



# 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

Lipid levels (mg/dl)	Diabetic patients	
	Without vascular complications	With vascular complications
Triglyceride	< 150	< 120
Total Cholesterol	< 200	< 180
LDL-Cholesterol	< 100	< 70
HDL-Cholesterol	> 45	> 45

# 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

Class of Drug	Effect on lipids	Drug & daily dose (mg)	Side-effects	Contra-indications
HMG-Co-A Inhibitors (Statins)	↓ TC ↓↓ LDL	Simvastatin (5-40)  Atorvastatin (5-80)  Rosuvastatin (5-20)	Myopathy, Altered LFT, Nausea, Vomiting	Pregnancy, impaired liver function

# Commonly used Lipid lowering agents

Class of Drug	Effect on lipids	Drug & daily dose (mg)	Side-effects	Contra-indications
Fibric acid derivatives (fibrates)	↓↓ TG ↑ HDL	Gemfibrozil (900-1500)  Bezafibrate (600-800)  Fenofibrate (67-200)	Myopathy, Altered LFT, ↑ Serum creatinine (fenofibrate).	Pregnancy, Impaired liver function, Gallstones

# Commonly used Lipid lowering agents

<b>Class of Drug</b>	<b>Effect on lipids</b>	<b>Drug &amp; daily dose (mg)</b>	<b>Side-effects</b>	<b>Contra-indications</b>
Niacin	↓ TC ↓ TG ↑↑HDL	Niacin (375-6000)	Flushing, Activation of peptic ulcer, Hyperglycaemia	Pregnancy, Hepatic disease Active Peptic ulcer
Ezetimibe	↓ LDL	Ezetimibe (10)	Diarrhoea, Abdominal pain	Pregnancy

# 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,  $\beta$ -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

Class of Drug	Drug & daily dose (mg)	Side-effects	Contra-indications
Diuretics	Hydrochlorothiazide (25-50) Indepamide (1.5-2.5)	Hypokalaemia, Hyponatraemia, Hyperuricaemia, Hyperglycaemia	Anuric renal failure, Hepatic failure Hypercalcaemia Pregnancy.



# Commonly used antihypertensive drugs

<b>Class of Drug</b>	<b>Drug &amp; daily dose (mg)</b>	<b>Side-effects</b>	<b>Contra-indications</b>
Beta-blockers	Atenolol (50-200) Metoprolol (100-450) Bisoprolol (5-10) Nebivolol (2.5-5)	Bradycardia, Fatigue.	Bronchial asthma, Heart block, PVD, Severe heart failure.

# Commonly used antihypertensive drugs

<b>Class of Drug</b>	<b>Drug &amp; daily dose (mg)</b>	<b>Side-effects</b>	<b>Contra-indications</b>
Angiotensin Converting Enzyme (ACE) Inhibitors	Enalapril (2.5-40) Ramipril (1.25-20) Lisinopril (2.5-40) Perindopril (2-4)	Dry cough, Hyperkalaemia, Renal failure.	Bilateral renal artery stenosis, Pregnancy.

# Commonly used antihypertensive drugs

<b>Class of Drug</b>	<b>Drug &amp; daily dose (mg)</b>	<b>Side-effects</b>	<b>Contra-indications</b>
Angiotensin Receptor Blockers (ARBs)	Losartan (25-100) Irbesartan(150-300) Valsartan (40-160) Telmisartan (20-80)	Headache, Dizziness, Hyperkalaemia.	Bilateral renal artery stenosis, Pregnancy.

# Commonly used antihypertensive drugs

<b>Class of Drug</b>	<b>Drug &amp; daily dose (mg)</b>	<b>Side-effects</b>	<b>Contra-indications</b>
Calcium Channel Blockers (CCBs)	Amlodipine (2.5-10) Nifedipine (5-40)	Headache, Pedal oedema, Flushing, Palpitation.	Cardiogenic shock, Acute MI.
	Verapamil (40-480) Diltiazem (60-240)	Nausea, Constipation	CCF, Heart block.

# 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.
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- 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.

