The Pharmacist’s Role in the Management of Chronic Kidney Disease

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Disclosures/Conflict of Interest

• Drs. Prasad-Reddy and Khan declare no conflicts of interest, real or apparent, and no financial interests in any company, product or service mentioned in this program, including grants, employment, gifts, stock holdings and honoraria.

Objectives

Pharmacists

At the conclusion of this program, the pharmacist will be able to:

• Compare and contrast different methods to evaluate kidney function.

• Discuss the pathogenesis of anemia and CKD, and evaluate the available options for treatment as they pertain to clinical guidelines.

• Discuss the pathogenesis of renal osteodystrophy, and given a patient case, recommend an appropriate treatment plan.

• Discuss the dosing of medications in patients with CKD, and identify different pharmacokinetic and pharmacodynamic characteristics that may present.

Pre-Test Questions

True/False. Hypertension is the leading cause of chronic kidney disease (CKD) in the United States.

True/False. Creatinine clearance is the most effective way to measure kidney function.

True/False. Patients with CKD have an increased risk of osteoporosis due to decreased calcium excretion from the tubules.

True/False. Patients with CKD have a 2-4 fold increase of cardiovascular disease when compared to the general population.

Methods to Evaluate Kidney Function

Audience Poll

Select the correct statement regarding GFR and creatinine clearance (CrCl):

A. GFR can be measured indirectly by assessing various filtration markers

B. Measurement of CrCl is one method used to estimate GFR

C. Creatinine is secreted by the proximal tubule and filtered by the glomerulus

D. CrCl exceeds actual GFR

E. All of the above
**Glomerular Filtration Rate (GFR)**

- National Kidney Disease Education Program (NKDEP).
- Retrieved from https://www.youtube.com/watch?v=J2YaULhMx5g&feature=youtu.be

**CKD Staging**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>GFR (mL/min/1.73 m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Normal or increased GFR</td>
<td>≥ 90</td>
</tr>
<tr>
<td>2</td>
<td>Mildly decreased GFR</td>
<td>60-89</td>
</tr>
<tr>
<td>3a</td>
<td>Moderately decreased GFR</td>
<td>45-59</td>
</tr>
<tr>
<td>3b</td>
<td>Severely decreased GFR</td>
<td>15-29</td>
</tr>
<tr>
<td>4</td>
<td>Kidney failure</td>
<td>&lt; 15 (or dialysis)</td>
</tr>
</tbody>
</table>

- GFR ≥ 90 considered normal in otherwise healthy persons.
- GFR between 60-89 may be normal for geriatric persons.
- GFR between 60-89 for 3 or more months PLUS kidney damage indicator for early kidney disease.
- GFR <60 for 3 or more months is considered CKD.
- Complications include CKD-MBD & anemia.

**Evaluation of GFR**

- Indicator of overall kidney function.
- How is it measured?
  - Filtration markers:
    - Achieve stable plasma concentration
    - Inert
    - Freely filtered by glomeruli
    - Not reabsorbed, secreted or metabolized
  - Gold standard: inulin, iothalamate, iohexol
  - Endogenous markers: serum creatinine, serum urea, serum cystatin C

**Serum Creatinine (SCr)**

- Secreted by proximal tubule & filtered by glomerulus → clearance exceeds GFR.
- Isolated use to assess renal function is not advised.
- Meiforms and SCr controversy.

**Factors Affecting SCr**

- Demographics:
  - Aging
  - Female gender
  - Ethnicity:
    - AA, Hispanic, Asian
  - Body Habitus:
    - Muscular
    - Malnourished/amputation
  - Medications:
    - Cimetidine, trimethoprim, probenecid, K-sparing diuretics

**GFR estimation methods**

- Cockroft-Gault 1973
- Jelliffe 1973
- Salazar-Corcoran 1968
- MDRD (6 variable) 1999
- MDRD (4 variable) 2009
- CKD-EPI 2009
- Schwartz (“bedside”) 2009
### Equations for Estimating GFR

<table>
<thead>
<tr>
<th>Equation</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jelliffe (2009)</td>
<td>CrCl(=0.813 \times \frac{SP}{HT}\times(0.85 \text{ if female}))</td>
</tr>
<tr>
<td>Salazar-Concoran (2009)</td>
<td>CrCl(=1.242 \times (\text{age}(\text{years})^{2} \times \text{weight}^{0.242} \times \text{height}^{0.422} + 0.331))</td>
</tr>
</tbody>
</table>

* Both the Jelliffe and Salazar-Concoran equations have since fallen out of favor.

