Diabetes Management Across the Spectrum of Kidney Function

Learning Objectives

• Identify the importance of following GFR trends to determine patient’s overall renal function
• Describe which diabetes medications require adjustments or discontinuation in renal dysfunction
• Explain the appropriateness of a patient’s diabetes regimen based on his/her renal function

Chronic Kidney Disease (CKD)

• CKD occurs in up to 40% of individuals with diabetes
• Associated with ↑ risk of CVD, death and healthcare costs
  – Medicare spending towards diabetes related kidney disease = $25 billion in 2011

Disclosure to Participants

Notice of Requirements For Successful Completion
Please refer to learning goals and objectives. Learners must attend the full activity and complete the evaluation in order to claim continuing education credit/hours

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Normal Renal Physiology

Nephron Hypertrophy

Stages of CKD

Defining CKD

Stages of CKD

Defining CKD

Estimating Equations

Do not use SCr ALONE to determine kidney function!
Serum Creatinine (SCr)

- Function of production, excretion, & ingestion

<table>
<thead>
<tr>
<th>Increase SCr</th>
<th>Decrease SCr</th>
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</thead>
<tbody>
<tr>
<td>CKD</td>
<td>Reduced muscle mass (elderly, females)</td>
</tr>
<tr>
<td>African American race</td>
<td>Malnutrition</td>
</tr>
<tr>
<td>Drugs that inhibit tubular secretion</td>
<td>Amputation</td>
</tr>
<tr>
<td>Ingestion of meat or creatine supplements</td>
<td>Vegetarian diet</td>
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</tbody>
</table>

Which option would you recommend?

1. Sulfonylurea (e.g. glimepiride)
2. Thiazolidinedione (e.g. pioglitazone)
3. DPP-4 Inhibitor (e.g. sitagliptin)
4. SGLT-2 Inhibitor (e.g. canagliflozin)
5. GLP-1 Agonist (e.g. dulaglutide)
6. Basal Insulin (e.g. insulin glargine)

Meet Ms. Jackson (40 y/o)

- Past Medical History:
  - Type 2 Diabetes & Hypertension
- Medications:
  - Metformin 1000 mg BID (x3 years)
  - Lisinopril 20 mg QDay
  - Atorvastatin 80 mg QDay
- Pertinent Labs:
  - A1C 9.2%; SCr 0.87; eGFR 84 mL/min

Ms. Jackson (43 y/o)

- Medications:
  - Metformin 1000 mg BID (x6 years)
  - Glimepiride 4 mg BID (x3 years)
  - Lisinopril 40 mg QDay
  - Atorvastatin 80 mg QDay
- Pertinent Labs:
  - A1C 8.4%; SCr 1.19; eGFR 56 mL/min
What do we do with the metformin?
1. Increase dose to 850 mg TID
2. Continue current dose of 1000 mg BID
3. Decrease dose to 500 mg BID
4. Discontinue use

What to do with glimepiride?
1. Keep it as is (4 mg BID)
2. Switch to a different sulfonylurea
3. Discontinue and look at another category

How should we modify her regimen?
1. Add Thiazolidinedione (e.g. pioglitazone)
2. Add DPP-4 Inhibitor (e.g. sitagliptin)
3. Add SGLT-2 Inhibitor (e.g. canagliflozin)
4. Add GLP-1 Agonist (e.g. dulaglutide)
5. Add Basal insulin (e.g. insulin glargine)

CKD Stage 3a (eGFR 45-59)
- Sulfonylureas
  - Glyburide/Glimepiride: beware active metabolites!
  - Glipizide preferred agent within class
    - Urinary (60-90%) and fecal (5-20%) elimination
    - Start at lower doses and increase slowly

CKD Stage 3b (eGFR 30-44)

Metformin in Renal Insufficiency
Table 1—Proposed recommendations for use of metformin based on eGFR
eGFR level (ml/min per 1.73 m²)

<30
  No need to modify dose of metformin
  Monitor renal function annually
  Continue use
  - Increase monitoring of renal function (every 3-4 months)
  - Proctor the metformin with caution
  - Use lower dose (e.g. 50%, or half-maximal dose)
  - Clarity monitor renal function (every 3 months)
  - Do not start new patients on metformin
<br>Additional advice is required in patients with other comorbidities or with uncontrolled hypertension or heart failure. Use in particular caution with chronic kidney disease, or potentially increasing renal function.

[Image: Metformin in Renal Insufficiency chart]
CKD Stage 3a (eGFR 45-59)

- SGLT-2 inhibitors (eGFR):
  - Empagliflozin: No adjustments (10-25 mg daily)
  - Canagliflozin: Max dose 100 mg daily
  - Dapagliflozin: Do not use
- Thiazolidinediones
  - No dose adjustments necessary
  - Beware fluid retention

What to do with glimepiride?
1. Keep it as is (4 mg BID)
2. Switch to a different sulfonylurea
3. Discontinue and look at another category

CKD Stage 3a (eGFR 45-59)

- DPP-4 inhibitors (eCrCl)
  - Alogliptin: 12.5 mg daily (eCrCl 30-59)
  - Saxagliptin: 2.5 mg daily (eCrCl <50)
  - Sitagliptin: 50 mg daily (eCrCl 30-49)
  - Linagliptin: No dose adjustments necessary!

How should we modify her regimen?
1. Add Thiazolidinedione (e.g. pioglitazone)
2. Add DPP-4 Inhibitor (e.g. sitagliptin)
3. Add SGLT-2 Inhibitor (e.g. canagliflozin)
4. Add GLP-1 Agonist (e.g. dulaglutide)
5. Add Basal insulin (e.g. insulin glargine)

CKD Stage 3a (eGFR 45-59)

- GLP-1 agonists (eCrCl)
  - Exenatide/Exenatide ER: use caution when 30-59
  - Liraglutide: no adjustments needed
  - Albiglutide/Dulaglutide/Lixisenatide: use caution
- Insulin: No dose adjustments necessary!
- Non-Steroidal Anti-Inflammatories (NSAIDs)

CKD Stage 3b (eGFR 30-44)

- Metformin
  - Consider dose reduction (~50%)
  - If not already on it, do not add
- SGLT-2 inhibitors (eGFR)
  - Avoid altogether
- All other recommendations as Stage 3a
Ms. Jackson (51 y/o)

- Medications:
  - Metformin 500 mg BID (x14 years)
  - Glipizide 10 mg BID (x8+ years)
  - Lisinopril 40 mg QDay
  - Atorvastatin 80 mg QDay

- Pertinent Labs:
  - A1C 8.3%; SCr 2.27; eGFR 24 mL/min

Other Comorbidities?

CKD Stages 4 & 5 (eGFR 15-29; <15)

- Stop Metformin
- DPP-4 Inhibitors:
  - Linagliptin full dose (5 mg daily)
  - Sita (25 mg); Saxa (2.5 mg); Alo (6.25 mg) daily
- GLP-1 agonists
  - Stop exenatide
  - Use caution with other agents

Closing Thoughts

- Important to follow eGFR along with A1C & blood sugars
- Follow the trends!
- Keep an eye on doses of diabetes medications
- Importance of individualizing therapy

CKD Stages 4 & 5 (eGFR 15-29; <15)

- Glipizide
  - Duration of diabetes?
  - Initiate at lower dose
  - Increase dose gradually

- Insulin
  - Initiate at lower dose
  - Increase dose gradually