Treatment of hypertension in pregnancy

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Objective

- To provide an update on the magnitude and consequences of hypertensive conditions in pregnancy
- To discuss treatment strategies for hypertension in pregnancy

Hypertension during pregnancy

DEVELOPING COUNTRIES			Rates (%) (95% CI)
ALL			
Pooled estimate**	36 371	Population-based	5.8 (4.9-6.8)
NULLIPAROUS			
Jamaica Aspirin Study	3026	Community-based antenatal clinics	11.0 (9.9-12.1)
INDUSTRIALISED COUNTRIES			
ALL			
North Carolina	289 125	Birth Certificate Data	3.7 (3.6-3.7)
NULLIPAROUS			
NIH Calcium Trial	2294	5 centres in the US	17.3 (15.8-18.9)
North Carolina	107 555	Birth Certificate Data	4.7 (4.6-4.8)

*data from recently conducted large studies
**calculated using logistic regression with adjustment for over-dispersion to account for the between-study variation

Pre-eclampsia*

DEVELOPING COUNTRIES			Rates(%)(%95CI)
ALL			
Trials /Pooled estimate**	71 054	Population or hospital-based	3.4 (2.0-5.6)
Latin American dataset	878 680	Hospital database	4.8 (4.8-4.9)
NULLIPAROUS			
Jamaica Aspirin Study	3026	Community-based antenatal clinics	4.6 (3.8-5.4)
INDUSTRIALISED COUNTRIES			
ALL			
Norway	1 869 388	Norwegian Birth Registry	2.8 (2.7-2.8)
South East Thames	48 865	All maternity units in the area	0.4 (0.3-0.4)
NULLIPAROUS			
NIH Calcium Trial	2294	5 centres	7.3 (6.3-8.5)

* data from recently conducted large studies
** calculated using logistic regression with adjustment for over-dispersion to account for the between-study variation

Eclampsia*

DEVELOPING COUNTRIES			Rates (%)(95%CI)
ALL			
Trials/Pooled estimate	67 260	Population or hospital-based	0.33 (0.16– 0.69)
Latin American dataset	878 680	Hospital database	0.21 (0.20-0.22)
NULLIPAROUS			
Jamaica Aspirin Study	3026	Community-based antenatal clinics	0.7 (0.5-1.1)
INDUSTRIALISED COUNTRIES			
ALL			
North Carolina	289 125	Birth Certificate Data	0.61 (0.58-0.64)
South East Thames	48 865	All maternity units in the area	0.02 (0.01-0.04)
NULLIPAROUS			
North Carolina	107 555	Birth Certificate Data	1.0 (0.9-1.1)

* data from recently conducted large studies

** calculated using logistic regression with adjustment for over-dispersion to account for the between-study variation

Variations in the incidence

		Pre-eclampsia (%)	Eclampsia (%)
WHO Antenatal Care Trial (2001) (control group)	Argentina (n= 3594)	1.81	0.11
	Cuba (n= 2721)	1.62	0.00
	Saudi Arabia (n= 1732)	1.15	0.06
	Thailand (n= 3074)	0.49	0.13
WHO RHL Impact trial (2003) (baseline data)	Mexico (n= 18 288)	6.7	0.70
	Thailand (n= 17 525)	2.0	0.30

Estimated numbers of pre-eclampsia and eclampsia cases per year*

	Developing countries (n=179)	Industrialised countries (n=44)
Births/year*	118 766 000	13 227 000
Incidence of pre-eclampsia (range %)	1.3 – 6.7	0.4 – 2.8
Estimated N of pre-eclampsia /year	**1 543 958 – 7 957 322**	**52 908 – 370 356**
Incidence of eclampsia among women with pre-eclampsia** (%)	2.3	0.8
Estimated N of eclampsia /year	**35 511 – 183 018**	**423 – 2963**

* Source:World Population Prospects:The 2000 Revision, vol I:Comprehensive Tables. United Nations. New York,2001

