Treatment of Diabetes Mellitus: Beyond glycaemic control

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Presentation Outline

• Introduction
• Concept of global cardiovascular risk
• Lipids
• Hypertension
• Antiplatelet agents
• Smoking
• Screening for complications of diabetes
• Conclusion
Introduction

Type 2 diabetes mellitus (T2DM)
• Leading metabolic disorder, 387 million (2014)
• India: > 65 million

• Macrovascular & microvascular complications
  – Cardiovascular disease
  – Cerebrovascular disease
  – Retinopathy
  – Nephropathy
  – Neuropathy
  – Foot problems
Introduction

• Landmark clinical trials -
  – Importance of tight glycaemic control.

• HbA1c levels of < 7%
  – ↓ diabetic retinopathy and nephropathy.
  – No ↓ cardiovascular disease

• Comprehensive programme of risk reduction
  – To reduce CV events in diabetic patients.
Concept of Global Cardiovascular Risk

• Conventional risk factors
  – Central obesity
  – Dyslipidaemia
  – Fasting hyperglycaemia
  – Hypertension

• Behavioural factors
  – Smoking and physical activity

• Newer markers
  – CRP and Plasminogen activator inhibitor-1
Lipids

‘Diabetic dyslipidaemia’
• Elevated levels of triglycerides
• Low levels of HDL-cholesterol
• High, normal or low levels of LDL-cholesterol, with increase in small dense LDL particles.

• Checked at least annually.
# Targets for lipid levels in diabetics

<table>
<thead>
<tr>
<th>Lipid levels (mg/dl)</th>
<th>Diabetic patients</th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Without vascular complications</td>
<td>With vascular complications</td>
</tr>
<tr>
<td>Triglyceride</td>
<td>&lt; 150</td>
<td>&lt; 120</td>
</tr>
<tr>
<td>Total Cholesterol</td>
<td>&lt; 200</td>
<td>&lt; 180</td>
</tr>
<tr>
<td>LDL-Cholesterol</td>
<td>&lt; 100</td>
<td>&lt; 70</td>
</tr>
<tr>
<td>HDL-Cholesterol</td>
<td>&gt; 45</td>
<td>&gt; 45</td>
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</table>
Important points

• Therapeutic lifestyle change
  Exceptions
  – Prior cardiovascular disease
  – LDL > 100 mg/dl
  – Risk of acute complications of hyperlipidaemia

• Improvement in glycaemic control
Important points

• Drug therapy – Statins

• If HDL ↓, Niacin.

• If TG ↑ + normal cholesterol levels, Fibrate.

• All three lipids ↑, statin + Fibrate OR statin + Niacin.
## Commonly used Lipid lowering agents

<table>
<thead>
<tr>
<th>Class of Drug</th>
<th>Effect on lipids</th>
<th>Drug &amp; daily dose (mg)</th>
<th>Side-effects</th>
<th>Contraindications</th>
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<tbody>
<tr>
<td>HMG-Co-A Inhibitors (Statins)</td>
<td>↓ TC ↓↓ LDL</td>
<td>Simvastatin (5-40)</td>
<td>Myopathy, Altered LFT, Nausea, Vomiting</td>
<td>Pregnancy, impaired liver function</td>
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<tr>
<td></td>
<td></td>
<td>Atorvastatin (5-80)</td>
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<td></td>
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<tr>
<td></td>
<td></td>
<td>Rosuvastatin (5-20)</td>
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<tr>
<td>Fibric acid derivatives (fibrates)</td>
<td>↓↓ TG ↑ HDL</td>
<td>Gemfibrozil (900-1500)</td>
<td>Myopathy, Altered LFT, ↑ Serum creatinine (fenofibrate).</td>
<td>Pregnancy, Impaired liver function, Gallstones</td>
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<tr>
<td></td>
<td></td>
<td>Bezafibrate (600-800)</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Fenofibrate (67-200)</td>
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<tr>
<td>Niacin</td>
<td>↓ TC, ↓ TG, ↑↑HDL</td>
<td>Niacin (375-6000)</td>
<td>Flushing, Activation of peptic ulcer, Hyperglycaemia</td>
<td>Pregnancy, Hepatic disease, Active Peptic ulcer</td>
</tr>
<tr>
<td>Ezetimibe</td>
<td>↓ LDL</td>
<td>Ezetimibe (10)</td>
<td>Diarrhoea, Abdominal pain</td>
<td>Pregnancy</td>
</tr>
</tbody>
</table>

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Hypertension

• Twice as common in diabetic patients.
• Major risk factor for stroke and diabetic retinopathy and nephropathy.

