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SPECIAL REPORT

Management of hypertensive disorders in pregnancy

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Which women should be referred?

What are the treatment options?

How should women be followed up?

HYPERTENSION IS THE MOST COMMON MEDICAL COMPLICATION OF PREGNANCY, AFFECTING 8-10% of pregnancies in the UK.[1] It is associated with risks to both the woman and the fetus, with increased risks of pre-eclampsia, preterm delivery, fetal growth restriction, placental abruption and perinatal death.[2]

Although secondary care services take the lead on pregnancies complicated by hypertensive disorders, GPs have an important role to play prior to, during, and after pregnancy.

In June this year, NICE updated its guidelines on hypertensive disorders in pregnancy to reflect advances in the evidence base and identify areas that require ongoing research.[3]

CHRONIC HYPERTENSION

GPs managing hypertension in women of reproductive age should discuss the use of antihypertensive drugs in pregnancy with them. It is important to explain the possible increased risk of congenital abnormalities associated with taking ACE inhibitors, angiotensin receptor blockers (ARBs), and thiazide diuretics in pregnancy, and to discuss the alternative treatments available.

Women with chronic hypertension who are planning a pregnancy should be offered referral to a specialist in hypertensive disorders of pregnancy to discuss the risks and benefits of treatment.

Pregnant women with chronic hypertension should have an immediate discussion regarding any treatment they are currently on, ensuring that they are not taking contraindicated antihypertensives (ACE inhibitors, ARBs, thiazide diuretics) and be referred to secondary care antenatal services.

Blood pressure control

Women who have been started on antihypertensives prior to pregnancy should continue with their existing antihypertensive if safe in pregnancy. ACE inhibitors and ARBs should be stopped in women if they become pregnant (preferably within two working days of notification of pregnancy) and alternative antihypertensive treatment should be discussed.

Consider reducing antihypertensive treatment if there is a sustained »

systolic blood pressure (SBP) < 110 mmHg or sustained diastolic blood pressure (DBP) < 70 mmHg, or if the woman has symptomatic hypotension.

Women who have chronic hypertension (see box 1, below) and are not already on treatment should be offered antihypertensive treatment if they have a sustained SBP ≥ 140 mmHg or DBP ≥ 90 mmHg (see table 1, below).

Labetalol should be considered first line to treat hypertension in pregnant women. If labetalol is not suitable, nifedipine should be considered. Methyldopa may be used if neither labetalol nor nifedipine are suitable.

When using antihypertensives in pregnancy, the target BP should be 135/85 mmHg. This lower target level was shown in the CHIPS trial to be associated with less progression to severe hypertension, with no increase in adverse outcomes for neonates.[5]

Aspirin

Aspirin has been shown to reduce the risk of pre-eclampsia.[6] Women at high risk for pre-eclampsia should be advised to take 75-150 mg per day from 12 weeks' gestation until the birth of the baby (see box 2, below). It remains unclear which dose is better, in terms of effectiveness and safety.

Although use of aspirin in women at high risk of pre-eclampsia is now common practice, it is not a licensed indication for use. Community pharmacies cannot legally sell aspirin for this indication and therefore it needs to be prescribed. This can be started in primary care.

Lifestyle

Women with chronic hypertension or at risk of hypertensive disorders in pregnancy should be given the same advice on exercise, rest and work as any pregnant woman.

Monitoring

Women with chronic hypertension in pregnancy will need more frequent antenatal appointments than women with uncomplicated pregnancies. They may need weekly appointments if BP is poorly controlled, or 2-4 weekly appointments if BP is well controlled.

Box 1

Hypertensive disorders in pregnancy: definitions

Hypertension
Hypertension is defined as a systolic blood pressure (SBP) ≥ 140 mmHg, or diastolic blood pressure (DBP) ≥ 90 mmHg. Severe hypertension is defined as SBP ≥ 160 mmHg or DBP ≥ 110 mmHg. Hypertension in pregnancy can be divided into chronic and gestational hypertension. Both of these are associated with increased risk of pre-eclampsia and HELLP syndrome.

Chronic hypertension
Chronic hypertension refers to hypertension that is present either at the antenatal booking visit or develops in the first 20 weeks. It includes women who have had hypertension (primary or secondary) diagnosed before pregnancy and are taking medication for this.

Gestational hypertension
Gestational hypertension refers to hypertension that develops after 20 weeks' gestation.

Pre-eclampsia
Pre-eclampsia is defined as new onset of hypertension after 20 weeks' gestation and the coexistence of either proteinuria, maternal organ dysfunction (renal, liver, neurological or haematological complications), or uteroplacental dysfunction (e.g. fetal growth restriction).

