scores at one minute (with recovery by five minutes with resuscitation). The unpredictability of the timing and magnitude of the blood pressure lowering effect of hydralazine may make its use in pregnancy problematic. The results of this meta-analysis do not support recent recommendations favouring initial use of hydralazine over other antihypertensives (including ketanserin).<sup>2</sup>

Nifedipine seems to be a reasonable alternative to hydralazine. In two case reports, profound muscle weakness and respiratory arrest were associated with concomitant use of nifedipine and magnesium sulphate.<sup>13-14</sup> However, no neuromuscular blockade was described in any of the trials comparing hydralazine with nifedipine or isradipine, even though magnesium sulphate was given to all or some women, and no such blockade was reported in the Magpie trial, in which 29% of women allocated to receive magnesium sulphate also received nifedipine.<sup>20</sup> Any risk of neuromuscular blockade is thus likely to be low, and the effect is reversible with calcium gluconate.

Parenteral labetalol also seems to be a reasonable alternative to hydralazine. Although it may be less effective in preventing recurrent severe hypertension, labetalol controlled severe hypertension in 87% of women and was similar to other antihypertensive agents in the need to prescribe further antihypertensives. No new trials were available to update the previously observed association between parenteral labetalol and (usually transient) neonatal bradycardia<sup>9</sup>; neonatologists should continue to be made aware when intravenous labetalol has been used during labour and delivery.

Ketanserin, an agent investigated most widely in the Netherlands and South Africa, compared favourably with hydralazine.

There are other limitations to this review that have not been discussed. Meta-analysis is based on a retrospective and observational study design, which relies on published data. However, trials provide the least biased form of information about therapeutic interventions and outcome, and the results of this meta-analysis are biologically plausible.

The most recent Cochrane review found no good evidence that one short acting antihypertensive is better than another, with the exception of ketanserin, which is associated with more persistent hypertension.<sup>21</sup> The Cochrane inclusion and exclusion criteria differed somewhat from those in this study, but the most important difference seems to be in the reviews' methods. In the absence of significant between-trial heterogeneity in outcome, we pooled the results from all trials comparing hydralazine and other antihypertensives, whereas the Cochrane review had five subgroups of trials comparing hydralazine and other antihypertensives, with different outcomes reported in each group. In our review, pooling had the advantage of not being based on the assumption that different antihypertensives would cause differences in maternal or perinatal outcome, and where differences between trials existed, pooling informed the reader about how

### What is already known on this topic

Hydralazine has been the recommended treatment for severe hypertension in pregnancy, but its side effects mimic symptoms of deteriorating pre-eclampsia

### What this study adds

The results of this meta-analysis do not support the use of hydralazine as first line treatment for severe hypertension in pregnancy

Adequately powered clinical trials, starting with a comparison of labetalol and nifedipine, are needed

differences in design of the studies and in the intervention may have influenced the results. Pooling resulted in greater statistical power where significant heterogeneity between trials did not exist, and allowed overall conclusions to be drawn from the data.

### Conclusions

The results of this review should generate uncertainty about the agent of first choice for treating severe hypertension in pregnancy. Definitive data from adequately powered clinical trials are needed, with the most promising comparison being that of nifedipine with labetalol (or perhaps ketanserin if it is available locally).

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## How my tonsils were saved

In 1937 I was a 7 year old schoolboy. One day the teacher moved me to sit at the front of the class, because, she said, I was deaf. I have no memory of deafness and in retrospect am reasonably certain that this was a misdiagnosis of my affectation of deafness in response to orders that I did not wish to obey.

The matter was reported to the school nurse at her next visit, and, after she tested me with whispered words and the clapping of hands behind my back, my parents were asked to present me at the next public health clinic. Here, a doctor with a mirror on his head and a cold metal spatula dripping with antiseptic looked down my throat. My father could not attend because he was working, and my mother was told that I would be put on the list for a tonsillectomy.

When my father heard of this, he was disinclined to accept it, saying that he thought the only problem with my hearing was hearing things I was not supposed to. I was taken to our general

practitioner, who declined to give an opinion because this was a matter for the public health doctors. My father, who was a carpenter at a ship chandler in Cardiff docks, made an appointment at the next public health clinic, and I was taken there again a week later.

I now know that this was quite something in the 1930s. "Doctors orders" were seldom questioned, and it also meant my father losing half a day's pay. We were eventually ushered in to see the doctor, my father wearing his best clothes as one did when seeing the doctor in those days. My father asked if it was really necessary for me to have my tonsils out. The doctor replied briskly, "Well please yourself," and we were dismissed.

So I still have my tonsils, which have never troubled me since.

David Crosby *honorary consultant surgeon, University Hospital of Wales, Cardiff*