Managing Complicated Diabetes

Graham McMahon MD MMSc
Associate Professor of Medicine, Harvard Medical School
Division of Endocrinology, Diabetes & Hypertension
Brigham & Women's Hospital

Disclosures:
- None

Learning Objectives
- Be able to identify and manage each of the following complications associated with diabetes mellitus
  - Nephropathy
  - Neuropathy
  - Retinopathy

Nephropathy

Diabetic Nephropathy
- Diabetic nephropathy is the most common cause of end-stage renal disease in the US
- Minorities experience higher than average rates of nephropathy and kidney disease
- Between 20-40% of patients with diabetes ultimately develop nephropathy.
- Mortality among diabetic patients with nephropathy is higher than in diabetic patients without nephropathy

Pathophysiology of Nephropathy in DM
- Decreased resistance in efferent and afferent arterioles
- Greater decrease in afferent resistance
- Glomerular hyperfiltration and hyperfusion
- Basement membrane thickening, mesangial proliferation
Screening Urine Microalbumin

- Urine microalbuminuria / creatinine ratio
  - Normal <30 mg/g
  - Microalbuminuria 30-300 mg/g
  - Macroalbuminuria >300 mg/g
- Spot morning sample; Repeat testing
- Reflects widespread vascular damage and endothelial dysfunction
- Independent predictor of
  - Overt nephropathy
  - Cardiovascular events
  - Early mortality

Protection with Glycemic Control

Arbencicid vs. Placebo

Treating Diabetes with Macroalbuminuria IDNT Study Results

- Irbesartan Diabetic Nephropathy Trial
  - 1715 patients- type 2 diabetes with nephropathy
  - Treatment:
    - irbesartan, amlodipine or placebo
  - Endpoints
    - Doubling of Cr, ESRD or death
      - reduced by 20% vs. placebo
      - reduced by 23% vs. amlodipine

Adding Spironolactone to ACEI or ARB

- 59 pts with type 2 diabetes and macroalbuminuria
- Spironolactone 25-50 mg qd or placebo added to ACEI or ARB for 1 year
- 5 pts with highest creatinine and K+ developed hyperkalemia with spironolactone
- Albuminuria decreased 41%
- BP reduced -7/-3 mmHg
- GFR declined in both groups, more in spironolactone grp

ADA Clinical Practice Recommendations 2011 Nephropathy

- Optimize glucose and BP control (A)
- Measure urine microalbumin + creatinine yearly (E)
- Initiate ACEI/ARB if malb present (A), monitoring potassium and creatinine (E)
- Consult nephrologist for stage 4 CKD [GFR<30] (E)
Neuropathy

Diabetic Neuropathy
- About 50% of people with diabetes have mild to severe forms of neural damage, including:
  - Impaired sensation or pain in the feet or hands
  - Slowed digestion of food in the stomach
  - Carpal tunnel syndrome
  - Other nerve problems
- More than 60% of nontraumatic lower-limb amputations in the United States occur among people with diabetes.

Diagnosing Neuropathy
- Prevalence from 8% at diagnosis to 42% at 10 yrs.
- Typical symptoms
  - Sharp, burning, tingling, superficial
  - Feet > calves
  - Present at rest; improves with walking
  - Worse in bed
- Typical signs
  - Loss of vibration/proprioception → large fiber loss
  - Impairment of pain, temp, touch → small fiber loss
  - Monofilament pressure sensation
  - Exclude PVD and disk lesion

Types of Diabetic Neuropathy
- Symmetric polyneuropathy
  - Glove and stocking
- Autonomic neuropathy
  - Bladder, sexual dysfunction, diarrhea, BP
  - Hypoglycemia unawareness
- Diabetic amyotrophy
- Mononeuropathies

Complications of Polyneuropathy
- Ulcers
- Charcot arthropathy
- Dislocation and stress fractures
- Amputation - Risk factors include:
  - Peripheral neuropathy with loss of protective sensation
  - Altered biomechanics (with neuropathy)
  - Evidence of increased pressure (callus)
  - Peripheral vascular disease
  - History of ulcers or amputation
  - Severe nail pathology

Detecting Neuropathy
- Pain index
- Inspection
  - Callus, hair loss, red areas
  - Asymmetry, loss of arch height, hammer toes
- Monofilament
  - 10g filament test
- Vibratory sense
Managing Neuropathy

- Foot care referral
  - Education, self-inspection, nail care
- Pain management
  - Duloxetine
  - Pregabalin
  - Tricyclics
  - Gabapentin
  - Lidocaine
  - Capsaicin
  - Opioids

Managing Neuropathy

Duloxetine (Cymbalta)
- FDA approved
- QD (60 mg)
- Onset within 1 wk
- Nausea problematic
- Only compared to placebo
- Can combine with gabapentin

