Why Dialysis Medications Matter?

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Objectives

- Discuss common medications used in dialysis and the importance of each for maintaining one’s health
- Define adherence and the impact of non-adherence on kidney transplant outcomes
- Provide an example of how to improve adherence
- Discuss common medications and side effects used in kidney transplant recipients
- Provide an example of a post-kidney transplant medication regimen
Patient KW

- KW is a 46 year old female who is being seen in clinic for pre-transplant evaluation
- She has end stage renal disease (ESRD) as a result of diabetes and high blood pressure
- She has been on hemodialysis (HD) for 3 years
KW Medications

- **Asthma**
  - Albuterol inhaler: 2 puffs every 4 hours as needed
  - Symbicort 80-4.5 mcg inhaler: 2 puffs two times daily

- **Blood Pressure**
  - Carvedilol 25 mg tablet two times daily
  - Clonidine 0.1 mg tablet two times daily
  - Enalapril 20 mg tablet daily

- **Diabetes**
  - Novolog insulin: 10 units with meals
  - Levemir insulin: 30 units at bedtime

- **Peripheral Neuropathy**
  - Gabapentin 200 mg capsule at bedtime
KW Medications

- **Heart Protection**
  - Aspirin 81 mg tablet daily
  - Atorvastatin 40 mg tablet at bedtime

- **Phosphate Binders**
  - PhosLo 667 mg capsule: 2 capsules with each meal
  - Sevelemer 800 mg tablet: 3 tablets with each meal

- **Vitamin D/PTH regulation**
  - Calcitriol 0.5 mcg capsule Mon, Wed, and Fri
  - Cinacalcet 30 mg tablet daily

- **Anemia**
  - Epogen 10,000 units every Mon, Wed, and Fri with HD
  - Ferrous sulfate (iron) 325 mg tablet three times daily

- **Overall Health**
  - Renal multivitamin daily
Timeline – Phosphate Binders

1950
• Aluminum hydroxide (1940s)

1980
• Calcium carbonate (1980s)

1990
• Sevelamer HCl (Renagel) – 1998

2000
• Calcium acetate (PhosLo) – 2001
• Lanthanum carbonate (Fosrenol) -2004
• Sevelamer carbonate (Renvela) – 2007
• Sucroferric oxyhydroxide (Velphoro) – 2013
• Ferric citrate (Auryxia) – 2014
Dialysis Medications: Phosphate Binders

- What can happen if I don’t take my phosphate binders?
  - Manifestations:
    - Ulcerating lesions that can become gangrenous wounds
  - Risk factors:
    - High Ca X Phos product from not taking your phos binders
    - Presence of uremia from missing dialysis
    - High levels of iPTH from missing vitamin D

What can happen if I don’t take my phosphate binders?

- **Manifestations:**
  - Cardiac calcifications → chest pain → heart attack

- **Risk factors:**
  - High Ca X Phos product from not taking your phos binders
  - Presence of uremia from missing dialysis
  - High of iPTH from missing vitamin D

Mortality Risk by Serum P and Ca Levels for Hemodialysis Patients

(N = 40,538)

How can I reduce my phosphorus levels?

- Reduce phosphorus intake from diet
  - AVOID frozen/processed foods, colas, bottled iced tea
  - Take phosphate binders with meals AND snacks

Where can I learn about low phosphorous foods?

- Ask your kidney doctor for referral to see a dietitian
- National Kidney Disease Education Phosphorous:
  - How to Read a Food Label
  - Tips for people with CKD
  - Available in English & Spanish
What Is Phosphorus?
Phosphorus is a mineral that helps keep your bones healthy. It also helps keep blood vessels and muscles working. Phosphorus is found naturally in foods rich in protein, such as meat, poultry, fish, nuts, beans, and dairy products. Phosphorus is also added to many processed foods.

Why Is Phosphorus Important for People with CKD?
When you have CKD, phosphorus can build up in your blood, making your bones thin, weak, and more likely to break. It can cause itchy skin, and bone and joint pain. Most people with CKD need to eat foods with less phosphorus than they are used to eating.

