

Prescribing for pregnancy: chronic hypertension

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Abstract

An increasing number of women who become pregnant have pre-existing hypertension. For this group of women, a proportion will develop pre-eclampsia or severe hypertension which can impact on maternal and fetal well-being. Women with raised blood pressure should be offered reliable contraception when they do not wish to conceive and pre-conception counselling to address pregnancy-related concerns and advice on preparation for pregnancy and the use of medicines. For women with a history of hypertension, the smallest number of safe medicines at the lowest effective doses should be used while preparing for and during pregnancy. This article forms part of the series of prescribing for pregnancy and discusses the impact of hypertension on pregnancy, the impact of pregnancy on hypertension and options for treatment.

Key learning points

- ▶ Most women with well-controlled hypertension, managed with labetalol, methyldopa or nifedipine can have normal pregnancy and birth.
- ▶ These women are, however, at an increased risk of developing pre-eclampsia, severe hypertension and stroke.
- ▶ Preconception counselling is useful to optimise general health, rule out secondary causes, ensure medication is compatible with pregnancy and screen for end-organ damage.
- ▶ Women with hypertension should have consultant-led care, additional scans to ensure adequate fetal growth, regular reviews to diagnose pre-eclampsia and prompt treatment of severe hypertension.

Introduction

There has been an increase in the proportion of pregnant women who have chronic hypertension.¹ This may be as a result of women delaying pregnancy and so conceiving at an age when hypertension is more common, as well as an increasing prevalence of obesity and diabetes in the population.¹ High blood pressure (BP) affects up to 10% of pregnancies with most having either gestational hypertension or pre-eclampsia (from 20 weeks onward); nevertheless, some women (up to 3%) will have pre-existing hypertension predating the pregnancy.²⁻⁵ Some women will not have had a formal diagnosis of hypertension if their BP was not checked prior to pregnancy, while others will already be taking antihypertensive medication. A quarter of women with pre-existing hypertension will develop super-imposed pre-eclampsia or develop severe hypertension which can impact on maternal and fetal well-being.⁴ The MBRRACE-UK (Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries across the UK) report from 2016 states that undertreatment of severe hypertension can have fatal consequences for mother and baby.⁶ The aim of antihypertensive medication is to avoid severe hypertension causing haemorrhagic stroke or end organ damage, without compromising placental perfusion pressure (which could lead to fetal growth restriction).^{6,7} Even with mild-to-moderate hypertension, women are more likely to have adverse outcomes in pregnancy, including fetal growth restriction, placental abruption, preterm birth and superimposed pre-eclampsia and it does not seem that tighter control of BP affects these endpoints.^{7,8}

The National Institute for Health and Care Excellence (NICE) recommends that women with pre-existing hypertension should have preconceptual counselling and be managed as a high-risk pregnancy with consultant-led care.⁹ Healthcare professionals who are involved in the care of women of childbearing age

with hypertension should discuss pregnancy plans and arrange access to reliable contraception for those who do not wish to conceive. Women who are considering pregnancy should be offered preconception counselling supported with high-quality information to address pregnancy-related concerns (see box 1). Prepregnancy planning should involve a discussion about maintaining an active lifestyle and optimising general health, including achieving or maintaining a healthy weight (ideally with body mass index [BMI] <30 kg/m²), avoiding excess dietary salt intake, advising on smoking cessation and reviewing medication (prescribed and over-the-counter).^{9,10} Women may need a referral to a maternal medicine clinic to discuss BP targets during pregnancy, monitoring arrangements and antihypertensive treatment options. There should be consideration of changing existing antihypertensive medication to those that are safe to use during pregnancy.

Women who are considering pregnancy should be given advice on vitamin supplementation, including folic acid 400 µg daily (5 mg daily if BMI >30 kg/m² or if another risk factor for neural tube defects is present), which should be started 3 months prior to conception and continued throughout the first trimester, and vitamin D (10 µg per day).¹¹ Women should be advised to avoid vitamin A supplementation as high levels may be teratogenic.

