The Role of the Consultant Pharmacist in CKD - ESRD

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Objectives

Define Chronic Kidney Disease (CKD) and criteria to stage CKD according to the KDOQI and KDIGO guidelines

Describe principles of hemodialysis and drug therapy in patients with reduced kidney function

Discuss challenges of managing CKD and ESRD patients residing in skilled nursing facilities

Recommend strategies for overcoming challenges of managing CKD and ESRD patients in the long-term care setting

CKD – ESRD Facts

The overall prevalence of CKD in the general population is approximately 14 percent.

High blood pressure and diabetes are the main causes of CKD. Almost half of individuals with CKD also have diabetes and/or well-reported cardiovascular disease (CVD).

More than 662,000 Americans have kidney failure. Of these, 468,000 individuals are on dialysis, and roughly 193,000 live with a functioning kidney transplant.

Kidney disease often has no symptoms in its early stages and can go undetected until it is very advanced. (For this reason, kidney disease is often referred to as a “silent disease.”)

The adjusted incidence rate of ESRD in the United States rose sharply in the 1980s and 1990s, leveled off in the early 2000s, and has declined slightly since its peak in 2006.

Compared to Caucasians, ESRD prevalence is about 3.7 times greater in African Americans, 1.4 times greater in Native Americans, and 1.5 times greater in Asian Americans.

Each year, kidney disease kills more people than breast or prostate cancer. In 2013, more than 47,000 Americans died from kidney disease.

2014 Prevalence of CKD

Prevalence of CKD Stages, 1999-2014 vs. 1999-2006 vs. 2007-2014 by CKD Stage and Year


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<th>Stage</th>
<th>Prevalence (%)</th>
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Prevalence of CKD Stages: 1999-2014 vs. 2007-2014 by CKD Stage and Year

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2014 Mortality with End-Stage Renal Disease

Medicare Spending for CKD

Medicare spending for patients with CKD ages 65 and older exceeded $50 billion in 2013 and represented 20 percent of all Medicare spending in this age group.

More than 70 percent of Medicare spending for CKD patients ages 65 and older was incurred by those who also had diabetes, congestive heart failure, or both.

Although spending was 12.7 percent higher for African Americans than Caucasians in 2013, this represented a reduction from the 19.6 percent gap that occurred in 2010.

Spending was more than twice as high for patients with all three chronic conditions of CKD, diabetes, and congestive heart failure ($36,203) than in patients with only CKD ($15,614).

Medicare fee-for-service spending for ESRD beneficiaries rose by 1.6 percent, from $30.4 billion in 2012 to $30.9 billion in 2013, accounting for 7.1 percent of the overall Medicare paid claims costs.

Definition of Chronic Kidney Disease (CKD)

- Abnormal measurements of the actual or estimated glomerular filtration rate (GFR) defined as either kidney damage or GFR of less than 60 mL/min/1.73 m² of body surface area for a minimum of 3 months (90 days).

Staging CKD using GFR

<table>
<thead>
<tr>
<th>Corresponding KDOQI Category</th>
<th>GFR (mL/min/1.73m²)</th>
<th>Kidney Function</th>
<th>KDOQI Category</th>
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<tr>
<td>Stage 1 CKD</td>
<td>&gt; 90</td>
<td>Normal Function</td>
<td>G1</td>
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<tr>
<td>Stage 2 CKD</td>
<td>60-89</td>
<td>Mild Decrease</td>
<td>G2</td>
</tr>
<tr>
<td>Stage 3 CKD</td>
<td>45-59</td>
<td>Mild-Moderate Decrease</td>
<td>G3a</td>
</tr>
<tr>
<td>Stage 3 CKD</td>
<td>30-44</td>
<td>Moderate Decrease</td>
<td>G3b</td>
</tr>
<tr>
<td>Stage 4 CKD</td>
<td>15-29</td>
<td>Severe Decrease</td>
<td>G4</td>
</tr>
<tr>
<td>Stage 5 CKD (ESRD if HD required)</td>
<td>≤ 15</td>
<td>Kidney Failure</td>
<td>G5</td>
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</tbody>
</table>

Staging CKD using Albuminuria

<table>
<thead>
<tr>
<th>Category</th>
<th>AER (mg/day)</th>
<th>ACR (mg/mmol)</th>
<th>ACR (mg/g)</th>
<th>Terms</th>
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<tr>
<td>A1</td>
<td>&lt; 30</td>
<td>&lt; 3</td>
<td>&lt;30</td>
<td>Normal to mildly increased</td>
</tr>
<tr>
<td>A2</td>
<td>30-299</td>
<td>3-30</td>
<td>30-299</td>
<td>Moderately increased</td>
</tr>
<tr>
<td>A3</td>
<td>&gt;300</td>
<td>&gt;30</td>
<td>&gt;300</td>
<td>Severely increased</td>
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</table>