### Cockcroft-Gault (CG) and MDRD Limitations

- Require stable kidney function and steady-state SCr concentrations
- Use cautiously in critically ill, those with AKI, and requiring RRT
- SCr rounding in elderly patients
- Rounding to 1.0 mg/dL may underestimate actual renal function resulting in under-dosing
- Obesity
  - May lead to increased renal plasma flow and GFR
  - 2009 MDRD study
    - Included 199 overweight patients (BMI > 30 kg/m^2) and 103 obese patients (BMI > 34.9 kg/m^2)
  - Tended to underestimate measured GFR
- Use of adjusted body weight has been validated in aminoglycoside dosing
- Use of lean body weight recommended by some experts

### Cockcroft-Gault Equation

- Used in pharmacokinetic studies
- Estimates used for drug dosage recommendations
- NKDEP recommend using either CG or MDRD for drug dosing
- Simple mathematical formulation and bedside applicability

### Equations for Estimating GFR

- Current recommendations:
  - The National Kidney Disease Education Program (NKDEP), National Kidney Foundation (NKF) and American Society of Nephrology (ASN) all recommend estimating GFR from SCr:
    - MDRD & Cockroft-Gault equation
      - Incorporate multiple factors to reduce limitation with SCr alone
      - CKD-EPI replaces MDRD equation
      - Most labs report GFR estimates using MDRD
      - NKF now recommends using CKD-EPI

### Considerations

- Role of the FDA
  - The 2009 FDA guidance on PK studies recommend use of creatinine clearance for renal dose adjustments
  - Recommendations to include both GFR derived creatinine clearance and equations based on eGFR
  - Unlikely to impact medications with existing renal dose adjustments
- Clinical Considerations
  - Renal function is a mosaic representation
  - Pharmacist/clinical should consider labs, clinical signs, symptoms in addition to renal function estimation equations
Anemia of Chronic Kidney Disease

Anemia in CKD: Pathogenesis
- Common complication of CKD
- Occurrence and severity vary with degree of renal dysfunction
- Hgb < 13.0 g/dL (men), < 12 g/dL (women)
- Compensatory mechanisms do not exist in patients with CKD
- Normochromic, normocytic anemia

Anemia in CKD: Symptoms
- Hemoglobin should be measured in ALL individuals with CKD regardless of disease stage

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shortness of breath</td>
<td>Heart failure</td>
</tr>
<tr>
<td>Extremity tingling</td>
<td>Left ventricular hypertrophy</td>
</tr>
<tr>
<td>Headaches</td>
<td>Angina</td>
</tr>
<tr>
<td>Chest pain</td>
<td>Increased hospitalizations</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>Decreased quality of life</td>
</tr>
<tr>
<td>General malaise</td>
<td>Increased all-cause mortality</td>
</tr>
</tbody>
</table>

Anemia in CKD: Treatment
- Erythropoiesis stimulating agents
  - Epoetin alpha
  - Darbepoetin alpha
- Iron therapy
- Red blood cell transfusions

Etiology of Anemia in CKD
- Multifactorial
  - Erythropoietin deficiency
  - Deficiencies in iron, folate, vitamin B
  - Shortened life-span of red blood cells
  - Uremic complications
    - Gastrointestinal bleeding, hemolysis
  - Bone marrow suppression

Audience Poll
Which of the following should be avoided in patients with chronic kidney disease who present with anemia?
A. Erythropoietin stimulating agents
B. Oral iron therapy
C. Intravenous iron therapy
D. Red blood cell transfusions

Erythropoiesis Stimulating Agents (ESAs)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Initial Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epoetin – α (Procrit®)</td>
<td>50-100 units/kg IV SQ 3 times weekly</td>
</tr>
<tr>
<td>Darbopoetin – α (Aranesp®)</td>
<td>0.45 mcg/kg/week IV SQ (~40 mcg)</td>
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</table>

Decrease dose by 25% if Hgb increases by >19 g/dL or is approaching 12 mg/dL

Reassess labs monthly – do not adjust doses more than once monthly

ESA's Adverse Effects

- Hypertension
- Seizures
- Vascular access thrombosis
- CV disease/Stroke
- Neutralizing antibodies
- Pure red cell aplasia (PRCA)
- Results in resistance to all ESA's

ESAs Cont.