With individualised well managed care, many women with hypertension can anticipate a good outcome for themselves and their baby. This is one of a series of articles that discuss prescribing for pregnancy and should be read in conjunction with the introductory article (*Prescribing for pregnancy: general pre-pregnancy care*).¹⁰

Box 1 Information sources**Family Planning Association (contraception advice and link to local clinics)**

<https://www.sexwise.org.uk/contraception>
<https://www.sexwise.org.uk/where-to-get-help/how-get-help-your-sexual-health>

Action on pre-eclampsia (including patient decision aid)

<https://action-on-pre-eclampsia.org.uk>
<https://action-on-pre-eclampsia.org.uk/wp-content/uploads/2019/11/High-blood-pressure-in-pregnancy-blood-pressure>

NHS Health A to Z

<https://www.nhs.uk/pregnancy/related-conditions/complications/high-blood-pressure/>

NICE Clinical Knowledge Summaries

<https://cks.nice.org.uk/topics/hypertension-in-pregnancy/>

NICE Hypertension in pregnancy

<https://www.nice.org.uk/guidance/ng133>

UK Best Use of Medicines in Pregnancy

<http://www.medicinesinpregnancy.org/>

UK Teratology Information Service

<http://www.uktis.org/>

UK Breastfeeding Network

<https://www.breastfeedingnetwork.org.uk/drugs-factsheets>

USA Lactmed Database

<https://www.toxnet.nlm.nih.gov/newtoxnet/lactmed.htm>

NICE, National Institute for Health and Care Excellence.

How might chronic hypertension affect pregnancy

Preconception counselling is an important opportunity to optimise BP control and improve overall health; it is also imperative, however, that a woman presenting in early pregnancy with a sustained systolic BP ≥ 140 mm Hg, or diastolic BP ≥ 90 mm Hg has a diagnosis of pre-existing hypertension considered and is treated appropriately.⁹ The majority of women with a prepregnancy diagnosis will have had investigations to exclude secondary causes of hypertension.^{12,13} Although the majority will have 'essential' hypertension, some investigations may be appropriate to rule out secondary causes such as renal artery stenosis or aortic coarctation. Assessment for end organ damage, left ventricular hypertrophy (with an ECG and echocardiogram), together with renal function (serum creatinine and quantitative estimate of proteinuria) is advised if this has not been checked before pregnancy.¹³

About a quarter of women with chronic hypertension risk developing superimposed pre-eclampsia, a multiorgan condition leading to widespread endothelial damage potentially causing significant proteinuria, renal and liver dysfunction, fetal growth restriction, intrauterine death, eclampsia and rarely maternal death.^{8,14} The only definitive cure for pre-eclampsia is delivery of the fetus and placenta, which may mean premature birth and operative intervention for the mother. Even without pre-eclampsia, chronic hypertension is associated with up to a 20% risk of fetal growth restriction (defined as birth weight less than the 10th centile) and a twofold increase in intrauterine death, adjusted for demographics (ethnicity, fetal sex, maternal smoking, etc).¹⁵ Furthermore, these women have an increased risk of placental abruption, compared with normotensive women.^{13,15}

All women with hypertension in the first trimester should be offered aspirin from 12 weeks of pregnancy.¹⁶ This intervention can

reduce the risk of developing pre-eclampsia by 15%.¹⁷ Although the standard dose of aspirin in the UK is 75 mg daily, a recent clinical guideline from the Royal College of Obstetricians and Gynaecologists suggests considering an aspirin dose of 150 mg per day for women with hypertension who have a BMI >35 kg/m².¹⁸

All women with hypertension will be offered monthly fetal growth scans from 28 weeks' gestation to exclude fetal growth restriction. Towards the third trimester, more regular appointments for BP monitoring and tests for proteinuria are offered to check for development of pre-eclampsia. As the physiological drop of BP starts to recover in the third trimester, women may need to start or increase antihypertensive medication at this point to avoid severe hypertension or to manage pre-eclampsia.¹⁹

The timing of birth will be based on BP control as well as development of pre-eclampsia or concerns regarding fetal growth.⁹ Most women with chronic hypertension who have had a straight-forward pregnancy with no additional complications are offered induction of labour on or by their estimated due date should they not have spontaneously laboured. Other factors, however, may necessitate moving this date forwards. New research is emerging which suggests that delivery between 38 and 39 weeks' gestation may be beneficial to avoid late onset severe hypertension.¹⁹ Women with pre-eclampsia are likely to be delivered at or by 37 weeks, or soon after diagnosis if affected after 37 weeks.

How might pregnancy affect BP?

There is a physiological reduction in systemic vascular resistance during pregnancy which results in a fall in BP of around 15–20 mm Hg. This may allow some women with a background of hypertension to reduce or stop their medication. BP rises naturally in the third trimester and women should be monitored closely as medication adjustments may be needed. BP monitoring may involve use of a validated home BP monitor suitable for use in pregnancy (<https://stridebp.org/bp-monitors>), which has been found to reduce the need for induction of labour and antenatal admissions.²⁰

Which antihypertensive medication is preferred?

