Hypertension and diabetes

Hypertension is the UK's single most common medical condition[1] and there is no greater evidence-base in clinical practice for the management of hypertension. Hypertension is also an important risk factor for the development and worsening of many complications of diabetes, including diabetic eye disease and kidney disease. Most people with diabetes develop high blood pressure during their life and having diabetes increases your risk of developing high blood pressure and other cardiovascular problems.

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Hypertension has a prevalence of 30–40% in the UK's adult population with its incidence increasing with age such that approximately 60% of 65 year olds are hypertensive.[2] It affects 50% of black people over 40 years of age and in patients with type 2 diabetes mellitus almost three quarters are hypertensive.[2]

Hypertension tends to cluster with other cardiometabolic risk factors such as age, gender, ethnicity, smoking, lipid status and family history.[2] For both men and women the effect of blood pressure increases the relative risk of cardiovascular disease by two to four-fold comparing optimal blood pressure <120/80mmHg to high normal blood pressure <140/90mmHg.[3]

Increasing age, the presence of obesity, and worsening renal function all contribute to an increased likelihood of hypertension in people with diabetes. With increasing obesity, physical inactivity, and the ageing of the population, diabetes and hypertension are crucial public health concerns for the 21st century. Control of blood pressure (BP) among patients with diabetes can affect important CVD outcomes because the relationship between BP and risk of CVD events is continuous, consistent, and independent of other risk factors.[4]

Diagnosis and assessment

The British Hypertension Society recommends checking BP every five years as a minimum and if >130/85mmHg then annually. To identify hypertension (blood pressure persistently >140/90mmHg) the new NICE/BHS guidance recommends ambulatory blood pressure monitoring (ABPM) is undertaken since this appears to be the best predictor of cardiovascular events[1] compared to clinic based-blood pressure monitoring (CBPM)/home blood pressure monitoring (HBPM). However, this has major resource implications either in terms of GP acquisition of costly ABPM machines or referral on to secondary care for such measurement.

If average daytime blood pressure on ABPM is >135/85mmHg hypertension is diagnosed. Stage 1 hypertension is >140/90mmHg (135/85 ABPM); stage 2 hypertension >160/100mmHg (150/95ABPM); severe hypertension >180/100mmHg. Stage 1 requires treatment if ten year cardiovascular risk is >20% or if target organ damage exists. Stage 2 requires treatment.

Pragmatically HBPM readings give a good approximation to ABPM. It is advised that blood pressure readings are taken twice daily ideally am and pm for at least four and preferably seven days. In calculating the average the first day's readings are discarded (as tend to be atypically high) and an average created (to confirm hypertension with blood pressure >135/85mmHg).

Both ABPM and HBPM appear to impress on patients the veracity of their hypertension diagnosis and therefore enhance concordance with lifestyle changes and use of pharmacotherapy.

Hypertension investigations aim to detect a secondary cause for raised blood pressure and target organ damage. So renal function tests, lipid profile, fasting blood sugar and urinalysis are undertaken along with electrocardiogram (to detect left ventricular hypertrophy).

In young hypertensives especially or those with refractory hypertension it is worth including an aldosterone: renin ratio to identify patients with primary hyperaldosteronism[5] and urinary vanillylmandelic acid for phaeochromocytoma. However, over 95% of patients will have essential/idiopathic hypertension. These patients require a more

comprehensive evaluation for associated obesity, salt and alcohol intake, diet and exercise patterns. Review of cardiovascular risk factors and comorbidities is essential to direct therapeutic interventions.

Diabetes

Hypertension is more prevalent in patients with type 2 diabetes than in the nondiabetic population. It is estimated that the prevalence of arterial hypertension (BP greater than 160/95mmHg) in patients with type 2 diabetes is in the range of 40-50%.[6]

Adults who have both diabetes and hypertension have more renal disease and atherogenic risk factors including dyslipidaemia, hyperuricaemia, elevated fibrinogen and left ventricular hypertrophy.

A recent United Nations report found that the number of people with high blood pressure and diabetes is drastically increasing in both developed and developing countries. The report said found that in high-income countries, widespread diagnosis and treatment with low-cost medication have reduced mean blood pressure across populations, leading in turn to a reduction in deaths from heart disease. In Africa, however, more than 40% of adults in many countries are estimated to have high blood pressure —most of them remain undiagnosed, even though many of these cases could be treated with low-cost medications, which would significantly reduce the risk of death.[7]

In the case of diabetes, the global average prevalence is around 10%, with up to one third of populations in some Pacific Island countries having this condition. Left untreated, diabetes can lead to cardiovascular disease, blindness and kidney failure.

Blood pressure targets

NICE points out that there have been no large trials randomising hypertensives to different blood pressure targets that have sufficient power to assess clinical outcomes in terms of optimal blood pressure targets. Therefore current guidance is based on blood pressure targets adopted in clinical trials.

The pragmatic targets set by NICE for uncomplicated hypertensives are <140/90mmHg for clinic readings or <135/85mmHg for ABPM/HBPM daytime average readings. In patients over 80 years of age there is a less stringent clinic blood pressure target of <150/90mmHg. Where patients have diabetes mellitus or target organ damage the target is reduced to 130/80mmHg.

The QOF target is currently set at 150/90mmHg as it is an easier target to attain. Blood pressure thresholds for intervention include >160/100mmHg in uncomplicated hypertensives and >140/90mmHg in patients with[8]:

- Target organ damage (cardiovascular disease, left ventricular hypertrophy (LVH), nephropathy, retinopathy)
- Diabetes mellitus
- 10 year cardiovascular disease risk >20%.