- Derived by recombinant DNA technology
- Extended T½ with Aranesp®
- Subcutaneous vs. intravenous administration
- Onset of action
  - Immediate reticulocyte demargination
  - ~2 weeks before erythrocytes mature
  - Hgb will continue to increase for lifespan of RBC

How High is Too High: An Analysis of Clinical Trials Utilizing ESAs

<table>
<thead>
<tr>
<th>Study Population</th>
<th>Population</th>
<th>Findings</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobinization trial</td>
<td>Healthy adults</td>
<td>Increased Hgb concentrations in all arms</td>
<td>No significant difference in outcomes</td>
</tr>
<tr>
<td>ESA Trials</td>
<td>Patients with CKD</td>
<td>Increased Hgb concentrations in all arms</td>
<td>No significant difference in outcomes</td>
</tr>
<tr>
<td>Non-EESA Trials</td>
<td>Patients with CKD</td>
<td>Increased Hgb concentrations in all arms</td>
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Clinical Practice Recommendations – Initiation of ESA's

- In patients on dialysis, initiate ESA's when Hgb is 9 – 10 g/dL
- In patients NOT on dialysis, decision to initiate ESA's when Hgb concentration <10 g/dL, should be based on an individualized approach
- In patients NOT on dialysis, do not initiate ESA's if Hgb > 10 g/dL
- When considering ESA initiation, always recommend balancing benefits of anemia-related adverse effects and risk of RBC transfusion, with potential agent harm

General Recommendations for ESA's

Non-Dialysis Dependent Patients on ESA's

- During initiation of phase of ESA's, monitor Hgb concentration at least monthly
- For CKD-NP patients, during the maintenance phase of ESA therapy, monitor Hgb concentrations at least every 3 months
- Utilize subcutaneous administration of ESA's for CKD-NP patients

Dialysis Dependent Patients on ESA's

- During initiation of phase of ESA's, monitor Hgb concentration at least monthly
- For CKD-NP patients, during the maintenance phase of ESA therapy, measure Hgb concentration at least monthly
- Utilize intravenous or subcutaneous administration of ESA's for HD patients
- Utilize subcutaneous administration of ESA's for PD patients

ESAs should not be used to maintain Hgb concentration above 15 g/dL (150 g/l) in adult patients with CKD

In all adult patients ESAs not be used to intentionally increase the Hgb concentration above 15 g/dL (150 g/l)
What is the most common cause of resistance to erythropoiesis-stimulating agents?

**Iron Deficiency**

**Anemia in CKD: Oral vs. IV Iron**

<table>
<thead>
<tr>
<th>Advantage</th>
<th>Oral Iron</th>
<th>IV Iron</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accessible, ready available, does not require intravenous access, relatively safe</td>
<td>Inexpensive, easily available, does not require intravenous access, relatively safe</td>
<td>Avoids concerns with medication adherence and absorption</td>
</tr>
<tr>
<td>Disadvantages</td>
<td>Requires multiple daily doses, GI adverse effects, variable GI absorption, DDI</td>
<td>Requirements for iron overload, adverse reactions, need for IV access</td>
</tr>
<tr>
<td>Potential candidates</td>
<td>All patients</td>
<td>Patients on hemodialysis</td>
</tr>
</tbody>
</table>

**Intravenous Iron Products**

| Iron Dextran | 100 mg IV over 2 minutes | Yes! | Requires in-office observation at first dose |
| Sodium ferric gluconate/ferric glomerate | 145 mg IV over 1 min, or diluted over an hour | No | May be considered as alternative option in patients with sensitivity to dextran |
| Iron sucrose | 200 mg IV over 2 – 5 minutes or diluted over 15 minutes | No | May be considered as alternative option in patients with sensitivity to dextran |
| Ferric carbohymalate | 500 mg IV over 15 minutes | No | Can affect accuracy of MRI. May be re-administered 3 – 8 days after initial infusion |
| Ferric carboxymaltose | 300 mg over 2.5 minutes or diluted over 15 minutes | No | Only indicated in patients with non-dialysis dependent kidney disease. Weight based dosing guides administration frequency |

**Methods of Iron Dosing in CKD**

**Maintenance Dosing**
- Provides patients with small doses of iron administered at regular intervals to maintain iron status
- Intended to avoid iron deficiency or decline in iron test parameters
- May be associated with lower ESA doses and lower cumulative iron doses
- May result in lower infection risk
- May resemble more physiologic processes when compared to loading doses
- Requires frequent monitoring and supply costs

