Cardiovascular Risk in Diabetes

Lipids

Hypercholesterolaemia is an important reversible risk factor for cardiovascular disease and should be tackled aggressively in all diabetic patients.

- In Type 1 patients, normal or high HDL-cholesterol concentrations are often seen. However an elevated HDL-cholesterol is not associated with the same cardio-protective effect as in non-diabetic individuals.
- The characteristic hyperlipidaemia of Type 2 diabetes is mild hypercholesterolaemia, low HDL-cholesterol and hypertriglyceridaemia.
- Triglyceride concentrations are elevated by poor glycaemic control. Triglycerides may normalise with good glycaemic control, attention to diet and increasing exercise. Excess alcohol consumption is also associated with elevated triglyceride concentrations.

Screening for Dyslipidaemia

- Lipids should be checked at diagnosis and annually thereafter.
- Assess more frequently if lipid-lowering therapy is prescribed.
- Total cholesterol, HDL-cholesterol and triglycerides should be requested. For ease, non-fasting estimation is usually adequate. Lipids should not be screened in people whose life expectancy is estimated to be less than five years.

Management

1. Lifestyle Advice

- Reinforce dietary advice and optimise glycaemic control.
- Provide weight reduction diet for those with BMI > 25.
- If BMI > 30, set target of 5-10 kg weight loss.
- Increase fruit and vegetable consumption (5 portions per day).
- Increase oily fish consumption (2 portions per week).
- Reduce saturated fat intake.
- Encourage regular physical activity.

2. Exclude (and Treat) Secondary Causes of Hypercholesterolaemia

- Alcohol excess.
- Hypothyroidism.
- Nephrotic Syndrome.
- Cholestasis.
- Drugs (e.g. diuretics, corticosteroids).

3. Drug Treatment: Patients with existing cardiovascular disease (Secondary Prevention)

Includes diabetic patients with angina, myocardial infarction, cerebrovascular disease and peripheral vascular disease.

- Treat with a Statin if Total cholesterol >3.5 mmol/L.
- All patients with existing cardiovascular disease should take Aspirin. If aspirin is contraindicated, alternative antiplatelet therapy, such as clopidogrel, should be considered.
4. Drug Treatment: Patients without cardiovascular disease (Primary Prevention)

- Most people with Type 2 diabetes aged above 40 should receive treatment with a statin and it should be considered in people with Type 1 diabetes. A positive decision NOT to prescribe lipid-lowering therapy may be considered in people aged 40-50 years who have no other risk factors for CVD and in people with a particularly high HDL cholesterol (e.g. >1.8mmol/l)
- **Type 1 and Type 2 patients with evidence of nephropathy** (microalbuminuria or proteinuria present) are at particularly high cardiovascular risk and should be treated aggressively.

5. Age Limits

- There should be no ‘upper age limit’ for prescribing lipid-lowering therapy. Each individual should be considered on his/her own merits and, if life expectancy is estimated to be greater than five years, lipid-lowering therapy should be prescribed if standard criteria are met
- Once treatment is established, it should not be discontinued at any particular age, unless clinically indicated due to other conditions.

Patients with Persistently Raised Triglyceride Concentrations

- Check fasting sample (Total-cholesterol, HDL-cholesterol & Triglycerides)
- Optimise glycaemic control
- Exclude co-existing pathology e.g. alcohol excess.

Lipid Lowering Drugs

First line lipid-lowering therapy is Simvastatin. Current NHS Lothian Lipid Management Guidelines state start with 40mg simvastatin at night. Atorvastatin should be commenced if patients fail to reach targets with Simvastatin. Monitoring of liver function and, if muscle pain, creatinine kinase is recommended.

Fibrates have been less well tested in clinical trials. They are mainly of benefit in those with mixed hyperlipidaemia and low HDL cholesterol. They may be considered in people who do not tolerate statin therapy.