Your health care provider may talk to you about taking a phosphate binder with meals to lower the amount of phosphorus in your blood.

<table>
<thead>
<tr>
<th>Foods Lower in Phosphorus</th>
<th>Foods Higher in Phosphorus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fresh fruits and vegetables</td>
<td>Meat, poultry, fish</td>
</tr>
<tr>
<td>Rice milk (not enriched)</td>
<td>Dairy foods</td>
</tr>
<tr>
<td>Breads, pasta, rice</td>
<td>Beans, lentils, nuts</td>
</tr>
<tr>
<td>Corn and rice cereals</td>
<td>Bran cereals and oatmeal</td>
</tr>
<tr>
<td>Light-colored sodas/pop</td>
<td>Colas</td>
</tr>
<tr>
<td>Home-brewed iced tea</td>
<td>Some bottled iced tea</td>
</tr>
</tbody>
</table>
How Do I Lower Phosphorus in My Diet?

- Know what foods are lower in phosphorus (see page 1).
- Eat smaller portions of foods high in protein at meals and for snacks.
  - **Meat, poultry, and fish:** A cooked portion should be about 2 to 3 ounces or about the size of a deck of cards.
  - **Dairy foods:** Keep your portions to \( \frac{1}{2} \) cup of milk or yogurt, or one slice of cheese.
  - **Beans and lentils:** Portions should be about \( \frac{1}{2} \) cup of cooked beans or lentils.
  - **Nuts:** Keep your portions to about \( \frac{1}{4} \) cup of nuts.
- Eat fresh fruits and vegetables—if you have not been told to watch your potassium.
- Many packaged foods have added phosphorus. Look for phosphorus, or for words with PHOS, on ingredient labels, like the one below. Choose a different food when the ingredient list has PHOS on the label.

**Ingredients:** Potatoes, Vegetable Oil (Partially Hydrogenated Soybean Oil), Salt, Dextrose, Disodium Dihydrogen Pyrophosphate...

**Examples of Foods that May Have Added Phosphorus**

- Fresh* and frozen uncooked meats and poultry
- Chicken nuggets
- Baking mixes
- Frozen baked goods
- Cereals, cereal bars
- Instant puddings and sauces

*Ask the butcher to show you which fresh meats do not have added phosphorus.
Dialysis Medications: Vitamin D Analogues

- Why do I need to take my vitamin D medication?
  - Low levels of active vitamin D (calcitriol) occur due to the kidney’s inability (kidney failure) to activate vitamin D.
  - Vitamin D is important for lowering PTH levels which have several detrimental effects on your body if remain high.
Why do I need to take my vitamin D medication?

- Vitamin D deficiency increases your risk for:
  - Bone disease
  - Heart disease
  - Autoimmune diseases
  - Cancers
  - Infections
## Available Vitamin D Analogues

<table>
<thead>
<tr>
<th>Vitamin D analogue</th>
<th>Oral Formulation</th>
<th>IV Formulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcitriol</td>
<td>Rocaltrol® 0.25, 0.5 mcg capsules</td>
<td>Calcijex® 1 mcg/ml</td>
</tr>
<tr>
<td></td>
<td>0.5mg/ml solution</td>
<td></td>
</tr>
<tr>
<td>Paricalcitol</td>
<td>Zemplar® 1,2,4 mcg capsules</td>
<td>Zemplar® 5 mcg/ml</td>
</tr>
<tr>
<td>Doxercalciferol</td>
<td>Hectorol® 0.5, 2.5 mcg capsules</td>
<td>Hectorol® 2 mcg/ml</td>
</tr>
</tbody>
</table>
Dialysis Medications: Cinacalcet (Sensipar)

- Why do I need to take my Sensipar?

- Helps lower parathyroid hormone (PTH) levels which has several detrimental effects on your body if remains high.