**Loading Dosing**
- Provides patients with periodic iron repletion to replenish stores when iron status indicates deficiency
- Critics suggest that total amount of iron administered may not be sufficient to maintain concentration of erythropoiesis in the long term
- May lead to periods of functional iron deficiency and fluctuations in hemoglobin concentrations
- “Redefining” effect may occur

**Management of the Complications of CKD:**

**Chronic Kidney Disease: Bone-Mineral Disorder (CKD-BMD)**
Chronic Kidney Disease-Bone Mineral Disorder

Biochemical Abnormalities
- Initial dose
  - Sevelamer HCL
  - Lanthanum
  - Calcium (Fosrenol®)
  - Calcium Phosphate acetate, carbonate (Renagel®)
  - Calcium carbonate (PhosLo®) 800

Soft Tissue and Vascular Calcification

Bone Deformities

Abnormalities in Bone Metabolism
- Secondary hyperparathyroidism
  - Phosphate retention
  - Decreased free calcium concentrations
  - Decreased 1,25 dihydroxyvitamin D concentrations
  - Increased fibroblast growth factor 23 concentrations
  - Reduced expression of various substances
    - Vitamin D receptors, calcium-sensing receptors, fibroblast growth factor receptors, klotho in PTH glands

Serum and Calcification

Renal Osteodystrophy Simplified
- Reduced GFR
- Decreased Phosphate Excretion
- Low Phosphorus
- Low PTH
- Low Ca Reabsorption

Calciuria

Vitamin D Therapy
- Established role in mineral homeostasis
  - Stimulates absorption of serum calcium
  - Down regulates synthesis/release of PTH
  - Modulates immune function and inflammatory response
  - Increases osteoblast activity
  - Negative endocrine regulator of renin system
  - Cardiovascular benefits

Phosphate Binders

<table>
<thead>
<tr>
<th>Phosphate Binder</th>
<th>Initial dose</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium carbonate (Tums®)</td>
<td>500 – 1000 with meals</td>
<td>No VD, calcification, DDI, hypercalcemia, large pill burden, affected by gastric pH</td>
</tr>
<tr>
<td>Calcium acetate (PhosLo®)</td>
<td>600 – 1354 with meals</td>
<td>No VD, calcification, DDI, hypercalcemia, large pill burden, minimally affected by pH</td>
</tr>
<tr>
<td>Aluminum hydroxide</td>
<td>600 – 1200 with meals</td>
<td>Constipation, CKD toxicity, consternation, utilize only for short term</td>
</tr>
<tr>
<td>Sevelamer HCL (Renagel®)</td>
<td>800 – 1600 with meals</td>
<td>Colonic obstruction, reflux, acidosis affected by gastric pH, large pill burden. No DDI, effectiveness when compared to other agents</td>
</tr>
<tr>
<td>Lanthanum carbonate (PhosLo®)</td>
<td>500 – 1000 with meals</td>
<td>Non-toxic, No DDI, no side effects</td>
</tr>
</tbody>
</table>

Hyperphosphatemia
- Initial alteration is excretion of phosphate
- Secondary effects on PTH, Ca, and Vitamin D
- Increases calcium x phosphate concentration

- Treatment
  - Dietary restriction to 900 mg/day
  - Phosphate Binding Agents
    - Bind dietary phosphorus in GI tract and are excreted in the feces minimizing absorption
    - Choice of agent is based upon other therapies, DDI adverse effects, patient preferences, cost, risk of hypercalcemia

Hyperphosphatemia

Notes
- Patients with CKD Stage 3, 4 on dialysis:
  - In patients with elevated PTH levels, correct abnormalities in phosphate, calcium, and vitamin D deficiency
  - Utilize native vitamin D
- Patients with CKD Stage 3, 4 on dialysis with persistent elevated PTH levels:
  - Once vascular access have been corrected, consider a treatment with calcitriol analog calciotriol if PTH levels are rising
- Patients with CKD Stage 3 who are dialysis dependent:
  - Treat patients with calcium or another vitamin D analog
  - Step or reduce treatment in the presence of hypercalcemia
### Vitamin D Therapy

- **Skin** (exposure to sunlight) → **Vitamin D3** (7-dehydrocholesterol) → **Vitamin D2** (supplements) → **Liver** → **Calcitriol** (1,25-dihydroxyvitamin D3)

- **Calcitriol** is the most active form of Vitamin D.