HELLP syndrome
HELLP syndrome is a triad of haemolysis, elevated liver enzymes and low platelet count; 10-20% of cases of pre-eclampsia are estimated to progress to HELLP syndrome.[4]

Table 1

Antihypertensive drugs used in pregnancy and postnatally[3]

	Pregnancy	Postnatal
First line	Labetalol	Enalapril OR nifedipine if black African/Caribbean ethnic origin (amlodipine if used previously)
Second line	Nifedipine	Enalapril + nifedipine/amlodipine
Third line	Methyldopa	Add atenolol/labetalol in addition to, or instead of, the second agent added
Contraindicated	ACE inhibitors ARBs Diuretics Spironolactone	
Avoid		Diuretics and ARBs if breastfeeding

Box 2

Use of aspirin to prevent pre-eclampsia

Women are considered to be at high risk if they have any of the following:
- A hypertensive disorder in a previous pregnancy
- Chronic kidney disease
- Autoimmune disease
- Diabetes (type 1 or 2)
- Chronic hypertension

They should also be considered high risk if they have more than one of the following moderate risk factors:
- First pregnancy
- Age ≥ 40
- Pregnancy interval ≥ 10 years
- BMI ≥ 35 kg/m^2 at first visit
- Multifetal pregnancy
- Family history of pre-eclampsia

GESTATIONAL HYPERTENSION AND PRE-ECLAMPSIA

Any woman with new onset of hypertension after 20 weeks or symptoms or signs suspicious of pre-eclampsia should be referred for same day assessment at a secondary care antenatal assessment unit.

Assessment

Initial assessment should include measurement of BP to assess severity of hypertension, and looking for symptoms and signs of pre-eclampsia. The most common symptoms are:

- Severe headache
- Visual changes (e.g. blurring, flashes)
- Severe epigastric pain
- Vomiting
- Sudden swelling of the hands, feet, or face

Proteinuria should initially be assessed by dipstick. If the urine dipstick is positive (1+ or more), the urine can be sent for either albumin: creatinine (8 mg/mmol diagnostic threshold) or protein: creatinine ratio (30 mg/mmol diagnostic threshold), to quantify proteinuria. Full blood count (FBC), renal and liver profile should be measured, usually in secondary care.

'Women presenting with suspected pre-eclampsia between 20 and 35 weeks should be offered placental growth factor (PlGF) as a rule-out test'

Women presenting with suspected pre-eclampsia between 20 and 35 weeks of pregnancy should be offered placental growth factor (PlGF) as a rule-out test for pre-eclampsia. PlGF is an angiogenic factor that has high sensitivity and negative predictive value in determining the need for delivery. Recent trial evidence has shown that the availability of PlGF reduces time to clinical diagnosis of pre-eclampsia, and reduces maternal adverse outcomes.[7] It is a relatively new diagnostic test that is being made increasingly available across many parts of the UK. This will allow clinicians to rule out pre-eclampsia with high certainty if the PlGF-based test is normal.

Management

Gestational hypertension: Antihypertensive medication should be started if BP remains ≥ 140/90 mmHg, using the same medication strategy as for women with chronic hypertension (see table 1, p22), and in all women with severe hypertension, aiming for a target BP of 135/85 mmHg or less. In women with severe hypertension, BP should be measured every 15-30 minutes until it is < 160/110 mmHg. BP should then be measured once or twice a week until it is 135/85 mmHg or less. FBC, renal profile, and liver profile should be measured at presentation and then weekly.

The fetal heart should be auscultated at every antenatal appointment. Ultrasound assessment of the fetus should be carried out at diagnosis, and then 2-4 weekly if normal.

Pre-eclampsia: In women with pre-eclampsia, BP should be measured at least every 48 hours, more frequently if admitted to hospital. They should also have FBC, renal profile and liver profile measured twice a week, or three times a week if severe hypertension persists. The fetal heart should be auscultated two weekly and a cardiotocogram should be performed at diagnosis.

Admission to hospital should be considered if there are any of the following concerns:

- Sustained SBP ≥ 160 mmHg
- Any maternal biochemical or haematological investigations that cause concern, for example, a new and persistent:
  — rise in creatinine (≥ 90 μmol/L, ≥ 1 mg/100 ml) or
  — rise in alanine transaminase (> 70 IU/L, or twice upper limit of normal range) or
  — fall in platelet count (< 150,000/μl)
- Signs of impending eclampsia
- Signs of impending pulmonary oedema
- Other signs of severe pre-eclampsia
- Suspected fetal compromise
- Any other clinical signs that cause concern.

INTRAPARTUM CARE

Timing of delivery

Early delivery (< 37 weeks' gestation) should not be planned in women with chronic or gestational hypertension if BP is ≤ 160/110 mmHg, unless there are other indications. Precise timing of delivery in these women should be based on discussions between the woman and a senior obstetrician.

