Hypertension - drug therapy

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Blood pressure achieved: continue therapy with regular follow-up
1 Background information

Quick info:

Scope:
- diagnosis and management of hypertension in adults in primary care
- aetiology of essential and secondary hypertension
- assessment and referral criteria for suspected secondary hypertension
- emergency referral criteria for suspected hypertensive crisis
- appropriate blood pressure (BP) measuring technique
- assessment of patients with previously known/unknown hypertension
- assessment of cardiovascular risk and managing other cardiovascular risk factors
- non-pharmacological and lifestyle interventions for treating hypertension
- pharmacological interventions for treating hypertension
- clinical conditions associated with hypertension
- assessment of end-organ damage

Out of scope:
- hypertension in children
- hypertension in pregnancy
- hypertension in patients with diabetes
- specialist management of secondary hypertension
- specialist management of hypertensive crises

Definition:
- sustained systolic blood pressure (SBP) of 140mmHg or more and/or diastolic blood pressure (DBP) of 90mmHg or more in the surgery
- thresholds for hypertension are:
  - stage 1 hypertension:
    - surgery BP 140/90mmHg or higher
    - ABPM daytime average or HBPM average 135/85mmHg or higher
  - stage 2 hypertension:
    - surgery BP 160/100mmHg or higher
    - ABPM daytime average or HBPM average 150/95mmHg or higher
  - severe hypertension:
    - surgery systolic BP 180mmHg or higher
    - surgery diastolic BP 110mmHg or higher
- 'white coat' hypertension – BP unusually raised when measured during consultations with clinicians, but normal when measured in 'non-threatening' situations:
  - occurs in approximately a third of people with mildly elevated BP
  - less likely to occur in people with higher BPs
- resistant/refractory hypertension – hypertension despite prescribing adequate doses of at least three drugs (including a diuretic) and lifestyle advice
- accelerated/malignant hypertension – BP higher than 180/110mmHg with signs of papilloedema or retinal haemorrhage (hypertensive retinopathy)

Aetiology:
- primary (or essential) hypertension:
  - no identifiable cause
  - accounts for approximately 95% of people with hypertension
- secondary hypertension:
  - a result of a known underlying cause
  - accounts for approximately 5% of people
Incidence and prevalence:
• 30-40% of adults in England – proportion increases with age
• in England and Wales, hypertension-related mortality is 3.5 times higher in people of African-Caribbean descent
• hypertension-associated mortality rate is 1.5 times higher in British Asian patients than the national average

Risk factors:
• age – over age 55 years for men and over age 65 years for women
• smoking
• race or ethnicity – higher risk with African, Caribbean, and South Asian origin
• genetic predisposition
• diet – high salt and fat intake
• physical inactivity
• obesity – body mass index (BMI) of 30kg/m² or more

Complications:
• hypertension is responsible for more deaths and disease than any other biomedical risk factor worldwide
• left ventricular hypertrophy
• angina pectoris
• risk of the following is increased by 2-4 times in patients with hypertension:
  • stroke
  • myocardial infarction (MI)
  • cardiac failure
  • peripheral vascular disease (PVD)

References:

2 Patient information

Quick info:
http://www.bpassoc.org.uk
http://www.hbpf.org.uk
http://www.patient.co.uk/health/High-Blood-Pressure-(Hypertension).htm

3 Key messages for this pathway

Quick info:
This pathway has been locally developed for South West Hampshire.
Key messages:
• first line treatment ACE inhibitor or ARB if <55 years, CCB (e.g. amlodipine) if >55 years)
• step 2 treatment should be ACE inhibitor or ARB, combined with a CCB
• NICE recommend clortalidone or indapamide if a thiazide type diuretic is used

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4 Adverse effects of treatment

Quick info:

Monitor for adverse effects from treatment:

- new symptoms:
  - cough (occurs in about 15% or patients taking an ACE inhibitor) – if troublesome, consider switching to an ARB
  - cold extremities, paraesthesia, and numbness (more common in patients with peripheral vascular disease) – consider stopping beta-blockers
  - fatigue
  - constipation – may occur when taking verapamil
  - impotence or loss of libido – reversible on withdrawal of treatment
  - gout
  - sleep disturbance or nightmares – less likely with water-soluble beta-blockers
  - gingival hyperplasia – commonly associated with calcium-channel blockers, and disappears on withdrawal
  - diabetes – thiazide-type diuretics may the increase risk of new-onset diabetes
  - signs of hypoglycaemia eg tremor, tachycardia – can be masked by non-selective beta-blockers
- biochemical:
  - deterioration in renal function
  - electrolyte imbalances
    - hyperkalaemia – check urea and electrolytes 1-2 weeks after starting ACE-inhibitor or angiotensin II receptor antagonist (ARB), or increasing dose
    - hypokalaemia – can occur with thiazide-type diuretics
- cardiovascular:
  - bradycardia – may occur when taking diltiazem or verapamil
  - orthostatic hypotension – consider reducing dose or stopping angiotensin converting enzyme (ACE) inhibitor/diuretic/any concomitant drugs known to reduce BP, and seek expert advice
  - vasodilatory adverse effects – less common with rate-limiting calcium-channel blockers than dihydropyridine calcium-channel blockers, and improve with continued use
  - dehydration

5 Recommended actions if biochemistry abnormal at review

Quick info:

- if serum creatinine or potassium increase unacceptably, consider stopping or reducing the dose of the following (if patient is taking them):
  - nephrotoxic drugs, such as nonsteroidal anti-inflammatory drugs (NSAIDs)
  - vasodilators, such as calcium-channel blockers and nitrates
  - potassium supplements or potassium-sparing diuretics
  - diuretics – reduce dosage if patient is hypovolaemic
- if serum creatinine:
  - persists above 50% of baseline (or greater than 265micromol/L) – halve the dose of ACE inhibitor or ARB and recheck in 5-7 days
  - persists above 100% of baseline (or greater than 310micromol/L) – stop ACE inhibitor or ARB immediately and seek specialist advice
  - increases by 30% or more with a large decrease in BP soon after starting treatment – investigate for possible renovascular disease
- if serum potassium:
6 Hypertension: indications for drug therapy

Quick info:
Drug therapy helps to reduce the incidence of stroke, coronary heart disease, and overall mortality.
Offer antihypertensive drug treatment to people aged <80 years with stage 1 hypertension (surgery BP $\geq 140/90$mmHg and ABPM or HBPM $>135/85$mmHg) if:

- target organ damage
- established cardiovascular disease
- renal disease
- diabetes
- 10 year cardiovascular risk $\geq 20$

Offer antihypertensive drug treatment to all people with stage 2 hypertension (surgery BP $\geq 160/100$mmHg and ABPM or HBPM $\geq 150/95$mmHg).

Offer antihypertensive drug treatment to all people with severe hypertension (surgery systolic BP $\geq 180$mmHg or diastolic BP $\geq 110$mmHg) without ABPM or HBPM.

7 Blood pressure goals on treatment

Quick info:
Target blood pressure on treatment using surgery blood pressure:

**In the absence of diabetes:**

- $<140/90$mmHg, in people under 80 years
- $<150/90$mm Hg in people aged 80 years and over

**In patients with type 2 diabetes mellitus:**


- $<130/80$mmHg if eye, kidney or cerebrovascular damage
- $<140/80$mmHg if no target organ damage

Consider ambulatory or home BP monitoring, especially if 'white-coat effect'. Target BP in people without diabetes is an average during usual waking hours of:

- $<135/85$mmHg, in people under 80 years
- $<145/85$mm Hg in people aged 80 years and over

NB: Provide appropriate guidance and materials to patients about the benefits of drugs and the side-effects sometimes experienced, to help the patient make an informed choice.

8 Manage other cardiovascular risk factors according to risk calculation

Quick info:
Consider using QRISK®2-2011 risk calculator [http://qrisk.org/]:

- Consider statin treatment (first line simvastatin 40mg) if patient has:
  - clinically-apparent CVD – aim for:
    - serum total cholesterol of less than 4.0mmol/L (minimum audit standard <5.0mmol/L)
    - low-density lipoprotein (LDL) cholesterol of less than 2.0mmol/L (minimum audit standard <3.0mmol/L)
    - 20% or higher 10 year risk of developing CVD
• Only consider low dose aspirin for secondary prevention in patients with cardiovascular disease. Consider clopidogrel for people who cannot tolerate aspirin

9 Provide lifestyle advice

Quick info:
Advertise patient on:
• stopping smoking
• losing weight if needed
• aerobic exercise (eg walking, jogging, cycling) for 30-60 minutes 3-5 times a week
• healthy eating:
  • reducing salt intake
  • increasing fruit and vegetable intake
• reducing:
  • alcohol consumption
  • caffeine intake
• relaxation techniques:
  • stress management
  • meditation
  • cognitive therapies
  • muscle relaxation
  • biofeedback
• avoiding nonsteroidal anti-inflammatory drugs (NSAIDs) if possible
Offer appropriate guidance and written or audiovisual materials to promote lifestyle changes.
NB: Trials have shown that the combination of exercise and diet can reduced systolic and diastolic BP by approximately 4-5mmHg. By lowering BP and cardiovascular risk, the need for long-term drug therapy may be reduced, delayed, or removed.

