Drug Interactions in the Heart/Lung Transplant Patient

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Objectives

– I. Describe prescription drug interactions with common immunosuppressants, cholesterol-lowering agents, steroids, antivirals and Bactrim.
– II. Describe over-the-counter (OTC) medication interactions and which OTCs to avoid
– III. Describe herbal medications that may be harmful and what interactions have been described in the literature.
Common Prescription Medications in Transplantation

• **Immunosuppressants**

• **Steroids**

• **Cholesterol-lowering agents** - Statins

• **Antivirals** - Cytomegalovirus (CMV) and Epstein-Barr Virus (EBV)

• **Antibiotics** - Pneumocystis carinii pneumonia (PCP)
Cyclosporine (CsA, Neoral®, Sandimmune®, Gengraf®)

• Prescription Drugs Which INCREASE CsA
  • **Calcium Channel Blockers**: diltiazem, nicardipine, verapamil
  • **Antifungals**: fluconazole, itraconazole, ketoconazole, voriconazole
  • **Antibacterials**: macrolides (erythromycin, clarithromycin, azithromycin)
  • **Glucocorticoids**: methylprednisolone
  • **Other**: birth control pills, glipizide, amiodarone, allopurinol, bromocriptine, colchicine, metoclopramide, propafenone, tacrolimus, sirolimus
Cyclosporine (CsA, Neoral®, Sandimmune®, Gengraf®)

– Prescription Drugs Which DECREASE CsA
  • **Antibacterials**: rifampin, nafcillin, IV Bactrim
  • **Anticonvulsants**: carbamazepine, phenobarbital, phenytoin, primidone
  • **Antiplatelets**: ticlopidine
  • **Other**: octreotide, orlistat
Tacrolimus (FK506, Prograf®)

- Prescription Drugs that INCREASE FK levels:
  - **Calcium Channel Blockers**: diltiazem, nicardipine, nifedipine, verapamil
  - **Antifungals**: clotrimazole, fluconazole, itraconazole, ketoconazole, voriconazole
  - **Antimicrobials**: (macrolides) erythromycin, clarithromycin, azithromycin
  - **Prokinetic Agents**: metoclopramide, cisapride
  - **Other**: bromocriptine, cimetidine, CsA, ethinylestradiol, methylprednisolone, omeprazole, nefazodone, danazol
Tacrolimus (FK506, Prograf®)

- Prescription Drugs that DECREASE FK levels:
  - **Anticonvulsants**: carbamazepine, phenobarbital, phenytoin
  - Other: Rifampin, rifamycins

- Be aware that use of the following agents WITH tacrolimus can worsen/induce kidney dysfunction: gentamicin, tobramycin, amphotericin B, cisplatin and cyclosporine.
Sirolimus (Rapamune®)

- Prescription Drugs That INCREASE Rapa levels:
  - **Calcium Channel Blockers**: Diltiazem, nicardipine, verapamil
  - **Antifungals**: ketoconazole, fluconazole, itraconazole, voriconazole
  - **Antimicrobials**: rifampin, clarithromycin, erythromycin
  - **Other**: cisapride, metoclopramide, bromocriptine, cimetidine, danazol, CYCLOSPORINE
Sirolimus (Rapamune®)

– Prescription Drugs That **DECREASE** Rapa levels:
  
  • **Anticonvulsants**: carbamazepine, phenobarbital, phenytoin
  
  • **Antibiotics**: rifabutin
Using Sirolimus and Cyclosporine Together

- Sirolimus levels increase by 80% when taken 4 hours after cyclosporine capsules
- Sirolimus levels increase by 230% when given at the SAME time as cyclosporine capsules
- Sirolimus levels increase by 67-86% when given at the SAME time as cyclosporine oral solution
Mycophenolate (MMF, Cellcept®)

• Prescription Drugs Which INCREASE MMF:
  • Acyclovir

• Prescription Drugs Which DECREASE MMF:
  • Cholestyramine, Antacids with aluminum and magnesium
Azathioprine

- **Prescription medications which INCREASE** Azathioprine: Allopurinol
- **Other**: Azathioprine can cause your INR to go DOWN if you are on warfarin. You may need higher doses of warfarin.
- *Azathioprine is a potent bone marrow suppressant, any drug with the potential to suppress bone marrow activity such as Bactrim, ganciclovir, cyclophosphamide, MTX may worsen this.*
Cholesterol-Lowering Agents

– HMG-CoA Reductase Inhibitors (Statins):
  • Pravastatin (Pravachol®)
  • Lovastatin (Mevacor®)
  • Fluvastatin (Lescol®)
  • Simvastatin (Zocor®)
  • Atorvastatin (Lipitor®)
  • Rosuvastatin (Crestor®)
Cholesterol-Lowering Agents