### Calcitriol

- **Most active form of Vitamin D (1,25 dihydroxyvitamin D)**
- **Utilized when PTH levels are high**
  - Up regulates Vitamin D receptors reducing parathyroid hyperplasia

- **Agents Clinical Paricalcitiol**

- **Analog available**
  - Calcitriol, Doxcalciferol, Paricalcitol

- **No difference in efficacy between agents**

- **Pharmacodynamic parameters guide usage**

### Calcimimetics

- **Cinacalcet HCL (Sensipar®)**

- **Risk of hyperparathyroidism among agents**

### Treatment of Hyperparathyroidism in Dialysis Patients: Calcimimetics

- **Cinacalcet HCL (Sensipar®)**
  - Attaches to calcium receptor on the PT gland and increases sensitivity to serum calcium thereby reducing PTH
  - Augments the signal caused by the binding of extracellular ionized calcium to CaR to increase intracellular calcium and decrease PTH release

### What Does the Data for Cinacalcet Say?

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palmer et al. 2005</td>
<td>Multicenter, randomized, placebo-controlled trial</td>
<td>Meta-analysis of 11 randomized controlled trials of cinacalcet therapy on mortality and adverse events in patients with CKD</td>
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<tr>
<td>Faxon et al. 2010</td>
<td>Multicenter, randomized, placebo-controlled trial</td>
<td>Meta-analysis of 11 randomized controlled trials of cinacalcet therapy for hyperparathyroidism</td>
</tr>
</tbody>
</table>

- **Cinacalcet had little or no effect on all cause mortality, positive risk, e.g., 30-day stroke incidence, subcutaneous injection site reactions, and edema**
- **Patients who received cinacalcet had greater reductions in median PTH levels, a greater proportion of patients with a greater reduction in levels, and experienced significant reductions in serum calcium, phosphorous, and calcium-phosphate ratio**

- **Cinacalcet and vitamin D analogs (calcitriol, doxercalciferol, paricalcitol)**
  - **No difference in efficacy between agents**

- **Pharmacodynamic parameters guide usage**
Senispar®

- **Dosing:** 30 mg daily, Max = 180 mg daily
- Potent inhibitor of CYP 2D6
- **Adverse effects**
  - Nausea, vomiting
  - Hypocalcemia (avoid initiation of corrected Ca < 8.4 mg/dL)
- **Monitoring**
  - Calcium, phosphorous, Ca × P, iPTH

Drug Dosing Considerations in CKD

Drug-Related ADRs in CKD

- Approximately half of patients with an estimated GFR <60 ml/min are at risk for ADRs
- **Risk Factors**
  - Non-white ethnicity
  - Older age
  - ACEi/ARB use
  - Diabetes
  - Advanced CKD

Rate of adverse drug events in ambulatory patients with CKD

<table>
<thead>
<tr>
<th>PATIENT REPORTED</th>
<th>N=267</th>
<th>Rate (per 100 patients)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoglycemia</td>
<td>57.6</td>
<td></td>
</tr>
<tr>
<td>Fainting/ severe dizziness</td>
<td>23.1</td>
<td></td>
</tr>
<tr>
<td>Nausea, vomiting &amp; diarrhea</td>
<td>21.1</td>
<td></td>
</tr>
<tr>
<td>Hyperkalemia</td>
<td>18.1</td>
<td></td>
</tr>
<tr>
<td>Confusion</td>
<td>16.9</td>
<td></td>
</tr>
</tbody>
</table>

DETECTED AT STUDY VISIT

| Hypoglycemia     | 8.3   |
| Hyperkalemia     | 8.3   |
| Bradycardia      | 6.4   |

*Adjusted for sociodemographic, comorbid conditions, GFR, and number of medications

Medication Safety in CKD

PK and PD Considerations: CKD

- Increased volume of distribution (Vd) in moderate to severe CKD & preexisting CKD with AKI
- Decreased protein binding
- Increased tissue binding
- Alteration in body composition (i.e. fluid overload)
- Metabolite accumulation
- Questionable pharmacologic action
- May contribute to adverse drug reactions
- Non-renal clearance
- CKD and AKI may effect activities of uptake and efflux transporters, and CYP enzymes
- Clinical dosing impact unknown
PK and PD Considerations: CKD

- Loading dose (LD):
  - Most guidelines do not recommend a LD
- Consider when:
  - Drug with long half-life
  - Need to rapidly achieve steady-state concentrations
  - If Vd of drug significantly increased
- Modified LD:
  \[ LD = \text{usual LD} \times \left( \frac{\text{patient's Vd}}{\text{normal Vd}} \right) \]