The primary role of antihypertensive medication is to reduce severe hypertension, thus avoiding haemorrhagic stroke and end-organ damage.²¹ The optimal BP for pregnant women with pre-existing hypertension is $\leq 135/85$ mm Hg.⁹ In a study of women with non-severe, non-proteinuric pre-existing hypertension or gestational hypertension, tight control of systolic BP has been shown to be beneficial in reducing the development of severe hypertension without affecting fetal growth.²² It is worth noting that the study excluded women with a systolic BP ≥ 160 mm Hg.

Outside of pregnancy and for women who do not have type 2 diabetes, the first-line treatment for mild hypertension in Caucasian women aged under 55 years is an angiotensin-converting enzyme inhibitor (ACEI) or an angiotensin II receptor antagonist (AIIIRA).¹² Some women will be prescribed these medications for their renoprotective effects in hypertension. In women who are of black African or African-Caribbean origin and who do not have type 2 diabetes, the first-line treatment is a calcium channel blocker (CCB). For women with type 2 diabetes and are of any age or family background, the recommendation is to offer an ACEI or AIIIRA, with AIIIRA being the preferred option for women of black African or African-Caribbean family origin. A beta-blocker is only used as a fourth-line treatment.¹²

NICE recommends continuing with existing antihypertensive treatment if it is safe to use in pregnancy, or switching to an alternative treatment, unless sustained systolic BP is less than 110 mm Hg or sustained diastolic BP is less than 70 mm Hg or the woman has symptomatic hypotension.⁹

In pregnancy, labetalol, nifedipine and methyldopa are recommended options to treat hypertension.⁹ The first-line antihypertensive, as recommended by NICE, is labetalol, a beta-blocker which is an antagonist at α - and β_1 and β_2 adrenergic receptors.^{9,23} This is usually started at a dose of 100 mg twice a day and can be increased to a maximum of 2400 mg daily in divided doses and is the only antihypertensive medication with a licence for the management of hypertension in pregnancy.^{9,24} The paediatric team need to be made aware of any baby exposed to labetalol *in utero* because of the potential increased risk of neonatal hypoglycaemia.²⁵ A modified-release formulation of nifedipine, a dihydropyridine CCB that relaxes smooth muscle and also has tocolytic activity, is a second-line option. The dose of modified-release nifedipine typically ranges from 10 mg twice a day to 40 mg twice a day.²⁴ Methyldopa, a centrally-acting α_2 -adrenergic receptor agonist that reduces sympathetic outflow and reduces blood vessel tone, is usually started at 250 mg 2–3 times per day and has a maximum dose of 3 g per day.^{24,26} Although research has now suggested that methyldopa is less effective at reducing severe hypertension, it has a long safety record for use in pregnancy with follow-up of children exposed *in utero* and therefore is still used preferentially in some units.²⁷ There is a helpful infographic and decision aid for patients to use when discussing these issues, which summarises the advantages and disadvantages of taking treatment, and the differences between the three main medication groups.^{9,28}

ACEIs and AIIIRAs are contraindicated in pregnancy due to their detrimental effects on fetal renal development in the first trimester and growth particularly in the second and third trimester.²⁹ Women should be advised to switch to an antihypertensive medication that is safe for use during pregnancy before conception. Ideally at preconception counselling, new antihypertensives can be prescribed and BP monitoring for early pregnancy organised, when there can be a physiological reduction in BP. NICE guidance states that ACEIs or AIIIRAs should be stopped if a woman finds she is unexpectedly pregnant (preferably within two working days of notification of pregnancy) and a safe alternative offered.⁹

Diuretics are not recommended as a maintenance treatment for hypertension during pregnancy.⁹ Diuretics cause maternal intravascular dehydration at a time where, physiologically, there is a significant increase in maternal plasma volume. In addition, there may be an increased risk of congenital abnormalities and neonatal complications if thiazides or thiazide-like diuretics are used as maintenance during pregnancy.⁹

Severe hypertension (BP $\geq 160/110$ mm Hg) is an emergency situation as the autoregulation of brain perfusion can be overwhelmed leading to haemorrhagic stroke. In these instances, rapid control of BP is required. This may require immediate release oral nifedipine (repeated dose at 30 min intervals) or labetalol (oral or intravenous) or intravenous hydralazine.^{9,26,30} Hydralazine has a direct effect to relax vascular smooth muscle causing vasodilation in arterioles, however, it is associated with a reflex tachycardia and needs consideration of simultaneous preloading with intravenous fluids. Beyond 20 weeks' gestation, severe hypertension can be an indicator for administering magnesium sulphate to prevent eclamptic seizures in women with pre-eclampsia.^{24,31,32}

Are any modifications needed in labour?

