Diabetes: Use of Adjunctive Therapy
ACEs, ARBs, ASA & STATINs --Oh My!

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Project ECHO
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Diabetes Warrior

William “Lee” Dubois
Points to Ponder

- ASCVD is the leading cause of morbidity and mortality among persons with diabetes.
- Persons with DM have a 2-fold increased risk of CHD or ischemic stroke.
- There is increased risk of silent MI among persons with DM.
- Up to 50% of persons with DM will develop heart failure.
- The presence of CKD in persons with T1DM & T2DM increases risk for CVD.

Endocrinology Advisor, 3/2018
Objectives

• Discuss association between diabetes and cardiovascular disease

• Discuss when to initiate adjunctive therapy in patients with diabetes

• Case studies
ASSOCIATION BETWEEN DIABETES AND CARDIOVASCULAR DISEASE
Prevalence of Type 2 Diabetes Mellitus Is Increasing

- Globally, 415 million people were living with diabetes in 2015; this will rise to 642 million by 2040\(^1\)
- CV death rates are higher among adults with diabetes when compared to those without diabetes\(^2\)

http://www.diabetesatlas.org/
National diabetes statistics report, 2014
Cardiovascular Disease Risk Factors in Diabetes Mellitus

**Traditional**
- Obesity
- Dyslipidemia
- Hypertension
- Abdominal obesity
- Lack of physical exercise
- Cigarette smoking

**Non-traditional**
- Insulin resistance and hyperinsulinemia
- Glucose variability
- Postprandial hyperglycemia
- Microalbuminuria
- Erectile dysfunction
- Hematological/Thrombogenic factors
- Inflammation C-reactive protein
- Genetics and epigenetics

Martin-Timon, et al. 2014
Why Is This Important?

The primary aim in the management of diabetes is comprehensive cardiovascular risk reduction (ADA-EASD)
Case

- S.B. is a 50 year old female with a 10 year h/o T2DM.
- Since her last visit she has experienced multiple episodes of hypoglycemia with BG ranging 42-70mg/dL.
- She currently test 3x/ day with BG ranging 42-347mg/dL at all times of the day.
- Current medications:
  - Basaglar 45 units at hs
  - Humalog 15 units TIDac
  - Lisinopril 20mg daily
  - Simvastatin 10mg daily
Case (cont)

- PMH- HTN, T2DM, Anemia (heavy periods), hyperlipidemia
- FH- mother and sister with DM, father deceased heart attack age 54
- Labs- A1c 9.7%, cholesterol-240, LDL-120, HDL- 42, GFR-111, micro/alb-45
- PE- BP 160/90, 86, BMI 30.4 weight- 90kg
MANAGEMENT OF RISK FACTORS FOR CVD
HYPERTENSION
Hypertension

• Current target <140/90 (lower is better if it can be achieved with undue burden)

• If BP >120/80 start lifestyle modification (DASH diet, ↓ sodium↑ potassium, moderate ETOH intake, ↑ physical activity)

• All patients with HTN should monitor BP at home

ADA standards of care, 2018, diabetes.org
Recommendations for the Treatment of Confirmed Hypertension in People With Diabetes

Initial BP between 140/90 mmHg and 160/100 mmHg

- Start one agent
  - Albuminuria*

  - No
  - Start one drug:
    - ACEI
    - ARB
    - CCB***
    - Diuretic**

  - Yes
  - Start:
    - ACEI or ARB

Initial BP ≥ 160/100 mmHg

- Start two agents
  - Albuminuria*

  - No
  - Start drug from 2 of 3 options:
    - ACEI or ARB
    - CCB***
    - Diuretic**

  - Yes
  - Start:
    - ACEI or ARB and
    - CCB*** or Diuretic**

Assess BP Control and Adverse Effects

Treatment tolerated and target achieved

- Continue therapy

Not meeting target or adverse effects using a drug from each of three classes

- Assess BP Control and Adverse Effects

Not meeting target

- Add agent from complementary drug class:
  - ACEI or ARB
  - CCB***
  - Diuretic**

Adverse effects

- Consider change to alternative medication:
  - ACEI or ARB
  - CCB***
  - Diuretic**

- Not meeting target and target achieved

- Continue therapy

Consider Addition of Mineralocorticoid Receptor Antagonist; Refer to Specialist With Expertise in BP Management

ADA standards of care, 2018, diabetes.org
DYSLIPIDEMIA
Dyslipidemia

• Obtain lipid profile at time a diagnosis and every 5 years (≥ age 40), at initiation of therapy, 4-12 after initiation/change and annually

• Lifestyle modification (↓ cholesterol, saturated and trans fat, ↑ omega 3 fatty acids and plant sterols/stanols, ↑ physical activity and weight loss)

• Statin Therapy- (based on presence of ACVD or risk for)
# Recommendation for statin and combination treatment in adults with DM