In women with pre-eclampsia, obstetricians may consider early delivery in the presence of the features of severe pre-eclampsia. In women with pre-eclampsia presenting from 37 weeks onwards, birth should be initiated within 24-48 hours.

During delivery

Women with hypertensive disorders in pregnancy should be managed according to NICE guidance on intrapartum care. Women with severe hypertension or severe pre-eclampsia may be given magnesium sulfate, either for prevention of eclamptic fits, or for fetal neuroprotection if very preterm delivery is being considered.

POSTNATAL CARE

Following hypertension in pregnancy

Women who have had chronic or gestational hypertension in pregnancy should have their BP measured:

- Daily for the first two days after birth
- At least once between days 3 and 5 after birth
- As clinically indicated if any medication is changed after birth

The aim should be to keep BP < 140/90 mmHg, with or without antihypertensives. Women should have a review of antihypertensive treatment two weeks after birth usually with their GP (or a specialist), and again at 6-8 weeks after birth. Women with gestational hypertension often need a similar duration of antihypertensive treatment postnatally to the duration of antenatal treatment they required.

'Women should be advised that the need to take antihypertensive medications should not prevent them from breastfeeding'

Women who have not required antihypertensive agents during pregnancy sometimes require medication postnatally. If BP is ≥ 150/100 mm Hg, they should be started on antihypertensive treatment.

In line with management of adults with hypertension outside pregnancy, enalapril should be offered first line to treat postnatal hypertension (see table 1, p22). In women of black African or Caribbean origin, nifedipine should be used first line (or amlodipine if used successfully by the woman previously). If a single agent is not sufficient, »

consider a combination of a calcium channel blocker (such as nifedipine or amlodipine) and enalapril. If not tolerated or ineffective, third line would be the addition of atenolol or labetalol (or swapping one of the agents already being used for atenolol or labetalol).

Women should be advised that the need to take antihypertensive medications should not prevent them from breastfeeding. Although antihypertensive medications can pass into breast milk, they do so in very small amounts and would therefore be unlikely to have any clinical effect on the baby. As most medications are not tested in pregnant and breastfeeding women there will be disclaimers on the manufacturers' information leaflets, but no specific safety concerns have been raised. However, women should be advised to monitor their babies for lethargy, pallor, cold peripheries and poor feeding. It is preferable to avoid diuretics and ARBs in women who are breastfeeding as they may have an effect on breast milk production.

Following pre-eclampsia in pregnancy

Women with pre-eclampsia who did not take antihypertensives before birth should have their BP measured:

- At least four times per day while an inpatient
- At least once on days 3 to 5
- On alternate days until normal (if abnormal on days 3 to 5)

If BP in these women is > 150/100 mmHg, they should be started on antihypertensive treatment.

In women who had pre-eclampsia and did take antihypertensives, BP should be measured:

- Four times a day while inpatients
- Every 1-2 days for up to two weeks after transfer to community care until off treatment and not hypertensive

Consider reducing antihypertensives if BP falls below 140/90 mmHg, and reduce treatment if it is < 130/80 mmHg.

Women should always be asked about epigastric pain and headaches when their BP is being measured. Transfer to community care should only happen when there are no symptoms of pre-eclampsia, BP is ≤ 150/100 mmHg, and blood test results are stable or improving.

Every woman should have a care plan which includes details about:

- Who will provide follow-up care
- Frequency of BP monitoring
- Thresholds for reducing or stopping treatment
- Indications for referral for review
- Self-monitoring for symptoms

GP or specialist review should take place two weeks after transfer to community care, and again at 6-8 weeks after birth (see box 3, above right).

Women who have had pre-eclampsia should have a urinary dipstick test at their 6-8 week check, and if they still have proteinuria, should be seen by their GP or specialist at three months postpartum to assess kidney function. If proteinuria is still present or kidney function is abnormal at three months consider referring for a specialist kidney assessment.

ADVICE ON LONG-TERM PROGNOSIS AND FOLLOW-UP

Women with a hypertensive disorder in pregnancy should be advised that the overall risk of recurrence in future pregnancies is approximately one in five. Consider referral for pre-pregnancy counselling for women who have had hypertensive disorders in pregnancy and delivery before 34 weeks, to discuss possible risks in future pregnancies and strategies to reduce risk.

Women should be advised to aim for or maintain a healthy BMI prior to another pregnancy (18.5-24.9 kg/m^2).

