Module 8 Drug Treatment in Type 2 Diabetes with Hypertension

- Hypertension is 1.5 – 2 times more prevalent in Type 2 diabetes (prevalence up to 80 % in diabetic subjects). This exacerbates the risk of cardiovascular disease by ~ two-fold.

- Drug therapy reduces the risk of cardiovascular disease and death. The United Kingdom Prospective Diabetes Study (UKPDS) has shown an 11% decrease in risk with each 10 mmHg reduction of systolic blood pressure. In the Hypertension Optimal Treatment (HOT) study, there was a 51% reduction in cardiovascular events in diabetics with target diastolic BP <80 mmHg as compared to those with target diastolic BP< 90mm Hg[1,2]. In the Action to Control Cardiovascular Risk in Diabetes (ACCORD) blood pressure study, aggressive blood pressure control targeting a systolic blood pressure level <120 mmHg in people with type 2 DM has not been shown to yield additional cardiovascular benefits as compared to a systolic blood pressure target of <140 mmHg. Further, adverse effects were more frequent in the intensive blood pressure lowering group [3].

- Thus, the target blood pressure for patients with diabetes is recommended to be below 130/80 mmHg.

- Albuminuria is a strong predictor of all-cause mortality and cardiovascular morbidity and mortality in Type 2 diabetes. Simultaneous presence of proteinuria with hypertension potentiates the mortality risk in patients with diabetes [6,7] .

Treatment of hypertension:

1. Non-pharmacological measures including smoking cessation, weight reduction, moderation of alcohol consumption, reduction in salt intake and alleviation in stress.

2. Pharmacological treatment takes into consideration the drug efficacy, safety profile/side effects, and the patient's factors including co-morbidities (Table 1 and Table 2):
   - Both Angiotensin-converting enzyme inhibitor (ACEI) and Angiotensin Receptor Blockers (ARB) have been confirmed to confer additional vascular and renoprotective effects; therefore either should be included in the anti-hypertensive regime, especially for those with diabetic kidney disease. (Hope Study [8,9,10,11]).
   - Most patients with diabetes and hypertension will require two or more anti-hypertensive medications to achieve blood pressure goal.
   - In the case of refractory hypertension (poor response to treatment), watch out for unsuspected secondary causes (renal or endocrine disorders), poor drug compliance, exogenous medications, and volume overload fluid status.

Table 1. Drug Treatment for Hypertension

Six main drug classes of anti-hypertensive drugs are available for the initiation and maintenance of blood pressure lowering therapy, but the choice of drugs is influenced by cost and many factors as illustrated below.

Class of Drug	Compelling Indications	Possible Indications	Compelling Contraindications	Possible Contraindications
ACE Inhibitors (ACEI)	Heart failure, Left ventricular dysfunction, Post myocardial infarction, Diabetic kidney disease	Proteinuric renal disease	Pregnancy, Bilateral renal artery stenosis, Hyperkalaemia	Renal impairment
Angiotensin II Receptor Blockers (ARB)	ACE inhibitor intolerance		Pregnancy, Bilateral renal artery stenosis, Hyperkalaemia	Renal impairment
Beta-Blockers	Angina, Post myocardial infarction Tachyarrhythmias	Heart failure (low dose)	Asthma, chronic obstructive pulmonary disease, Heart block	Peripheral vascular disease
Calcium Channel Blockers (dihydropyridine)	Elderly patients, Isolated systolic hypertension	Angina, Peripheral vascular disease		Congestive heart failure
Calcium Channel Blockers (rate limiting, e.g. verapamil, diltiazem)	Angina		Heart block	Congestive heart failure, combination with beta-blockers
Thiazide / thiazide-like Diuretics	Heart failure, Elderly patients, Isolated systolic hypertension		Gout	Dyslipidaemia, Pregnancy, Sexually active males

Table 2. Possible Combination and Effects of Anti-hypertensive Therapy in Diabetes

Combination	Specific benefits	Disadvantages
ACE inhibitor + calcium-channel blocker	Calcium-channel blocker has a neutral effect on lipid and glucose metabolism. Combination of calcium-channel blocker with ACEI or ARB is effective in the treatment of diabetic hypertension.	---
Diuretic + ACE inhibitor	ACE inhibitor prevents activation of angiotensin-aldosterone system due to diuretic-induced extracellular fluid volume contraction, and helps to retain potassium	High risk of 'first dose' hypotension with ACE inhibitor in patients over treated with diuretics
Diuretic + β-blocker	---	Possibly aggravate hyperglycaemia in Type 2 diabetes
Diuretic + calcium-channel blocker	Diuretic reduces mild ankle swelling due to calcium-channel blocker	---
β-blocker + calcium-channel blocker	β-blocker counteracts tachycardia due to calcium-channel blocker's vasodilator action, Effective anti-anginal therapy	May aggravate or provoke cardiac failure (both are negative inotropes)

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