10 Consider step 1 drug treatment

Quick info:
Consider pharmacological treatment with:
• once or twice daily dosing where possible as this may improve adherence compared with multiple daily dosing
• non-proprietary (generic) medication where appropriate to minimise cost

11 Patients younger than age 55 years and not black African/Caribbean

Quick info:
For patients under age 55 years (not black African/Caribbean), begin with an angiotensin converting enzyme (ACE) inhibitor – consider:
• ramipril capsules (first line)
• enalapril
• lisinopril
If ACE inhibitor is not tolerated or unsuitable, prescribe an angiotensin-II receptor antagonist (ARB):
• losartan
• candesartan
ACE inhibitors and ARBs are contra indicated if the patient:
• has a history of angioedema associated with previous exposure to an ACE inhibitor

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Hypertension - drug therapy

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• has hereditary or idiopathic angioedema
• has bilateral renal artery stenosis
• is pregnant or of child bearing age
If the patient is breastfeeding, consider captopril or enalapril.
If ACE inhibitors or ARBs are not suitable, start a calcium-channel blocker or low dose thiazide-type diuretic.
Consider a beta-blocker for initial treatment only if the patient meets the following criteria:
• intolerance or contraindication to ACE inhibitors and ARBs
• women of child bearing potential
• has increased sympathetic drive
Consider the following beta-blockers:
• atenolol – preferred for low cost
• if patient has heart failure consider:
  • bisoprolol
  • carvedilol

12 Patients older than age 55 years or black African/ Caribbean

Quick info:
For patients age 55 years and older or those of African or Caribbean descent (any age):
• begin with dihydropyridine calcium-channel blocker (CCB):
  • amlodipine
  • modified-release nifedipine (specify brand, e.g Coracten XL or Adalat LA)

• if CCB not suitable (e.g. oedema, intolerance or heart failure) offer a thiazide-like diuretic:
  • Bendroflumethiazide is no longer recommended as first choice thiazide-like diuretic in hypertension, but should be continued in existing patients if BP is stable and well controlled.
  • If a diuretic is started or changed, give:
    • chlortalidone - NICE Guidelines advise 12.5-25mg once daily (licensed dose 25-50mg daily) . The 50mg tablets are scored and may be halved. The 12.5mg dose is difficult to deliver accurately in the UK currently and so should therefore be avoided where possible.
    • indapamide - 2.5mg once daily or 1.5mg modified release once daily.
  • rate-limiting calcium-channel blockers:
    • diltiazem (modified-release) – once daily (specify brand, e.g. Viazem XL or Slozem)
    • verapamil (modified-release) – once daily

13 Review

Quick info:
Review patient:
• measure blood pressure (BP) at least once a month until BP is less than 140/90mmHg
• the maximum effect of almost all antihypertensive drugs is achieved within 3 weeks of starting or changing doses
• the majority (over two thirds) of patients will fail adequate BP control with monotherapy. Combination of two or more drugs has been most widely used to reduce BP effectively
• consider factors affecting BP control, eg:
  • use of over the counter medication, prescription medication, illicit drugs, or alcohol
  • poor adherence to therapy
Check biochemistry:
14 Consider step 2 drug treatment

Quick info:
If blood pressure (BP) is not adequately controlled, consider step 2 drug therapy. Using two drugs at less than maximum dosage (usually half maximum recommended dosage) often gives better blood pressure control than titrating a single drug to maximum dosage. Dosages can be increased once two drug treatment is established.