- Consequences of high PTH:

<table>
<thead>
<tr>
<th>Skeletal Associations</th>
<th>Extraskeletal Associations</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-turnover bone lesions</td>
<td>Nervous system</td>
</tr>
<tr>
<td>Osteitis fibrosa</td>
<td>Neuropathy</td>
</tr>
<tr>
<td>Brown tumors</td>
<td>Heart</td>
</tr>
<tr>
<td>Bone pain</td>
<td>Hypertension</td>
</tr>
<tr>
<td>Osteopenia</td>
<td>LVH, interstitial fibrosis</td>
</tr>
<tr>
<td>Fractures</td>
<td>Myocardial/valvular calcification</td>
</tr>
<tr>
<td>Hypercalcemia</td>
<td>Glucose intolerance</td>
</tr>
<tr>
<td>Hyperphosphatemia</td>
<td>Hyperlipidemia</td>
</tr>
<tr>
<td>Calciphylaxis</td>
<td>Anemia</td>
</tr>
</tbody>
</table>
Dialysis Medications: Erythropoietin Stimulating Agents (ESAs)

- **What are ESAs?**

- ESAs help your bone marrow make red blood cells and thus improve your anemia

- Your ability to make red blood cells decreases as your kidney disease progresses

- **2 major types:**
  - Epoetin alfa (Epogen or Procrit): 3 times a week
  - Darbepoetin alfa (Aranesp): weekly or every 2 weeks
Dialysis Medications: Erythropoietin Stimulating Agents (ESAs)

- Why does my doctor prescribe ESAs?
- To help treat your anemia and improve how you feel

Symptoms of Anemia:
- Central
  - Fatigue
  - Dizziness
  - Fainting
- Blood vessels
  - Low blood pressure
- Heart
  - Palpitations
  - Rapid heart rate
  - Chest pain
  - Angina
  - Heart attack
- Spleen
  - Enlargement
- Respiratory
  - Shortness of breath
- Muscular
  - Weakness
- Intestinal
  - Changed stool color
- Skin
  - Paleness
  - Coldness
  - Yellowing
- Eyes
  - Yellowing

Red = In severe anemia
Dialysis Medications: Iron Supplements

- Why does my doctor prescribe iron?
  - To help treat your anemia and improve how you feel
  - Iron is an important component of your red blood cells as it allows for oxygen to bind → oxygen is required for your organs to function properly
Dialysis to Kidney Transplant
Dialysis to Kidney Transplant

- Adherence to dialysis medications is assessed by the transplant team in order to ensure you are a suitable candidate for transplant.

- Your adherence NOW while you're on dialysis will predict your future adherence to your transplant medications.
Adherence: Definition

- The extent to which a person’s behavior corresponds with agreed recommendations from a health care provider
  - Taking medications
  - Following a diet
  - Executing lifestyle changes

- Non-adherence is defined as the deviation from the prescribed medication regimen sufficient to influence adversely the regimen’s intended effect
Pre-Kidney Transplant Workup

- Referral from a physician

- Patient schedules evaluation appointment for candidacy at hospital
  - Transplant coordinator
  - Transplant surgeon and nephrologist
  - Financial coordinator
  - Social worker
  - Dietician
  - Pharmacist
Adherence Scale

- Do you sometimes forget to take your medications?
- Over the past 2 weeks, were there any days when you did not take your medications?
- Have you ever cut back or stopped taking your medicine without telling your doctor because you felt worse when taking them?
- When you travel or leave home, do you sometimes forget to bring along your medicine?
- Did you take your medication yesterday?
- When you feel your health is under control, do you sometimes stop taking your medicine?
- Taking medication everyday is a real inconvenience for people. Do you ever feel hassled about sticking to your treatment plan?
- How often do you have difficulty remembering to take all your medications
  - Never/Rarely, Once in a while, Sometimes, Usually, All the time?
Post-Transplant Expectations

- On average patients take 8-9 medications per day
  - Anti-rejection medications
  - Prophylactic antibiotics
  - Medications for underlying disease states
  - Medications for side effects