- Statin levels INCREASED by alcohol, itraconazole, ketoconazole, CYCLOSPORINE, erythromycin, gemfibrozil, niacin, warfarin

- Statin levels DECREASED by antacids, bile acid sequestrants, rifampin
Steroids

• **Prescription medications that REDUCE steroid concentrations**: phenytoin, phenobarbital and rifampin

• **Prescription medications that INCREASE steroid concentrations**: birth control pills, cyclosporine, ketoconazole
Antivirals: Ganciclovir/Valganciclovir

• Using CsA or tacrolimus with ganciclovir/valganciclovir can worsen kidney toxicity

• Prescription medications which INCREASE ganciclovir/valganciclovir levels: Mycophenolate
Bactrim

• Bactrim is an antibacterial which tends to affect OTHER drugs:

• Prescription medications whose levels are INCREASED when given with Bactrim: Digoxin, phenytoin, glipizide, glyburide, metformin, methotrexate, procainamide, ganciclovir, valganciclovir, warfarin

• Prescription medications whose levels are DECREASED when given with Bactrim: CsA

• *Bactrim given with ACE inhibitors can cause or worsen hyperkalemia (high potassium levels)
Over the Counter Medications: Which Ones Are Safe?

• Pain
  – Non-Steroidal AntiInflammatories (NSAIDS): ibuprofen (Motrin®), naproxen (Aleve®)
    • Used long term, this class of medications has the potential to affect platelet function, reduce kidney function and cause stomach bleeding. This class of medications is NOT to be used with warfarin
  – Acetaminophen (Tylenol®)
    • the safest of all OTC pain-relievers
Over the Counter Medications: Which Ones Are Safe?

• Allergies
  – diphenhydramine (Benedryl®), clemastine (Tavist), chlorpheniramine (Chlor-Trimeton®), loratidine (Claritin®)

  • Antihistamines are completely safe and have very few drug interactions. Be aware that allergy products which contain pseudoephedrine should be avoided. Many of them end in the letter “D” such as Tavist-D. The “D” stands for decongestant which usually means pseudoephedrine.
Over the Counter Medications: Which Ones Are Safe?

• Cough/Cold/Congestion
  • Be advised that almost ALL cold/flu preparation and any OTC product that has the word “Sinus” in its name most likely contains the decongestant, pseudoephedrine (Pseudofed®).
  • Pseudoephedrine is a sympathomimetic which can cause your heart rate to increase and your blood pressure to go up.
  • When you have a cold, avoid “cold” preparations with pseudoephedrine and instead use nasal sprays like Afrin® and pain relievers such as Tylenol®.
Over the Counter Medications: Which Ones Are Safe?

- Upset stomach, heartburn
  - Antacids (Maalox, Tums) are safe to use EXCEPT when taking them with MMF or CsA. Separate immunosuppressants and antacids by at least 2 hours.
  - Zantac®, Pepcid®, and Aclid® are all safe to use but please avoid Tagamet as this drug interacts with many medications especially warfarin.
  - Use antacids, Zantac, Pepcid, Aclid, Pravastatin/Prilosec with CAUTION if you are taking itraconazole. Itraconazole is absorbed in your stomach ONLY if your stomach is very acidic.
Over the Counter Medications: Which Ones Are Safe?

• **Diarrhea**
  
  • Be very cautious about using OTC antidiarrheal medications when you are experiencing diarrhea. Diarrhea in an immunosuppressed patient can be caused by numerous infectious agents and should be treated promptly by a physician. This is especially true if the diarrhea is accompanied by vomiting, a fever, severe dehydration and significant weight loss.
  
  • Diarrhea caused by antibiotic usage can be reduced by eating yogurt or taking acidophilus preparations.
Over the Counter Medications: Which Ones Are Safe?

• **Diet Aids/Caffeine**
  
  – Please avoid ALL diet aid products that pharmacies sell over the counter. These all contain stimulants which will cause your heart rate and blood pressure to soar!
  
  – Caffeine ingestion can lead to an increase in heart rate and blood pressure as well. Caffeine is also found in many migraine medications including Excedrin®.
Herbal Regulatory Issues

• 1994 Dietary Supplement Health and Education Act
  • Herbs, enzymes, glandulars, amino acids, etc are “dietary supplements”
  • FDA must prove supplement is unsafe
  • Supplements may give truthful info on effects on body or function, but must make disclaimer that FDA hasn’t evaluated the claim and is not intended for prevention, cure or treatment of disease
  • Purity, accuracy of labeling unregulated
Herbals You Should AVOID!