If patient is taking:
- angiotensin converting enzyme (ACE) inhibitor or angiotensin-II receptor blockers (ARB), add one of the following:
  - calcium-channel blocker - preferred treatment
  - thiazide-like diuretic
  - calcium-channel blocker or thiazide-like diuretic, add either:
    - ACE inhibitor; or
    - ARB (if ACE intolerant to inhibitors or for black people of African or Caribbean family origin)

Important notes:
- do not use an ACE inhibitor in combination with an ARB (except for diabetic nephropathy; in other situations combination less effective)
- do not use a beta-blocker with a thiazide-like diuretic (increased risk of developing diabetes)
- do not use a beta-blocker with verapamil (risk of bradycardia and heart failure)

Local Formulary Choices are as follows:
ACE Inhibitors
- Ramipril capsules (first choice)
- Enalapril or Lisinopril tablets

ARBs
- Losartan
- Candesartan

Calcium Channel Blockers
- Amlodipine tablets
- Nifedipine modified-release (e.g Coracten XL or Adalat LA)

Calcium Channel Blockers (rate-limiting)
- Diltiazem modified-release (e.g. Viazem XL or Slozem)
- Verapamil modified-release

Thiazide-like Diuretic
- Bendroflumethiazide is no longer recommended first line (but can still be used for existing patients)
- Chlortalidone or Indapamide

15 Target blood pressure achieved: continue therapy with regular follow-up

Quick info:
If blood pressure (BP) is adequately controlled:
- continue with medication
• monitor for adverse effects – monitor renal function (urea and electrolytes) in people on thiazide diuretics, angiotensin converting enzyme (ACE) inhibitors, or angiotensin-II receptor antagonists (ARB)
• reassess cardiovascular risk and monitor for symptoms of cardiovascular disease (CVD)
• follow-up:
  • at least annually to provide patients with support, discuss their lifestyle, symptoms, and medication
  • may need to be done every 3-6 months depending on co-morbidities, associated diseases, and need for laboratory testing
Consider decreasing dosage or number of antihypertensive drugs while continuing lifestyle modification only if BP is adequately controlled for at least 1 year. If appropriate, withdraw drugs gradually.

16 Review

Quick info:
Review patient:
• measure blood pressure (BP) at least once a month until BP is less than 140/90mmHg
• the maximum effect of almost all antihypertensive drugs is achieved within 3 weeks of starting or changing doses
• the majority (over two thirds) of patients will fail adequate BP control with monotherapy. Combination of two or more drugs has been most widely used to reduce BP effectively
• consider factors affecting BP control, eg:
  • use of over the counter medication, prescription medication, illicit drugs, or alcohol
  • poor adherence to therapy
Check biochemistry:
• if using thiazide diuretic – check serum potassium at:
  • baseline; and
  • 4-6 weeks after starting treatment
• if using ACE inhibitor or ARB – check serum urea and electrolytes, and estimated glomerular filtration rate (eGFR) at:
  • baseline; and
  • 1-2 weeks after starting treatment
See “recommended actions if biochemistry abnormal at review” box.

17 Consider step 3 drug treatment

Quick info:
If blood pressure (BP) is not adequately controlled, review medication to ensure step 2 treatment is at optimal or best tolerated doses. Then consider step 3 drug therapy:
• a combination of ACE inhibitor or angiotensin II receptor blocker, calcium channel blocker and thiazide diuretic should be used
Local Formulary Choices are as follows;
ACE Inhibitors
• Ramipril capsules (first choice)
• Enalapril or Lisinopril tablets
ARBs
• Losartan
• Candesartan
Calcium Channel Blockers
• Amlodipine tablets
• Nifedipine modified-release (e.g Coracten XL or Adalat LA)
Calcium Channel Blockers (rate-limiting)
• Diltiazem modified-release (e.g. Viazem XL or Slozem)
• Verapamil modified-release
Thiazide-like Diuretic

- Bendroflumethiazide is no longer recommended first line (but can still be used for existing patients)
- Chlortalidone or Indapamide

18 Target blood pressure achieved: continue therapy with regular follow-up

Quick info:
If blood pressure (BP) is adequately controlled:
- continue with medication
- monitor for adverse effects – monitor renal function (urea and electrolytes) in people on thiazide diuretics, angiotensin converting enzyme (ACE) inhibitors, or angiotensin-II receptor antagonists (ARB)
- reassess cardiovascular risk and monitor for symptoms of cardiovascular disease (CVD)
- follow-up:
  - at least annually to provide patients with support, discuss their lifestyle, symptoms, and medication
  - may need to be done every 3-6 months depending on co-morbidities, associated diseases, and need for laboratory testing
Consider decreasing dosage or number of antihypertensive drugs while continuing lifestyle modification only if BP is adequately controlled for at least 1 year. If appropriate, withdraw drugs gradually.

