A CASE OF HYPERTENSION IN DIABETES

This case study aims to:

- Help understand the association between hypertension and type 2 diabetes mellitus.
- State the goals for treatment of hypertension in patients with diabetes mellitus.
- Discuss the choice of antihypertensives in hypertensive patients with diabetes.
- List the various antihypertensives their mechanisms of action.
- Describe the routine primary management for a patient with type 2 diabetes.

History

Mr. G is a 45-year-old gentleman with a history of type 2 diabetes, obesity, and hypertension. The patient was diagnosed with type 2 diabetes 7 years ago when during an insurance examination. Mr. G. is 172 cms and has always been overweight, with his weight fluctuating between 85 and 90 kg.

Initial treatment for his diabetes consisted of a Tab glimepiride 1 mg/day with metformin. His diabetes has been under fair control with a most recent hemoglobin A1c of 7.4%.

Hypertension was diagnosed about 5 years ago when blood pressure (BP) measured in the family physician’s clinic was noted to be consistently elevated in the range of 160/90 mmHg on three occasions. Mr. G. was initially treated with ramipril, starting at 5 mg daily and increasing to 10 mg daily, yet his BP control has fluctuated.

One year ago, microalbuminuria was detected on an annual urine screen, with 2010 mg/dl of microalbumin identified on a spot urine sample.

Mr. G. comes for his usual follow-up visit for diabetes. Physical examination reveals an a BP of 150/90 mmHg and a pulse of 80 bpm.

1. What is the relationship between hypertension and diabetes?

Hypertension is more common in diabetics than non-diabetics. Hypertension is a major factor in development of macro vascular and micro vascular complications in a diabetic patient. The patient is at a greater risk of developing cardiovascular complications. Isolated systolic hypertension is more common in diabetics than non diabetics and is a risk factor for macro vascular disease.

Diabetes mellitus is a major risk factor for cardiovascular disease (CVD). Approximately two-thirds of people with diabetes die from complications of CVD. Patients with diabetes are prone to a number of cardiovascular risk factors beyond hyperglycemia. These risk factors, including hypertension, dyslipidemia, and a sedentary lifestyle, are particularly prevalent among patients with diabetes. To reduce the mortality and morbidity from CVD among patients with diabetes, aggressive treatment of glycemic control as well as other cardiovascular risk factors must be initiated.

2. Target BP for patients with diabetes and hypertension is

   a)  < 130/89 mm Hg
   b)  < 140/90 mm Hg
   c)  < 150/100 mm Hg
   d)  Neither of the above

The correct answer is a < 130/80 mm Hg.

Blood pressure should be measured at every routine diabetes visit. Patients found to have systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg should have
blood pressure confirmed on a separate day. Repeat systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg confirms a diagnosis of hypertension. The United Kingdom Prospective Diabetes Study (UKPDS), which followed patients with diabetes for an average of 8.5 years, found that patients with tight BP control (<150/<85 mmHg) versus less tight control (<180/<105 mmHg) had lower rates of myocardial infarction (MI), stroke, and peripheral vascular events. In the UKPDS, each 10-mmHg decrease in mean systolic BP was associated with a 12% reduction in risk for any complication related to diabetes, a 15% reduction for death related to diabetes, and an 11% reduction for MI.

The Hypertension Optimal Treatment (HOT) trial has shown that patients assigned to lower BP targets have improved outcomes. In the HOT trial, patients who achieved a diastolic BP of <80 mmHg benefited the most in terms of reduction of cardiovascular events. Other epidemiological studies have shown that BPs >120/70 mmHg are associated with increased cardiovascular morbidity and mortality in people with diabetes. The American Diabetes Association has recommended a target BP goal of <130/80 mmHg.

3. The antihypertensive agents recommended for patients with diabetes are
   a) ACE inhibitors
   b) ARBs
   c) Both of the above
   d) Neither of the above

   The correct answer is c- both ACEIs and ARBs.