Anti-platelet Therapy

Advice has been that Aspirin, or clopidogrel if aspirin intolerant, should be prescribed to patients whose 10 year risk of an event is >15%. However, the 2008 POPADAD trial shows that there is no benefit from daily prophylactic aspirin in type 1 or type 2 diabetes. This is borne out in advice from the drug and therapeutics bulletin.

Management of Hypertension for Type 1 or Type 2 Diabetes

**Type 1 Diabetes**

- In the absence of nephropathy (microalbuminuria or proteinuria), the prevalence of hypertension in Type 1 diabetes is similar to non-diabetic individuals
- Blood pressure rises as microalbuminuria becomes established
- Anti-hypertensive therapy reduces urinary albumin excretion and delays progressive loss of glomerular function. The greatest benefit is seen with ACE Inhibitors.

**Type 2 Diabetes**

- 40-50% of patients with Type 2 diabetes have hypertension at the time of diagnosis
- Hypertension accelerates the decline in renal function in established nephropathy.
Confirm the Diagnosis of Hypertension

Measurement of BP – see appendix 5 page 104

Thresholds and Targets for CV Risk in Diabetes

- The threshold for anti-hypertensive therapy is BP > 140/90mmHg
- The target BP is < 130/80mmHg in the absence of nephropathy
- In patients with Type 1 diabetes and nephropathy, ACE Inhibitors are first-line therapy and a target BP as low as possible is recommended

- In uncomplicated patients (no target organ damage, BP < 140/90mmHg), delay pharmacological intervention and reassess after 3-6 months of lifestyle measures
- If target organ damage (retinopathy, nephropathy, left ventricular hypertrophy) present, start anti-hypertensive therapy immediately
- If hypertension is sustained or severe (Diastolic BP > 110mmHg) or multiple cardiovascular factors are present, institute therapy within 1-2 weeks
- All hypertensive patients should receive lifestyle advice.

Diagnosis: Use of Ambulatory Blood Pressure Monitoring (ABPM)

- The average daytime BP and not the average 24 hour BP should be used to make treatment decisions
- BP measured by ABPM is systematically lower than surgery or clinic measurements in hypertensive patients; the average difference in techniques is 12/7mmHg; the target ABP is < 130/80mmHg
- Outcome trials in hypertension have all been based on surgery or clinic BP measurement, not on ABPM data.

ABPM is available via the Edinburgh Direct Access ABPM service whereby GPs can refer patients to the Diabetes Out-patient Departments at the WGH, RIE and SJH. A recent study involving patients attending the Direct Access service at the WGH found that results gained from Ambulatory Blood Pressure Monitoring were comparable with those for patients using self blood pressure monitors. Consequently self BP monitors are now routinely used instead of ABPM’s as these are preferred by the majority of patients attending the Diabetes Out-patient clinics. The home BP monitors are used in accordance with the European Society of Hypertension guidelines whereby patients record their own BPs twice a day for seven consecutive days. The BPs recorded in the first two days are ignored and an average of the remaining BPs is calculated to give the average daytime BP measurement. Ambulatory Blood Pressure Monitors used are Spacelabs 90207 (Spacelabs Inc., Redmond, Washington, USA.) Self BP monitor used are Microlife Watch BP Home.


Treatment of Hypertension in Type 1 Diabetes

- All drugs effective, therefore choice should be tailored to individual patient’s needs. For further information, see Lothian Joint Formulary.

If microalbuminuria or proteinuria is present in Type 1:

- ACE Inhibitors are first-line choice
• Angiotensin II antagonists can be used if ACE Inhibitors produce adverse effects e.g. cough
• Other classes of drugs may be added, with the exception of short acting dihydropyridine calcium channel blockers (e.g. Nifedipine), which are not as effective at limiting protein excretion.

Treatment of Hypertension Type 2 Diabetes
• All classes of drugs are effective at lowering BP, therefore choice should be tailored to individual patient’s needs
• ACE inhibitors and long acting calcium channel blockers are the preferred first-line agents.
• ACE Inhibitors are the recommended first-line therapy if nephropathy is present, as they are renoprotective.
• Polypharmacy is likely: 30% will require 3 or more drugs to achieve target BP.