Pregabalin (Lyrica)
- FDA approved
- TID
- Onset within 1 wk
- Schedule V (habit forming)
- Dizziness, sedation, confusion
- Combine with TCA

Gabapentin (Neurontin)
- Not FDA approved
- QD (100 mg)
- Onset within 2-6 wks
- Can combine with pregabalin

Cardiovascular Autonomic Neuropathy

- Symptoms/Signs
  - Exercise intolerance
  - Postural hypotension
- Treatment
  - Discontinue aggravating drugs
  - Change posture (make postural changes slowly, elevate bed)
  - Increase plasma volume

Postural Hypotension

- Treatment
  - Foot care/elevate feet when sitting
  - Eliminate aggravating drugs
  - Reduce edema
    - midodrine
    - diuretics
  - Support stockings
  - Screen for CVD

Genitourinary Autonomic Neuropathy

<table>
<thead>
<tr>
<th>Sign/Symptom</th>
<th>Treatment</th>
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<tbody>
<tr>
<td>Bladder dysfunction</td>
<td>Voluntary urination; catheterization</td>
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<tr>
<td>Retrograde ejaculation</td>
<td>Antihistamine</td>
</tr>
<tr>
<td>Erectile dysfunction</td>
<td>Sildenafil, tadalafil</td>
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<tr>
<td>Dyspareunia</td>
<td>Lubricants; estrogen creams</td>
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Diabetic Retinopathy

- Diabetic retinopathy is the most common cause of new cases of blindness among adults 20-74 years of age.
- Each year, between 12,000 to 24,000 people lose their sight because of diabetes.

Stages of Diabetic Retinopathy

- Mild nonproliferative diabetic retinopathy (NPDR)
- Moderate NPDR
- Severe NPDR
- Proliferative diabetic retinopathy (PDR)

Mild NPDR

- Clinical Findings
  - Increased vascular permeability
  - Microaneurysms
  - Intraretinal hemorrhages
  - Clinically Significant Macular Edema (CSME)
- Management/Treatment
  - Annual follow-up
  - If CSME present: color fundus photography, fluorescein angiography, and photocoagulation
Moderate NPDR

- Clinical Findings
  - Venous caliber changes
  - Intraretinal Microvascular Abnormalities (IRMAs)
  - CSME possible

- Management/Treatment
  - 6-12 month follow-up w/out CSME (unless preg)
  - Color fundus photography
  - CSME present: color fundus photography, fluorescein angiography, focal photocoagulation, 3-4 month follow-up

Severe NPDR

- Clinical Findings
  - Retinal ischemia
  - IRMAs
  - Extensive hemorrhage and microaneurysms
  - CSME possible

- Management/Treatment
  - 3-4 month follow-up
  - Color fundus photography
  - Possible panretinal photocoagulation
  - CSME present: color fundus photography, fluorescein angiography, focal photocoagulation, 3-4 month follow-up

PDR

- Clinical Findings
  - Ischemia induced neovascularization (disk or elsewhere)
  - Vitreous hemorrhage, retinal traction, tears, and detachment

- Management/Treatment
  - 2-4 month follow-up
  - Color fundus photography
  - Panretinal photocoagulation (3-4 mo f/u)
  - Vitrectomy

Reasons for Visual Loss

- Leakage of fluid in the macula (area of the eye where there is fine vision) from leaky vessels in Macular Edema
  - Laser photocoagulation
  - VEGF inhibitors

- Bleeding and scarring from abnormal blood vessels in PDR
  - Pan retinal photocoagulation
  - Vitrectomy

Event Rates of Severe Visual Loss: Diabetic Retinopathy Study

Treatment Effects of Panretinal Photocoagulation.
Prevention of Diabetic Retinopathy Associated Vision Loss

- Intensive glycemic control
- Tight blood pressure control (<130/80 mmHg)
- Comprehensive eye examinations

Type 1 Diabetes: DCCT

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<tr>
<th>Year of Study</th>
<th>Primary Prevention</th>
<th>Secondary Intervention</th>
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<tr>
<td>1983-1989</td>
<td>76%</td>
<td>54%</td>
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<td>1992-1995</td>
<td>81%</td>
<td>60%</td>
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DCCT Research Group
N Engl J Med 1993;342:381

Summary

- Diabetes complications are common and make management more difficult
- Obesity:
  - motivational interviewing, GLP1, bariatrics
- Retinopathy
  - Importance of macular edema, photocoag, referral
- Nephropathy
  - Screening, Importance of BP mgmt, ACEI/ARB
- Neuropathy
  - Recognition, appropriate management
- Empower and educate patients

Question

A 54-year-old man with type 2 diabetes for 8 years develops early satiety, nausea, belching and occasional vomiting. He has no lower gastrointestinal symptoms. Which of the following treatment approaches would you recommend?

- A. Gastric pacemaker
- B. Metoclopramide
- C. Pyridostigmine
- D. Somatostatin

References