   - Patients with a systolic blood pressure of 130–139 mmHg or a diastolic blood pressure of 80–89 mmHg may be given lifestyle therapy alone for a maximum of 3 months and then, if targets are not achieved, treated with addition of pharmacological agents.
   - Patients with more severe hypertension (systolic blood pressure ≥140 or diastolic blood pressure ≥90 mmHg) at diagnosis or follow-up should receive pharmacologic therapy in addition to lifestyle therapy.
   - Pharmacologic therapy for patients with diabetes and hypertension should be with a regimen that includes either an ACE inhibitor or an angiotensin receptor blocker (ARB). If one class is not tolerated, the other should be substituted. If needed to achieve blood pressure targets, a thiazide diuretic should be added to those with an estimated glomerular filtration rate (GFR) (see below) ≥30 ml/min per 1.73 m² and a loop diuretic for those with an estimated GFR <30 ml/min per 1.73 m².
   - Multiple drug therapy (two or more agents at maximal doses) is generally required to achieve blood pressure targets.
   - If ACE inhibitors, ARBs, or diuretics are used, kidney function and serum potassium levels should be closely monitored.
   - In pregnant patients with diabetes and chronic hypertension, blood pressure target goals of 110–129/65–79 mmHg are suggested in the interest of long-term maternal health and minimizing impaired fetal growth. ACE inhibitors and ARBs are contraindicated during pregnancy.

The UKPDS showed no significant differences in outcomes for treatment for hypertension using an ACE inhibitor or a β-blocker. In addition, both ACE inhibitors and angiotensin II receptor blockers (ARBs) have been shown to slow the development and progression of diabetic nephropathy.

In the Heart Outcomes Prevention Evaluation (HOPE) trial, ACE inhibitors were found to have a favorable effect in reducing cardiovascular morbidity and mortality, whereas recent trials have shown a renal protective benefit from both ACE inhibitors and ARBs.
ACE inhibitors and β-blockers seem to be better than dihydropyridine calcium-channel blockers to reduce MI and heart failure. However, trials using dihydropyridine calcium-channel blockers in combination with ACE inhibitors and β-blockers do not appear to show any increased morbidity or mortality in CVD, as has been implicated in the past for dihydropyridine calcium-channel blockers alone.

The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) in high-risk hypertensive patients, including those with diabetes, demonstrated that chlorthalidone, a thiazide-type diuretic, was superior to an ACE inhibitor, lisinopril, in preventing one or more forms of CVD.

4. What are the various antihypertensives used in diabetics

<table>
<thead>
<tr>
<th>Drug, daily dosage</th>
<th>Recommended in</th>
<th>Avoid in</th>
<th>Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium channel blockers</td>
<td>Asthmatics, patients with concomitant angina (except nifedipine), PVD,</td>
<td>Heart blocks (verapamil and diltiazem)</td>
<td>Flushing, headaches, ankle oedema, gum hyperplasia</td>
</tr>
<tr>
<td>Nifedipine 15-60mg, Amlodipine 5-10mg, Felodipine 5-20 mg, Nitrendipine 5-40mg</td>
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<td>ACE inhibitors</td>
<td>CHF, LVH</td>
<td>Renal artery stenosis, pregnancy, use with caution in patients with CRF, and with diuretics</td>
<td>Cough, angioneurotic oedema</td>
</tr>
<tr>
<td>Captopril 25-150mg, Enalapril 2.5-15 mg, Lisinopril 5 –30 mg, Ramipril 1.25-10 mg, Perindopril 4-8 mg</td>
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<tr>
<td>ARBs</td>
<td>CHF, LVH</td>
<td>Renal artery stenosis, pregnancy, use with caution in patients with CRF, and with diuretics</td>
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<tr>
<td>Losartan K 25-100 mg/day, Valsartan 80-160 mg/day, Olmesartan 20-40 mg/day, Telmisartan 20-80 mg/day</td>
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<td></td>
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<tr>
<td>Alpha blockers</td>
<td>Asthmatics, PVD, prostatic symptoms, impotence, hyperlipidemias</td>
<td>Severe aortic stenosis</td>
<td>Headache, dry mouth, first dose syncope</td>
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<tr>
<td>Prazosin 1-5 mg, Terazosin1-20 mg</td>
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Case contd.
Hydrochlorothiazide 12.5 mg/day was added to the treatment regimen.
The blood pressure dropped to 130 m/84 mm of Hg over a period of 2 weeks

Take home messages.
1. Hypertension is a risk factor for cardiovascular complications of diabetes.
2. Clinical trials demonstrate that drug therapy versus placebo will reduce cardiovascular events when treating patients with hypertension and diabetes.
3. A target BP goal of < 130/80 mmHg is recommended.
4. Pharmacological therapy needs to be individualized to fit patients' needs.
5. ACE inhibitors, ARBs, diuretics, and β-blockers have all been documented to be effective pharmacological treatment.
6. Combinations of drugs are often necessary to achieve target levels of BP control.
7. ACE inhibitors and ARBs are agents best suited to retard progression of nephropathy.

References
1) ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group: Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel-blocker vs. diuretic: the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial. JAMA 288:2981-2997, 2002