Management of Hypertension in the Elderly (Age 75+)
• Treating hypertension in the elderly confers protection against future stroke.
• Make a clinical decision on the relative benefits and risks of treating frail, very elderly patients
• Consider low dose Thiazide or long acting Calcium Channel Blocker as first line therapy
• Examine for signs of postural hypotension.
• BP targets may be relaxed.

Management of Isolated Systolic Hypertension
• Defined as SBP > 160 mmHg with DBP < 90 mmHg
• Common in middle-aged and elderly Type 2 patients
• Consider long acting Calcium Channel Blockers or low dose Thiazides diuretics for initial drug choice.

Indications for Hospital Referral
• Evidence of nephropathy (persistent microalbuminuria, overt proteinuria or serum creatinine > 150 µmol/L)
• Presence of cardiac failure or retinopathy
• Clinical possibility of renovascular disease or other secondary cause of hypertension
• BP difficult to control despite appropriate therapy
• Rise in serum creatinine (>50% from baseline) after ACE Inhibitor started

Use of ACE Inhibitors
• Consider the presence of renal artery stenosis in patients with Type 2 diabetes
• Suspect underlying renovascular disease if widespread atheroma present (e.g. carotid or abdominal bruits, aortic aneurysm, absent peripheral pulses)
• Before starting ACE Inhibitor, measure baseline urea, creatinine & electrolytes
• Repeat after 4-7 days, again after 3 months and thereafter annually
• Stop drug if significant hypotension or a significant rise in creatinine occurs (>50% from baseline)
• Refer or discuss with secondary care physician if in doubt

*SIGN recommend that ACE inhibitor therapy should be given to patients with diabetes who fall into any of the following categories:
• following Myocardial Infarction (MI)
and should be considered in:
• heart failure due to left ventricular systolic dysfunction
• patients with stable angina
General Advice

- All classes of anti-hypertensive drugs are effective at lowering BP
- Select drug with once (or maximum twice) daily dosage to improve adherence.
- Remember patients with diabetes are likely to be on multiple drugs
- Drug choices should, if possible, be tailored to an individual patient’s needs e.g.
  - ACE Inhibitor if previous MI with left ventricular dysfunction or persistent microalbuminuria or proteinuria present.
  - Cardio selective Beta-blocker or rate-lowering Calcium Channel Blocker if coexisting angina.
  - Thiazide diuretics are especially useful in older patients or patients with systolic hypertension. Bendroflumethiazide should not be prescribed in doses higher than 2.5mg daily.
  - Angiotensin II Receptor Antagonists should be reserved for patients experiencing adverse effects on ACE Inhibitors e.g. cough

Dosage Adjustment

- An interval of at least 4 weeks should be allowed to observe the full response, unless it is necessary to lower BP more urgently
- The 2.5mg dose of Bendroflumethiazide should not be titrated up

Combination Therapy

- Less than half of patients with hypertension will be controlled by monotherapy
- Sub-maximal doses of two drugs result in larger BP responses and fewer adverse effects than maximal doses of a single drug
- Fixed dose combination preparations should be avoided due to cost and lack of flexibility in dose titration
Algorithm: Recommendations for combining blood pressure drugs/ABCD rule

Step 1
- Younger [e.g. < 55 years] and non-black → A (or B*)
- Older [e.g. ≥ 55 years] or black → C or D

Step 2
- A (or B*) + C or D

Step 3
- A (or B*) + C + D

Step 4
- Resistant hypertension
  - Add: either α blocker or spironolactone or other diuretic

A: ACE inhibitor or angiotensin receptor blocker
B: β blocker
C: Calcium channel blocker
D: Diuretic (thiazide/thiazide-like)

*Combination therapy involving B and D induces more new onset diabetes compared to other combination therapies

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*See Appendix 5 (pg 104) for guidelines on measurement of blood pressure