If hypertension has been well controlled with medication and the pregnancy has been straightforward, women can aim for a vaginal birth.⁹ Any antihypertensive medication can be continued, although it may not be required if the BP is lowered with regional anaesthesia. During labour, hourly monitoring of the BP is warranted to ensure any increase can be promptly treated.

Ergometrine, an ergot alkaloid, is a uterotonic used in the management of primary postpartum haemorrhage, and should

be avoided in women with a background of hypertension as administration can cause a significant spike in BP.^{33,34} Other uterotonics, such as oxytocin, carboprost and misoprostol (unlicensed indication) can all be used as these do not increase BP. Should there be concerns about renal impairment (either transiently from pre-eclampsia or secondary to chronic hypertension) non-steroidal anti-inflammatory drugs should not be prescribed for analgesia postnatally.

What are the options after birth?

In the postnatal period optimal control of BP remains the goal. The NICE guidance on postpartum management of BP is based on its guideline on the management of hypertension in adults with some modifications for breastfeeding women.^{9,12} Many women with chronic hypertension can convert to their prepregnancy medication immediately after birth. Once-daily regimens are preferred to aid adherence.⁹ NICE recommends offering enalapril to treat hypertension during the postnatal period, or nifedipine or amlodipine for women of black African or Caribbean origin.⁹ Methyldopa needs to be discontinued postpartum due to the association with low mood.³⁵

The ACEI enalapril, beta-blockers (labetalol and atenolol), and CCBs (nifedipine and amlodipine) are compatible with breast feeding.⁹ Although, a small amount will be transferred to breast milk, the level will be lower than the level found in maternal serum and is unlikely to have any clinical effect.⁹ The benefits of breastfeeding outweigh the theoretical risk to the infant from antihypertensive medication.^{36,37} Nevertheless, women are advised to monitor their babies for drowsiness, lethargy, pallor, cold peripheries or poor feeding.⁹ Women who had not received antihypertensive medication prior to pregnancy but whose BP was elevated in early pregnancy and therefore may have had undetected chronic hypertension may require long-term treatment as outlined above. However, if hypertension onset was after 20 weeks, postnatal antihypertensive treatment may only be needed for a few weeks.

For women with chronic hypertension or gestational hypertension, NICE recommends daily BP readings on the first 2 days after birth and at least once between day 3 and 5 postpartum, when there is a physiological rise in BP.⁹ After discharge, the BP and any medication should be reviewed at 2 weeks post partum and again at 6 weeks by the GP or Maternity Unit. This review should include contraceptive advice if this was not provided prior to discharge after birth and prepregnancy counselling for future pregnancy.⁹ Guidance on the choice of contraceptive in women with hypertension is included in the UK Medical Eligibility Criteria for Contraceptive Use published by The Faculty of Sexual Health of the Royal College of the Obstetricians and Gynaecologists.³⁸

Conclusion

The numbers of women with pre-existing hypertension during pregnancy is likely to increase. These women need specialist care to ensure they embark in pregnancy in optimal health, with knowledge of pregnancy-safe medications and potential outcomes. The Action on Pre-eclampsia website (<https://action-on-pre-eclampsia.org.uk>) can be a useful resource for women and health professionals. With good care, many women will maintain good BP control and will have healthy babies. The added risks for pregnant women with hypertension need to be discussed and frequent antenatal reviews need to screen for developing pre-eclampsia and fetal growth restriction. Any changes in BP need to be effectively managed, potentially requiring an increase in antihypertensive medication, and severe hypertension rapidly treated.

Information for patients

If you are taking medicines to manage high blood pressure you should use reliable contraception when you do not wish to be pregnant. When you are considering becoming pregnant, please discuss this with your healthcare team before stopping contraception. In order to achieve the best outcome for mother and baby, any medication that you are taking to manage high blood pressure should be reviewed before pregnancy. Some changes may be needed to ensure the most appropriate medicines are used for treating your high blood pressure. Please speak to your doctor before making any changes to your medication.

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