American Journal of Kidney Diseases

Volume 63, Issue 5, Pages 713-735 (May 2014)
DOI: 10.1053/j.ajkd.2014.01.416
KDOQI US Commentary on the 2012 KDIGO Clinical Practice Guideline for the Evaluation and Management of CKD

Staging CKD using Albuminuria Categories: KDOQI 2012

Prospective of CKD by GFR and Albuminuria Categories: KDOQI 2012

Peritoneal albinuria categories description and stage

- A1: Normal or high
- A2: Mildly decreased
- A3: Moderately or severely decreased

- Normal to mildly increased
- Moderately increased
- Severely increased

- G1: Normal or high
- G2: Mildly decreased
- G3: Moderately or severely decreased
Estimating Kidney Function

- The National Kidney Disease Education Program (NKDEP) of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Kidney Foundation (NKF), and American Society of Nephrology (ASN) recommend estimating GFR from serum creatinine.
- Two commonly used equations are the Modification of Diet in Renal Disease (MDRD) Study equation and Cockcroft-Gault equation.
- Both equations use serum creatinine in combination with age, sex, weight, or race to estimate GFR and therefore improve upon several of the limitations with the use of serum creatinine alone.
- The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation is a new equation based on serum creatinine.

Cockcroft – Gault Formula

- The Cockcroft-Gault formula was developed in 1973 using data from 249 men with creatinine clearance (ClCr) from approximately 30 to 130 mL/m2. It is not adjusted for body surface area.
- $\text{CCr} = \frac{(140 - \text{age}) \times \text{weight}}{(72 \times \text{SCr})} \times 0.85 \text{ if female}$

MDRD Equation

- The 4-variable MDRD Study equation was developed in 1999 using data from 1628 patients with CKD with GFR from approximately 5 to 90 milliliters per minute per 1.73 m2. It estimates GFR adjusted for body surface area and is more accurate than measured creatinine clearance from 24-hour urine collections or estimated by the Cockcroft – Gault Equation.
- The equation was modified in 2005 to:
  - $\text{GFR} = \frac{175 \times (\text{Standardized SCr})^{-1.154}}{(\text{age})^{-0.203}} \times (0.742 \text{ if female}) \times (1.210 \text{ if African American})$

Limitations of estimating ClCr using Serum Creatinine

- Table & Indications for a Clearance: Measured values underestimate GFR at low SCr.

Hemodialysis

- Treatment of ESRD
- Reduces uremic toxins in the blood
- Removes/Reduces excessive fluid
- Corrects metabolic imbalances

Principles of Hemodialysis

- Diffusion: movement of solutes from a high concentration to a low concentration
- Convection: movement of larger molecules through semi-permeable membranes
- Ultrafiltration: movement of fluid through a semi-permeable membrane
- Adsorption: adhesion of molecules through a semi-permeable membrane
Principles of Drug Therapy -- HD

- Centers around how drugs are metabolized and eliminated from the body
- Renal clearance versus non-renal clearance (ClNR) pathways
- Size matters -- size of drug molecules
- Large molecules not removed (varies by dialyzer)
- Volume of Distribution
- Vd can be altered, but in general, the larger the Vd, not likely to be dialyzed
- Protein Binding
- Only free drug (unbound) usually removed

Non-renal clearance

Challenges in LTC

- Identifying medications contraindicated or not recommended in CKD and ESRD
- Identifying medications that are dialyzable for timing of doses
- New medication orders “default” time of administration
- “HOLD” orders while at dialysis
- No hold orders
  - Doses being held 3x/week impacting outcomes (i.e. insulin)
- “Tricky” medications like Midodrine

Questions for Consultant Pharmacists

- Are you calculating estimated ClCr for all residents?
- Are you looking for eGFR in the chart on the lab results?
- Are you checking the MAR for held doses and documentation and orders?