- Rigorous clinic follow-up schedule
  - 2 to 3 times weekly for at least one month after transplant
Adherence After Transplant

- Significant long-term problem
  - Compliance worsens 1 year after transplant

- Post-transplant non-adherence rates
  - ~35% of kidney transplant recipients

- Odds of graft failure increase 7 fold in kidney transplant recipients that are non adherent
  - $12,840 increase in 3-year medical costs
Strategies to improve adherence:

- Pillbox
- Set a timer on watch or phone
- Phone apps
  - MediSafe
  - DoseSmart
  - My Pillbox
Immunosuppression

"BOY! TALK ABOUT ORGAN REJECTION!"
Balance of Immunosuppression

Drug Toxicity

Rejection

Infection & Malignancy
Early Immunosuppression

- Induction - early, generally more potent medications, around the time of transplant
  - Thymoglobulin ~50%
  - Basiliximab (Simulect) ~20%
  - Alemtuzumab (Campath) ~10%

- Purpose of induction is to buy you time to get maintenance immunosuppression on board
Maintenance Immunosuppression

- Started anywhere from pre-transplant to first few days after transplant
  - Tacrolimus or cyclosporine
  - Mycophenolate
  - Prednisone
  - Sirolimus/Everolimus
  - Belatacept

- This is your long term medication – “lifelong”
Maintenance Medications
Tacrolimus
Prograf/Astagraf/Envarsus

- Strong immunosuppressant
  - Used for higher risk patients
  - May allow for less of other medications

- Measure levels in your body
  - Target higher levels early and lower levels later

- Once a day and twice a day formulations
Maintenance Medications
Cyclosporine
Neoral/Gengraf/Sandimmune

- Less potent than tacrolimus
- Almost 30 years of experience
- Measure level in your body
- Less use in minimizing other medications
Maintenance Medications
Tacrolimus & Cyclosporine

- Toxic to kidney
- Headache and tremor
- Increased blood pressure
- Increased blood sugar
- Increased cholesterol
- Low magnesium
- High potassium
Maintenance Medications
Belatacept
Nulojix

- 30 minute infusion once a month
- Decrease toxicities seen with tacrolimus or cyclosporine
- Issues with insurance coverage
- Minimal toxicities
Maintenance Medications
Mycophenolate
Myfortic/Cellcept

- Used in majority of transplants
  - In combination with tacrolimus/cyclosporine

- Side Effects
  - Nausea/vomiting
  - Diarrhea
    - May help to split up the dose
    - Take anti-diarrheals
  - Anemias
Maintenance Medications
Sirolimus/Everolimus
Rapamune/Zortress

- Generally in combination with tacrolimus/cyclosporine
- Start at time of transplant or for patients unable to tolerate other medications
- Measure level in your body

- Side Effects
  - Increase cholesterol
  - Anemia
  - Mouth sores
  - Problems with wound healing
  - Protein in urine
“Oldie but goody”
- 50 years of use

Use for maintenance and rejection (high dose)

Prolific list of side effects

Trend to avoidance and minimization over last 10-15 years
- Now trending back?
Increased blood sugars (diabetes)
Fluid retention
High blood pressure
Acne
Wound healing
Weight gain
Bone loss

Psychosis
Cataracts/glaucoma
Hormone imbalance
Impaired growth

Pediatrics
Which Combination is Best?

Drug Toxicity

Rejection

Infection & Malignancy
Maintenance Immunosuppression (United States 2012)

- **Calcineurin Inhibitor**
  - Tacrolimus (91%)
  - Cyclosporine (3.2%)

- **Antimetabolite**
  - Mycophenolic acid (93%)

- **Corticosteroids**
  - (67.6%)

Organ Procurement and Transplantation Network (OPTN).
Which Combination is Best?

- Take into account many patient factors

- Individualize therapy
  - More drugs available now
  - Side effects/toxicity

- What is the risk for rejection?

