Clinical Pharmacology of Hypertension

Defining hypertension

Normal blood pressure is 120/80
Grade 1 Hypertension is 140/90
Grade 2 Hypertension is 160/100
Grade 3 Hypertension is 180/110

Lifestyle advice

People with high blood pressure should be provided with the following advice to try and bring it under control:

- Adopt a healthy, low-calorie diet
  - Shown to lower systolic and diastolic BP by about 5-6mmHg over the course of a year
- Take regular aerobic exercise
  - 30-60 minutes three to five times per week - brisk walking, cycling, jogging
  - Shown to lower systolic and diastolic BP by about 2-3mmHg over the course of a year
- If alcohol consumption is excessive, cut it down
  - Shown to lower systolic and diastolic BP by about 3-4mmHg over the course of a year
- Reduce caffeine consumption
- Reduce salt consumption
- Stop smoking
  - Though there is little conclusive evidence to say that this helps.

Drug therapy

Drug therapy should be offered to patients

- Whose BP is persistently above 160/100
- Whose BP is persistently above 140/90 if there are significant other CV risk factors (10yr risk of CVD of 20% or more)

Target BP should be 140/90
In patients under 55, drug sequence should be...

- ACE inhibitor
- Add Calcium channel blocker or Thiazide diuretic
- Add Calcium channel blocker or Thiazide diuretic (whichever is not already being used!)
- Add a higher dose of diuretic, beta blockers, or selective alpha-blockers
In patients over 55, drug sequence should be...

- Calcium channel blocker or Thiazide diuretic
- Add ACE inhibitor
- Add Calcium channel blocker or Thiazide diuretic (whichever is not already being used!)
- Add a higher dose of diuretic, beta blockers, or selective alpha-blockers

All patients on medication for hypertension should be reviewed at least yearly.

ACE inhibitors

1) Angiotensin-converting enzyme inhibitors such as enalapril or lisinopril are effectively vasodilators.
2) ACEI reduce amounts of Angiotensin II and Aldosterone
   a) ACE normally converts Angiotensin I to Angiotensin II, so stopping this effect leads to a reduced amount of Angiotensin II, and hence a reduced amount of aldosterone, whose release is stimulated by Angiotensin II.
   b) Angiotensin II normally causes vasoconstriction - ACE inhibitors block this.
   c) Aldosterone normally makes the kidneys retain sodium, and hence increases blood volume, and hence increases blood pressure. With ACE inhibitors, sodium is more easily lost, and hence blood volume reduced.
3) ACEI increase amounts of bradykinin (but this is something of a secondary effect)
   a) ACE usually inactivates bradykinin. If you inhibit this effect, bradykinin levels will increase.
   b) Bradykinin is a vasodilator. It also increases vascular permeability, causes secretion of fluids in the GI tract and respiratory tract, and contracts intestinal and uterine smooth muscle.
4) ACEI can cause coughs, hypotension (with associated dizziness and headache), diarhoea, and muscle cramps.
   a) Coughs are caused by increased fluid secretion caused by increased bradykinin
   b) Diaorhoea is caused by increased contraction of gut smooth muscle
   c) Because of hypotension, the drug should be given just before bed
5) ACEI should not be given in pregnancy, renovascular disease, or aortic stenosis
   a) Contraindicated in pregnancy due to increased uterine muscle contraction
   b) Renovascular disease refers primarily to renal artery stenosis
      i) If the renal artery is permanently stenosed, then GFR is maintained by constricting the efferent arteriole, and thus increased glomerular pressure.
      ii) If you then give something that causes vasodilation, the efferent arteriole will dilate, and GFR will not be maintained
      iii) Renal failure follows, because the kidneys are not adequately perfused
6) ACEI are really good because...
   a) They reduced blood pressure without affecting heart rate or cardiac output
   b) They also protects diabetics from functional renal nephropathy (though why is not known...)
Calcium channel blockers

1. Some of these work as vasodilators, whereas others work on smooth muscle or cardiac muscle.
   a. Muscle actions...
      i. Calcium is needed for muscle to contract.
      ii. Calcium channel blockers delay this calcium getting into the cell.
      iii. Therefore, each cell is able to contract a little less strongly.
   b. Vasodilatory actions...
      i. Certain types of calcium channel blockers cause vasodilation, by working on vascular smooth muscle via a similar process.

2. Nifedipine works primarily on vascular smooth muscle, and has very little effect on the heart itself.
   a. This is good because...
      i. It rarely causes heart failure
      ii. It dilates the coronary arteries, which helps with angina pain
      iii. The vasodilation is good for Reynaud's
   b. But bad because...
      i. It doesn't help with arrhythmias
      ii. Like ACEI, it can't be used in renal artery stenosis

3. Verapamil works primarily on the heart, and has little effect on vascular smooth muscle.
   a. This is good because...
      i. It reduces cardiac output, slows the heart, and impairs AV conduction, thus reducing strain on the heart and reducing blood pressure.
      ii. The slowed AV conduction helps with arrhythmias
   b. But bad because...
      i. It can go too far and precipitate heart failure
      ii. It can exacerbate underlying conduction disorders
      iii. It cannot be used alongside beta-blockers
      iv. You can't drink grapefruit juice with it, as it impairs its metabolism
      v. It can give you constipation

4. Diltiazem is somewhere in the middle, doing a bit with the heart and a bit with smooth muscle
   a. This is good because...
      i. It's an all-rounder, and does nothing to excess
   b. But bad because...
      i. It can't be used alongside beta-blockers

Thiazide Diuretics

The traditional view is that these work by reducing blood volume, but recent research says that they actually work via a calcium-channel blocking mechanism.

Bendroflumethiazide works by inhibiting the sodium / chloride co-transporter in the early distal tubule of the kidney. You pee out more magnesium and potassium whilst on them, but retain sodium and uric acid.

Angiotensin II Antagonists

The place for these in hypertension therapy is fairly uncertain. They work by inhibiting angiotensin II receptors. Since (as discussed above) angiotensin II normally causes vasoconstriction, these drugs effectively cause vasodilation. The important one to know the name of is losartan.
Beta-blockers

Beta-receptors normally cause increased force and rate of heart contraction, so it is logical that beta-blockers reduce these things, and thus cause lower blood pressure. However, as this is the only way that beta-blockers work to reduce hypertension, and given that there are many side effects, other hypertensives are generally considered to be better. Therefore, beta blockers have suddenly gone out of fashion.

Like other drugs that slow the heart, it is important not to prescribe them in people that already have heart conduction problems. Propranolol has lots of non-cardiac side effects, including GI disturbances, sleep disturbances, and visual disturbances. Atenolol is water, rather than fat, soluble, and so avoids many of the side effects, as it is less likely to cross the blood-brain barrier. Carvedilol is a specially modified beta-blocker, manufactured to cause vasodilation; unfortunately, it's not particularly effective, and so doesn't have much benefit over the other beta-blockers.

Hypertension in pregnancy

This is quite a difficult subject, since none of the normal drugs can be used. Instead, methyldopa must be used, which is a centrally acting antihypertensive.

Please Note

These notes were written by Simon Howard as a medical student in 2007. They are presented in good faith and every effort has been taken to ensure their accuracy. Nevertheless, medical practice changes over time and it is always important to check the information with your clinical teachers and with other reliable sources. Disclaimer: no responsibility can be taken by either the author or publisher for any loss, damage or injury occasioned to any person acting or refraining from action as a result of this information.