Women should also be made aware of the increased risk of hypertension and cardiovascular disease in later life following a hypertensive disorder in pregnancy (see table 2, below). Whether pre-eclampsia and gestational hypertension result as manifestations of already pre-existing cardiovascular risk or whether they contribute to the pathogenesis of cardiovascular disease

Box 3

Six week postnatal visit checklist for women who have had hypertensive disorders in pregnancy

- Check blood pressure
- Check dipstick urinalysis for proteinuria
- Consider weight check if raised BMI
- Review antihypertensive medication and dose titration
- Discuss feeding method (explain that it is alright to breastfeed while using antihypertensives identified in table 1, p22)
- Discuss mood and mental health
- Discuss contraception
- Discuss risk of recurrence in future pregnancies
- Discuss future cardiovascular risk and how to reduce risk

Table 2

Approximate increases in future cardiovascular risk in women who have had a hypertensive disorder in pregnancy compared with those who have not[3]

Risk of future cardiovascular disease*	Any hypertension in pregnancy	Chronic hypertension	Gestational hypertension	Pre-eclampsia
Hypertension	2-4 times	N/A	2-4 times	2-5 times
Major adverse cardiovascular event	2 times	1.7 times	1.5-3 times	1.5-3 times
Cardiovascular mortality	2 times	No data	No data	2 times
Stroke	1.5 times	1.8 times	May be increased	2-3 times

*Risks are overall estimates summarised from risk ratios, odds ratios and hazard ratios

key points

SELECTED BY

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Hypertension is the most common medical complication of pregnancy, affecting 8-10% of pregnancies in the UK. It is associated with risks to both the woman and the fetus, with increased risks of pre-eclampsia, preterm delivery, fetal growth restriction, placental abruption and perinatal death.

GPs managing hypertension in women of reproductive age should discuss the use of antihypertensives in pregnancy with these women. It is important to explain the possible increased risk of congenital abnormalities associated with taking ACE inhibitors, ARBs, and thiazide diuretics in pregnancy, and discuss the alternative treatments available. Pregnant women with chronic hypertension should have an immediate discussion regarding any treatment they are currently on, ensuring that they are not taking contraindicated antihypertensives (ACE inhibitors, ARBs, thiazide diuretics) and be referred to secondary care antenatal services.

Labetalol should be considered first line to treat hypertension in pregnant women. If labetalol is not suitable, nifedipine should be considered. Methyldopa may be used if neither labetalol nor nifedipine are suitable. When using antihypertensives in pregnancy, the target blood pressure should be 135/85 mmHg. This lower target level was shown in the CHIPS trial to be associated with less progression to severe hypertension, with no increase in adverse outcomes for neonates. Aspirin has been shown to reduce the risk of pre-eclampsia. Women with a high risk for pre-eclampsia should be advised to take aspirin 75-150 mg per day from 12 weeks' gestation until the birth of the baby.

Any new onset of hypertension after 20 weeks or symptoms or signs suspicious of pre-eclampsia should be referred for same day assessment at a secondary care antenatal assessment unit. Women presenting with suspected pre-eclampsia between 20 and 35 weeks of pregnancy should be offered placental growth factor (PlGF) as a rule-out test for pre-eclampsia. PlGF is an angiogenic factor that has high sensitivity and negative predictive value in determining the need for delivery. Recent trial evidence has shown that the availability of PlGF reduces time to clinical diagnosis of pre-eclampsia, and maternal adverse outcomes.

Women with a hypertensive disorder in pregnancy should be advised that the overall risk of recurrence in future pregnancies is approximately one in five. Consider referral for pre-pregnancy counselling for women who have had hypertensive disorders in pregnancy and delivery before 34 weeks, to discuss possible risks in future pregnancies and strategies to reduce risk. Women should be advised to aim for, or maintain, a healthy body mass index prior to another pregnancy (18.5-24.9 kg/m^2). Women should also be made aware of the increased risk of hypertension and cardiovascular disease in later life following a hypertensive disorder in pregnancy.

development later on is unclear.[8] In light of the increased risks, discussions around secondary prevention should include the benefits of stopping smoking, maintaining a healthy lifestyle and a healthy weight.

Women who have suffered from pre-eclampsia but do not have hypertension or proteinuria at the six week check (see box 3, p24) should be informed that the absolute risk of developing end-stage kidney disease is low (although the relative risk is increased), so no further follow-up is necessary.

MENTAL HEALTH AND SUPPORT

Women who have had hypertensive disorders in pregnancy may have had difficult experiences during and after their pregnancy, and physical complications are associated with an increased risk of mental health problems.[9,10] They may need extra support from primary care as well as signposting to appropriate services. Women may find it useful to access information from APEC (Action on Pre-eclampsia), a UK based charity providing information and support to women and families affected by pre-eclampsia, see Useful information box, below.[11]

Competing interests: None

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Useful information

For patients
Action on Pre-eclampsia
https://action-on-pre-eclampsia.org.uk/about-pre-eclampsia

We welcome your feedback

If you wish to comment on this article or have a question for the authors, write to: **editor@thepractitioner.co.uk**