- Quality of the donor organ
  - Age
  - Function
  - Length of time from donor to recipient
  - Other donor risk factors
Other Medications Post-Transplant

- Antimicrobials
- Antivirals
  - Valganciclovir to prevent CMV infection
- Bactrim for UTI and PJP prophylaxis
- Thrush prophylaxis
- Pain management
- Bowel regimen
- Osteoporosis prophylaxis
- Home medications
### University of Illinois Medical Center

**Transplant Medication List for *** ***

**As of *** *** ***

(Transplant Date *** *** ***)

<table>
<thead>
<tr>
<th>Medication</th>
<th>Indication</th>
<th>Side Effects</th>
<th>9am</th>
<th>1pm</th>
<th>6pm</th>
<th>9 pm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tacrolimus (Astagraf XL) 1 mg capsule</td>
<td>To prevent rejection</td>
<td>High blood pressure, tremors, headache, high blood sugar</td>
<td>0 cap</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tacrolimus (Astagraf XL) 5 mg capsule</td>
<td>To prevent rejection</td>
<td>High blood pressure, tremors, headache, high blood sugar</td>
<td>3 cap</td>
<td>3 cap</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myfortic (mycophenolate) 360 mg tablet</td>
<td>To prevent rejection</td>
<td>Nausea, vomiting, diarrhea</td>
<td>2 tab</td>
<td></td>
<td></td>
<td>1 tab</td>
</tr>
<tr>
<td>Sulfameth/Trimeth (Bactrim SS) 400/80 mg tablet</td>
<td>To prevent pneumonia and urinary tract infection</td>
<td>Sun sensitivity, rash</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Valcyte 450mg tablet End Date:</td>
<td>To prevent viral infection</td>
<td>Low blood counts</td>
<td>1 tab</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Furosemide 40mg tablet</td>
<td>Water pill</td>
<td>Increased urination, low magnesium</td>
<td>1 tab</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitamin D 50,000 units capsule</td>
<td>Bone health</td>
<td>Constipation</td>
<td>1 cap every week at 9PM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Magnesium Oxide 400mg tablet</td>
<td>Supplement</td>
<td>Diarrhea</td>
<td>1 tab</td>
<td>1 tab</td>
<td>1 tab</td>
<td></td>
</tr>
<tr>
<td>Sodium Phos/Potasphos (Phospha Neutral) 250mg tablet</td>
<td>Supplement</td>
<td>-</td>
<td>2 tab</td>
<td>2 tab</td>
<td>2 tab</td>
<td></td>
</tr>
<tr>
<td>Cinacalcet (Sensipar) 30mg tablet</td>
<td>Low phosphate</td>
<td>Loss of appetite, muscle pain</td>
<td>1 tab</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amlodipine (Norvasc) 10mg tablet</td>
<td>High blood pressure</td>
<td>Swelling in legs, Headache, Fatigue</td>
<td>1 tab</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metoprolol tartrate 100mg tablet</td>
<td>High blood pressure</td>
<td>Dizziness, Fatigue</td>
<td>1 tab</td>
<td>1 tab</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clonidine 0.2mg tablet</td>
<td>High blood pressure</td>
<td>Dry mouth, fatigue</td>
<td>1 tab</td>
<td>1 tab</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydralazine 100mg tablet</td>
<td>High blood pressure</td>
<td>Headache, palpitations</td>
<td>1 tab</td>
<td>1 tab</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin 81mg tablet</td>
<td>Anti-coagulation</td>
<td>Bruising</td>
<td>1 tab</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gliimepiride 2mg tablet</td>
<td>High blood sugar</td>
<td>Low blood sugar (dizziness, weakness, sweating, tremors)</td>
<td>1 tab</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Docusate (Colace) 100mg capsule</td>
<td>For constipation</td>
<td>Cramps</td>
<td>Take 2 capsules by mouth daily as needed for constipation</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Final Thoughts

- Know your medications
- Know ABOUT your medications
- Ask questions of your transplant team
  - We need to hear from you
- Adherence, Adherence, Adherence
Questions?