Table 1: NICE guidance on initiating and monitoring antihypertensive drug treatment

- Offer antihypertensive drug treatment to people aged under 80 years with stage 1 hypertension who have one or more of the following:
  - target organ damage
  - established cardiovascular disease
  - renal disease
  - diabetes
  - 10-year cardiovascular risk equivalent to 20% or greater.
- Offer antihypertensive drug treatment to people of any age with stage 2 hypertension.
- For people aged under 40 years with stage 1 hypertension and no evidence of target organ damage, cardiovascular disease, renal disease or diabetes, consider seeking specialist evaluation of secondary causes of hypertension and a more detailed assessment of potential target organ damage. This is because 10-year cardiovascular risk assessments can underestimate the lifetime risk of cardiovascular events in these people.

Treatment algorithm

The BHS have utilised an algorithm based on work done

by Brown et al[9] to guide initial and subsequent choices of pharmacotherapy. This is based on renin levels such that white patients <55 years of age will have high renin and those >55 years and black patients of all ages will have low renin levels. A (ACE inhibitor /angiotensin receptor blocker [ARB]) and B (beta-blockers) agents will be effective in the high renin state whilst C (calcium channel blockers [CCBs]) and D (diuretics) agents work best at low renin levels. Since beta-blockers may cause an increased incidence of diabetes and atrial fibrillation[10] they have been consigned to level four of the joint BHS/NICE algorithm. The current BHS/NICE guidance goes further and suggest diuretics are consigned to level 3 since A+ C give a 20% greater reduction in cardiovascular disease risk compared with A + D.[1] NICE nominate indapamide and chlortalidone as preferred diuretics (these are not thiazides) as these are both more potent than thiazides with a better evidence-base[1] and have less metabolic side effects.

Only 25% of hypertensives are controlled by monotherapy so the medication for the remaining 75% involves a stepwise approach via ACD to attain target blood pressure. At level 4 there is the option of beta-blockers, alpha-blockers or further diuretics. Hitherto this has been largely guesswork. However there is a view that assessing renin at this stage could guide informed choice via an alpha/beta/delta acronym. At normal renin levels an alpha-blocker (alpha) would be the most appropriate addition, whilst for elevated renin a beta-blocker (beta) would best suit and for the low renin state a diuretic (delta) would be ideal.

Hypertension management

Lifestyle modification

Lifestyle factors need to be formally addressed since there tends to be a clustering of risk factors around cardiovascular disease.

Drug management

The ALLHAT trial[11] inspected the relative benefits of thiazides, CCBs, ACE inhibitors and alpha-blockers in hypertension control by assessing subsequent cardiovascular events. There was almost no difference in any of the groups though arguably alpha-blockers had a negative effect on chronic heart failure. There was demonstrable evidence of the benefits of combination therapy to hit target blood pressure. Several other trials reached the same conclusion such as the HOT study revealing almost three quarters of patients needing two or more drugs to hit target blood pressure.[12]

The ideal treatment for hypertension would be a once-daily dose of the fewest tablets required as this would improve concordance and might make use of potential drug synergy.

Other risk factors for cardiovascular disease must be considered where appropriate such as use of aspirin (where blood pressure <150/90mmHg) and statins. Where patients have comorbidities such as coronary heart disease/congestive heart failure there must be consideration of A and B drugs (ie ACE inhibitors, or ARB if ACE inhibitor is not tolerated, plus evidence-based beta-blockade).

For a five year period from 1998–2003 monotherapy became less often used whilst combination therapy increased by 50% and this has continued in the interim. Since other risk factors cluster (eg. metabolic syndrome) there are inevitably complex drug regimes required. The resultant pill burden equates with patient-perceived level of ill-health thus patients are eager to take fewer tablets. Fixed drug combination (FDC) has much to commend it in terms of psychology and patient concordance. This has been utilised in Wald and Law's[13] polypill and conducted in Yusuf's[14] polycap studies. In the USA there is greater use of FDCs compared to UK/Europe with concomitant greater success in target attainment.[15]

JNC7 guidelines suggested that FDCs are more convenient, simplify treatment and may cost less than separate prescriptions of individual components. JNC7 also suggested first line FDC usage where blood pressure is >160/100mmHg at presentation.[16] JNC8 is currently imminently awaited.

Feely et al[17] compared the results of polypill preparations versus standard dosed of single agents (atenolol/amlodipine/captopril/bendroflumethiazide) for hypertension management. The individual components were included at 25% of their usual dosage. 60% of patients treated with the polypill hit blood pressure target compared with atenolol 40%, amlodipine 32%, captopril 45% and bendroflumethiazide 15%. Synergy is important in use of drug combinations. Various trials have revealed up to 25% better concordance using an FDC compared with two separate agents.[18,19] There is further reduced concordance with increased number of pills.

The pharmacology of mode of action of drug groups helps guide combination regimes eg. diuretics have a relatively flat dose-response curve in the main but a high

increased incidence of side effects with dose elevation. This is also true of CCBs and beta-blockers. ACE inhibitors and ARBs have a better dose-response effect with minimal increase of side effect profile. It is therefore sensible to maintain a low dose of diuretics and CCBs but to uptitrate ACE inhibitors and ARBs.

Combining medications may also reduce side effects eg. potassium retention with ACE inhibitor/ARB treatment will mitigate potassium reduction with diuretics (though care must be exercised with the potassium conserving spironolactone and amiloride). The USA and Europe use 500% more FDCs than the UK especially in cardiovascular medicine.[20] Furthermore FDCs are now the norm for diabetes, asthma, analgesia, skin products and HRT etc.

Conclusion

Hypertension is the cause of a large number of deaths and morbidity and hospital admissions annually. Its management is therefore of great importance. We must strive to make accurate diagnoses and manage appropriately and aggressively with both lifestyle modification and pharmacotherapy driven by the dynamic evidence-base.

Conflict of interest: none declared

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