Case study #1 2008

- 94 yo female resident dies at the hospital. Hospital gives family cause of death as “acute digoxin toxicity secondary to renal failure”
- Upon review of the chart, I calculated her estimated ClCr to be about 12ml/min
- Resident had been dig toxic off and on for 3 months
- No mention of this in CRPh's reports, but CRPh did report that several doses of Omeprazole had not been charted on MAR-- “holes in MAR”
- When CRPh’s supervisor questioned, supervisor answered that it was “hard to find lab results” at that facility

Strategy for case #1

- Identify high risk drugs (digoxin)
- Calculate an estimated creatinine clearance -- HUNT DOWN THE LAB RESULTS
- Read the chart. Telephone orders to hold dose of digoxin and then restarted digoxin at same dose
- Should the CRPh have noticed the held doses of digoxin on the MAR?
- Recommend decrease dose of digoxin, extend dosing interval or eval to discontinue.
Quick list of medications contraindicated in ESRD

- Acetazolamide
- Amiloride
- Amoxicillin (875mg ER, Augmentin XR)
- Baclofen
- Buspirone
- Canagliflozin
- Desmopressin
- Fenofibrate
- Fenofibric Acid
- Furosemide
- Gemfibrozil
- Indomethacin
- Ketorolac
- Labetelol (in acute HF, bradycardia, hypotension)
- Levocarnitine (oral dose)
- Metaxalone
- Metformin **
- Nitrofurantoin
- Sotalol
- Triamterene

Quick list of meds generally not recommended or use with caution

- Duloxetine
- Glimepiride
- Glyburide
- HCTZ (not effective when ClCr <30)
- Alendronate
- Firobromate
- Glibenclamide
- Sucralfate

Quick list of meds to dose AFTER hemodialysis—dialyzable meds

- Acyclovir 200-800mg Q12 hr
- Allopurinol 100mg QD or QOD
- Amoxicillin 250-500mg QD extra dose after HD
- Atenolol 25-50mg 3x/week
- Cefdinir 300mg QOD
- Cephalexin 250-500mg QD
- Dialyvite/Nephrocaps/Nephrovite/Renocaps
- Enalapril
- Folic Acid
- Gabapentin 100-300mg QD xtra dose 4hrs after HD
- Isosorbide Mononitrate
- Lisinopril
- Metoprolol
- Minoxidil
- Ranitidine 150mg QD at end of HD
- SMX-TMP decrease dose by 50% dose after HD
- Tenofovir 300mg weekly
- Tramadol do not take ER, inc. interval to Q12 hr max 200mg/day
- Tumor necrosis factor inhibitors

What should you be looking for when reviewing an ESRD-HD resident?

- Nursing facility/Dialysis facility communication forms
- Lab results from dialysis facility and nursing home—specific labs?
- Calcium & Phosphate product
- Calcium
- Phosphate
- Potassium
- Hemoglobin and iron studies
- pTH
- Calcium binder: calcium acetate or sevelamer
- Antioxidant vitamins: vitamin C, vitamin E, and menadione
- Cathecholamin excess

Case #2

TW is a 53 yo AAF living in nursing home

PMHx:
- DM2
- ESRD on HD Th-Sa @0515
- HTN
- Hypothyroidism
- muscle weakness
- microcalcifications
- left knee osteoarthritis
- Allergies: morphine
- Diet: sodium restriction 2g/day

Medications:
- Multiple vitamins with mineral
- Warfarin 3mg QD at 5pm
- Canestril 1.25mg 12hr & 8hr
- Insulin Detemir (Levemir) 10 units BID
- Human Regular insulin per sliding scale
- Levothyroxine 150mcg QD at 6am
- Pantoprazole 40mg QD at 6:30am
- Advair 250-50 2 puffs BID PRN meds: Albuterol, APAP, Tramadol, bisacodyl supp., Alum/Mag/simethicone

Labs and vitals 2/1/17

<table>
<thead>
<tr>
<th>Date</th>
<th>Calcium</th>
<th>Phosphate</th>
<th>Potassium</th>
<th>Magnesium</th>
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Potassium 4.3

Phosphorus 2.2 L

Albumin 2.6 L

Serum Creatinine 9.54 H

RBC 3.52 (normal 4.0-5.5)

Hemoglobin 8.9 (increased from 7.7 on 1/24)

A1c: 12/14/16 = 9.2%
What are your initial thoughts?
- Missing medications?
- Medication-related problems or concerns?
- Receiving multiple vitamins with minerals?
- How many doses of meds is she missing the mornings she is at dialysis?
- Carvedilol
- Insulin Detemir
- Pantoprazole
- Levothyroxine

What would you recommend or would you?

Hennie’s critical observations for discussion

- Get familiar with Renal Osteodystrophy (Mineral Bone Disorder)
- Secondary Hyperparathyroidism will rock your world
- Disappearing Diabetes Phenomenon
- Respiratory issues: COPD vs Asthma vs CHF vs Fluid Overload
- Intradialytic hypotension is a problem

Case study data example

<table>
<thead>
<tr>
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<th>Test</th>
<th>Result</th>
<th>Reference Range</th>
<th>Notes</th>
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More case study data—hypotension 90 year old male

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Questions/Discussion??

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