• In all diabetics, Target BP < 130/80 mm Hg.
• With proteinuria, goal 125/75 mm Hg.

• Measured at every follow-up visit.
Hypertension

Lifestyle modifications

• For SBP 120-139 or DBP 80-89 mm Hg.
  – ↓ sodium intake and body weight.
  – ↑ fruits, vegetables and low-fat dairy products
  – Exercise
  – Moderation in alcohol consumption
  – Increasing activity levels

Drug therapy

– Failed to lifestyle modification
– SBP > 140 or DBP > 90 mm Hg.
Important points

• Initial drug therapy with ACEIs, ARBs, β-blockers, CCBs.
• All regimens should have ACEI or ARB.
  – ↓ risk of CVD
  – Prevent and retard diabetic nephropathy

• If needed, thiazide diuretic.
• Gradual reduction in elderly patients.
• Orthostatic hypotension.
## Commonly used antihypertensive drugs

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<tr>
<td></td>
<td>Indepamid (1.5-2.5)</td>
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<td>Beta-blockers</td>
<td>Atenolol (50-200)</td>
<td>Bradycardia, Fatigue.</td>
<td>Bronchial asthma, Heart block, PVD, PVD, Severe heart failure.</td>
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<tr>
<td></td>
<td>Metoprolol (100-450)</td>
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<td></td>
<td>Bisoprolol (5-10)</td>
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<tr>
<td></td>
<td>Nebivolol (2.5-5)</td>
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<tr>
<td></td>
<td>Ramipril (1.25-20)</td>
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<td></td>
<td>Lisinopril (2.5-40)</td>
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<td>Perindopril (2-4)</td>
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<tr>
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<td>Irbesartan (150-300)</td>
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<td>Valsartan (40-160)</td>
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<tr>
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<td>Telmisartan (20-80)</td>
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<td>Calcium Channel Blockers (CCBs)</td>
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<tr>
<td>Amlodipine (2.5-10)</td>
<td></td>
<td>Headache, Pedal oedema, Flushing, Palpitation.</td>
<td>Cardiogenic shock, Acute MI.</td>
</tr>
<tr>
<td>Nifedipine (5-40)</td>
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<tr>
<td>Verapamil (40-480)</td>
<td></td>
<td>Nausea, Constipation</td>
<td>CCF, Heart block.</td>
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<tr>
<td>Diltiazem (60-240)</td>
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Antiplatelet agents

Aspirin

• Effective in reducing CV morbidity and mortality - secondary prevention

• Failed to show significant reduction in CV end points - in primary prevention.
Restricted use of Aspirin (ADA)

• For secondary prevention in diabetic patients with H/o prior CVD.

• As primary prevention in T1DM & T2DM –
  At increased CV risk (10-year risk > 10%).
  – Men above 50 years and Women above 60 years.
  – At-least one other major risk factors
    • Family history of CVD
    • Hypertension
    • Smoking
    • Dyslipidaemia
    • Albuminuria
Antiplatelet agents

• Evidence - Not sufficient for CV risk < 5%.
• Dose of aspirin – 75 to 325 mg/day.

Clopidogrel
• Unable to tolerate aspirin

Aspirin + Clopidogrel
• Severe and progressive cardiovascular and cerebrovascular disease.
Cessation of Smoking

• Modifiable cause of premature death.
• Accelerate macrovascular complications,
• Adversely affect microvascular complications.

• Strongly advised to quit.
• Counselling for cessation of smoking.
Screening for Complications of Diabetes

• Regular assessment of CV risk factors.
• Diagnostic cardiac stress testing
  – With symptoms of CVD
  – With abnormal resting ECG
• Estimation of microalbuminuria, serum creatinine and eGFR at least annually.
  – From 5 years after diagnosis for type 1 DM,
  – At diagnosis for type 2 diabetes.
Screening for Complications of Diabetes

• Annual dilated retinal examinations
  – At diagnosis in T2DM
  – At 5 years after diagnosis in T1DM.

• Detailed foot examination with assessment of sensation and pedal pulses at each visit.

• More frequently, if any abnormality.
Conclusion

• **T2DM** – epidemic proportions in India.
  • Huge population at-risk for complications.
  
• **Important aspect** – tight glycaemic control.
  
• **Diabetes care programme** – address each of the cardiovascular risk factors.
  • Long-lasting reduction in the prevalence of complications of diabetes.
thank you