19 Review

Quick info:
Review patient:
- measure blood pressure (BP) at least once a month until BP is less than 140/90mmHg
- the maximum effect of almost all antihypertensive drugs is achieved within 3 weeks of starting or changing doses
- the majority (over two thirds) of patients will fail adequate BP control with monotherapy. Combination of two or more drugs has been most widely used to reduce BP effectively
- consider factors affecting BP control, eg:
  - use of over the counter medication, prescription medication, illicit drugs, or alcohol
  - poor adherence to therapy
Check biochemistry:
- if using thiazide diuretic – check serum potassium at:
  - baseline; and
  - 4-6 weeks after starting treatment
- if using ACE inhibitor or ARB – check serum urea and electrolytes, and estimated glomerular filtration rate (eGFR) at:
  - baseline; and
  - 1-2 weeks after starting treatment
See "recommended actions if biochemistry abnormal at review" box.

20 Consider step 4 drug treatment

Quick info:
If blood pressure (BP) is not adequately controlled with optimal or best tolerated doses of step 3 treatment, the patient has resistant hypertension.
Consider step 4 drug therapy or seek expert advice.
Consider:
- adding another diuretic, eg spironolactone if serum potassium ≤4.5mmol/L. Caution if reduced eGFR
- increasing dose of thiazide-like diuretic if serum potassium >4.5mmol/L
- if further diuretic therapy is not tolerated, contraindicated or ineffective, add an alpha blocker or beta blocker
  - doxazosin (avoid if history of postural hypotension)
21 Target blood pressure achieved: continue therapy with regular follow-up

Quick info:
If blood pressure (BP) is adequately controlled:
- continue with medication
- monitor for adverse effects – monitor renal function (urea and electrolytes) in people on thiazide diuretics, angiotensin converting enzyme (ACE) inhibitors, or angiotensin-II receptor antagonists (ARB)
- reassess cardiovascular risk and monitor for symptoms of cardiovascular disease (CVD)
- follow-up:
  - at least annually to provide patients with support, discuss their lifestyle, symptoms, and medication
  - may need to be done every 3-6 months depending on co-morbidities, associated diseases, and need for laboratory testing
Consider decreasing dosage or number of antihypertensive drugs while continuing lifestyle modification only if BP is adequately controlled for at least 1 year. If appropriate, withdraw drugs gradually.

22 Review

Quick info:
Review patient:
- measure blood pressure (BP) at least once a month until BP is less than 140/90mmHg
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- the majority (over two thirds) of patients will fail adequate BP control with monotherapy. Combination of two or more drugs has been most widely used to reduce BP effectively
- consider factors affecting BP control, eg:
  - use of over the counter medication, prescription medication, illicit drugs, or alcohol
  - poor adherence to therapy
Check biochemistry:
- if using thiazide diuretic – check serum potassium at:
23 Blood pressure uncontrolled or symptomatic postural hypotension

Quick info:
Consider referral to specialist if:
- secondary hypertension suspected
- postural hypotension is symptomatic, or systolic blood pressure (SBP) decreases by 20mmHg or more on standing up
- blood pressure (BP) is unusually variable
- BP is not adequately controlled on optimal primary care treatment
- multiple drug intolerance

24 Target blood pressure achieved: continue therapy with regular follow-up

Quick info:
If blood pressure (BP) is adequately controlled:
- continue with medication
- monitor for adverse effects – monitor renal function (urea and electrolytes) in people on thiazide diuretics, angiotensin converting enzyme (ACE) inhibitors, or angiotensin-II receptor antagonists (ARB)
- reassess cardiovascular risk and monitor for symptoms of cardiovascular disease (CVD)
- follow-up:
  - at least annually to provide patients with support, discuss their lifestyle, symptoms, and medication
  - may need to be done every 3-6 months depending on co-morbidities, associated diseases, and need for laboratory testing

Consider decreasing dosage or number of antihypertensive drugs while continuing lifestyle modification only if BP is adequately controlled for at least 1 year. If appropriate, withdraw drugs gradually.
Hypertension - drug therapy

Key Dates

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Evidence summary for Hypertension - drug therapy

This pathway has been developed according to the Map of Medicine editorial methodology (http://mapofmedicine.com/whatisthemap/editorialmethodology). The content of this pathway is based on high-quality guidelines [1,2,4,5,6], critically appraised meta-analyses and systematic reviews [8]. Practice-based knowledge has been added by contributors with front-line clinical experience [3,7], including any literature endorsed by the contributor group [9].

References

This is a list of all the references that have passed critical appraisal for use in the care map Hypertension

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