- **Androstenedione** (synthetic androgen)
- **Chapparal** (used to stop the aging process): liver tox
- **Comfrey** (used as an antiinflammatory): liver tox
- **DHEA** (synthetic androgen)
- **Digitalis**
- **Dong Quai** (used for menstrual flow): may be carcinogenic
- **Ma Huang** (used for energy): increases heart rate, BP, has been known to cause heart attacks/stroke
Herbals You Should AVOID!

- **Germander, Kava kava, Licorice Extracts, Life Root**: can cause liver toxicity
- **Mistletoe**: liver toxicity
- **White Willow** (herbal source of aspirin)
- **Yohimbe** (used for impotence): can increase heart rate and BP
- **Echinacea** and **Astragalus** should be avoided due to their potential to stimulate the immune system
- **Guarana, Kola nut**: sources of caffeine
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<th>Safe Herbals With Data Suggesting Efficacy</th>
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<tr>
<td>Co-Enzyme Q</td>
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Safe Herbals With Data Suggesting Efficacy

- **Co-Enzyme Q** - may decrease INR while on warfarin
- **Chamomile** - may increase INR if on warfarin
- **Feverfew** - has antiplatelet activity, avoid with warfarin, not for use in pregnancy
- **Garlic** - has antiplatelet activity, avoid with warfarin
- **Gingko** - has antiplatelet activity, avoid with warfarin
- **Glucosamine/Chondroitin**
- **Grapeseed Extract**
- **Milk Thistle**
Safe Herbals With Data Suggesting Efficacy

- Peppermint Oil
- Pygeum
- Saw Palmetto
- Slippery Elm
- St. John’s Wort - AVOID taking if you are on other antidepressants. AVOID if you are taking CYCLOSPORINE. St. John’s Wort causes CsA levels to DROP substantially! Lowers Dig levels
- Valarian - avoid other agents which aid sleep
Safe Herbals Which Have Insufficient Evidence Regarding Efficacy

- Alpha-lipoic Acid
- American Centaury
- Avena Sativa Extract
- Barley Grass
- Bee pollen: avoid if allergic to bees
- Bee propolis
- Beet Powder
- Betaine
Safe Herbals Which Have Insufficient Evidence Regarding Efficacy

- **Bilberry**
- **Black cohosh**
- **Black radish**
- **Blueberry**
- **Blue Green Algae**
- **Bromelain**
- **Cats Claw**
- **Cayenne Pepper**: Avoid in pregnancy, can increase BP
- **Chaste Berry**: Avoid in pregnancy/lactation
Safe Herbals Which Have Insufficient Evidence Regarding Efficacy

- **Choline**
- **Creatine**: do not use if on protein restriction
- **Dandelion**: avoid if gallbladder obstructed
- **Evening Primrose**: may interact with warfarin
- **Eyebright**
- **Fennel Seed**
- **Fenugreek**: may increase INR if on warfarin
- **Goldenseal**: Avoid in pregnancy/lactation
Safe Herbals Which Have Insufficient Evidence Regarding Efficacy

- **Ginseng**: may increase INR while on warfarin, avoid if you are on MAOIs, avoid in preg/lactation, avoid in psychotic and bipolar disorders
- **Green tea**: avoid if on warfarin! This tea contains large amounts of vitamin k
- **Hawthorn**: avoid if on ACE-inhibitors/digoxin
- **Ho-shou-wu tea**
- **Inositol**
Safe Herbals Which Have Insufficient Evidence Regarding Efficacy

- Lutein
- Lycopene
- Melatonin
- **Mexican wild yam**: avoid in pregnancy/lactation
- Nettle root
- Oyster extract
- **PABA**: may interact with sulfa antibiotics
- Parsley (volatile oil should be avoided in pregnancy)
- Passion Flower
- Pumpkin Seed
Safe Herbals Which Have Insufficient Evidence Regarding Efficacy

- Quercitin
- Rutin
- Schisandra/Schizandra
- Shark cartilage: avoid in pregnancy
- Siberian ginseng
- Soy extracts
- Tumeric
- Wheat Grass, Wood betony
A Word on Grapefruit Juice

– Be advised that the following medications can NOT be taken safely if you are consuming grapefruit juice:
  • **Calcium Channel Blockers**: felodipine, nimodipine, nisoldipine
  • **Immunosuppressants**: Cyclosporine-causes levels to go UP by 67%!, tacrolimus-causes levels to double!
  • **Statins**: Lovastatin, atorvastatin, pravastatin, simvastatin-all are increased by grapefruit juice
A Word on Grapefruit Juice

- **Seizure/Psych Meds**: Buspirone, carbamazepine, diazepam, midazolam, triazolam
- **Others**: Cisapride, methadone, sildenafil
QUESTIONS?