<table>
<thead>
<tr>
<th>Age</th>
<th>ASCVD</th>
<th>Statin intensity and combination treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 40 years</td>
<td>No</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>High</td>
</tr>
<tr>
<td></td>
<td></td>
<td>* If LDL cholesterol ≥ 70mg/dL despite maximally tolerated statin dose consider adding additional LDL-lowering therapy (i.e. ezetimibe or PCSK9 inhibitor)</td>
</tr>
<tr>
<td>&gt; 40 years</td>
<td>No</td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>High</td>
</tr>
<tr>
<td></td>
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<td>* If LDL cholesterol ≥ 70mg/dL despite maximally tolerated statin dose consider adding additional LDL-lowering therapy (i.e. ezetimibe or PCSK9 inhibitor)</td>
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ADA, Standards of Care, 2018
Low, moderate and high intensity statins (once daily dosing)

<table>
<thead>
<tr>
<th>High intensity statin (lowers LDL by ≥50%)</th>
<th>Moderate-intensity statin (lowers LDL by 30-50%)</th>
<th>Low-intensity statin (lowers LDL by &lt;30%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atorvastatin 40-80mg</td>
<td>Atorvastatin 10-20mg</td>
<td>Simvastatin 10mg</td>
</tr>
<tr>
<td>Rosuvastatin 20-40mg</td>
<td>Rosuvastatin 5-10mg</td>
<td>Pravastatin 10-20mg</td>
</tr>
<tr>
<td></td>
<td>Simvastatin 20-40mg</td>
<td>Lovastatin 20mg</td>
</tr>
<tr>
<td></td>
<td>Pravastatin 40-80mg</td>
<td>Fluvastatin 20-40mg</td>
</tr>
<tr>
<td></td>
<td>Lovastatin 40 mg</td>
<td>Pitavastatin 1mg</td>
</tr>
<tr>
<td></td>
<td>Fluvastatin XL 80mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pitavastatin 2-4mg</td>
<td></td>
</tr>
</tbody>
</table>

modified from: ADA, Standards of Care, 2018
Combination Therapy

- Statin & Ezetimibe– reduction of major CV events; may be beneficial for those who can not tolerate statins

- Statin & PCSK9 inhibitors– 15% relative risk reduction (for those on maximum dose of statin & h/o ASCVD

- Statin & fibrate– shown no improvement in CVD outcomes

- Statin & niacin– no CVD benefit; may increase risk of stroke
ASCVD risk calculator

http://www.cvriskcalculator.com/

- Makes recommendations for ASA, statin and BP control
- Does not account for duration of diabetes or presence of complications
KIDNEY DISEASE
ACE or ARB

• ACE or ARB recommended for non-pregnant patients with DM and HTN with modestly elevated urinary microalbumin/creatinine ratio (>30-299mg/g creatinine)

• Strongly recommended for patient with microalbumin/creatinine ≥300mg/g creatinine/GFR <60ml/min/1.73m²
# Other Therapies

<table>
<thead>
<tr>
<th>Drug</th>
<th>Benefit</th>
<th>Risk/contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin (75-162mg/d)</td>
<td>CVD risk &gt;10% (w/one risk factor) ↓ ischemic vascular events</td>
<td>Bleeding</td>
</tr>
<tr>
<td>ACE inhibitor</td>
<td>↓ infarct size, ↓mortality, limit ventricular remodeling</td>
<td>Hyperkalemia, worsening renal insufficiency</td>
</tr>
<tr>
<td>Beta blockers</td>
<td>↓ risk of recurrent ischemia, ↓infarct size, improve mortality</td>
<td>? Mask symptoms of hypoglycemia, bradycardia, bronchospasm</td>
</tr>
</tbody>
</table>
Management of S.B.'s CVD Risk

- **Add ASA** (based on FH)
- **Switch to high intensity statin** (based on age, ASCVD risk and LDL)
- **Add ligraglutide** (due to HTN, hyperlipidemia, and family history, as well as being obese) *(if no contraindications)*
- **Add additional BP medication** (BP above target)
- **Prescribe a home BP monitor**
CASE STUDIES
AH

- AH is a 47 year old female with a 5 year h/o T1DM.
- Vitals: BP 102/70, P-78
- Labs:
  - A1c -7.2%
  - GFR- >60
  - Creatinine -1.2
  - Urine micro/albumin -3
  - LDL- 78mg/dL

Does she need an ACE/ARB or statin?
BG

• BG is a 33 year old female with a 25 year h/o T1DM. No FH of CVD. She is planning to have children in the near future.
• Vitals: BP 132/85, 72
• Labs:
  – A1c 7.5%
  – LDL-101mg/dL

Does she need an ACE/ARB or statin?
THANK YOU!!

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Questions???