PK and PD Considerations: HD

- Drug-related factors:
  - Molecular weight or size
  - Degree of protein binding
  - Distribution volume

Kidney Disease Program
https://kdpnet.kdp.louisville.edu/drugbook/adult/

Assessment Question

A 52 year old male (60 kg) is being treated empirically for cellulitis with vancomycin 750 mg IV every 12 hours. Estimated CrCl is 45 ml/min. Steady-state trough returns at 15 mcg/ml (goal: 10-15 mcg/ml). What is the next appropriate step?
A. Decrease dose to 500mg, continue same interval
B. Decrease dose to 500mg, extend interval
C. Continue same dose, decrease interval
D. Continue same dose, extend interval

ACEI/ARB in CKD

- Effectively lower glomerular capillary pressure
- Protective in CKD, especially diabetes
- Decreased pressure in hypo-perfused states
- Volume depletion, cirrhosis, congestive heart failure

Drug Selection Considerations
Prostaglandins in CKD
- Dilate afferent arterioles
- Preserve GFR
- NSAIDs block this protective action
- NSAIDs and RAAS-inhibitors may result in afferent vasoconstriction and efferent dilation, respectively

Iodinated Contrast
- Leads to acute kidney injury
- Risk factors: CKD, diabetes, CHF, dehydration, concurrent nephrotoxic agents
- Minimize risk:
  - Low or iso-osmolar agents at lowest doses
  - Avoid concurrent nephrotoxic agents
  - Optimize volume status
- NO benefit of prophylactic hemofiltration/HD

IV Fluid Selection
- **Group A:** NS 1 ml/kg/h starting @ BTW 2nd and continued ±12h post-procedure
- **Group B:** NaHCO3 (166 mEq/L) 3 ml/kg/h 1h pre- and 1ml/kg/h for 1h post-procedure
- **Group C:** NaHCO3, 1ml/kg bolus 200ml pre + 1.500 ml/hr 10kg + 100-200 ml mineral water orally and 100 ml of mineral water post-procedure

RAAS Antagonists
- Expect a 10-30% rise in SCr
- Hyperkalemia
- Practice recommendations:
  - Assess eGFR and potassium 1 week after initiation or dose increase
  - Discontinue/reduce dose if SCR increases > 30% or K+ > 5.5 mEq/L

Antimicrobials & CKD
- Most require renal dose adjustments:
  - Common exceptions: Ceftriaxone, moxifloxacin, macrolides, doxycycline, dexamethasone
  - Imipenem/cilastatin:
    - High vescic risk in CKD patients
    - Consider carbapenem in CKD
  - Limited dosing recommendations in HD and PD
- Ceftriaxone, doxycycline
- Review PK/PD of ase (AUC, MIC)
- Consult ID pharmacist

Treatment Considerations in CKD Patients with UTI
- **Ampicillin**: Achieve good urine concentration
- **Cephalosporins**: Generally low urine concentrations
- **Carbapenems**: 50% of active drug present in urine
- **Quinolones**: Ciprofloxacin and levofloxacin achieve good urine concentrations
- **Nitrofurantoin**: Low renal excretion, avoid if eGFR < 50 ml/min
- **Trimethoprim**: Achieve good urine concentration
- **Aminoglycosides**: Achieve high urine concentrations
- Nephrotoxic
* Requires dose adjustment in CKD

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Treatment Considerations in CKD Patients with UTI
- **Ampicillin**: Achieve good urine concentration
- **Cephalosporins**: Generally low urine concentrations
- **Carbapenems**: 50% of active drug present in urine
- **Quinolones**: Ciprofloxacin and levofloxacin achieve good urine concentrations
- **Nitrofurantoin**: Low renal excretion, avoid if eGFR < 50 ml/min
- **Trimethoprim**: Achieve good urine concentration
- **Aminoglycosides**: Achieve high urine concentrations
- Nephrotoxic
* Requires dose adjustment in CKD
Antimicrobials & CKD

- Example: long-term amphotericin needed for a HD (receives TIW) patient who is unable to come to infusion center daily for amphotericin dose. Physician requests dose to be given on dialysis days.
- Recommendations per packet insert to dose daily
  - Review PK/PD of abx
  - Consult ID pharmacist

The Pharmacist’s Role in the Management of Chronic Kidney Disease

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