** Magpie Trial, 2002

*Villar *et al*, 2003

Estimated number of maternal deaths due to pre-eclampsia/eclampsia per year

	Developing countries	Industrialised countries
Case-fatality rate of pre-eclampsia	0.4*	0.034**
Estimated number of deaths due to pre-eclampsia*** (range)/year	6176 – 31 829	18 - 126
Case-fatality rate of eclampsia	5.2****	0.72**
Estimated number of deaths due to eclampsia*** (range)/year	(1846 – 7862)	(3 – 22)
Maternal deaths due to pre-eclampsia/ eclampsia*** (range)/year	**8022 – 39 691**	**21 - 148**

* Magpie Trial, 2002
** MacKay, 2001
*** Calculated with corresponding case-fatality rates
**** Eclampsia Trial, 1995

***Villar *et al*, 2003**

worldwide each year;

- between 1 500 000 and 8 000 000 women will develop pre-eclampsia
- up to 150 000 women will have eclamptic convulsions
- over 90 % in developing countries

Complications of pre-eclampsia
(Magpie trial, 2002 – placebo group)

Complication	%
Perinatal mortality	11.5
Stillbirth	8.6
Macerated stillbirth	3.7
Low birth weight (<2500 g)	48.0
Induced labour	43.0
Caesarean section	48.0
Maternal mortality	0.4

Complications of pre-eclampsia
(Magpie trial, 2002 – placebo group)

	Women with severe pre-eclampsia at enrollment (%)	Eclampsia (%)	Baby death (%)
High risk countries (n= 2812)	**28**	**2.3**	**16.6**
Middle risk countries (n= 1461)	**24**	**1.8**	**8.2**
Low risk countries (n= 782)	**28**	**0.8**	**4.3**

Lancet 2002

Complications of pre-eclampsia
(Magpie trial, 2002 – placebo group)

At trial entry	Eclampsia (%)	Neonatal death (%)
Severe pre-eclampsia (n=1345)	**2.7**	**19.7**
Mild-moderate pre-eclampsia (n=3710)	**1.6**	**9.7**

Lancet , 2002

Limitations: definitions

- variety of definitions
- some of them impractical: need for a second BP measurement
- relationships between different components of definitions and the adverse outcomes

Limitations: diagnosis / BP measurement

- poor agreement between observers, terminal digit bias, expected normal value bias
- equipment

Limitations: diagnosis / proteinuria

- gold standard - 24-hr collection - impractical
- dipstick - affected by the tonicity
- protein/creatinine ratio - best option but still may not be practical and valid due to hour-to-hour variety of protein excretion

Treatment

Effective medical actions

- antihypertensive drugs
- magnesium sulphate
- early delivery

Antihypertensive drugs

- Mild to moderate hypertension

Unclear whether antihypertensive drug therapy for mild-moderate hypertension during pregnancy is worthwhile

(Cochrane review: Abalos et al, 2002)

Antihypertensive drugs

- Very high blood pressure

- recommended
- which antihypertensive ?

- Little evidence on the choice of the antihypertensive; better to avoid diazoxide and ketanserin

(Cochrane review, Duley and Henderson-Smart, 2002)

Anticonvulsants

- Magnesium sulphate vs placebo

Mg SO_4 more than halves the risk of eclampsia and probably reduces the risk of maternal death. It does not improve outcome for the baby, in the short term.

(Cochrane review, Duley et al, 2003)

Anticonvulsants for pre-eclampsia

- Magnesium sulphate vs other anticonvulsants

- better than phenytoin for reducing the risk of eclampsia, but with an increased risk of c/s

- better than nimodipine

- comparison with diazepam: insufficient evidence to conclude

(Cochrane review, Duley et al, 2003)

Anticonvulsants for eclampsia

- Magnesium sulphate vs other anticonvulsants

- Mg SO_4 is substantially more effective than phenytoin and diazepam for treatment of eclampsia

(Cochrane reviews, Duley and Henderson-Smart, 2003)

Treatment strategies for pre-eclampsia/eclampsia

	FIGO Survey* (percentage of countries where treatment is commonly used)	Obstetricians' survey** (percentage of obstetricians using the treatment in the UK and Ireland)
$MgSO_4$ only	40	21
$MgSO_4$ with antihypertensives	24	_

* FIGO Survey, 2001 (61/95)
** Gulmezoglu, 1998